

CD-ROM INSIDE

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the **NAPLEX**[®] format and
drug name flashcards!

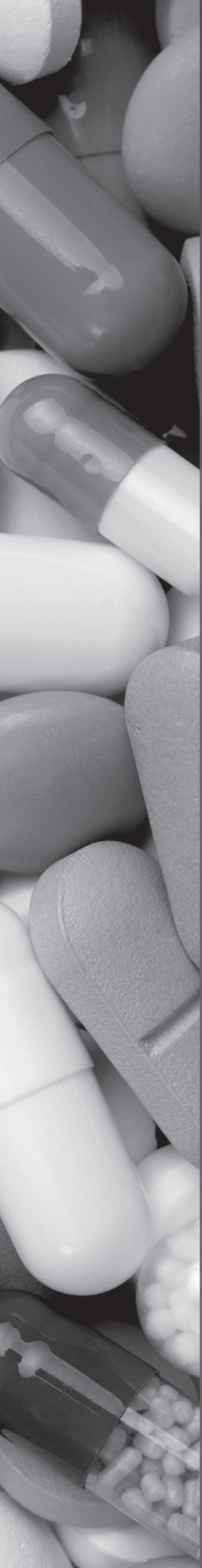


MOSBY'S
Pharmacy
for the
Review
NAPLEX[®]

Content patterned
after outline for
NAPLEX[®]

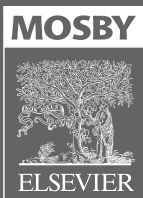
Over 2,000
questions provide
a complete review

Rationales for
answers provided
for each question



MOSBY'S

Pharmacy Review for the NAPLEX[®]



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Introduction

Mosby's Pharmacy Review for the NAPLEX® reflects the unique attributes and dynamic role of the pharmacist in healthcare. The main objective of the text is to provide a useful, current, and comprehensive review of relevant pharmacy topics to the candidate in preparation for the NAPLEX® examination.

Although this text is for use primarily by NAPLEX® candidates, the concise format of the materials would make an excellent review for pharmacy students, pharmacy instructors, or for practicing pharmacists. Users of this guide will benefit from the review of a variety of topics relating to the science and art of pharmacy practice, including general reviews of medication treatments for commonly encountered disease states and therapeutic areas. Candidates will benefit from keeping this book handy as they enter practice to provide a quick go-to reference regarding pharmaceutical calculation methods, patient counseling, and more.

Key features of this review include:

Over 1,600 NAPLEX®-oriented study questions.

An easy to follow outline format for each chapter to organize and quickly overview each area of importance.

Pharmacist-oriented questions at the conclusion of each chapter include thorough rationales at the end of the book to aid in comprehensive review and study. The rationales help ensure comprehension and understanding of the material, rather than focus on direct memorization or rote review.

Patient-based review questions within the therapeutic review chapters are presented with an emphasis on appropriate patient counseling by the pharmacist.

Electronic flashcards and **two mock timed examinations** on the enclosed CD-ROM allow the student to test comprehension and to demonstrate competency under testing conditions. The NAPLEX®'s focus on three areas of pharmaceutical practice is accurately reflected in the CD-ROM content.

How to Use This Book

It is best for a candidate to approach preparation for the NAPLEX® in a logical and orderly manner, with time given to consistent review of all areas of importance to the examination. The format of this text will help the student with his or her review and organization of study. The subject matter, including patient-based cases, will address all areas of the NAPLEX® competency statements, in roughly the same proportion that they are represented on the NAPLEX® examination. The three main areas of study are:

Area One: Assure Safe and Effective Pharmacotherapy and Optimize Therapeutic Outcomes

Area Two: Assure Safe and Accurate Preparation and Dispensing of Medications

Area Three: Provide Health Care Information and Promote Public Health

After a thorough review of the text contents, the student can use the CD-ROM to test medication familiarity and competency under simulated test circumstances. A well-prepared student who has studied to learn and understand the material will be able to display his or her knowledge and will enhance his or her potential for licensure.

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Preparing for the NAPLEX®

1

CHAPTER

GENERAL INFORMATION

NAPLEX

The North American Pharmacy Licensure Exam (NAPLEX) is the clinical aptitude test developed by the National Association of Boards of Pharmacy (NABP) and administered to pharmacy graduates to assess the competency of candidates for pharmacy practice. It is a requirement to obtain pharmacy licensure in all 50 states.

MPJE

The Multistate Pharmacy Jurisprudence Examination (MPJE) is the examination developed by the NABP to test the candidate's competency and knowledge of federal and state pharmacy law. The questions are customized to the specific law in each state. It is required for a pharmacy license by 44 states and the District of Columbia.

REGISTRATION

Candidates wishing to register for the NAPLEX with or without the MPJE must contact the board of pharmacy in the state they are seeking licensure or their school of pharmacy and complete a paper examination registration form for each examination. Candidates may also choose to register online for the NAPLEX or MPJE at www.napb.net. Candidates should check the website to see if their state participates in online registration.

Candidates may submit their registration, paper or online, before graduation; however, the state board of pharmacy will authorize eligibility only after all graduation requirements have been met.

The NAPLEX and MPJE may be taken on the same day, if time permits; however, it may be beneficial to take the examinations on separate days due to the diversity of the material.

FEES

Examination fees:

- NAPLEX: \$465 per examination
- MPJE: \$185 per examination

For those who wish to change their appointments, an additional fee of \$50 will be charged. Candidates who withdraw from taking the NAPLEX will receive a partial refund of \$140; those who withdraw from taking the MPJE will receive a partial refund of \$65. Cancellations or

rescheduling the exam must be done at least two business days before the scheduled appointment.

Fees are payable to the National Association of Boards of Pharmacy or NABP and submitted in the form of a money order, bank draft, or certified check. Personal check or cash is not accepted.

After registration, candidates will receive an authorization to test (ATT) letter, which confirms the candidate's eligibility by the state board of pharmacy. Upon receipt, candidates can schedule their appointments for examination and have one year to do so. The ATT and application expires after one year.

The NABP website, www.nabp.net, can provide the most current information.

ANSWER FORMAT OF THE NAPLEX

The computer-adaptive NAPLEX examination consists of 185 multiple-choice questions; however, only 150 questions are scored. The remaining 35 are considered pretest questions, which have no impact on the final score. These questions are used to help develop future tests. Because no indication is given to determine the scored questions versus the nonscored questions, it is to test-takers' advantage to answer all questions to the best of their knowledge.

The test also uses case/scenario-based format (i.e., patient profiles) and K-type multiple choice questions in which three choices are given and candidates select from five combinations of those three choices:

- I. Choice 1
- II. Choice 2
- III. Choice 3
- A. I only
- B. III only
- C. I and II
- D. II, III
- E. I, II, III

TEST STRUCTURE OF THE NAPLEX

The NAPLEX has three core areas:

1. Ensure safe and effective pharmacotherapy and optimize therapeutic outcomes (approximately 54% of the exam).
2. Ensure safe and accurate preparation and dispensing of medications (approximately 35% of the exam).

3. Provide health care information and promote public health (approximately 11% of the exam).

Candidates may refer to the NAPLEX blueprint for more detailed dissection of the topics covered on the examination at www.nabp.net.

If the candidate does not pass the exam, he/she may retake the exam after 91 days for the NAPLEX and after 30 days for the MPJE.

ADMINISTRATION PROCESS

NAPLEX

The NAPLEX has 185 questions to be taken in a 4 hour and 15 minute time period. There is an optional 10 minute break after approximately two hours of testing time.

The test is presented in a computer-adaptive testing format, which means that each answered question will determine the difficulty of the next. A correctly answered question in a series will be followed by a harder question. An incorrect response will be followed by an easier question.

Every question must be answered in the order it is presented. The test-taker cannot return to previous questions and change answers, so all responses are final. Due to the adaptive nature of the exam, questions also cannot be skipped because each response determines the next question.

MPJE

The test consists of 90 questions; only 60 are scored. The exam is to be taken in two hours with no break.

TEST TAKING STRATEGY

- Arrive to the testing center at least 30 minutes before the examination to allow time to check-in.
- Take a snack for the 10-minute break during the NAPLEX.
- Take proper identification (refer to candidate bulletin).
- Relax the night before the exam and eat a nutritious breakfast the morning of the examination.
- Although there is no penalty for guessing, you still want to make your best effort to choose a correct response.
- Make educated guesses. If you can rule out one or more answer choices, you have a better chance of selecting the right answer.
- Limit your time on any one question; as a general rule of thumb, be halfway through the NAPLEX by the 10 minute break.
- Use various study guide materials, including text books, flashcards, class notes, and practice tests. Take a full-length practice test before the examination.

- Do not try to “cram” new material. Create a study schedule that allots adequate time for the various sections of the NAPLEX.

SCORE RESULTS

NAPLEX

The scaled NAPLEX scores range from 0 to 150 with a minimally acceptable level of performance on the examination reflected by a score of 75. To obtain a score, the candidate has to complete at least 162 questions. Test scores are not given directly to the candidate; instead, they are forwarded by the NABP to the board of pharmacy from which the candidate is seeking licensure.

Depending on the state, candidates may transfer their scores to more than one state. Candidates should check the website (www.nabp.net) about the score transfer program. The state to which they wish to transfer their scores should also be contacted for more information.

MPJE

The minimum acceptable passing score on the MPJE scale is 75. To obtain a score, the candidate has to complete at least 77 questions. MPJE scores cannot be transferred between states. Candidates must take the law portion for each individual state in which they are seeking licensure.

THE PRE-NAPLEX

The NABP also offers the pre-NAPLEX. It is designed to familiarize the test-taker with the testing experience. The pre-NAPLEX is the only practice exam written and developed by the NABP.

There are 50 questions on the pre-NAPLEX and two forms are available. The cost for each practice examination is \$50. The candidate must register with the website and set up a username and password. Each candidate may take the pre-NAPLEX two times but must complete the first test before starting another one and pay for each test. The test may be taken with any computer with Internet access, including at home, a school, a library, and at any time. The scores are scaled and interpreted similar to the NAPLEX.

NAPLEX AND MPJE REGISTRATION BULLETIN

A free bulletin regarding the NAPLEX and MPJE is offered to all candidates. Topics covered include registration procedures, testing appointment information, NAPLEX and MPJE administration, NAPLEX and MPJE score results, the pre-NAPLEX, and NAPLEX score transfer information. It is available online at <http://www.nabp.net/ftpfiles/bulletins/NAPLEXMPJE.pdf> or through your state board of pharmacy.

Pharmaceutical Calculations

SYSTEMS OF MEASURE

Summary of conversion between metric, apothecaries' and avoirdupois systems:

Note that in the apothecaries' and avoirdupois systems there is only one common unit of measure, the grain. The other measurement units carry different values when comparing the systems. When converting between the two, the pharmacist should convert the value down to the grain amount in the one system, then convert to the other system.

Per the United States Pharmacopeia, 1 grain = 64.8 mg.

METRIC SYSTEM

Mass = gram (g)

Length = meter (m)

Volume = liter (L)

= 1 cubic centimeter (cc) equals approximately 1 milliliter (mL) and weighs 1 g

Prefixes

kilo-	10^3	1 thousand (1000) times the basic unit
hecto-	10^2	1 hundred (100) times the basic unit
deka-	10	1 ten (10) times the basic unit
deci-	10^{-1}	1 tenth (0.1) times the basic unit
centi-	10^{-2}	1 hundredth (0.01) times the basic unit
milli-	10^{-3}	1 thousandth (0.001) times the basic unit
micro-	10^{-6}	1 millionth times the basic unit
nano-	10^{-9}	1 billionth times the basic unit
pico-	10^{-12}	1 trillionth times the basic unit

APOTHECARIES' SYSTEM

Volume (fluid)

60 minims	= 1 fluid drachm (or dram)
8 drams	= 1 fluidounce
16 fluid ounces	= 1 pint
2 pints	= 1 quart
8 pints (4 quarts)	= 1 gallon

Mass (weight)

12 ounces	= 1 pound
8 drams (480 grains)	= 1 ounce (apothecaries')
1 drams	= 27.34375 grains

1 dram	= 1.772 grams
3 scruples	= 1 dram
20 grains	= 1 scruple

AVOIRDUPOIS SYSTEM

A system of masses based on a pound weighing 16 ounces mostly commonly used in the United States for commercial purposes.

Volume

1 fluid ounce	= 8 fluidram

Mass

437.5 grains	= 1 ounce
28.349523 grams	= 1 ounce
16 drams	= 1 ounce (avoirdupois)
16 ounces	= 1 pound (lb.)

UNITS OF AMOUNT OF SUBSTANCE

1 Mole = Molecular Weight in grams or Relative Molecular Mass in grams

1 Molar solution = Gram Molecular Weight or Relative Molecular Mass in grams in 1 Liter

1 mol = 1000 millimols (normally written as 1000 mmol)

1 millimole = 1000 micromoles

1 micromole = 1000 nanomoles

1 mol / liter = 1 mmol / mL, 1 mmol / liter = 1 micromole / mL

Millimole (mmol): A millimole (mmol) is a molecular weight expressed in milligrams.

The number of millimoles of a substance is calculated by dividing the number of milligrams of a substance by the molecular weight (MW) of the substance:
mmols = mg/MW

RATIO AND PROPORTIONS

RATIO

A ratio is a comparison of two numbers. In pharmacy calculations, a ratio can be used to express strength of drug concentration.

Example: A 1:25 solution of wintergreen oil means that 1 mL of wintergreen oil is contained in each 25 mL of solution.

PROPORTIONS

A proportion represents the equality between two ratios. A proportion is an equation with a ratio on each side. It is a statement that two ratios are equal. This mathematical concept is often used in community pharmacy.

Example:

If 5 tablets contain 1625 mg of acetaminophen, how many tablets should contain 2925 mg?

Solution:

$$5 \text{ (tablets)} = 1625 \text{ milligrams}$$

$$X \text{ (tablets)} = 2925 \text{ milligrams}$$

$$X = 9 \text{ tablets, answer}$$

$$\frac{5 \text{ tablets}}{1625 \text{ mg}} = \frac{X \text{ tablets}}{2925 \text{ mg}} \quad X = 9 \text{ tablets}$$

Relevant measurements and conversions

$$1 \text{ in} = 2.54 \text{ cm}$$

$$1 \text{ m} = 39.37 \text{ in}$$

$$1 \text{ kg} = 2.2 \text{ lb}$$

$$1 \text{ g} = 15.4324 \text{ gr (round to 15.4 gr)}$$

$$1 \text{ fl oz.} = 29.5729 \text{ mL (round to 29.6 or 30 mL)}$$

DIMENSIONAL ANALYSIS

Dimensional analysis is a method of manipulating units to solve mathematical equations. The process allows you to cancel out unwanted units leaving only those units you want your answer to be expressed as.

Example:

A pharmacist wants to know how many inhalers should be dispensed to a patient to provide a 60-day supply of fluticasone. The recommended daily dose is 250 mcg twice daily. The commercial inhaler delivers 220 mcg per metered dose and contains 60 metered inhalations.

Solution:

$$220 \text{ mcg} \times 2 \text{ (twice daily)} = 440 \text{ mcg/day}$$

$$\frac{440 \text{ mcg}}{\text{day}} \times \frac{1 \text{ inhalation}}{220 \text{ mcg}} \times \frac{1 \text{ inhaler}}{60 \text{ inhalations}} \times 60 \text{ days} = 2 \text{ inhalers}$$

The pharmacist should dispense 2 inhalers for a 60-day supply.

INTERPRETATION OF MEDICATION ORDERS*Example 1:*

A prescription for prednisone 5 mg should be taken as follows:

2 tablets three times daily the first day; 1 tablet three times daily on the second day; 1 tablet twice daily for 7 days; and 1 tablet daily thereafter.

How many tablets should be dispensed for a 30-day supply?

Solution: Dispense 44 tablets in total

Example 2:

A prescription is to be taken as follows: "1 tablespoon ac and hs for 7 days." What is the minimum volume that should be dispensed?

Solution:

achs = before meals and at bedtime

1 tablespoon = 15 mL

Patient needs to receive four doses per day for 7 days.

$$15 \text{ mL} \times 4 \text{ doses} \times 7 \text{ days} = 420 \text{ mL}$$

DOSAGE BASED ON DROPS

Certain medications that are administered or dispensed to a patient come in the form of liquids and are administered as drops. This section provides practice for calculations for these types of prescriptions.

If a pharmacist counted 30 drops of a drug in filling a graduated cylinder to the 1.5 mL mark, how many drops per milliliter did the dropper deliver?

Solution:

$$\frac{30 \text{ drops (gtt)}}{X \text{ gtts}} = \frac{1.5 \text{ mL}}{1 \text{ mL}}$$

$$X = 20 \text{ drops per mL, answer}$$

PERCENTAGE AND RATIO STRENGTH CALCULATIONS EXPRESSED AS V/V, W/W, AND W/V

Certain prescriptions are expressed in weight/weight (w/w), volume/volume (v/v), and weight/volume (w/v) percentages. To properly process prescription orders of this nature, the pharmacist must be able to make conversions and calculations with these units.

Concentration = quantity of solute divided by the quantity of preparation.

V/V: If the solute and the preparation are expressed in the same units, then concentration is dimensionless. For example, 10 mL of alcohol dissolved in a sufficient quantity of water to make 40 mL of solution is dimensionless: $10 \text{ mL}/40 \text{ mL} = 0.250$ (or 25% v/v).

W/W: If the quantity of solute and of the preparation are expressed in the same units of weight, the concentration is dimensionless. If 10 g of charcoal are mixed with 65 g of another powder to make a total of 75 g, the charcoal concentration is $10 \text{ g}/75 \text{ g} = 0.133$ by weight (or 13.3% w/w).

W/V: When a solute is measured by weight and the solution by volume, concentration is *not* dimensionless. If 1.25 g of NaCl is dissolved in sufficient water to make 55 mL of solution, the concentration is $1.25 \text{ g}/55 \text{ mL} = 0.0227 \text{ g/mL}$ (w/v). The % w/v is expressed as #g/100 mL (e.g., 2.27% or 2.27 g/100 mL).

Example 1:

How many grams of drug should be used to prepare 120 grams of a 2% w/w solution in water?

Solution:

$$120 \text{ grams mixture} \times \frac{2 \text{ grams drug}}{100 \text{ grams drug}} = 2.4 \text{ grams, answer}$$

Example 2:

What is the percentage strength (w/v) of a solution of drug if 40 mL contain 5 grams?

Solution:

$$\frac{40 \text{ mL}}{5 \text{ grams}} = \frac{100 (\%)}{X (\%)}$$

$$X = 12.5\%, \text{ answer}$$

PPM AND PPB (PARTS PER MILLION AND PARTS PER BILLION)

When ppm or ppb is used as a designation for concentration, some systems are w/w, some are v/v and some are w/v. Concentration is always a ratio or fraction in w/w and v/v situations. Weight by volume (w/v) concentrations are always defined in terms of grams and milliliters. The same default rules are followed as for percentage systems.

Example:

Express 2 ppm of ferrous gluconate in water in percentage strength and ratio strength.

Solution:

$$2 \text{ ppm} = 2 \text{ parts in } 1,000,000 \text{ parts}$$

$$= 1:500,000 - \text{ratio strength}$$

$$0.0002\% - \text{percentage strength}$$

DILUTION, CONCENTRATION, AND ALLIGATION**DILUTION OF AN INGREDIENT**

Dilution is the addition of diluent to the ingredient or an admixture of the ingredient with solutions to achieve a lower concentration of solution.

Example:

A 1:5000 dilution of drug A is requested. If 1 mL of drug A injection 1:200 is mixed with sterile water for injection, how many mL of water will be needed?

Solution:

$$\frac{1}{200} 1 \text{ mL} = \frac{1}{5000} (X)$$

$$0.005 = 0.0002(X)$$

$$25 \text{ mL} = X$$

$$25 \text{ mL} - 1 \text{ mL} = 24 \text{ mL}, \text{ answer}$$

CONCENTRATION OF AN INGREDIENT

Concentration is the addition of an active ingredient or evaporation of the diluent from an active ingredient to create a more concentrated solution.

Example:

How many grams of coal tar containing 25% (w/w) should be added to petrolatum to prepare 240 grams of coal tar containing 15% (w/w)?

Solution:

The coal tar (active ingredient) is added to a diluent (petroleum) currently containing no coal tar.

$$\frac{25\%}{15\%} = \frac{240 \text{ grams}}{X \text{ grams}}$$

$$X = 143.7 \text{ grams}$$

$$144 \text{ grams of coal tar, answer}$$

ALIUOT METHOD (ALLIGATION)

Alligation is a method that is particularly useful when mixing two or more preparations of known strengths to prepare a mixture of an intermediate desired strength. The final mixture will be an average of the individual strengths, which are calculated as proportional parts.

Alligation Alternate and Alligation Medial are methods that can be used to solve any type of dilution or concentration problem, including concentrations expressed in mg/mL, ratios, mixtures of liquids of known specific gravities, etc. The strengths of all preparations being mixed and the final mixture are expressed in a common denomination (of weight, volume, percentage, etc.) when setting up the alligation equation. When diluting a preparation, the strength of the diluent is considered to be 0%. When increasing the strength of a given mixture by adding more drug/active ingredient, the strength of the active ingredient to be added is considered to be 100%. A final proportion allows a correlation between the parts and any specific denomination needed.

Example 1:

A pharmacist has a 60% solution and a 15% solution. She needs a 40% solution to compound a medication. What is the proportion of the 60% and 15% solutions that would make a 40% solution? This example will use the process of Alligation Alternate to calculate the quantities of each mixture needed to make the final mixture of the desired strength:

Solution:

60%	25	60 - 40 = 20
40%		15 - 40 = 25
15%	20 parts	25 + 20 = 45

25 parts of the 60% solution combined with 25 parts of 15% solution would yield 45 parts of a 40% solution.

ISOTONIC SOLUTIONS

Osmosis occurs when a solvent (e.g., water) passes through a semipermeable membrane from a low-concentration solution into a high-concentration one, with the result that the concentrations become equalized. The pressure that causes this occurrence is known as osmotic pressure.

A solution that exerts the same osmotic pressure as a specific body fluid is known as isotonic. If the solution exerts an osmotic pressure lower than that of specific body fluid, the solution is hypotonic. If the actual solution exerts an osmotic pressure higher than that of specific body fluid, the solution is considered hypertonic.

Example:

How much sodium chloride is needed to adjust the following prescription to isotonicity? (E value [sodium chloride equivalents] for zinc sulfate is 0.15)

Zinc sulfate 2%

NaCl q.s.

Purified water q.s. 60 mL

Make isotonic solution

Solution:

If sodium chloride is only being used to provide the 60 mL isotonic solution: $60 \text{ mL} \times 0.9\% = 0.54 \text{ g}$ (or 540 mg)

Step 1: $60 \text{ mL} \times 2\% = 1.2 \text{ g}$ (or 1200 mg) of zinc sulfate required to fill the prescription

Step 2: 1200 mg is equivalent to $1200 \times 0.15 = 180 \text{ mg}$ of sodium chloride

Step 3: $540 \text{ mg} - 180 \text{ mg} = \mathbf{360 \text{ mg (or 0.36 g, answer)}}$

ELECTROLYTE SOLUTIONS

Electrolyte solutions are used to treat fluid and electrolyte disturbances. They may be prepared as oral solutions, syrups, dry granules intended to be dissolved in water or juice to make an oral solution, or oral tablets or capsules, and they are also commonly prepared as intravenous infusions.

To convert electrolytes in solution (expressed as milliequivalents [mEq] per unit volume to weight per unit volume or vice versa), the following calculation may be used:

$$\text{mEq} = \frac{\text{mg} \times \text{Valence}}{\text{Atomic, molecular, or formula weight}}$$

$$\text{mg} = \frac{\text{mEq} \times \text{Atomic, molecular, or formula weight}}{\text{Valence}}$$

Table 2-1 Valences and Atomic Weights of Select Ions

Ion	Formula	Atomic/Formula Weight	Valence
Aluminum	Al^{3+}	27	3
Ammonium	NH_4^+	18	1
Acetate	$\text{C}_2\text{H}_3\text{O}_2^-$	59	1
Bicarbonate	HCO_3^-	61	1
Calcium	Ca^{+2}	40	2
Carbonate	CO_3^{2-}	60	2
Chloride	Cl^-	35.5	1
Citrate	$\text{C}_6\text{H}_5\text{O}_7^{3-}$	189	3
Ferrous	Fe^{2+}	56	2
Ferric	Fe^{3+}	56	3
Gluconate	$\text{C}_6\text{H}_5\text{O}_3^-$	195	1
Lactate	$\text{C}_3\text{H}_5\text{O}_3^-$	89	1
Lithium	Li^+	7	1
Magnesium	Mg^{2+}	24	2
Phosphate (mono)	H_2PO_4^-	97	1
Phosphate (di)	HPO_4^{2-}	96	2
Potassium	K^+	39	1
Sodium	Na^+	23	1
Sulfate	SO_4^{2-}	96	2

From Zatz J: *Pharmaceutical Calculations*, ed 4, Hoboken, NJ, 2005, John Wiley & Sons, Inc., p. 267.

Example:

How much calcium chloride ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) is required to prepare 100, 1 mL ampules containing 10 mEq per mL? (mw = 147)

Solution:

$$100 \text{ mL} \times 10 \text{ mEq/mL} = 1000 \text{ mEq}$$

$$1 \text{ mEq} = \frac{147 \text{ mg}}{2} = 73.5 \text{ mg}$$

$$\frac{1 \text{ mEq}}{73.5 \text{ mg}} = \frac{1000 \text{ mEq}}{X} = 73,500 \text{ mg}$$

$$X = \mathbf{73.5 \text{ g, answer}}$$

TPN CALCULATIONS

Total parenteral nutrition (TPN) provides all of the patient's daily nutritional requirements and generally contains dextrose (carbohydrate), amino acids (protein source), vitamins, trace minerals, electrolytes, and fat emulsions. TPN solutions may also include insulin and occasionally therapeutic drugs. The amount of protein, dextrose, and fat are calculated based on the patient's daily kcal (calories) needed and available stock solutions. Other ingredients do not contain calories.

Example:

A patient needs 1600 kcal/day. The physician has ordered that the patient receive 65% of the daily calories (kcal) from carbohydrates, 10% from protein, and 25% from fat.

Calculate the amount (volume) needed to supply the dextrose, protein, and fat calories from these pharmacy stock solutions:

Dextrose 65%, amino acid 10%, fat 25%

First, determine how many kcal the patient needs from each component:

$$1600 \text{ kcal} \times 65\% = 1040 \text{ kcal from dextrose}$$

$$1600 \text{ kcal} \times 10\% = 160 \text{ kcal from protein}$$

$$1600 \text{ kcal} \times 25\% = 400 \text{ kcal from fat}$$

Next, convert these kcals into grams:

$$1040 \text{ kcal} \times 1 \text{ gram}/3.4 \text{ kcal} = 305.9 \text{ grams dextrose}$$

$$160 \text{ kcal} \times 1 \text{ gram}/4 \text{ kcal} = 40 \text{ grams protein}$$

$$400 \text{ kcal} \times 1 \text{ gram}/9 \text{ kcal} = 44 \text{ grams fat}$$

Then, calculate how many milliliters are needed from each stock solution:

$$305.9 \text{ grams} \times 100 \text{ mL}/65 \text{ grams} = 470.6 \text{ mL from dextrose 65\%}$$

$$40 \text{ grams} \times 100 \text{ mL}/10 \text{ grams} = 400 \text{ mL from amino acid 10\%}$$

$$44.4 \text{ grams} \times 100 \text{ mL}/25 \text{ grams} = 177.6 \text{ mL from fat 25\%}$$

NOTE:

Carbohydrate contains 3.4 kcal/g

Amino acid contains 4 kcal/g

Fat contains 9 kcal/g

CALCULATION OF DOSES

There are a variety of ways to determine doses of drugs including by age, body weight, surface area, creatinine clearance, and other pharmacokinetic parameters.

CREATININE CLEARANCE

When using the below equations, two factors to consider are (1) the serum creatinine is at steady state and (2) the weight, gender, and age of the individual reflect normal muscle mass.

Cockcroft-Gault equation

To estimate renal function for the purpose of drug dosing, creatinine clearance should be measured or estimated.

For males:

$$\text{CrCl} = \frac{(140 - \text{Patient's age in years}) \times \text{Body weight in kg}}{72 \times \text{Serum creatinine in mg/dL}}$$

For females:

$\text{CrCl} = 0.85 \times \text{CrCl determined using formula for males}$

If the individual is obese or not within 30% of their ideal body weight, other methods of calculating creatinine clearance should be used. Ideal body weight (IBW) or adjusted body weight (ideal body weight plus 40% of obese weight) instead of actual body weight in the Cockcroft-Gault equation will provide a better estimate of creatinine clearance.

IBW for males in kg = $50 + (2.3)(\text{Height in inches} - 60)$

IBW for females in kg = $45 + (2.3)(\text{Height in inches} - 60)$

BODY SURFACE AREA

The practitioner may need to take into account body surface area as a possible variable when determining drug dosage (e.g., chemotherapy).

Body Surface Area (BSA) – The Mosteller Formula:

$$\text{BSA}(\text{m}^2) = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

The average BSA of an adult is 1.73 m^2 .

CALCULATIONS FOR PEDIATRIC DOSES

Various pediatric formulas have been used historically to calculate APPROXIMATE pediatric dosages.

Young's rule, based on age:

$$\frac{\text{Age}}{\text{Age} + 12} \times \text{Adult dose} = \text{Dose for child}$$

Fried's rule for infants:

$$\frac{\text{Age (in months)}}{150} \times \text{Adult dose} = \text{Approx. dose for infant}$$

Clark's rule, based on weight:

$$\frac{\text{Weight (in lb)} \times \text{Adult dose}}{150} = \text{Dose for child}$$

BSA approximation of child's dose:

$$\frac{\text{Child BSA}}{1.73 \text{ m}^2} \times \text{Adult dose} = \text{Approx. dose for child}$$

STOCK SOLUTIONS

A stock solution, commonly referred to as bulk bottle, is a large volume of a reagent (in chemistry) or in this case, medication. These stock solutions can be prepared by a manufacturer or compounded in the pharmacy. Pharmacists typically take stock solutions and use them to prepare weaker solutions of medications or chemicals for laboratory or clinical use.

Example:

How many mL of a 0.5% gentian violet stock solution is needed to prepare 1 pint of a 1:2000 solution?

Solution:

Step 1: Determine the quantity of the final solution:

1 pint = 946 mL,

$$\text{so} \quad \frac{1 \text{ g}}{200 \text{ mL}} = \frac{X \text{ grams}}{946 \text{ mL}}$$

$$X = 0.473 \text{ grams}$$

Step 2: Determine the amount of available solution needed to obtain the determined quantity (0.5% gentian violet solution contains 0.5 grams in 100 mL of solution):

$$\frac{0.5 \text{ g}}{100 \text{ mL}} = \frac{0.473 \text{ grams}}{X \text{ mL}}$$

$$X = 94.6 \text{ mL, estimate } 95 \text{ mL}$$

RECONSTITUTION OF DRY POWDERS

Many drugs (antibiotics, steroids, and biologics) that are not stable in solution are prepared as dry-filled solids or lyophilized powders. Prior to use, these dry powders must be reconstituted as a solution with a suitable diluent in the proper volume to give specified concentration (usually provided in the package insert). Occasionally, the physician may prescribe a final concentration different from the one provided by the manufacturer. Also, in some cases, the pharmacist needs to determine if the powdered drug contributes to the final volume of the reconstituted solution before modifying the label instructions.

Example:

The package information of a vial containing 30 million units of penicillin G potassium specifies that when the appropriate amount of sterile solvent is added to dry powder, the resulting concentration is 500,000 units per mL. How many milliliters of sterile water for injection are needed to prepare the following solution?

(Note: the powder accounts for 8 mL of the final volume)

Penicillin G potassium 30,000,000 units

Sterile water for injection

Provide a solution containing 500,000 units per mL

$$\frac{500,000 \text{ units}}{30,000,000 \text{ units}} = \frac{1 \text{ mL}}{X \text{ mL}}$$

$$X = 60 \text{ mL}$$

$$60 \text{ mL} - 8 \text{ mL} = 52 \text{ mL, answer}$$

INTRAVENOUS INFUSIONS, PARENTERAL ADMIXTURES, AND FLOW RATES

Intravenous infusions are large volumes of sterile, aqueous preparations administered intravenously (through a vein) over an extended period of time.

Example:

An order is written for 25,000 units of heparin in 250 mL of D5W to infuse at 2000 units/hr. What is the correct rate of the infusion (in mL/hr)?

Solution:

$$\text{Concentration of IV} = \frac{\text{Total amount of drug}}{\text{Total volume}}$$

$$\text{IV rate} = \frac{\text{Dose desired}}{\text{Concentration of IV}}$$

$$\text{Concentration of IV} = \frac{25,000 \text{ units of heparin}}{250 \text{ mL of D5W}}$$

$$\text{Concentration of IV} = 100 \text{ units/mL of heparin}$$

$$\text{IV rate} = \frac{2000 \text{ units/hr}}{100 \text{ units/mL}}$$

$$\text{IV rate} = 20 \text{ mL/hr}$$

Parenteral admixtures are a sterile preparation that involves the combination of one or more drugs to large-volume.

Example:

A patient weighs 170 pounds. A pharmacist receives a prescription order for 0.25 mg amphotericin B per kilogram body weight. How many milliliters of a 25 mg/10 mL solution are needed to supply the dose, which will then be diluted in 500 mL of 5% dextrose?

Solution:

$$\frac{170 \text{ lb}}{2.2 \text{ lb}} = 77 \text{ kg patient}$$

$$0.25 \text{ mg} \times 77 \text{ kg} = 19.25 \text{ mg dose needed}$$

$$\frac{25 \text{ mg}}{19.25 \text{ mg}} = \frac{10 \text{ mL}}{X \text{ mL}}$$

$$X = 7.7 \text{ mL, answer}$$

Calculating IV flow or drip rates are necessary to ensure that the patient is receiving the desired amount of drug that was ordered.

Example:

If 20 mg of drug is added to a 750 mL parenteral fluid, what flow rate, in milliliters per hour, will deliver 2 mg of drug per hour?

Solution:

$$\frac{20 \text{ mg}}{2 \text{ mg}} = \frac{750 \text{ mL}}{X \text{ mL}}$$

$$X = 75 \text{ mL per hour, answer}$$

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REVIEW QUESTIONS

(Answers and Rationales on page 313.)

- A patient is prescribed 10 mEq of potassium daily. The source of potassium chloride in the pharmacy is 5 mEq/mL in 1 mL vials. How many vials per day is needed for the patient?
 - 0.5 vial
 - 1 vial
 - 2 vials
 - 1.5 vials
- How much elemental iron is present in every 150 mg of ferrous sulfate ($\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$)? (Atomic weights are iron = 55.9; sulfur = 32.1; oxygen = 16.0; and hydrogen = 1.0. Iron has valences of +2 and +3)
 - 25 mg
 - 30 mg
 - 48 mg
 - 54 mg
 - 60 mg
- A 130-lb patient has a creatinine clearance rate of 40 mL/min. Assuming Drug X is eliminated exclusively by renal mechanisms, what maintenance dose should be administered if the normal maintenance dose is 3 mg/lb of body weight?
 - 50 mg
 - 100 mg
 - 150 mg
 - 200 mg
 - 250 mg

4. An IV medication is available as 3.5 g/ 500 mL with a strength calculation of 0.25 mg/kg/min is prescribed to a 130-lb patient. What is the infusion rate in mL/hour?
 - a. 2.1 mL/ hr
 - b. 126.6 mL/ hr
 - c. 278.6 mL/ hr
 - d. 6,203.4 mL/ hr
5. Which of the following is an invalid DEA number?
 - a. BT5555555
 - b. DB1294658
 - c. AR7532648
 - d. MA2643713
 - e. All of the above are valid
6. How many quarts are in two gallons?
 - a. 2 quarts
 - b. 4 quarts
 - c. 8 quarts
 - d. 16 quarts
7. How many fluid ounces are in a quart?
 - a. 4 fluid ounces
 - b. 8 fluid ounces
 - c. 16 fluid ounces
 - d. 32 fluid ounces
8. How many teaspoons are in one pint?
 - a. 31.5
 - b. 47.3
 - c. 94.6
 - d. 104.2
9. A patient is prescribed 20 mEq of potassium chloride daily. The source of potassium chloride in the pharmacy is 2 mEq/ mL in 20 mL vials. How many mL per day are needed for this patient?
 - a. 1 mL
 - b. 2 mL
 - c. 10 mL
 - d. 20 mL
10. A patient is prescribed 10 mEq of potassium chloride daily. The source of potassium chloride in the pharmacy is 2 mEq/ mL in 20 mL vials. How many mL per day are needed for this patient?
 - a. 0.5 mL
 - b. 1 mL
 - c. 5 mL
 - d. 10 mL
11. How much sodium chloride is needed to make an isotonic 100 mL solution?
 - a. 0.45 g
 - b. 0.90 g
 - c. 1.32 g
 - d. 1.53 g
12. What volume of diluent (assume sterile water) is needed to make an isotonic solution from 0.45 g of sodium chloride?
 - a. 25 mL
 - b. 50 mL
 - c. 100 mL
 - d. 125 mL
13. The ratio strength of a solution is 1:900 (w/v). What is the percent weight by volume [(w/v)%] of the solution?
 - a. 0.1%
 - b. 1.1 %
 - c. 0.9%
 - d. 9%
14. The ratio strength of a solution is 1:5000 (w/v). What is the percent weight by volume [(w/v)%] of the solution?
 - a. 0.02%
 - b. 2 %
 - c. 0.8%
 - d. 8%
15. A vial of tobramycin sulfate contains 40 mg of drug per mL of injection. A patient was given 0.5 mL. How much tobramycin sulfate was administered?
 - a. 10 mg
 - b. 20 mg
 - c. 30 mg
 - d. 40 mg
16. How many days will the following prescription supply?
Rx
Penicillin VK suspension 250 mg/5 mL
Sig. 1 tsp. qid t.a.t. disp 200 mL
 - a. 7 days
 - b. 10 days
 - c. 14 days
 - d. 21 days
17. A medication is available in a 200 mg/5 mL vial. An Rx calls for 150 mg bid $\times$ 10d. How many milliliters are needed for a single day?
 - a. 5 mL
 - b. 7.5 mL
 - c. 10 mL
 - d. 75 mL
18. A medication is available in a 200 mg/5 mL multiple-use vial. An Rx calls for 300 mg bid $\times$ 10d. How many vials are needed for the full course?
 - a. 15 vials
 - b. 30 vials
 - c. 60 vials
 - d. 75 vials
19. JK is a 42 year-old woman who has a prescription for 32 mEq of oral potassium chloride. However, your pharmacy only has 600 mg controlled-release potassium chloride tablets in stock. How many tablets are required each day to provide this dose? (MW = 75)
 - a. 8
 - b. 3
 - c. 2
 - d. 4
 - e. 6

20. If a patient has a temperature of 102.2° F, what is the patient's temperature in degrees Celsius?
- 37.6 °C
 - 38.4 °C
 - 39 °C
 - 40.1 °C
21. If 500 mL of a 15% (v/v) solution of methyl salicylate in alcohol is diluted to 1500 mL, what will be the percentage strength (v/v)?
- 225%
 - 5%
 - 45%
 - 0.45%
22. A medication is available in a 150 mg/5 mL vial. An Rx calls for 300 mg bid × 10d. How many mL are needed for a single dose?
- 5 mL
 - 10 mL
 - 50 mL
 - 100 mL
23. What is the day supply for this prescription?
Amoxicillin 125 mg/5 ml (100 ml)
SIG: ss tsp tid
- 2 days
 - 100 days
 - 25 days
 - 13 days
 - 10 days
24. What is the percent weight by volume [% (w/v)] if 250 grams of dextrose is dissolved in 300 mL of water to make a final volume of 500 mL?
- 4.5%
 - 5%
 - 45.45%
 - 50%
25. If a prescription reads "Dispense: XVIII capsules," how many capsules should be dispensed?
- 12 tablets
 - 18 tablets
 - 22 tablets
 - 30 tablets
26. What total quantity of tablets should be dispensed for the following prescription?
Rx: Prednisone 5 mg
Sig: 10 mg qid × 2 days
10 mg tid × 2 days
10 mg bid × 2 days
5 mg tid × 2 days
5 mg bid × 2 days Then stop.
Qty qs
- 23 tablets
 - 25 tablets
 - 46 tablets
 - 50 tablets
27. What quantity should be dispensed for the following prescription?
- Rx: Prednisone 10 mg
Sig: 2 tabs bid × 3 days
1 tab bid × 3 days
1 tab qd × 3 days
1/2 tab qd × 3 days Then stop.
Qty qs
- 9 tablets
 - 10 tablets
 - 22 tablets
 - 23 tablets
28. How many grams of NaCl are there in 1000 mL of D5W/0.45% NaCl solution?
- 4.5 g
 - 0.6 g
 - 0.45 g
 - 0.25 g
29. How many grams of dextrose are in 1000 mL of D5W/0.45% NaCl solution?
- 100 g
 - 50 g
 - 20 g
 - 15 g
30. How many grams of dextrose are in 500 mL of a 10% dextrose solution?
- 500 g
 - 50 g
 - 150 g
 - 200 g
31. How many grams of NaCl are in 500 mL of 0.9% sodium chloride (NS) solution?
- 5 g
 - 2.5 g
 - 4.5 g
 - 1.5 g
32. How many milligrams of neomycin are in 25 mL of a 1% neomycin solution?
- 250 mg
 - 125 mg
 - 400 mg
 - 500 mg
33. How many grams of amino acids are in 500 mL of a 5% amino acid solution?
- 2.5 g
 - 22.5 g
 - 25 g
 - 50 g
 - 10 g
34. A pharmacist has 25 mL of 0.5% gentian violet solution. What will be the final ratio strength if he or she dilutes this solution to 600 mL with purified water?
- 1:8
 - 1:200
 - 1:500
 - 1:1000
 - 1:4800

35. An order is written for 1 g of lidocaine in 250 mL of D5W to infuse at 60 mg/hr. What is the correct infusion in (mL/hr)?
- 15 mL/hr
 - 20 mL/hr
 - 35 mL/hr
 - 45 mL/hr
36. An order is written for 25,000 units of heparin in 250 mL of D5W to infuse at 17 mL/hr. How many units of heparin will the patient receive in 6 hours?
- 10,200 units
 - 40,000 units
 - 10,800 units
 - 20,400 units
37. An order calls for 2.5 million units of aqueous penicillin. How many milliliters are needed if the vial concentration is 500,000 units/mL?
- 6 mL
 - 2 mL
 - 10 mL
 - 5 mL
38. How many milliliters are needed for 5 million units of penicillin if the vial concentration is 1 million units per mL?
- 15 mL
 - 5 mL
 - 10 mL
 - 20 mL
39. Valproic acid syrup comes in a 250 mg/5 mL concentration. How many mg are present in 7.5 mL of solution?
- 1000 mg
 - 500 mg
 - 375 mg
 - 250 mg
40. How many milliliters of 250 mg/5 mL valproic acid syrup are needed for a 0.5-g dose?
- 1 mL
 - 5 mL
 - 10 mL
 - 15 mL
41. If a drug comes in a 250 mg/1.5 mL solution, how many milliliters are required for a 2 g dose?
- 1.5 mL
 - 2 mL
 - 4.5 mL
 - 6 mL
 - 12 mL
42. How many grams of ampicillin are in 3 mL of a 500 mg/1.5 mL solution?
- 1 gram
 - 4 grams
 - 3.5 grams
 - 2 grams
43. How many milliliters contain 2.5 g of cephalothin if the concentration of the solution is 1 g/4.5 mL?
- 16.5 mL
 - 13.5 mL
 - 14.25 mL
 - 11.25 mL
44. How many grams of iodine are in 4 mL of a 50% iodine solution?
- 1 g
 - 2 g
 - 3 g
 - 4 g
45. How many milliliters of a 50% dextrose solution are needed for a 7.5-g dextrose dose?
- 7.5 mL
 - 10 mL
 - 15 mL
 - 20 mL
46. How many grams of sodium are in 50 mL D5W solution?
- 0
 - 1
 - 2.5
 - 3
47. The unit of weight measurement that is the same in both the apothecaries' and avoirdupois systems is the?
- Dram
 - Grain
 - Ounce
 - Pound
 - Scruple
48. One microgram equals one thousand (1000):
- Centigrams
 - Grams
 - Kilograms
 - Nanograms
 - Milligrams
49. Calculate the drip rate for 120 mL of IV fluids to be given over a half hour via an IV set that delivers 15 gtt/mL.
- 13 gtt/min
 - 25 gtt/min
 - 60 gtt/min
 - 33 gtt/min
 - 50 gtt/min
50. If a patient is given IV fluids at a rate of 25 gtt/min over 1 hour, how much fluid will be administered? The drop factor is 15 gtt/mL.
- 50 mL
 - 100 mL
 - 125 mL
 - 200 mL
 - 225 mL

51. In order to achieve better pain control, codeine phosphate 0.7 mL SC $\times$ 1 is ordered for a patient. The injectable form of codeine phosphate is available in a concentration of 50 mg/mL. How much codeine will this patient receive in this dose?
- 20 mg
 - 30 mg
 - 35 mg
 - 60 mg
 - 100 mg
52. Morphine is ordered for a patient, and the nurse gives him 1.9 mL from a vial with a concentration of 40 mg/2.5 mL. How much morphine was the patient given?
- 5 mg
 - 10 mg
 - 20 mg
 - 30 mg
 - 40 mg
53. The vial of hydromorphone that you have in stock has a concentration of 1.5 mg/0.5 mL. If the patient is given 0.7 mL, how much hydromorphone did she receive?
- 1.8 mg
 - 2.1 mg
 - 2.2 mg
 - 2.4 mg
 - 3 mg
54. What is the concentration (in percent) of a solution containing 20 mEq of potassium chloride per 15 mL of liquid? (MW = 75)
- 10
 - 15
 - 20
 - 25
 - 2.5
55. Diazepam is to be administered by the IV route to an adult patient. It is given at a rate of 5 mg/min over 90 seconds. How much diazepam is given to this patient?
- 5 mg
 - 6 mg
 - 7.5 mg
 - 8 mg
 - 10 mg
56. How many milligrams of morphine were given to a patient who received 6.2 mL of a 5 mg/mL solution?
- 31 mg
 - 22 mg
 - 25 mg
 - 35 mg
 - 46 mg
57. A nurse wants to give 300 mcg of levothyroxine IV to a patient, from a vial containing 0.4 mg/mL. How many milliliters should be given to the patient?
- 0.6 mL
 - 0.8 mL
 - 1.0 mL
 - 1.2 mL
 - 7.5 mL
58. A patient is to take 2.6 mL of oral furosemide, and each teaspoon contains 40 mg. How much furosemide will the patient be taking in their 2.6 mL dose?
- 20.8 mg
 - 40 mg
 - 33.1 mg
 - 16.5 mg
 - 24 mg
59. What is the percent weight=weight (%[w/w]) if 250 grams of dextrose is dissolved in 300 mL of water to make a final volume of 500 mL?
- 4.5%
 - 5%
 - 45.45%
 - 50%
60. According to USP specifications, how many milligrams is equal to 1/2 grain?
- 64.8 mg
 - 32.4 mg
 - 32.4 g
 - 3.24 mg
61. If the adult dose of a drug is 200 mg, what is the estimated dose for a child with a BSA of 0.8 m², using the BSA estimation method?
- 92 mg
 - 150 mg
 - 50 mg
 - 75 mg
62. If Lanoxin Pediatric Elixir contains 0.1 mg of digoxin per mL, how many mcg of digoxin are in 6 mL elixir?
- 6 mcg
 - 60 mcg
 - 600 mcg
 - 6000 mcg
63. What is the percentage of alcohol in a mixture of 200 mL of 95% v/v alcohol, 1000 mL of 70% v/v alcohol, and 200 mL of 80% v/v alcohol?
- 75%
 - 82%
 - 0.75%
 - 7.5%
64. A TPN order requires 500 mL of D5W. How many mL of D50W should be used if the D5W is not available?
- 450 mL
 - 550 mL
 - 50 mL
 - 25 mL

65. How much sodium chloride is needed to make the following prescription isotonic given E value for zinc sulfate is 0.15?
Zinc sulfate 2%
Sodium chloride q.s.
Purified water q.s 60 mL
a. 540 mg
b. 1200 mg
c. 180 mg
d. 360 mg
66. How much elemental iron is present in 500 mg of ferrous sulfate ($\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$) with atomic weights are Fe = 55.9; sulfur = 32.1; oxygen = 16.0; and hydrogen = 1.0. Iron has valences of +2 and +3)?
a. 100.5 mg
b. 167.7 mg
c. 111.8 mg
d. 120 mg
67. What will be the final ratio strength of a solution if one wishes to dilute 100 mL of 0.5% gentian violet solution to 1250 mL with purified water?
a. 1:500
b. 1:1000
c. 1:2500
d. 1:5000
68. How many beclomethasone (Qvar) inhalers should be dispensed to provide a 90-day supply? The recommended dose is 168 mcg BID. The commercial inhaler delivers 42 mcg per metered dose and contains 200 inhalations
a. 2 inhalers
b. 3 inhalers
c. 4 inhalers
d. 5 inhalers
69. If 6.25 g of boric acid are dissolved in sufficient alcohol to make a total volume of 100 mL, what is the strength of boric acid in the solution in mg/mL?
a. 62.5 mg/mL
b. 6.25 mg/mL
c. 625 mg/mL
d. 62.5 g/mL
70. If 50 mL of 4% (w/v) Xylocaine solution are added to 100 mL bag of D5W injection, what is the percentage strength (w/v) of Xylocaine in the final product?
a. 1%
b. 2.5%
c. 1.3%
d. 2%
71. A blood glucose reading shows 200 mg% of glucose. Express this value in mg/mL.
a. 0.2 mg/mL
b. 20 mg/mL
c. 2 mg/mL
d. 200 mg/mL
72. How many grams of solute are there in 250 g of a 1:50 w/w solution?
a. 50 g
b. 5 g
c. 0.5 g
d. 5 mg
73. How many milligrams of drug are there in 50 mL of a 5% w/v solution?
a. 0.25 g
b. 5 g
c. 2500 mg
d. 250 mg
74. How many milligrams of drug are there in 100 g of a 1:200 w/w mixture?
a. 500 mg
b. 5 mg
c. 5 g
d. 5000 mg
75. How many mg of sodium bicarbonate (NaHCO_2) contain 400 mg of sodium?
a. 1496 mg
b. 1.496 mg
c. 0.922 mg
d. 922 mg
76. What is the percentage (based on weight) of Na in Na_2CO_3 ?
a. 21.7%
b. 43.4%
c. 4.34%
d. 0.434%
77. How many milligrams of sodium chloride are there in a 2 mmol solution? (MW of NaCl = 58.5)
a. 117 mg
b. 11.7 mg
c. 1.17 mg
d. 1.17 g
78. How many millimoles of calcium fluoride are present in 5 g? (MW of calcium fluoride = 78)
a. 0.641 mmol
b. 6.41 mmol
c. 64.1 mmol
d. 64.1 mol
79. How many grams of KCl are needed to prepare 50 mmols solution? (MW of KCl = 74.6)
a. 3730 mg
b. 37.30 mg
c. 3.730 g
d. 37.30 g
80. What is the percentage strength of 1:200 solution of oil in alcohol?
a. 0.5% v/v
b. 0.005% v/v
c. 5% v/v
d. 0.5 mL

81. What is the percentage concentration of a 2:2000 solution of benzalkonium chloride?
- 0.01% w/v
 - 1% w/v
 - 0.1% w/v
 - 10% w/v
82. To make 100 mL of 1:1000 w/v solution, how many milligrams of NaHCO_2 are needed?
- 10 mg
 - 100 mg
 - 0.1 mg
 - 1 mg
83. If the reorder point for simvastatin 40 mg is 2 and the maximum is 5, how many bottles should be ordered if there is 1 bottle of simvastatin 40 mg?
- 0
 - 1
 - 4
 - 5
84. You have a bottle of 1 g amoxicillin powder for oral suspension. How many mL of purified water are needed to prepare a 125 mg/5 mL suspension?
- 10 mL
 - 1.0 mL
 - 40 mL
 - 4.0 mL
85. How much dilutant needs to be added to a 500 mg vial of Merrem to obtain a concentration of 50 mg/mL?
- 1 mL
 - 5 mL
 - 10 mL
 - 50 mL
 - 100 mL
86. A patient is to receive 1000 mL of solution over 8 hours. If the administration set delivers 20 gtt/mL, at how many gtt/min should the solution be infused?
- 4 gtt/min
 - 20 gtt/min
 - 40 gtt/min
 - 0.4 gtt/min
87. A solution is to be administered by IV infusion at a rate of 100 mL/hr. How many gtt/min should be infused if the administration set delivers 20 drops/mL?
- 5 gtt/min
 - 50 gtt/min
 - 3.3 gtt/min
 - 33 gtt/min
88. A patient is to receive 1 L of a normal saline by IV infusion over 12 hours. What is the rate of infusion expressed as gtt/min if the infusion set delivers 20 gtt/mL?
- 28 gtt/min
 - 2.8 or 3 gtt/min
 - 28 gtt/hr
 - 280 gtt/hr
89. An IV infusion for a 22-lb child calls for 4 mcg/kg/min at a rate of 1.2 mL/hr. How many milligrams of a drug are required in a 100-mL infusion solution to supply the required dose?
- 440 mg
 - 200 mg
 - 3.3 mg
 - 20 mg
90. If 100 g dextrose is dissolved in 100-mL water to make a final volume of 150 mL, what is the %w/v of this solution?
- 50% w/v
 - 66.7%w/v
 - 5% w/v
 - 6.67% w/v
91. What is the %w/v concentration of a 100 mL of amoxicillin oral suspension containing 150 mg/5 mL?
- 30% w/v
 - 1.5% w/v
 - 3% w/v
 - 15% w/v
92. If a patient has a temperature of 37°C, what is the patient's temperature in Fahrenheit?
- 69°F
 - 100°F
 - 98°F
 - 98.6°F
93. If a solution has a ratio strength of 1:10000 w/v, what is the % w/v of the solution?
- 0.01% w/v
 - 1.0% w/v
 - 0.1% w/v
 - 10% w/v
94. The required dose for a 110-lb patient is 0.5 mg/kg/min. If the concentration of the medication is 1 g/100 mL, what is the infusion rate in mL/hr?
- 2.5 mL/min
 - 25 mL/min
 - 150 mL/hr
 - 15.0 mL/hr
95. If 2.54 g of a drug is used to make 1000 tablets, roughly how many milligrams will 60 tablets contain?
- 25 mg
 - 50 mg
 - 100 mg
 - 150 mg
 - 200 mg
96. What is the %w/w of 1000 mL solution when 200 g dextrose is dissolved in 900 mL of water?
- 18.2%
 - 20%

- c. 1.82%
d. 2.0%
97. A 16 oz. 10 g/15 mL lactulose bottle contains how many tablespoon-doses?
a. 96 doses
b. 3.2 doses
c. 320 doses
d. 32 doses
98. If the required dose is 1 tsp bid, how long will an 180-mL bottle of clemastine fumarate syrup 0.5 mg/5 mL last?
a. 36 days
b. 18 days
c. 30 days
d. 60 days
99. How many milligrams of prochlorperazine are in a 5 mL injection containing 5 mg/mL?
a. 5 mg
b. 1 mg
c. 10 mg
d. 25 mg
100. The recommended daily adult dose of a medication is 2 mg/kg body weight in 4 divided doses. What is the daily dose for a person weighing 110 lb?
a. 100 mg daily
b. 25 mg daily
c. 220 mg daily
d. 10 mg daily
101. Kefzol is ordered at a dose of 30 mg/kg/day divided three times daily for an elderly female patient who weighs 88 lbs. How much Kefzol will be given to her daily?
a. 400 mg
b. 800 mg
c. 1200 mg
d. 1.5 g
e. 1 g
102. How much Kefzol would have to be drawn up from the vial and injected into an IV bag to make one dose of Kefzol for the patient in question 101? The vial you have on hand was compounded to a concentration of 325 mg/mL.
a. 5.45 mL
b. 6.25 mL
c. 1.65 mL
d. 1.23 mL
e. 0.68 mL
103. A bag with 250 mL of NS will be infused over 2 hours using a microdrip set (60 gtt/mL). What is the flow rate in drops per minute?
a. 60 gtt/min
b. 100 gtt/min
c. 115 gtt/min
d. 125 gtt/min
e. 140 gtt/min
104. An IV bag with 1250 mL of IV fluids is to be infused over 3 hours with a 15 gtt/mL set. How many milliliters will be infused over each hour?
a. 300 mL/hr
b. 345 mL/hr
c. 416 mL/hr
d. 427 mL/hr
e. 458 mL/hr
105. A 240 lb male patient is prescribed zidovudine at a dose of 2 mg/kg three times daily. How much zidovudine will this patient receive daily?
a. 218 mg
b. 436 mg
c. 654 mg
d. 245 mg
e. 186 mg
106. A patient weighing 155 lbs is ordered dobutamine at a rate of 5 mcg/kg/min. When the drug is admixed, 200 mg of dobutamine was put into a 500 mL bag of normal saline (NS). What is the final concentration of the solution in mcg/mL?
a. 5 mcg/mL
b. 40 mcg/mL
c. 200 mcg/mL
d. 400 mcg/mL
e. 444 mcg/mL
107. The required dose of Drug X for a 150-lb patient is 1 mg/kg/min. If the concentration of the medication is 5 g/100 mL, what is the infusion rate in mL/hr?
a. 2.1 mL/min
b. 5 mL/min
c. 82 mL/hr
d. 400 mL/hr
108. What is the milliosmolarity of normal saline (0.9% NaCl) solution? Na=23, Cl=35.5
a. 145 mOsm/L
b. 220 mOsm/L
c. 255 mOsm/L
d. 285 mOsm/L
e. 308 mOsm/L
109. If a solution contains 1 g of sodium chloride dissolved in 100 mL of D5W, how many milliosmoles are present? (Na = 23; Cl = 35.5; hydrous dextrose = 198)
a. 60
b. 120
c. 240
d. 300
e. 360
110. An order is received in the pharmacy for an irrigation solution of 0.25% w/v acetic acid. The acetic acid in stock is 99.9% w/w, and must be added to 128 oz of purified water. How many grams of 99.9% w/w acetic acid must be added to the purified water in order to prepare the final irrigation solution?
a. 6.7
b. 8.2

- c. 9.6
d. 10.8
e. 12.3
111. One gram of a given chemical is soluble in 10 mL of alcohol. What is the specific gravity of alcohol if a saturated solution is made with this chemical into an 11.1% w/w solution?
a. 0.75
b. 0.8
c. 0.9
d. 1.0
e. 1.15
112. How many grams of iodine are consumed daily from 0.3 mL tid of 5% w/v strong iodine solution?
a. 450
b. 45
c. 4.5
d. 0.045
e. 0.0045
113. A technician is preparing a potassium chloride infusion for a hypokalemic patient. The IV bag contains 250 mL of normal saline and 5.86 g of KCl (KCl molecular weight = 74.6). In the final infusion preparation, how many milliequivalents of potassium chloride are present?
a. 12.7 mEq
b. 78.5 mEq
c. 43.7 mEq
d. 22.5 mEq
e. 36.4 mEq
114. What is the volume of distribution of a drug with a clearance of 9 L/hr, $F = 50$, and an elimination half life of 7.8 hours?
a. 70 L
b. 93 L
c. 101 L
d. 149 L
115. How many mL of tetracycline suspension 250 mg/5 mL must be given in order for the patient to receive 150 mg?
a. 3 mL
b. 6 mL
c. 12 mL
d. 7.5 mL
e. 15 mL
116. An acidic drug has a pK_a of 5.4. What percentage of the drug is ionized in urine with a pH of 6.0?
a. 25.1%
b. 74.9%
c. 20.1%
d. 79.9%
117. A weakly basic drug has a pK_a of 8.6. What percent would be un-ionized in circulation?
a. 0.059%
b. 0.941%
c. 5.9%
d. 94.1%
118. A patient is to receive 2 mg/min of labetalol hydrochloride that has been prepared by adding 200 mg of labetalol hydrochloride injection to 250 mL of D5W to attain a final concentration of 2 mg/3 mL. How many milliliters per hour should the nurse infuse?
a. 2.5 mL/h
b. 150 mL/h
c. 3 mL/h
d. 180 mL/h
119. A patient is to receive 4 L of D5NS over 24 hours. If the IV tubing has a drip factor of 15 gtt/mL, what is the drip rate?
a. 18 gtt/min
b. 42 gtt/min
c. 55 gtt/min
d. 250 gtt/min
120. What is the day supply for this prescription? Persantine 25 mg (quantity 100) SIG: 1 tab qod
a. 200
b. 100
c. 50
d. 25
e. 20
121. Which erythromycin salt(s) is/are available by IV infusion?
I. Erythromycin lactobionate
II. Erythromycin stearate
III. Erythromycin ethylsuccinate
a. I only
b. II only
c. I and II
d. I and III
e. II and III
122. The hydrogen ion concentration of a topical solution is 1×10^{-8} . What is the pH of this solution?
a. 8
b. 4
c. 2
d. 6
e. None of the above
123. A 3-mEq/mL solution of KCl contains how many milligrams per milliliter? (MW of KCl = 74.5)
a. 0.04 mg/mL
b. 24.8 mg/mL
c. 111.8 mg/mL
d. 223.5 mg/mL
124. A patient is prescribed 10 mEq KCl once daily to compensate for the potassium wasting effects of furosemide. How many mg of KCl is in each dose? (MW of KCl = 74.5)
a. 3.73 mg
b. 7.45 mg

- c. 372.5 mg
d. 745 mg
125. CH is a 72-year-old woman who requires empiric vancomycin treatment for pneumonia. She is 5' 2" and weighs 125 lbs. Her SCr is 1.2 mg/dL. What is her calculated creatinine clearance?
- a. 33.5 mL/min
b. 39.4 mL/min
c. 38.0 mL/min
d. 44.7 mL/min
126. JW is a 64-year-old man with a prior medical history positive for hypertension and poorly controlled diabetes. He presents to the ED today complaining of fever and chills that have progressively worsened over the last 24 hours. His physical exam is unremarkable with the exception of an oozing foot ulcer. The medical team wants to begin empiric antibiotic treatment including an aminoglycoside. What is his calculated creatinine clearance? (height = 5' 8", weight = 247 lbs, SCr = 1.1 mg/dL)
- a. 61.3 mL/min
b. 55.8 mL/min
c. 65.6 mL/min
d. 107.8 mL/min
127. A patient's labs show serum calcium of 8.7 mg/dL and serum albumin of 3.2 g/dL. What is her corrected calcium concentration?
- a. 8.7 mg/dL
b. 9.34 mg/dL
c. 8.06 mg/dL
d. 14.46 mg/dL
128. How many milliliters of water should be added to 100 mL of a 1:125 (w/v) solution to obtain a solution such that 25 mL diluted to 100 mL will yield a 1:4000 strength solution?
- a. 300 mL
b. 400 mL
c. 500 mL
d. 600 mL
e. 700 mL
129. Using the following WBC and differential, calculate this patient's absolute neutrophil count (ANC).
WBC: $2.0 \times 10^3/\text{mm}^3$
Segs: 14.8%
Bands: 5%
Lymphocytes: 55%
Monocytes: 22%
Eosinophils: 1.7%
Basophils: 1%
- a. $99/\text{mm}^3$
b. $196/\text{mm}^3$
c. $396/\text{mm}^3$
d. $540/\text{mm}^3$
130. What is the pH of a buffer solution containing 0.25 M of acetic acid and 0.75 M of sodium acetate? ($K_a = 1.75 \times 10^{-5}$)
- a. 3.87
b. 4.28
c. 5.24
d. 6.53
131. A drug is available as both a 150-mg tablet and 100 mg capsule. The AUC for the tablet was calculated to be 76.3 mg.hr/L and for the capsule 84.2 mg.hr/L. What is the relative bioavailability of the tablet with respect to the capsule?
- a. 0.61
b. 0.73
c. 0.91
d. 1.37
132. If a person is 138 pounds and 66 inches, what is their BMI (Body mass index) (kg/m^2)?
- a. 46
b. 22.2
c. 2.2
d. 703
e. 12.5
133. TJ is a 23-year-old woman who has a long history of poorly controlled asthma. She is admitted to the hospital with a severe asthma attack and is started on aminophylline. She is currently receiving a continuous infusion of aminophylline at 40 mg/hour. The patient has not experienced any adverse effects and is responding well to therapy. Her steady-state theophylline concentration is 12.6 mg/mL. What dose of oral theophylline sustained-release formulation may she be converted to?
- a. 600 mg q12h
b. 400 mg q12h
c. 200 mg q12h
d. 800 mg q12h
e. None of the above
134. What statement is true regarding first order kinetics?
- I. Drug is metabolized at a rate that is constant overtime.
II. Aspirin is metabolized through first order kinetics.
III. $V = V_{\text{max}} [C]/K_m$
- a. I only
b. III only
c. I and II
d. II and III
e. I, II and III

The Federal Drug Administration (FDA) defines *traditional pharmacy compounding* as “the combining, mixing, or altering of ingredients to create a customized medication for an individual patient in response to a licensed practitioner’s prescription (www.fda.gov). Compounding is often used when the patient is intolerant of a manufactured drug. It may also be needed when an alternative route of administration is needed and not available commercially. It also allows physicians to prescribe customized strengths and dosage systems.

I. Regulation

The FDA established current Good Manufacturing Practices (cGMP) to ensure that minimum standards are met for drug product quality. The National Association of Boards of Pharmacy (NABP) formulated “Good Compounding Practices” that are used by many states. These can be found in the United States Pharmacopeia-National Formulary (USP-NF) and establish standards for extemporaneous compounding of nonsterile and sterile preparations.

II. Quality assurance

- A. Nonsterile products¹: The following questions are to be considered carefully before compounding:
1. Have the physical and chemical properties and medicinal, dietary, and pharmaceutical uses of the drug substances been reviewed?
 2. The first time a product was compounded, was documentation made of the materials and equipment used, method of mixing, labeling requirements, and dating determination?
 3. Are the quantity and quality of each active ingredient identifiable?
 4. Will the active ingredients be effectively absorbed, locally or systemically according to the prescribed purpose, from the preparation and route of administration?
 5. Are there added substances, confirmed or potentially present from manufactured products, that may be expected to cause an allergic reaction, irritation, toxicity, or undesirable organoleptic response from the patient? Are there added substances, confirmed or potentially present, that may be unfavorable (e.g., unsuitable pH or inadequate solubility)?
 6. Were all calculations and measurements confirmed to ensure that the preparation will be compounded accurately?
 7. Were expiration dates of all compounding materials being used checked?
 8. Are there clear labeling and directions?

9. Are there instructions regarding proper handling and storage of the medication?
10. Does it look or smell like it should?

B. Sterile products

1. Check compatibilities between drug-vehicle, drug-drug, and drug-container.
2. The finished product should be free of contamination, such as particles, bacteria, pyrogens.
3. All compounding materials should be checked for expiration date and proper function before use.
4. The solution should be clear, with all drugs completely in dissolution.
5. Final products should have seals or appropriate closures to indicate that the product has not been contaminated or manipulated since it was compounded and that it was checked and verified by the pharmacist so that nothing is added to the final product.
6. Clear labeling and directions should be present.
7. Labeling and instructions for proper handling and storage of medication should be present.
8. Logs/documentation/lot numbers should be present.

III. Requirements for Compounding

A. Materials

B. Equipment

1. Beaker
2. Biologic safety cabinet
3. Flask
4. Mortar
5. Ointment slab
6. Pestle
7. Scale
8. Stirring rod
9. Syringe/needle
10. Weighing paper/weighing boat
11. Spatula

C. Compounding area

1. The product may be flammable (e.g., alcohol), highly reactive (e.g., phenol), or cytotoxic (e.g., chemotherapy). The pharmacist may need to prepare the medication in a vertical flow hood to prevent harm to himself/herself. The pharmacist should use appropriate attire (e.g., gloves, gowns, facial covering).

IV. Achieving Stabilization of the Preparation

A. Temperature

- B. pH
- C. Stability and degradation
- D. Shelf life
- E. Special handling of product while in transport/delivery (e.g., do not shake)
- F. Precipitation
- G. Exposure to light and air
- H. Storage
 1. Glass bottles for certain medications to avoid adhesion to plastic, such as nitroglycerin in polyvinyl chloride (PVC) bags, and to avoid the release of plastic contaminants in the medication
 2. Refrigeration or freezing to prevent drug degradation or microbial growth
 3. Light-resistant container to prevent photo degradation
- V. Compounded Preparations
 - A. Solutions
 - A liquid preparation in which the ingredients are completely soluble
 - B. Suspensions
 - A liquid preparation in which the particles are mixed with but remain undissolved in a fluid or solid. *Note:* contents generally settle to the bottom of the bottle, so shake well before dispensing, and the patient should shake the item well prior to each use.
 - C. Emulsions
 - Emulsions are two-phase systems that consist of two immiscible liquids, one of which is uniformly dispersed throughout the other as fine droplets. They are classified as oil-in-water (o/w) or water-in-oil (w/o). There may also be multiple emulsions (e.g. w/o/w emulsion where a water droplet enclosed in an oil droplet is itself dispersed in water). They may be used internally to mask the bitter taste or odor of drugs or externally as creams or lotions.
 - D. Capsules
 - Solid dosage forms in which medicinal and/or inert substances are closed in a hard or soft gelatin shell.
 - E. Molded Tablets
 - Also known as tablet triturates, the preparation of tablets by molding has been replaced by tablet compression. Molded tablets dissolve rapidly in the mouth and do not contain disintegrants, lubricants, or any other component that slows the rate of dissolution.
 - F. Wafers
 - An oral dosage form consisting of a case, usually of rice-flour paste, containing the medication
 - G. Troches
 - A solid dosage form that is meant to be sucked, not swallowed, for drug absorption; also known as a lozenge
 - H. Suppositories
 - A suppository is a medicine that melts after insertion into the rectum (rectal suppository), the vagina (vaginal suppository), or the urethra (urethral insert)
 - I. Parenteral preparations
 - Desired effect is systemic when substance is given by routes other than the digestive tract. Parenteral administration generally has the greatest bioavailability because it avoids an absorption phase and possible inactivation by first-pass metabolism by the liver. It can be further divided into two subgroups: parenteral by injection or infusion and other nonoral parenteral administration (transdermal patch)
 - J. Powders
 - Used internally or externally, powders are often mixed with water or other liquid solvent
 - K. Creams, ointments, gels
 - Cream: A water-based preparation that is water-washable
 - Ointment: An oil-based preparation that is not water-washable
 - Gel: Semisolid systems consisting of suspensions of small inorganic particles or large organic molecules interpenetrated by a liquid
 - L. Tincture
 - A solution of a medicinal substance in an alcoholic or hydroalcoholic solvent
- VI. Examples of References Pharmacists May Use for Compounding
 - A. The United States Pharmacopeia–National Formulary (USP–NF): The compendium for pharmaceutical medicines and excipients for use in the United States
 - B. Trissel's Stability of Compounded Formulations: The handbook of stability and compatibility of injectable products
 - C. International Journal of Pharmaceutical Compounding
 - D. Drug Facts and Comparisons
 - E. Material Safety Data Sheets (MSDSs)
 - F. USP 797 Guidebook to Pharmaceutical Compounding: Sterile Preparations.

Excipients

Binders	Keep ingredients together, particularly in tablets Example: candelilla wax, corn starch
Buffer	Maintain the pH of a product to prevent drug degradation and can also protect the user from GI irritation Example: disodium hydrogen phosphate, sodium bicarbonate
Coatings	Can protect the drug product from degradation from the environment or from the GI tract for long-acting or delayed-release Example: gelatin, ethyl cellulose
Coloring agents	Generally used to match flavor Example: FD & C Red 40, tartrazine (FD&C #5)
Diluents/ Fillers	Allow for filling of a capsule or increase the size of a tablet for greater ease in handling; also used for creating aliquots or dissolving medications

	Example: magnesium stearate, anhydrous calcium phosphate
Emulsifiers	Promote solubility of one liquid into another
	Example: methyl cellulose, glyceryl monostearate
Flavoring agents	Make a drug product more palatable
	Example: cherry syrup
Preservatives	Reduce bacterial growth or protect the drug
	Example: benzyl alcohol, butyl paraben
Antioxidants	Prevent oxidation of active substances
	Example: ascorbic acid, sodium metabisulfite
Alcohols	Used as solubilizing agent or preservative (not for use in infants or epidurals)
	Example: benzyl alcohol
Parabens	Type of preservative
	Example: methylparaben, propylparaben
Chelators	Complex heavy metals, can improve efficacy of antioxidants or preservatives
	Examples: citric acid, tartaric acid, ethylenediamine-tetraacetic acid sodium (EDTA)
Sweeteners	Offset the poor taste of a product
	Example: sorbitol, simple syrup

Compounding Terms

Aliquot	A stock product made for a quantity below the least measurable quantity; see also least measurable quantity
Aseptic technique	The process of making a sterile product while reducing contamination of any particles, pathogens, or pyrogens; particularly important for parenteral, ophthalmic, and inhaled preparations
Biologic safety cabinet	A work area designed to aseptically prepare sterile medications; the vertical flow hood is ideal for preparing chemotherapeutic drugs, volatile substances, and other cytotoxic medications; the horizontal flow provides no protection to the user
Eutectic mixture	The combination of two solid substances at room temperature, which become liquid when combined
Geometric dilution	Mixing two powders of unequal size

Infusion (herbal medicine)	The steeping of a medicine in water; making a tea
Infusion (modern medicine)	Continuous delivery of a solution over a prolonged period of time
Least measurable quantity	The smallest amount that can be quantified by a scale or other measuring device; if a quantity must be used for which the device cannot measure, an aliquot must be made
Levigate	To make into a smooth, fine powder or paste, as by grinding when moist
Liniment	A liquid or semifluid preparation that is applied to the skin as a counterirritant
Mortar	A bowl for grinding and mixing ingredients
Muddle	The process of grinding a solid in a mortar with a pestle into a fine powder
Pestle	A rod used to grind and mix ingredients
Spatulation	Blending small amounts of powder by movement of a spatula on a paper or tile
Topical	A dosage form meant to treat an affected area without systemic effects
Transdermal	A medicated adhesive patch that is placed on the skin to deliver a time-released dose of medication through the skin and into the bloodstream; not to be confused with a topical medication
Triturate	To rub, crush, grind, or pound into fine particles or a powder; pulverize; also known as muddling

Reference

1. Schnatz RG: *Pharmaceutical Compounding Nonsterile Drug Products*, USP33-NF28 Online. Chapter 795, Proposed 2010 revision.

REVIEW QUESTIONS

(Answers and Rationales on page 317.)

1. What is the percent weight/weight (w/w) if 250 grams of dextrose is dissolved in 300 mL of water to make a final volume of 500 mL?
 - a. 4.5%
 - b. 5%
 - c. 45.45%
 - d. 50%

2. How many day's worth of medication is provided by the following prescription?
Penicillin VK suspension 250 mg/5 mL
Sig tsp i qid tat disp 200 mL
- 7 days
 - 10 days
 - 14 days
 - 21 days
3. What volume was dispensed by the pharmacist if the percent concentration (weight/volume) of cefaclor was 3.7%?
Cefaclor oral suspension 187 mg/5 mL
Sig 1 tsp bid
- 50 mL
 - 75 mL
 - 100 mL
 - 150 mL
4. To prepare a 2% w/w hydrocortisone cream, how many grams of pure hydrocortisone powder must be mixed with 30 g of 1% hydrocortisone cream?
- 0.31 g
 - 3.1 g
 - 1.5 g
 - 15 g
5. What is the final concentration (w/w) of zinc oxide ointment when 200 g of a 5% zinc oxide ointment and 400 g of a 10% zinc oxide ointment are mixed?
- 7.5%
 - 0.83%
 - 8.3%
 - 83%
6. A pharmacist is asked to compound a 200 mL mixture containing maldroxy 50 mL, diphenhydramine elixir 50 mL, and viscous lidocaine 2%. How much viscous lidocaine 2% is needed to prepare the order?
- 200 mL
 - 4 mL
 - 100 mL
 - 60 mL
7. A pharmacist is trying to make 10% w/w sodium chloride solution and has 1 lb of 28% w/w sodium chloride solution on hand. How many grams of 10% w/w sodium chloride solution can be made from the amount on hand?
- 65
 - 127
 - 684
 - 1271
 - 1582
8. A pharmacist is to prepare 500 g of an ointment containing 5% w/w glycerin. The density of glycerin is 1.25 g/mL. How many milliliters of glycerin are needed to prepare this formulation?
- 6.8 mL
 - 7.3 mL
 - 8.4 mL
 - 9.1 mL
 - 20 mL
9. A pharmacist wants to prepare 4 L of 10% w/v hydrochloric acid from a stock bottle of 36.8% w/w hydrochloric acid (specific gravity 1.19). How many milliliters of the stock solution should be used to prepare the final 10% w/v hydrochloric acid solution?
- 125
 - 243
 - 512
 - 815
 - 913
10. A compounding pharmacy gets an order for 2 lb of 2% mupirocin ointment. The stock ointment on hand is 5% mupirocin ointment. How many grams of the 5% formulation should be mixed with white petrolatum in order to prepare this order?
- 14
 - 85
 - 127
 - 243
 - 363
11. How much ointment would fit into 80 2-oz jars?
- 80 oz
 - 4 lb
 - 875 g
 - 10 lb
 - 1271 g
12. For a 7-year-old female patient:
Sodium fluoride 500 mcg
M & Ft cap DTD # LX
Sig 1 qd
How many grams of sodium fluoride are required to prepare the prescription?
- 0.5
 - 30
 - 50
 - 0.03
 - 0.05
13. Sodium fluoride 250 mcg
M & Ft cap DTD # LX
Sig 1 qd
How many milligrams of sodium fluoride are required to prepare the prescription?
- 0.25
 - 15
 - 25
 - 150
 - 250

14. What problem(s) should the pharmacist anticipate in preparing this prescription?
- Caustic nature of sodium fluoride
 - Poor water solubility of sodium fluoride
 - Difficulty in weighing small quantity of powder
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
15. For a 23-year-old female patient:
Diphenhydramine 50 mg
Acetaminophen 325 mg
M & Ft cap DTD # XXX
Sig 1 qhs
Lactose will be the preferred filler agent because of its solubility. The appropriate capsule size for the above prescription will be capsule size #1 with an approximate capacity of 0.5 mL. The tapped density of the ingredients are as follows: diphenhydramine 800 mg/mL, acetaminophen 850 mg/mL, and lactose 950 mg/mL. Determine the amount of lactose needed to prepare this prescription.
- 52.4 mg
 - 111.8 mg
 - 1.57 g
 - 3.35 g
 - Cannot be determined
16. Which of the following is true regarding emulsions?
- One-phase systems
 - May be used internally or externally
 - May be classified as oil-in-water or water-in-oil
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
17. Which of the following statements about laminar flow hoods are FALSE?
- Laminar flow hoods provide clean air to the working area.
 - Laminar flow hoods provide a constant flow of air out of the work area to prevent room air from entering.
 - The air flowing out from the hood suspends and removes contaminants introduced into the work area by personnel.
 - The room air is taken into the HEPA filter and is then passed through a different filter to remove gross contaminants, such as lint or dust.
- I only
 - III only
 - II and III only
 - I, II, and III
 - IV only
18. Objects in the hood are arranged in a manner to get full benefit of the laminar flow of air. In a horizontal hood, the items should be placed:
- individually left to right, equidistance from the front and back of the laminar airflow hood working space as well as from each other
 - grouped left to right, equidistance from the front and back of the laminar airflow hood working space
 - individually back to front, equidistance from each other
 - grouped on only one side of the hood
19. Which of the following is NOT available as large-volume parenterals (LVP)?
- Dextrose and sodium chloride injection USP
 - Mannitol injection USP
 - Lactated Ringer's injection USP
 - Sodium chloride injection USP
 - None of the above
20. Which of the following statements about laminar flow hoods are FALSE?
- Laminar flow hoods provide clean air to the working area.
 - Laminar flow hoods provide a constant flow of air out of the work area to prevent room air from entering.
 - The room air is taken into the HEPA filter and is then passed through a different filter to remove gross contaminants such as lint or dust.
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
21. To remove 5 mL of solution from a 30-mL multidose vial, what is the correct order of steps?
- Place point of syringe needle onto the vial's rubber closure at a 45° angle with the bevel opening facing upwards.
 - Inject the air.
 - Draw 5 mL of air into the syringe.
 - Raise the needle angle to 90° and insert needle through the rubber closure.
 - Remove 5 mL of solution.
- I, II, III, IV, V
 - III, I, IV, II, V
 - III, IV, I, II, V
 - I, III, IV, II, V
 - I, III, II, IV, V
22. To maintain sterility, what part(s) of the syringe should never be touched?
- Luer-lok tip
 - Plunger
 - Barrel
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III

23. Needle size is determined by the gauge and the length. Which of the following statements are correct?
- The larger the gauge number, the larger the diameter of the needle's bore.
 - The larger the gauge number, the finer the diameter of the needle's bore.
 - Needle length is measured in inches.
 - Needle length is measured in centimeters.
 - Needle length is measured in millimeters.
- I and III
 - I and IV
 - I and V
 - II and III
 - II and V
24. A concentrated vancomycin solution of 10 mL is added to a 100 mL piggyback bag of normal saline. The solution is to be infused over one hour. What is the infusion rate?
- 10 mL/hr
 - 100 mL/hr
 - 110 mL/hr
 - 200 mL/hr
 - 210 mL/hr
25. How many milliliters of water should be mixed with 120 mL of syrup containing 75% w/v sucrose to make a syrup containing 50% w/v sucrose?
- 60 mL
 - 80 mL
 - 100 mL
 - 120 mL
 - 200 mL
26. Which of the following statements is INCORRECT?
- To prevent contamination, swab rubber closure of the vial with 70% alcohol using firm strokes in any direction or manner.
 - To prevent core formation, insert needle to penetrate the rubber closure at same point with both tip and heel of bevel.
 - To prevent vacuum formation, inject an equal amount of air for the volume of fluid to be removed.
 - When reconstituting drug powder, remove an equal amount of air for the volume of diluent added.
 - None of the above.
27. Which of the following statements about pyrogens is/are CORRECT?
- Pyrogens are bacterial endotoxins.
 - Pyrogens are metabolic products of living microorganisms.
 - Pyrogens cause a pyretic response upon injection.
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
28. Which of the following is NOT a method used to sterilize pharmaceutical products?
- Steam
 - Dry heat
 - Filtration
 - Gas
 - All of the above are used to sterilize products
29. True or False: When preparing a dose from an ampule, one should use a 0.22- μ m inline filter rather than the 5- μ m filter straw.
- True
 - False
30. True or False: Nitroglycerin should always be prepared in glass because it is adsorbed to polyvinyl chloride (PVC), the plastic in the bags, and intravenous (IV) tubing.
- True
 - False
31. Drugs that are adsorbed to the inner lining of IV containers and tubing or administration sets, resulting in loss of drug delivered to the patient, include:
- Nitroglycerin
 - Insulin
 - Heparin
- I only
 - II only
 - I and II
 - III only
 - I, II, and III
32. Which of the following is not an example of an irrigation solution?
- Neomycin and polymyxin B sulfates
 - Ringer's solution
 - Sodium chloride
 - Dextrose
 - Sterile water
33. Which of the following is a common base for ointments?
- Bentonite
 - Methylcellulose
 - VEEGUM 6%
 - Hydrophilic petrolatum
 - All of the above
34. Answer the question based on the following prescription:
For a 7-year-old patient:
Omeprazole 10 mg/tsp
Sig 1 tsp q day, dispense 200 mL
Recipe:
Dissolve omeprazole in sodium bicarbonate 8.4% 200 mL
When preparing the above recipe, the pharmacist should be concerned with which of the following?
- The purpose of sodium bicarbonate 8.4%
 - The absence of alcohol
 - The acid-base reaction between sodium bicarbonate 8.4% and gastric acid

- a. I and II only
b. III only
c. II and III only
d. I, II, and III
e. None of the above
35. Answer the question based on the following prescription:
For a 7-year-old patient:
Omeprazole 10 mg/tsp
Sig 1 tsp q day, dispense 200 mL
Recipe
Dissolve omeprazole in sodium bicarbonate 8.4% 200 mL
Using the information given in the prescription and the recipe above, what is the final concentration for this oral suspension?
a. 0.05 mg/mL
b. 0.67 mg/mL
c. 2 mg/mL
d. 200 mg
e. 400 mg
36. Answer the question based on the following prescription:
For a 7-year-old patient:
Omeprazole 10 mg/tsp
Sig 1 tsp q day, dispense 200 mL
Recipe
Dissolve omeprazole in sodium bicarbonate 8.4% 200 mL
What is the amount of omeprazole required for this prescription?
a. 10 mg
b. 20 mg
c. 40 mg
d. 200 mg
e. 400 mg
37. Medicinal agents can either be weak acids or weak bases. Weak bases include the following EXCEPT:
I. codeine.
II. diphenhydramine.
III. phenobarbital.
a. I only
b. II only
c. III only
d. I and II
e. I and III
38. Burow's solution 15 mL
White petrolatum 45 g
Sig Apply bid AM and hs
The "% w/v" expression is commonly used as an abbreviation for percent weight in volume for solutions or suspensions of solids in liquids. What is the meaning of 2% w/v?
a. 2 mg/100 mL
b. 2 mg/1 L
c. 2 g/100 mL
d. 2 g/1 L
e. 0.02 g/100 mL
39. Please refer to the following prescription:
Rx
Starch
Talc aa 5 g
Lanolin 10 g
Petrolatum qs ad 60 g
What amount of starch should be weighed?
a. 1 g
b. 5 g
c. 15 g
d. 45 g
e. Cannot be determined
40. Which of the following statements is FALSE?
a. Water for injection, USP, is purified by distillation or by reverse osmosis.
b. Water for injection, USP, meets the same standards for the presence of total solids as purified water, USP.
c. Water for injection, USP, may not contain added substances.
d. Water for injection, USP, must be both sterile and pyrogen free.
e. Sterile water for injection, USP, is used for reconstitution of antibiotics.
41. Limewater is commonly used interchangeably for:
a. aluminum acetate.
b. hydrogen peroxide.
c. aluminum subacetate.
d. coal tar solution.
e. calcium hydroxide.
42. Which of the following best describes wool fat?
a. Oleaginous
b. Absorption (anhydrous)
c. Emulsion (water-in-oil [w/o] type)
d. Emulsion (oil-in-water [o/w] type)
e. Water soluble
43. Which of the following best describes hydrophilic ointment?
a. Oleaginous
b. Absorption (anhydrous)
c. Emulsion (W/O type)
d. Emulsion (O/W type)
e. Water soluble
44. Which of the following best describes Lubriderm products?
a. Oleaginous
b. Absorption (anhydrous)
c. Emulsion (W/O type)
d. Emulsion (O/W type)
e. Water soluble
45. Which of the following best describes Eucerin products?
a. Oleaginous
b. Absorption (anhydrous)
c. Emulsion (W/O type)
d. Emulsion (O/W type)
e. Water soluble

46. For an 8-year-old female patient:
Rx
Sodium fluoride 250 mcg
M & Ft cap DTD # XC
Sig 1 qd
How many milligrams of sodium fluoride are required to prepare this prescription?
- 2.75
 - 22.5
 - 25
 - 27.5
 - 225
47. Needle size is determined by the gauge and the length. Which of the following statements is/are correct?
- The larger the gauge number, the larger the diameter of the needle's bore.
 - The larger the gauge number, the finer the diameter of the needle's bore.
 - Needle length is measured in inches.
- I only
 - III only
 - I and II only
 - II and III
 - I, II, and III
48. When obtaining a 3-mL dose from a 5-mL ampule, which one of the following steps is INCORRECT?
- Disinfect the neck of the ampule using an alcohol swab.
 - Leave the swab in place.
 - Break ampule neck by snapping neck toward the back wall of the laminar flow hood and away from you.
 - Place needle tip into solution while holding the ampule almost horizontally.
 - After drawing approximately 4 mL of solution, aspirate excess into alcohol swab.
49. If the infusion rate for drug X is 120 mL/hr, what is the infusion rate in drops (gtt) per minute if drug X is administered using an infusion set that delivers 20 gtt/mL?
- 20 gtt/min
 - 40 gtt/min
 - 60 gtt/min
 - 80 gtt/min
 - 100 gtt/min
50. The pharmacist needs to prepare 100 capsules, each containing 4 mg of estriol and 0.5 mg of estradiol. A size 3 capsule is chosen for the prescription and separate capsules are filled with drug and lactose. Weights of contents are as follows: estriol = 250 mg, estradiol = 180 mg, lactose = 300 mg
How much of each ingredient are needed to prepare this prescription.
- 100 mg estriol; 50 mg estradiol; 32.54 g lactose
 - 200 mg estriol; 50 mg estradiol; 20.7 g lactose
 - 300 mg estriol; 100 mg estradiol; 63.7 g lactose
 - 400 mg estriol; 50 mg estradiol; 29.637 g lactose
 - 500 mg estriol; 100 mg estradiol; 15.2 g lactose
51. Which of the following statements is/are true for a vertical flow hood?
- Air blows towards worker.
 - Air blows from top down to maintain sterility and protect the worker.
 - It is used to make chemotherapy.
- I only
 - III only
 - I and II only
 - II and III
 - I, II, and III
52. Lactose, microcrystalline cellulose, and starch are commonly used:
- as a diluent or filler.
 - to provide bulk.
 - to provide cohesion to the powder blend of active and inactive components for transfer into capsule shells.
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
53. The total fill weight (drug plus excipients) for one capsule of a prescription was determined to be 280 mg. Which of the following choices is/are appropriate?
- #1 capsule
 - #3 capsule
 - #2 capsule
 - #5 capsule
 - b or c
54. Question refers to the following prescription:
An 18-year-old female patient
Room No. 1827
Theophylline 200 mg
Potassium chloride 10 mEq
D5W 250 mL
Infuse over 4 h at 0800, 1400, 2000 for 4 days
How many vials of theophylline injection (25 mg/mL, 20 mL per vial) are needed to complete this order for 4 days?
- 3
 - 4
 - 5
 - 6
 - 7
55. Question refers to the following prescription:
An 18-year-old female patient
Room No. 1827
Theophylline 200 mg
Potassium chloride 10 mEq
D5W 250 mL
Infuse over 4 h at 0800, 1400, 2000 for 4 days
A pharmacist reviewing this order should:
- call the prescriber to inform of a drug interaction between theophylline and potassium chloride.

- b. call the prescriber because the dose of theophylline is too low.
 - c. talk to the IV room technician to make sure the IV is put in a light-blocking bag.
 - d. call the prescriber and inform that potassium chloride is not compatible in D5W.
 - e. fill the prescription as is.
56. Sintering is:
- a. a method of mixing in a mortar and pestle.
 - b. a process of steeping and soaking a substance.
 - c. a method of extraction by boiling dissolved chemicals.
 - d. a process in which powdered materials are heated to form a coherent mass.
57. Which of the following is/are considered by USP-NF to be tablet and/or capsule lubricants?
- I. Magnesium stearate
 - II. Sodium benzoate
 - III. Sodium lauryl sulfate
- a. I only
 - b. II only
 - c. III only
 - d. I and III
 - e. All of the above
58. Which of the following are considered by USP-NF to be antimicrobial preservatives?
- I. Methylparaben
 - II. Sodium benzoate
 - III. Alcohol
- a. I only
 - b. II only
 - c. I and II
 - d. I and III
 - e. All of the above
59. How many grams of coal tar must be incorporated into 450 grams of zinc oxide paste to prepare a 10% coal tar ointment?
- a. 10 g
 - b. 45 g
 - c. 50 g
 - d. 90 g
 - e. 95 g
60. A 0.22- μ m filter is able to remove which of the following from a parenteral solution?
- I. Glass particles from an ampule
 - II. Bacteria
 - III. Viruses
- a. I only
 - b. II only
 - c. I and II
 - d. II and III
 - e. All of the above
61. An order is written for 60 mL of 0.5% (w/v) lidocaine hydrochloride solution. The pharmacy has 2% (w/v) lidocaine hydrochloride solution in stock. To fill this order, how many milliliters of normal saline (NS) should the pharmacist mix with what volume of lidocaine stock solution?
- a. 5 mL 2% solution and 55 mL NS
 - b. 15 mL 2% solution and 45 mL NS
 - c. 55 mL 2% solution and 5 mL NS
 - d. 45 mL 2% solution and 15 mL NS

Drug Information Resources

4

CHAPTER

The pharmacist is the healthcare professional who is the point-person for all drug information. Because it is impossible for any one person to know everything, the pharmacist should be able to know where to get information. In addition to locating the information, the pharmacist must be able to interpret, evaluate, and apply it. Equally important is communication of this information. If a physician asks for information, the pharmacist can likely share the information with the language in which it was discovered. However, if the information is intended to be passed along to a patient, the pharmacist may need to explain it in a way that reflects the patient's health literacy (explained in further detail in Chapter 6, Patient Education).

I. Hierarchy of Pharmacy and Medical Literature

A. Primary

1. Original journal articles
2. Case reports
3. Descriptive reports
4. Expert communication
5. Unpublished literature
6. Peer-reviewed journals
 - a) *New England Journal of Medicine*
 - b) *Journal of the American Medical Association* (JAMA)
 - c) *Annals of Internal Medicine*
7. Non-peer-reviewed journals
 - a) Supplements
 - b) "Throw away" journals
8. Advantages
 - a) Most timely
 - b) Provides vital information on which therapeutic decisions are based
9. Disadvantages
 - a) Cost (e.g., cost of journal subscriptions)
 - b) Access
 - c) Inconsistencies (e.g., conflicting journal articles)
 - d) Requires basic statistic knowledge to interpret study design and results

B. Secondary

1. Abstracting and indexing systems of primary literature
2. Medline
3. EMBASE
4. International Pharmaceutical Abstracts (IPA)
5. Advantages
 - a) Organizes volumes of literature

- b) Versatile
 - c) IPA is a more pharmacy-specific database
6. Disadvantages
 - a) Cost (e.g., EMBASE is more than \$40,000/year)
 - b) Access
 - c) Scope (some systems may search more or different journals so not always comprehensive)
7. Medline
 - a) Abstracting service created by National Library of Medicine
 - b) Uses MeSH (Medical Subject Headings) terms
 - c) PubMed is a free search engine for accessing Medline

C. Tertiary (Table 4-1)

1. Assembled information or interpretations of primary literature
2. Textbooks
3. Drug compendia
4. Full-text electronic books and databases
5. Review articles
6. Internet sources of various levels of reliability: It is critical to educate patients about web sources that provide misinformation.
7. Advantages
 - a) Access
 - b) Compactness
 - c) Conciseness
 - d) Cost
 - e) Ease of use/easy to read
8. Disadvantages
 - a) Timeliness
 - b) Errors in transcription
 - c) Incomplete detail

II. Components of a Clinical Trial

A. Population

1. Sample: subset of the population
 - a) Individuals from whom data are collected for the study
2. Sample size/power analysis
 - a) Determination of the number of patients required to adequately power a study
 - (1) A large sample size can detect a small difference.
 - (2) A small sample size can detect a large difference.

Table 4-1 Common Examples of Tertiary Literature (NOTE: lists are not comprehensive)

Topic of Interest	Literature in which to Find Topic
Alcohol/sugar/gluten free	<i>Red Book</i> (Drug Topics)
Adverse effects	<i>Meyler's Side Effects of Drugs</i> <i>Drug-Induced Diseases</i>
Bioequivalence	<i>Orange Book</i> (electronic version on FDA website)
Compounding	<i>Remington's Pharmaceutical Sciences</i> <i>Extemporaneous Formulations</i>
Consumer health information	USP DI Vol II: Advice for the Patient (obsolete) Clinical Pharmacology Lexi-Comp Micromedex Websites: www.drugdigest.org www.webmd.com
Diseases/General Medicine	<i>Cecil Textbook of Medicine</i> <i>Harrison's Principles of Internal Medicine</i>
Dosing	<i>AHFS Drug Information</i>
Dosing: Special populations	Clinical Pharmacology Drug Facts and Comparisons Micromedex <i>Harriet Lane Handbook</i> (pediatric) <i>Drugs in Pregnancy and Lactation</i> (Briggs) <i>Drug Prescribing in Renal Failure</i>
Drug Interactions	<i>Hansten and Horn Drug Interaction Analysis and Management</i> Clinical Pharmacology Drug Facts and Comparisons Micromedex
Foreign Drug Identifications	Index Nominum Martindale: The Complete Drug Reference
IV Compatibility	<i>Trissel's Handbook on Injectable Drugs</i> <i>King's Guide to Parenteral Admixtures</i>
Natural Products	Natural Standard Natural Medicines Comprehensive Database
Pharmacology/Pharmacokinetics	<i>Goodman and Gilman's The Pharmacologic Basis of Therapeutics</i> <i>Pharmacotherapy: A Pathophysiologic Approach</i> (DePiro) <i>Applied Therapeutics: The Clinical Use of Drugs</i> (Koda-Kimble)
Tablet Identification	IDENTIDEX (Micromedex) IDENT-A-DRUG WebMD Clinical Pharmacology's Drug Identifier
Unlabeled use	Drug Facts and Comparisons Micromedex USP DI Volume 1 (obsolete) <i>AHFS Drug Information</i> Clinical Pharmacology
Vaccines	www.cdc.gov

3. Randomization
 - a) Blocked
 - b) Stratified
 - c) Cluster
 - d) Systematic assignment
- B. Baseline assessment
- C. Study location
 1. Single center: use of one site to conduct a research study
 2. Multicenter: use of multiple sites to conduct a research study

3. International: use of multiple countries to conduct a research study
- D. Blinding
 1. Single blind: patient masked, or investigator masked, but not both
 2. Double blind: patient and investigator masked
 3. Open label: no masking; all patients and investigators aware of treatment
- E. Controls
 1. Placebo controlled: administration of an inactive substance for a control

2. Double dummy: use of multiple controls to maintain blinding
 - a) Example: To compare two medicines, one presented as blue tablets and one as red capsules, researchers could also supply blue placebo tablets and red placebo capsules so that both groups of patients would take one blue tablet and one red capsule
3. Active control: use of an established therapy as the comparative group
4. Crossover: patients serve as their own control by receiving multiple interventions
- F. Methods
- G. Institutional review board (IRB), ethics committees
- H. Intervention, duration of treatment
- I. Monitoring
- J. Follow-up
- K. Compliance
 1. Measure of adherence
- L. Outcome Measures
 1. Primary/secondary endpoints
 2. Surrogate endpoints: easily measured substitute markers in place of more clinically meaningful endpoints (e.g., CD4 count used as a surrogate endpoint for a trial regarding HIV infection)
- M. Statistics
 1. Goal: to be confident that the probability statement (p value) is valid and to maximize the possibility of detecting a difference when one actually exists¹
- N. Results
- O. Reporting adverse effects (MedWatch)
- III. Assessing Trial Results
 - A. Findings related to primary outcomes
 1. What type of data are presented?
 - a) Categorical (qualitative data)
 - (1) Nominal: named categories (e.g., blood type, gender, race)
 - (a) Mutually exclusive
 - (2) Ordinal: ordered categories of data; often sequenced (e.g., poor, good, excellent)
 - (a) Mutually exclusive
 - b) Numerical (quantitative data)
 - (1) Continuous: ordered, sequenced, and has a set of distance or values between rank (e.g., blood pressure, glucose levels)
 - B. Were the findings statistically significant?
 1. Hypothesis testing
 - a) Tests against the null hypothesis
 - (1) Null hypothesis (H_0): states that the variable of interest is equal to a given value or that no relationship exists between various variables
 2. Statistical and clinical significance
 - a) Statistical: probability that the results are due to chance or due to a true effect of treatment
 - b) Clinical: importance of the practical relevance or variation of a difference in outcomes
 - (1) A statistically significant outcome may not be clinically significant
 3. P value
 - a) The probability of the observed result or a more extreme result occurring by chance alone
 - C. How large is the treatment effect (when the primary outcome shows a statistically significant difference)?
 1. Relative risk (RR)
 - a) The reduction in the risk from one therapy relative to another ($RR = \text{events in treatment group} \div \text{events in placebo group}$)
 - (1) A RR of 1 means that there is no difference.
 - (2) A RR that is <1 (e.g., 0.75) means that risk is decreased
 - (3) A RR that is >1 (e.g., 1.15) means that risk is increased
 - b) Commonly used to express the therapeutic benefit of a drug
 2. Absolute reduction risk (ARR)
 - a) The absolute difference between the probabilities of the treatment event rate and control event rate ($ARR = \text{Probability of events in placebo group } [P_B] - \text{Probability of events in the active treatment group } [P_A]$)
 - b) Expressed as a percentage
 4. Types of error
 - a) Type I error (false-positive error)
 - (1) Rejecting the null hypothesis when it should be accepted
 - (2) Relates to validity
 - (3) Alpha level
 - (a) It is the risk of finding a difference when there is not one (risk of experiencing a type I error)
 - (b) Usually 5% by designation, indicating there is a less than 5% possibility that a finding is due to chance (does not really exist)
 - b) Type II error (false-negative error)
 - (1) Accepting the null hypothesis when it should have been rejected (there was a difference that was not detected)
 - (2) Relates to power
 - (3) Beta level
 - (a) The chance researchers are willing to risk that a difference will not be detected
 - (b) The probability of committing a Type II error
 - (c) Type II error (or beta)
 - (d) Usually 20% by designation
 5. Confidence interval (CI)
 - a) The range of values in which researchers can be certain that the true point estimate will fall
 - b) 95% CI most commonly reported
 - (1) 95% probability that the true result lies within the range of results found, and there is a 5% probability that the true range lies outside the interval
 - c) CI is calculated by subtracting from and adding to the sample mean the appropriate number of standard errors of the mean
 - d) The narrower the CI, the greater the reliability and more precise the data

3. Number needed to treat (NNT)
 - a) Number of subjects needed to treat over a defined period of time to experience one benefit of therapy
 - b) $NNT = 1/ARR$
- IV. Evaluating Clinical Trials
 - A. Questions to consider
 1. Why was this study conducted?
 2. Were previous trials conducted?
 - B. Consider the power/significance of the study
 1. Statistically
 2. Clinically
 - C. Critique the trial
 1. Population
 2. Intervention
 3. Endpoints: were they appropriate?
 4. Statistics
 - a) Consider the appropriateness of each statistical test and result
 - D. Can the findings from this study be extrapolated to patient/consumer?
- V. Study Types in Clinical Research
 - A. Randomized controlled trial
 1. An experiment in which investigators assign, by random allocation, eligible subjects into intervention groups to receive or not to receive one or more interventions that are being compared
 2. Gold standard: Randomized controlled trials are considered to have the highest validity and reliability of various research designs, as they eliminate causes of bias and provide a high level of experimental control.
 3. Necessary for Food and Drug Administration (FDA) approval
 - B. Cohort studies
 1. Group of subjects who have not yet experienced the outcome of interest
 2. Subjects exposed to a factor of interest are compared to a group not exposed and followed prospectively over time
 - C. Case-control studies
 1. Subjects with a particular characteristic are compared to a similar group without the characteristic to determine the cause
 2. Retrospective
 - D. Case reports
 1. No control
 2. No designed intervention
 3. Descriptive account of a subject
 - E. Meta-analysis
 1. A method of combining results of previous and similar research to determine a single estimate of treatment
 - F. Cross-sectional studies
 1. Measurements taken at a single point in time
 - G. Survey
 1. Research used to study the incidence, distribution, and relationship
 - H. "N-of-1" trials
 1. Randomized controlled study involving a single subject
 2. Crossover design
 3. Lack of generalizability to a population

- VI. Research involved in the FDA Drug Approval Process
 - A. Preclinical research
 1. Goal: assess potential therapeutic effects
 2. Does not predict human response
 - B. Phase I
 1. Initial study, usually in healthy human volunteers
 2. Small number of subjects (fewer than 100 subjects); brief length of study (less than 1 year)
 3. Determines toxicology, metabolism, and pharmacologic activities; early evidence of effectiveness
 - C. Phase II
 1. Expanded drug study to obtain preliminary efficacy data and safety in humans
 2. Small and highly homogeneous population of patients for whom the drug is intended (N = several hundred participants)
 - D. Phase III
 1. Pivotal trials
 2. Larger study (N = hundreds to thousands of participants)
 3. Long-term (up to several years)
 4. Semidiverse population (representing target population)
 5. Establishes final formulation, marketing claims, product stability, packaging, and storage concerns
 6. Successful completion may mean ready to submit compound to FDA for approval
 - E. Phase IV (postmarketing surveillance)
 - F. New Drug Application (NDA) form
 - G. Abbreviated NDA (aNDA) form: generic drug approval
 - H. Supplemental NDA (sNDA): approval for new indication

Reference

Haney MS, Meek PD: *Essential clinical concepts of biostatistics*, Kansas City, 1999, ACCP.

REVIEW QUESTIONS

(Answers and Rationales on page 320.)

1. A customer requests a recommendation for a "reliable brand" for ginseng. To ensure that she gets a ginseng product that has been tested for quality, what website(s) should a pharmacist consult?
 - I. ConsumerLab.com
 - II. ConsumerReports.org
 - III. American Society of Health-System Pharmacists (ASHP) Essentials
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
2. A customer requests a recommendation for a "reliable brand" for honeysuckle. To ensure that she gets a honeysuckle product that has been tested for quality, a pharmacist should NOT consult which of the following websites?
 - a. ConsumerLab.com
 - b. ConsumerReports.org

- c. www.USP.org
 - d. www.nsf.org
 - e. www.fda.gov
3. How is Drug Facts and Comparisons organized?
 - a. Alphabetically by generic name
 - b. Alphabetically by manufacturer name
 - c. By imprint code
 - d. By therapeutic use
 - e. None of the above
 4. How is Trissel's Handbook of Injectable Drugs organized?
 - a. Alphabetically by generic name
 - b. Alphabetically by manufacturer name
 - c. By imprint code
 - d. By therapeutic use
 - e. None of the above
 5. In which of the following resources could you have found information on unlabeled uses for a drug?
 - I. Lexi-Comp
 - II. Drug Facts and Comparisons
 - III. United States Pharmacopeia (USP) Volume 1 (obsolete)
 - a. I only
 - b. II only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
 6. Which of the following resources would you NOT use to identify a drug?
 - a. IDENTIDEX System
 - b. Clinical Pharmacology
 - c. Facts and Comparisons eAnswers
 - d. WebMD
 - e. Natural Standard
 7. In which resource would you find separate age, height, and weight charts for boys and girls?
 - I. Drugs in Pregnancy and Lactation (Briggs)
 - II. Harriet Lane Handbook
 - III. NeoFax
 - a. I only
 - b. II only
 - c. III only
 - d. I and II only
 - e. I, II, and III
 8. The FDA's MedWatch is a service through which one can report:
 - I. product quality problems.
 - II. product use errors.
 - III. adverse reactions.
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
 9. Any original published research in regards to a medication is considered to be:
 - a. primary literature.
 - b. secondary literature.
 - c. tertiary literature.
 10. Where would you best find a list of sound-alike look-alike drugs?
 - a. AHFS
 - b. EMBASE
 - c. IPA
 - d. MEDLINE
 - e. Institute for Safe Medication Practices (ISMP)
 11. True or False: PubMed requires the use of MeSH terms.
 - a. True
 - b. False
 12. If given a "PMID," what is the quickest way to locate the article?
 - a. Micromedex
 - b. EMBASE
 - c. PubMed
 - d. Ovid
 13. Why is it difficult to detect new or rare adverse drug reactions (ADR)?
 - a. It is not mandated to report ADRs to a program such as MedWatch.
 - b. Patients are taking too many medications to determine which causes an ADR.
 - c. Patients are poorly monitored while on therapy.
 - d. Patients are hesitant to report an ADR.
 14. True or False: Because MedWatch is an FDA program and not a manufacturer, MedWatch does not publish safety-related drug labeling changes.
 - a. True
 - b. False
 15. What do P and T in "P & T Committee" stand for?
 - a. Pharmacy and Therapeutics
 - b. Pharmacology and Therapeutics
 - c. Pharmacy and Times
 - d. Pharmacy and Toxicology
 16. True or False: The P & T Committee, like the IRB, reviews, monitors, and has the authority to approve or disapprove research.
 - a. True
 - b. False
 17. A recent formulary protocol has taken effect at your hospital and the proton pump inhibitor (PPI) of choice is Prilosec (omeprazole). The clinical pharmacist receives a prescription for Protonix (pantoprazole) and automatically switches to Prilosec. This is an example of:
 - a. generic substitution.
 - b. pharmaceutical alternative.
 - c. pharmaceutical equivalence.
 - d. therapeutic interchange.
 18. Which of the following are disadvantages in retrospective data collection?
 - a. There is no impact on clinical outcome.

- b. There are limited resources.
 - c. It is time consuming.
 - d. All of the above.
19. Results of a study show that, compared with placebo, the investigational agent decreases blood pressure by 10 mm Hg with p value of 0.006. What is the best description of this result?
- a. Statistically significant and clinically significant
 - b. Statistically significant but not clinically significant
 - c. Clinically significant but not statistically significant
 - d. Not clinically significant and not statistically significant
20. Which of the following are limitations of clinical studies to detect adverse effects?
- a. ADR studies use healthy, nonsymptomatic patients.
 - b. ADR studies use a relatively small sample size when compared to the numbers of patients estimated to be prescribed a drug.
 - c. ADR studies use a relatively short study duration when compared to the duration of treatment used for most chronic medications.
 - d. All of the above.
 - e. None of the above.
21. Type A adverse drug reactions:
- I. are usually dose-dependent and predictable.
 - II. are unrelated to pharmacological actions.
 - III. are caused by immunological mechanisms.
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
22. A type of data analysis in which the results of several studies are lumped together and analyzed refers to which type of study?
- a. Randomized controlled study
 - b. Cohort study
 - c. Case study
 - d. Meta-analysis
23. The outcome measure of a study comparing the efficacy of a new sepsis drug with existing therapy is mortality at 28 days. What is this type of outcome?
- a. Surrogate measure
 - b. Primary outcome measure
 - c. Secondary outcome measure
 - d. None of the above
24. The primary outcome measure for a study comparing the efficacy of a new sepsis drug with existing therapy is mortality at 28 days. What type of data is this outcome?
- a. Continuous
 - b. Ordinal
 - c. Nominal
 - d. None of the above
25. Which source contains information regarding foreign drugs?
- a. Martindale: The Complete Drug Reference
 - b. Red Book Drug Topics
 - c. Lexi-Comp
 - d. AHFS Drug Information
26. Which of the following people are blinded in a triple-blind study?
- I. Statistician
 - II. Investigators
 - III. Experimental subjects
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
27. Which of the following is the form to report adverse drug reactions to the FDA?
- a. Naranjo Causality Scale
 - b. Vaccine Adverse Event Reporting System (VAERS)
 - c. MedWatch
28. The statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings. This definition refers to what type of study?
- a. Meta-analysis
 - b. Randomized controlled trial
 - c. Crossover study
 - d. Case-control study
 - e. Cohort study
29. To achieve the least amount of bias, what study design should be used?
- a. Open label
 - b. Single blind
 - c. Double blind
30. Which type of error is made if the researcher concludes that there is difference between the studied groups when there is NO difference?
- a. Type II error
 - b. Type I error
 - c. Both a and b
 - d. None of the above
31. True or False: MEDLINE is the database that is available to anyone free of charge.
- a. True
 - b. False
32. What type of literature is readily available in most pharmacies?
- a. Primary literature
 - b. Secondary literature
 - c. Tertiary literature
33. The National Institutes of Health and the National Library of Medicine worked to develop what online drug information database?

- a. DailyMed
 - b. Clinical Pharmacology
 - c. Medscape Drug Reference
 - d. Natural Standard
 - e. UpToDate
34. What is currently the name for the PDA counterpart of Micromedex?
- a. DailyMed
 - b. Clinical Pharmacology
 - c. mobileMicromedex
 - d. Epocrates
 - e. Thomson mobile
35. Through which of the following is MEDLINE available free to the public?
- a. Blackwell Synergy
 - b. EBSCOHost
 - c. EMBASE
 - d. OVID
 - e. PubMed
36. The truncation symbol for PubMed is:
- a. #
 - b. \$
 - c. *
 - d. &
 - e. ^
37. The primary function of the Peer Review Process is to:
- a. Reduce subscription costs
 - b. Ensure accuracy and quality of content
 - c. Increase the journal revenues via reviewer fees
 - d. Advance the publication process
 - e. Decrease the number of research papers submitted for publication
38. A nurse working on the pediatric unit of a hospital incorrectly administers 3 units of regular insulin to a child intramuscularly rather than subcutaneously. The nurse is at fault for a(n):
- a. Vaccine scheduling error
 - b. Immunization injury
 - c. Medication error
 - d. Adverse drug event
 - e. All of the above
39. A girl enters your pharmacy and asks you to identify a drug she found in her boyfriend's gym bag. The ethical principle that would prohibit you from providing the answer is:
- a. Autonomy
 - b. Equality
 - c. Sincerity
 - d. Privacy
 - e. None of the above
40. Copyright Law is a subsection of which of the following laws?
- a. Criminal Law
 - b. Administrative Law
 - c. Civil Law
 - d. Intellectual Property Law
 - e. None of the above
41. Which of the following is an example of continuous data?
- a. Gender
 - b. NHYA class
 - c. Blood pressure
 - d. Mortality
42. Copying words or ideas without giving credit for the original idea or language is referred to as:
- a. Plagiarizing
 - b. Copyrighting
 - c. Broadcasting
 - d. Referencing
 - e. Reproducing
43. A unique alphanumeric string assigned to an object such as an electronic journal article is a(n):
- a. Digital Object Identifier (DOI)
 - b. HyperTextMarkup Language (HTML)
 - c. Extensible markup locator (XML)
 - d. Uniform Resource Identifier (URI)
 - e. HyperText Transfer Protocol (HTTP)
44. Which of the following resources may be used to check the compatibility of a drug with other drugs?
- I. Trissel's Handbook of Injectable Drugs
 - II. King's Guide to Parenteral Admixtures
 - III. Drug-Induced Diseases
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
45. Any undesirable effect associated with the use of a drug at a normal dose is referred to as a(n):
- a. Adverse drug reaction
 - b. Medication error
 - c. Medication misadventure
 - d. All of the above
 - e. None of the above
46. Which of the following is most likely to be an example of primary literature?
- a. A chapter in Harrison's *Principles of Internal Medicine* entitled "Women's Health"
 - b. A monograph in *Natural Standard Database* entitled "Saw Palmetto"
 - c. A journal entitled "The Annals of Pharmacotherapy"
 - d. An article in *New England Journal of Medicine* titled "The Relation between Blood Pressure and Mortality Due to Coronary Heart Disease among Men in Different Parts of the World"
 - e. All of the above
47. True or False: Double-blind, randomized controlled trials are associated with the least amount of bias.
- a. True
 - b. False

48. True or False: A well-conducted study has internal validity only.
- True
 - False
49. The results of a randomized controlled trial that compares insulin delivered via a pump with insulin injected 3 times daily shows 18% reduction in HbA1C for patients on the pump (95% confidence interval, 1%–22%). True or False: The result is statistically significant.
- True
 - False
50. True or False: The confidence interval determines whether the result is clinically significant.
- True
 - False
51. Continuous data are used to describe which of the following?
- Blood sugar level
 - Blood pressure
 - Mortality
 - Gender
 - a and b only
52. The combination of key words that will return the highest number of results is:
- Propranolol AND hypertension
 - Propranolol NOT hypertension
 - Propranolol OR hypertension
 - Propranolol WITH hypertension
 - Propranolol WITHOUT hypertension
53. To find out if daptomycin and ceftazidime can be safely administered through a Y-site, it would be best to consult:
- Cecil Textbook of Medicine
 - Drugs in Pregnancy and Lactation (Briggs)
 - King Guide to Parenteral Admixtures
 - Merck Index
 - Stockley's Drug Interactions
54. Yahoo.com is an example of a:
- Search directory
 - Search engine
 - Web site
 - Web dictionary
 - None of the above
55. The Weber Effect states:
- Adverse drug reactions always follow a normal distribution
 - Healthcare professionals must report adverse drug reactions in an online database
 - Reporting of adverse drug reactions increases until the middle to end of the second year of marketing
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
56. A well-conducted study will have:
- internal validity but no external validity.
 - both internal and external validity.
 - external validity but no internal validity.
 - no internal and external validity.
57. Phase IV clinical studies are commonly known as?
- Pharmacokinetic study
 - Preclinical study
 - Post-Marketing Surveillance study
 - Prevention study
 - Quality of life study
58. In clinical research, beta refers to which of the following:
- the null hypothesis being true
 - the probability of making a type II error
 - degree to which conclusions about causes of relations are likely to be true
 - cause-effect relationships
 - None of the above
59. Statistical power of a study is:
- used to determine sample size.
 - determined after enrollment.
 - determined before enrollment.
 - a and c only.
 - All of the above.
60. A medication use evaluation is:
- An evaluative method; reviewing practitioner prescribing, pharmacist dispensing, and patient use of medications is considered
 - An ongoing, systematic process designed to maintain the appropriate and effective use of the drug
 - Designed to improve quality of care for patients
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
61. What is nominal data?
- Categorical data in which the order of the categories is arbitrary
 - A type of data in which order is important
 - A type of measurement data
 - All of the above
62. Which of the following are ethical considerations when conducting a study?
- Institutional Review Board approval
 - Informed consent
 - Power of Study
 - Confidentiality
 - All of the above
63. Which of the following would be best describing this example: a prescription for Protonix is being switched to Prevacid due to formulary protocol in a hospital pharmacy.

- a. Therapeutic interchange
 - b. Generic substitution
 - c. Pharmaceutical equivalence
 - d. Pharmaceutical alternative
64. The role of a pharmacist in evidence-based medicine includes which of the following:
- I. Accurately integrating medical literature
 - II. Evaluating levels of evidence from clinical studies
 - III. Comprehensively reviewing literature
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
65. A regularly updated list of medication used in the diagnosis, prophylaxis, or treatment of disease is called a:
- a. Compendium
 - b. Policy
 - c. Formulary
 - d. Medication Account
 - e. Guideline
66. An analysis of all patients randomized in a study, even if they fail to comply or drop out is called?
- a. Regression analysis
 - b. Intention to treat analysis
 - c. Per-protocol analysis
 - d. Epidemiologic surveillance
 - e. None of the above
67. Oversight of policies and procedures related to all aspects of medication use within an institution are the responsibility of which committee?
- a. Institutional Review Board
 - b. Pharmacy and Therapeutics Committee
 - c. Safety group
 - d. Quality Assurance Committee
 - e. Drug Formulary Committee
68. Additions to the formulary with restrictions in place for improved therapeutic outcomes are considered:
- a. Guided-use strategies
 - b. Drug use evaluations
 - c. Orphan drugs
 - d. Non-label use
 - e. None of the above
69. Which of the following principles should guide the off-label use of medications?
- a. Patient safety
 - b. Pharmacy and Therapeutics Committee protocol for use
 - c. Comprehensive and balanced review of the evidence
 - d. All of the above
70. If a pharmacist evaluates a patient's planned drug therapy before dispensing the medication, this is considered a:
- a. Concomitant medication use evaluation
 - b. Prospective medication use evaluation
 - c. Retrospective medication use evaluation
 - d. Prevention medication use evaluation
 - e. None of the above
71. A patient who just started taking atenolol presents to a pharmacy with a blood pressure of 132/78 and pulse of 54 beats per minute. What is the most appropriate action?
- a. Advising the patient that these are normal values and not to worry
 - b. Calling the physician and suggesting that metoprolol might have a less-pronounced effect on the patient's heart rate
 - c. Asking the patient if he has noted any dizziness on standing or decreased exercise tolerance
 - d. Advising the patient to discontinue atenolol immediately
72. When counselling a patient on the use of Nexium, which of the following is most appropriate for the pharmacist to make?
- a. Take this medication once a day before breakfast.
 - b. This medication may cause sedation.
 - c. This medication is used to treat your toenail infection.
 - d. This medication is used to treat your high blood pressure condition.
73. The purpose(s) of a meta-analysis include:
- I. Decrease the chance of a type I error
 - II. Increase sample size
 - III. Decrease the likelihood of beta error
- a. I only
 - b. II only
 - c. I and III
 - d. II and III
 - e. I, II, and III
74. The most common instrument used in a meta-analysis to assess data heterogeneity is the:
- a. Paired t-test
 - b. Chi square
 - c. Cochran's Q
 - d. Pearson's correlation
 - e. None of the above
75. Which of the following is an example of nominal data?
- a. Gender
 - b. Blood glucose
 - c. Likert scales
 - d. Visual analog scales
 - e. All of the above
76. Which of the following are TRUE regarding a Phase I study for a new hypoglycemic agent?
- I. It includes patients for which the drug is intended.
 - II. Over 1,000 patients are usually included in the study.
 - III. It includes only healthy volunteers.

- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
77. Which of the following databases is available free of charge to the public?
- a. IPA
 - b. EMBASE
 - c. MEDLINE
 - d. Current Contents
78. A cohort study enrolled 800 cancer-free women receiving hormone replacement therapy (HRT) and 800 matched controls. By the end of the study, 75 of the cohort had developed breast cancer and 38 of the controls had developed breast cancer. Given these data, what is the relative risk of developing breast cancer associated with exposure to HRT?
- a. 0.507
 - b. 1.97
 - c. 1.05
 - d. 0.95
79. What source is used to find information on drug compatibility and stability?
- a. Remington's Pharmaceutical Sciences
 - b. Trissel's Handbook of Injectable Drugs
 - c. Martindale: The Complete Drug Reference
 - d. Drugs in Pregnancy and Lactation (Briggs)
 - e. Merck Index
80. Which of the following references provides "Drug information for the Health Care Professional"?
- a. USP DI Vol I
 - b. USP DI Vol II
 - c. USP DI Vol III
 - d. USP NF
 - e. None of the above
81. A woman informs a pharmacist that she is 36 weeks pregnant. The pharmacist recommends that she avoid ibuprofen. What reference provides the best support for this recommendations?
- a. Drugs in Pregnancy and Lactation (Briggs)
 - b. Merck Index
 - c. Physician's Desk Reference (PDR)
 - d. Trissel's Handbook of Injectable Drugs
 - e. None of the above
82. Which of the following is not considered tertiary literature?
- a. AHFS Drug Information
 - b. International Pharmaceutical Abstracts (IPA)
 - c. Micromedex
 - d. Physician's Desk Reference (PDR)
 - e. None of the above
83. What source should be used to obtain information on pharmaceutical compounding?
- a. AHFS
 - b. Hansten and Horn's
 - c. Martindale: The Complete Drug Reference
 - d. Remington's Pharmaceutical Sciences
 - e. Trissel's Handbook of Injectable Drugs
84. What source should be used for information on foreign drugs?
- a. Harrison's
 - b. Drugs in Pregnancy and Lactation (Briggs)
 - c. Martindale: The Complete Drug Reference
 - d. Remington's Pharmaceutical Sciences
 - e. Trissel's Handbook of Injectable Drugs
85. What source should be used to determine if there is an interaction between citalopram and clindamycin?
- a. Hansten and Horn Drug Interaction Analysis and Management
 - b. Index Nominum
 - c. Drugs in Pregnancy and Lactation (Briggs)
 - d. Remington's Pharmaceutical Sciences
 - e. None of the above
86. What source does NOT contain information regarding foreign drugs?
- a. Index Nominum
 - b. Red Book Drug Topics
 - c. Micromedex
87. Which of the following resources provides a package insert of atorvastatin calcium (Lipitor)?
- a. AHFS Drug Information
 - b. Drug Facts and Comparisons
 - c. Physician's Desk Reference (PDR)
 - d. Red Book Drug Topics
 - e. All of the above
88. What is the name of the program developed by the USP to report and evaluate medication errors?
- a. MEDMARX
 - b. MedWatch
 - c. VAERS
 - d. None of the above
 - e. a, b, and c
89. Which of the following is NOT an example of how to randomize patients in a study?
- a. Blocked
 - b. Cluster
 - c. Stratified
 - d. Multi-center
 - e. None of the above

- I. Definitions and Purpose
 - A. Dispensing is the physical act of giving, providing, or delivering a drug, chemical, device, or medication for later oral ingestion, insertion, application, injection, or other use.
 - B. The goal of dispensing is to select and dispense medications in a manner that promotes safe and effective use.
 1. Use the National Drug Code (NDC) number and other attributes to identify the correct drug product.
 - a. The key identifier when selecting a product in the U.S. is the NDC number, which is unique to every drug product.
 - b. NDC is an 11-digit, three-segment number. The format for all medications follows 55555-4444-22. The first segment of five numbers is a labeler code assigned by the Food and Drug Administration (FDA). A labeler is any firm that manufactures, repackages, or distributes a drug product. The second segment of four numbers is the product code, which indicates a specific strength, dosage form, and formulation for a particular product. Lastly, the third segment of two numbers identifies the package size.
 - c. When filling a prescription, one can use an NDC number to verify one has the correct drug. Generics for the same medication each have their own NDC.
 - d. When filling a prescription, verify the product against its image (if available) and confirm that it is in good condition. Confirm the expiration date, dosage form, and imprint code.
 2. Use barcode technology: Newer systems can include barcode technology that can scan for the appropriate product and even prevent dispensing unless the correct product is selected. This practice is used in hospitals and retail settings.
 3. Check for expiration dates.
 4. Check for drug interactions. When checking for interactions, a pharmacist must review the patient's medication, evaluate and consider the indication, consider the patient's age and hepatic/renal function, and whether or not the patient is pregnant. These factors may alter drug therapy.
 - a. There are many types of drug interactions:
 - 1) Drug-drug interactions
 - 2) Drug-food interactions
 - 3) Drug-disease interactions
 - 4) Drug-herb interactions
 - 5) Drug-pregnancy/lactation effects
 - b. Many pharmacy computer systems will have a drug-interaction screening software program in place. The integrated applications are usually provided through vendors such as First DataBank. As each prescription is filled, the system automatically checks the medication against other medications the patient is taking. However, this system is not always accurate because some people get prescriptions filled at multiple pharmacies and the computers are not on the same network. Ask patients about their use of all prescriptions, over-the-counter (OTC) medications, herbal remedies, vitamins, minerals, and other supplements. Determine if the patient has any known allergies.
 - c. There are other resources available to check for drug interactions including Clinical Pharmacology, Facts and Comparisons, Micromedex, and many others.
 - d. Herb-drug interactions are a concern due to uncertainty as to how herbs and supplements will interfere with other medication. Resources and data are limited in this area.
 - 1) An example of an herb-drug interaction is St. John's wort and cyclosporine. The mechanism for this interaction is proposed to be induction of cytochrome P-450 enzymes by St. John's wort.
 - 2) It is important to counsel patients on the possibility of food-drug interactions. Grapefruit or grapefruit juice has the potential to alter the effects of various medications, including antiarrhythmic agents, immunosuppressive agents, statins, and calcium channel blockers. The interaction is likely the result of inhibition of intestinal or liver metabolism by cytochrome P-450.
 - e. The pharmacist should notify the prescriber of serious drug interactions (those where the patient risk exceeds any benefit from the

- drug combination) and discuss alternative therapy.
5. Identify and verify drugs by their generic, brand, and/or common names. Most drugs have several names: a chemical name, a generic name, and a brand name. For example: [R-(R*, R*)]-2-(4-fluorophenyl)- β , δ -dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate is the chemical name for atorvastatin calcium, the generic name for Lipitor®.
 - a. Generic products contain the same active ingredient but are not likely to contain the same excipients (inactive ingredients). Generic drugs may differ in shape, scoring, configuration, release mechanisms, packaging, colors, flavors, and preservatives from the brand name product. The generic version delivers the same amount of its active ingredient and must have the same dosage form, safety, strength, route of administration, and conditions of use as the innovator/brand name product. Generic drugs are subject to the same FDA standards as all drugs and must be manufactured under the same strict standards of the FDA's good manufacturing practice (GMP) regulations. Generic drugs must pass stringent bioequivalency tests in humans to ensure the generic version delivers the same amount of active ingredient as the innovator/brand equivalent.
 - b. Excipients, or inactive ingredients in drug products, include fillers, binders, colors, and coatings. An individual may be allergic or sensitive to a specific excipient. Patients should be asked about all of their allergies, not just allergies to medications.
 - c. Therapeutic interchange is the process of dispensing prescribed medications that are chemically different but are therapeutically similar to the medication prescribed. Normally there are approved written guidelines or protocols in a formulary system.
 - 1) Therapeutic interchange is common in the hospital setting. For example, a doctor may prescribe esomeprazole (Nexium®) 40 mg, but the hospital pharmacy substitutes the preferred drug, pantoprazole (Protonix®). However, this practice varies from institution to institution and state to state. Some states do not allow any therapeutic interchange unless the prescriber is contacted. Other states do not address the issue at all.
 - d. Generic interchange is the process of dispensing a medication produced by another manufacturer that is the exact same chemical entity as the brand name prescribed.
 - 1) This practice also varies from state to state. Some use positive formularies, meaning that generics may be dispensed if the drug appears on the formulary. Other states use negative formularies that prohibit generic interchange of selected drugs. Using generic medications saves money because the price can be 30% to 80% less than the brand name.
 - 2) Consult the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book") for bioequivalence when determining appropriate generic products to dispense in lieu of a brand name/innovator product.
 6. Determine whether a particular drug dosage strength or dosage form is commercially available and whether it is available on a nonprescription basis.
 - a. Some medications are available as a prescription and an OTC product. Ibuprofen 200 mg (Motrin®, Advil®) is available OTC; ibuprofen 400 mg, 600 mg, and 800 mg are available by prescription. Other medications have become OTC products after previously being a prescription-only product. Cetirizine (Zyrtec®), loratadine (Claritin®), and omeprazole (Prilosec®) are a few of the medications that have made the switch from prescription to OTC.
 - b. Often there are different routes of administration are available for a therapeutic agent. The route of administration is determined by the therapeutic objective and the properties of the drug used. Each route has advantages and disadvantages, and the administration should be suited to the patient's needs. The two most common routes of administration are enteral and parenteral.
 - 1) Enteral: Oral is the most common route of administration. It is the easiest, most convenient, and least expensive. There are some disadvantages to the oral route: slower onset of absorption and action; variation in rate and degree of absorption with gastrointestinal contents and motility; cannot be used with nausea and vomiting; cannot be used with patients who are unconscious, have difficulty swallowing, or can take nothing by mouth (NPO). The patient's ability and willingness to swallow a solid dosage form is also a factor.
 - a) Sublingual, or under the tongue, administration allows the drug to enter the systemic circulation directly and bypass the liver.
 - 2) Rectal: Rectal administration may be used in patients who have difficulty swallowing or have nausea. In this form, the drug is not inactivated by intestinal enzymes if the drug is placed properly in the rectum.
 - 3) Parenteral: Some examples of the parenteral route are intravenous, subcutaneous, and intramuscular. Some drugs must be given by this route to stay in their active form. Insulin glargine (Lantus®) can only be given as an injection because oral administration would break down the medication before

absorption could occur. Bioavailability of drugs administered parenterally is usually more rapid, extensive, and predictable. Another advantage is that a parenteral route can be used during emergency therapy when a patient is unable to take medications by mouth.

- a) Intravenous is a common parenteral route. Drug absorption is not dependent on the GI tract and the effects are rapid. However, rapid administration may cause hemolysis and other adverse effects.
 - b) Intramuscular injections permit the administration of more irritating drugs and larger volumes of solutions that cannot be tolerated by other routes.
 - c) Subcutaneous (SC or SQ): SC injections are given under the skin and provide a rapid onset of action.
 - d) Transdermal administrations are applied to the surface of a body part.
- 4) Inhalation: Inhaled drugs are those that are administered through mucous membranes of the respiratory tract by nebulizer, face mask, pumps, or breathing machine. Examples of inhaled drugs include bronchodilators, corticosteroids, and mucolytic agents.
- E. Identify commercially available drug products by their characteristic physical attributes.
1. Imprint codes
 - a. Imprint codes are used for quick identification of solid dosage forms in drug overdose cases, to identify unknown drug products, and to allow patients to check that they have been dispensed the correct medication. Until 1995, there were no regulations regarding imprint data on solid-dosage forms of medications. Drugs exempt from federal regulations are in Table 5-1.²
 - b. The FDA only requires drug firms to provide their imprint information, along with their listing forms, to the agency's Drug Listing

Team, where it is entered into a database. The data captured include identifiers such as shape, size, color, imprint code, scoring, and coating. The database also incorporates imprint graphics, which describe a logo that does not consist of conventional characters.

- c. For example, tadalafil 10 mg (Cialis®) is a teardrop shaped, yellow tablet imprinted with C 10; tadalafil 20 mg (Cialis®) is a teardrop shaped, yellow tablet imprinted with C 20.
 - d. The Division of Drug Information can identify oral-dosage drugs based on physical appearance and markings. This service offered by the FDA is free to the American public. Drug-identification inquiries can be sent to the Division of Drug Information via telephone at 888-INFOFDA (888-463-6332), via fax (301-827-4577), or via e-mail (druginfo@cder.fda.gov).
 - e. Dietary supplements are not required to have imprint information.
2. Packaging and labeling
 - a. For some medications, the original package is important to the proper storage of the medication, or to reference manufacturer labeling. For example, nitroglycerin sublingual tablets must be stored in their original, tightly closed, glass bottle because potency can be lost by adsorption if repackaged. Packaging can vary between different strengths or types of medications.
 3. OTC medications: The drug facts label format was based on the nutrition facts food label. It uses an easy to read format and includes:
 - a. The product's active ingredients, including the amount in each dosage unit.
 - b. The purpose of the medication.
 - c. The uses and indications for the drug.
 - d. Specific warnings, including when the product should not be used, and when it is appropriate to consult a doctor or pharmacist. The warnings section also describes side effects that could occur and substances or activities to avoid.
 - e. Dosage instructions addressing when, how, and how often to take the medication.
 - f. The product's inactive ingredients, which is important for those with specific allergies.
 4. Dietary supplements:
 - a. The FDA regulates dietary supplements (defined by the FDA as being composed only of essential nutrients, such as vitamins, minerals, proteins, herbs, or similar nutritional sources) differently than food or OTC/prescription drug products. Dietary supplement manufacturers do not have to get FDA approval or register their products before producing or selling them. The Dietary Supplement Health and Education Act of 1994 (DSHEA) states that the dietary supplement manufacturer is responsible for ensuring that the supplement is safe before it is marketed. The FDA is responsible for monitoring safety via adverse event reporting and product

Table 5-1 Exemptions to Imprint Code Regulations

Drug products used in clinical investigations	When physical characteristics of the drug make it impossible to imprint
Drug products intended for use in bioequivalence studies	When the medication is dispensed in a controlled health care setting (i.e., doctor's office)
Prescribed drug products compounded extemporaneously by pharmacists	When the drug is not dispensed to patients for self administration.
Drugs classified as radiopharmaceutical drug products	

information. The manufacturers must ensure that the label is truthful and not misleading. Good Manufacturing Processes (GMP), determined by the FDA, must be in place. These govern the preparation, packing, and holding of dietary supplements under conditions that ensure their safety. The manufacturer, however, does not have to prove supplement quality.⁴

- b. There are third-party testing organizations that certify dietary supplements, which include USP, NSF International, and Consumer Lab. Certifications are important because many herbs and supplements have no identifying features on the pill or capsule. Keeping the consumer well informed about herbs and supplements is an important role for a pharmacist.
 - 1) USP is an independent, nongovernmental, nonprofit public health organization that verifies the identity, strength, purity, and quality of dietary supplements. Products that pass USP scrutiny receive a USP Verified mark on the label (Figure 5-1).
 - 2) NSF International verifies products for content and label accuracy, purity, contaminants, and good manufacturing processes.
 - 3) Consumer Lab tests various products against various claims in a qualitative manner (Figure 5-2).



Figure 5-1 — **USP Verified Dietary Supplement mark.** (Courtesy www.uspverified.org).

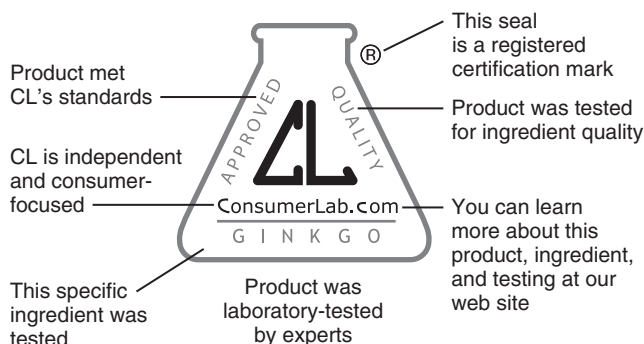


Figure 5-2 — **Consumer Lab Qualitative Testing.** (ConsumerLab.com, LLC).

- F. Interpret and apply pharmacokinetic parameters and quality assurance data to determine bioequivalence among manufactured drug products and identify products for which documented evidence of inequivalence exists.
 1. Drug products are considered pharmaceutical equivalents if they contain the same active ingredient, are of the same dosage form and route of administration, and are identical in strength or concentration.
 2. Generic drugs must pass stringent pharmacokinetic and bioequivalency tests in humans to be noted as bioequivalent to the innovator/brand product. The tests ensure the generic version delivers the same amount of active ingredient as the innovator/brand equivalent.
 3. The *Orange Book* is published by the FDA and aides in determining bioequivalence between drug products made by different manufacturers.³ The *Orange Book* uses a two-letter coding system to help determine which drug products are therapeutically equivalent.
 - a. Codes that begin with A are considered to be therapeutically equivalent to other pharmaceutically equivalent products.
 - 1) Drugs that have no known equivalence or suspected bioequivalence problems are designated AA, AN, AO, AP, or AT, depending on the dosage form.
 - 2) The *Orange Book* has a list with therapeutic equivalence (TE) evaluations for FDA-approved drug products. TE codes are composed of 2 letters (e.g., AB, AB2, BX). The first letter indicates whether the approved product is therapeutically equivalent to the reference-listed drug (RLD). If it is, then the drug will be designated with the letter "A." Drug products with a TE code starting with "B" are not considered to be therapeutically equivalent, or there is a problem in bioequivalence. The second letter provides additional information on the basis of the FDA's evaluations, such as route of administration or formulation.
 - b. Drug products with codes that begin with B are not considered therapeutically equivalent to other pharmaceutically equivalent products. Drugs fall under this category for one of three reasons: 1) the drug has documented bioequivalence problems or significant potential for problems, 2) quality standards are inadequate or the FDA has insufficient basis to determine therapeutic equivalence, or 3) the drug products are under regulatory review. B* indicates that the drug previously received an A or B code, but new information has been received by the FDA that raises questions regarding therapeutic equivalence, and the FDA will not take a position on the drug until it completes an investigation and review.

G. Identify and communicate appropriate information regarding packaging, storage, handling, administration, and disposal of medications.

a. Packaging

1. The Poison Prevention Act of 1970 states that child resistant closures must be on prescription containers unless the prescription is for an exempted drug or if the patient has authorized easy-open packaging.
2. Examples of exemptions from this rule are sublingual dosage forms of nitroglycerin, potassium supplements in unit dose forms, and oral contraceptives in mnemonic packaging.

b. Storage

1. Expiration date: The expiration date of a medication as determined by USP states that the expiration date must be no later than the expiration date on the manufacturer's container or one year from the date the drug is dispensed, whichever date is earlier. The expiration date for certain products such as insulin is different. For example, the expiration date on insulin products is 24 months from the date of manufacture. However, the stability of the insulin is altered once the product is opened and it therefore bears a new expiration date. The expiration information can be found in the product's package insert. For example, insulin glargine (Lantus®) and other insulin vials should be discarded 28 days after the product is opened. Other drug products may also have new expiration dates when opened. For example, Latanoprost (Xalatan®) needs to be stored in the refrigerator until first use, then may be stored at room temperature for 6 weeks.

c. Handling

1. Certain medications need careful handling to prevent degradation of the product.
2. The pharmacist should take precaution when preparing medications for patients. An example of this would be not shaking a vial of colistimethate for reconstitution, but rather gentle swirling.
3. Overall handling of sterile products is briefly reviewed in Chapter 3 on compounding.

d. Administration

1. When a medication is dispensed to the patient, the prescription label must have specific information*:
 - Pharmacy name, address, and telephone number
 - Assigned prescription number

- Date of the prescription or the date of its filling or refilling (state law often determines which date is to be used)
- Name of patient
- Name of prescriber
- Directions for use and any cautionary statements
- Controlled substance schedules II, III, or IV must contain the following warning: CAUTION: Federal law prohibits the transfer of this drug to any person other than the patient for whom it was prescribed.

2. Most medications are to be discarded in the trash, not flushed down the toilet. This should be done by taking the medications out of their original container and mixing with an undesirable substance such as coffee grounds or cat litter. However, the Office of National Drug Control Policy states that certain medications (e.g., fentanyl) can be disposed of in the toilet.

3. Patients should be aware of safe and legal disposal of drug devices. (e.g., needles disposed in appropriate sharp's containers).
4. Disposal instruction is not limited to patient knowledge but this knowledge is also important for the pharmacist, who may have to dispose of hazardous materials such as chemotherapeutic drugs.

H. Identify and describe the use of equipment and apparatus required to administer medications.

- a. The pharmacist should be able to describe in patient-appropriate language, how each medication should be used. This is particularly important for describing proper use of inhalers, nebulizers, insulin administration, auto injectors (e.g., EpiPen®), and ophthalmic and otic preparations.
- b. In addition to education regarding how to use a device, the pharmacist should be able to describe other elements of medication use (described in greater detail in Chapter 6, Patient Education).
 1. Possible adverse effects and their management
 2. Therapeutic drug monitoring including needed laboratory tests
 3. What to do in the event of a missed dose
 4. Helpful nondrug activities

References

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- FDA: *Electronic orange book*. Available at <http://www.fda.gov/cder/ob/default.htm>. Accessed September 2008.
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*Specific state laws may require additional information.

REVIEW QUESTIONS

(Answers and Rationales on page 324.)

1. The mechanism of action of Maxair® is closely related to which of the following agents?
 - a. Zafirlukast
 - b. Albuterol
 - c. Ipratropium
 - d. Nedocromil
 - e. None of the above
2. Which of the following is/are available dosage strength(s) of oral Norvasc®?
 - I. 2.5 mg
 - II. 10 mg
 - III. 25 mg
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II and III
3. Which of the following auxiliary labels should be affixed to the container for Xalatan®?
 - a. May discolor urine
 - b. Refrigerate before opened
 - c. Do not freeze
 - d. b and c only
4. A consulting pharmacist in a nursing home is asked by a nurse for advice regarding selegiline and sertraline administration for an 85-year-old patient. The patient has received the following new orders:
Sertraline 25 mg PO q AM
Selegiline 5 mg PO at breakfast and lunch
What is the most appropriate recommendation?
 - a. Administer the sertraline at bedtime.
 - b. Separate the morning medication administration by at least 2 hours.
 - c. Call the physician to warn of a potential drug interaction.
 - d. Call the physician to recommend a higher dose of sertraline.
5. A 62-year-old patient is transferred from a skilled nursing facility to the emergency department after a fall. The emergency department doctor writes an order for IV meperidine 15 mg/h. During medication reconciliation, the pharmacist notices that the patient has been taking 10 mg selegiline q AM. What is the most appropriate action?
 - a. Ensure timely delivery of the meperidine to the patient.
 - b. Recommend changing to oral meperidine.
 - c. Recommend an alternative medication for pain management because of a potential drug interaction.
 - d. Recommend an alternative medication for pain management because of the patient's age.
6. A patient brings in a vial of cloudy NPH insulin. Examination of the medication profile reveals simultaneous use of NPH and regular insulin. Which of the following is the MOST PROBABLE explanation for the cloudy appearance of the NPH insulin?
 - a. The insulin has been improperly stored.
 - b. The insulin has expired.
 - c. The insulin has been contaminated.
 - d. The insulin is expected to be cloudy.
7. What is the generic name of Invirase®?
 - a. Ritonavir
 - b. Saquinavir
 - c. Nelfinavir
 - d. Indinavir
8. A patient has a prescription for Lansoprazole, which is not on the formulary of his insurance. The pharmacist calls the prescriber to recommend a change to a similar medication that is on the formulary. Which of the following would be the most appropriate recommendation?
 - a. Latanoprost
 - b. Fluconazole
 - c. Pantoprazole
 - d. Aripiprazole
9. An uninsured patient has a prescription for Lipitor® 10 mg daily. After discussing the cost of the prescription with the patient, the pharmacist calls the prescriber to recommend a change to a similar medication that is less expensive. Which of the following would be the most appropriate recommendation?
 - a. Simvastatin 10 mg daily
 - b. Simvastatin 20 mg daily
 - c. Crestor® 5 mg daily
 - d. Crestor® 10 mg daily
10. What is the generic name of Aciphex®?
 - a. Aripiprazole
 - b. Rabeprazole
 - c. Pantoprazole
 - d. Albentazole
11. What is the generic name of Noxafil®?
 - a. Posaconazole
 - b. Methimazole
 - c. Voriconazole
 - d. Albentazole
12. What is the generic name of Terazol®?
 - a. Tramadol
 - b. Tioconazole
 - c. Terconazole
 - d. Miconazole
13. A patient who has been seizure free on phenytoin suspension 3.5 mL PO twice a day is now receiving feedings and medication through a nasogastric tube. What would be the most appropriate recommendation to ensure that the patient's phenytoin level stays at a therapeutic level?

- a. Recommend enteral feeding that contains less protein and more fat.
 - b. Hold tube feedings for 1 hour before and after phenytoin administration.
 - c. Obtain daily phenytoin serum levels and adjust the dose accordingly.
 - d. Ensure that the phenytoin is diluted with distilled water before instillation.
14. Which of the following brand(s) can be used for the treatment of pruritus that is associated with partial biliary obstruction?
- I. Prevalite®
 - II. Questran®
 - III. Megace®
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
15. Which of the following may produce significant hypotension with the initial dose?
- a. Reserpine
 - b. Prazosin
 - c. Clonidine
 - d. Propanolol
 - e. Methyldopa
16. What is the rationale for prescribing benztropine with a phenothiazine?
- a. Benztropine reduces extrapyramidal side effects.
 - b. Benztropine enhances absorption.
 - c. Benztropine decreases the required phenothiazine dose.
 - d. Benztropine prevents gastric irritation.
 - e. Benztropine is an antidepressant.
17. Which of the following is most dangerous when infecting the orbit?
- a. *Pseudomonas aeruginosa*
 - b. *Streptococcus thermophilus*
 - c. *Bacillus subtilis*
 - d. *Aspergillus niger*
 - e. *Escherichia coli*
18. Which of the following is used to selectively increase neutrophil production?
- a. Thrombopoietin
 - b. Filgrastim
 - c. Erythropoietin
 - d. Interleukin 11
 - e. Sagramostim
19. Which of the following may be used in the treatment of a 5-year-old child with diarrhea?
- a. Intravenous saline
 - b. Antibiotics
 - c. Oral rehydration
 - d. All of the above
 - e. None of the above
20. Which of the following may occur with bulimia?
- a. Hyponatremia, hypokalemia, and hypochloremia
 - b. Hyponatremia, hypokalemia, and hypochloremia
 - c. Hyponatremia, hyperkalemia, and hyperchloremia
 - d. a and b
 - e. a and c
21. Adderall® is a:
- a. stimulant
 - b. narcotic
 - c. depressant
 - d. antidepressant
 - e. diuretic
22. It is recommended that patients take prazosin just before bedtime to minimize which side effect?
- a. Insomnia
 - b. Rash
 - c. Dizziness
 - d. Urinary frequency
 - e. Palpitations
23. Which of the following products may be directly substituted for Claritin®?
- a. Sudafed®
 - b. Bonine®
 - c. Allegra®
 - d. Alavert®
 - e. Contact®
24. Which of the following is NOT an indication for nitroglycerin?
- a. Angina
 - b. Chronic hypertension
 - c. Perioperative hypertensive emergency
 - d. Pulmonary hypertension
 - e. Congestive heart failure
25. Sulfonylureas:
- a. may cause an adverse reaction when consumed with alcohol.
 - b. stimulate insulin release from the pancreas.
 - c. carry a risk of hypoglycemia.
 - d. a and b
 - e. a, b, and c
26. Simethicone is most likely included in which of the following OTC products?
- a. Stool softener
 - b. Cough suppressant
 - c. Decongestant
 - d. Antacid
 - e. None of the above
27. What are the available dosage strength(s) of oral Lexapro®?
- I. 5 mg
 - II. 20 mg
 - III. 40 mg

- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
28. Metformin:
- a. may cause lactic acidosis.
 - b. is safe to use in patients with renal failure.
 - c. shows maximum effect after the first dose.
 - d. is excreted predominantly in the feces.
 - e. works by stimulating insulin release.
29. Acarbose:
- a. is an alpha-glucosidase inhibitor
 - b. is safe to use in patients with chronic intestinal disease.
 - c. is less than 2% absorbed.
 - d. a and b
 - e. a and c
30. Glyburide:
- a. may cause a disulfiram-like reaction.
 - b. has an onset of action of 15–60 minutes.
 - c. can be used to treat type 1 diabetes mellitus.
 - d. a and b
 - e. a, b, and c
31. Ranitidine:
- a. is a histamine-2 antagonist.
 - b. can be used to treat peptic ulcer disease.
 - c. may cause dizziness.
 - d. is excreted in both the urine and feces.
 - e. All of the above
32. True or False: Metformin can be used to treat type 1 diabetes mellitus.
- a. True
 - b. False
33. True or False: *H pylori* can cause peptic ulcer disease.
- a. True
 - b. False
34. What is the DEA schedule for Ultram®?
- a. C-I
 - b. C-II
 - c. C-III
 - d. C-IV
 - e. None of the above
35. Captopril is a(n):
- a. angiotensin-receptor blocker.
 - b. angiotensin-converting enzyme inhibitor.
 - c. beta blocker.
 - d. thiazide diuretic.
 - e. loop diuretic.
36. Which of the following products is/are not appropriate for a patient taking warfarin (Coumadin®)?
- I. Percodan®
 - II. Demerol®
 - III. Dilaudid®
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
37. Furosemide is a(n):
- a. angiotensin-receptor blocker.
 - b. angiotensin-converting enzyme inhibitor.
 - c. beta blocker.
 - d. thiazide diuretic.
 - e. loop diuretic.
38. How many tablets of Darvocet-N 100® is in the maximum adult daily dose?
- a. 6 tablets
 - b. 8 tablets
 - c. 10 tablets
 - d. 12 tablets
 - e. 14 tablets
39. Metoprolol is a(n):
- a. angiotensin-receptor blocker.
 - b. angiotensin-converting enzyme inhibitor.
 - c. beta blocker.
 - d. thiazide diuretic.
 - e. loop diuretic.
40. Hydrochlorothiazide is a(n):
- a. angiotensin-receptor blocker.
 - b. angiotensin-converting enzyme inhibitor.
 - c. beta blocker.
 - d. thiazide diuretic.
 - e. loop diuretic.
41. Candesartan is a(n):
- a. angiotensin-receptor blocker.
 - b. angiotensin-converting enzyme inhibitor.
 - c. beta blocker.
 - d. thiazide diuretic.
 - e. loop diuretic.
42. Tamoxifen is a(n):
- a. rapid-acting insulin.
 - b. HMG-CoA reductase inhibitor.
 - c. antiestrogen.
 - d. corticosteroid.
 - e. sulfonylurea.
43. Glipizide is a(n):
- a. rapid-acting insulin.
 - b. HMG-CoA reductase inhibitor.
 - c. antiestrogen.
 - d. corticosteroid.
 - e. sulfonylurea.
44. Simvastatin is a(n):
- a. rapid-acting insulin.
 - b. HMG-CoA reductase inhibitor.
 - c. antiestrogen.
 - d. corticosteroid.
 - e. sulfonylurea.

45. Methylprednisolone is a(n):
a. rapid-acting insulin.
b. HMG-CoA reductase inhibitor.
c. antiestrogen.
d. corticosteroid.
e. sulfonyleurea.
46. Lispro is a(n):
a. rapid-acting insulin.
b. HMG-CoA reductase inhibitor.
c. antiestrogen.
d. corticosteroid.
e. sulfonyleurea.
47. Nedocromil is a(n):
a. mast cell stabilizer.
b. β -agonist.
c. calcium-channel blocker.
d. H_2 antagonist.
e. H_1 antagonist.
48. Albuterol is a(n):
a. mast cell stabilizer.
b. β -agonist.
c. calcium-channel blocker.
d. H_2 antagonist.
e. H_1 antagonist.
49. Diphenhydramine is a(n):
a. mast cell stabilizer.
b. β -agonist.
c. calcium-channel blocker.
d. H_2 antagonist.
e. H_1 antagonist.
50. Verapamil is a(n):
a. mast cell stabilizer.
b. β -agonist.
c. calcium-channel blocker.
d. H_2 antagonist.
e. H_1 antagonist.
51. Ranitidine is a(n):
a. mast cell stabilizer.
b. β -agonist.
c. calcium-channel blocker.
d. H_2 antagonist.
e. H_1 antagonist.
52. A patient has been taking prednisone for 5 days following an exacerbation of asthma symptoms. He begins treatment with cromolyn sodium. True or False: He should immediately stop prednisone with the first dose of cromolyn.
a. True
b. False
53. Flexeril® is available in which of the following strength(s)?
I. 2.5 mg
II. 5 mg
III. 10 mg
- a. I only
b. III only
c. I and II
d. II and III
e. I, II, and III
54. Fluticasone is a:
a. H_1 antagonist.
b. H_2 antagonist.
c. β -agonist.
d. corticosteroid.
e. β antagonist.
55. Which of the following is useful in the treatment of acute, productive cough?
a. Guaifenesin
b. Montelukast
c. Ipratropium
d. a and b
e. a, b and c
56. Which of the following is first-line treatment for intermittent asthma?
a. Cromolyn sodium
b. Albuterol
c. Prednisone
d. 100% oxygen
e. Ipratropium
57. Guaifenesin:
a. is an expectorant.
b. is a cough suppressant.
c. thins bronchial secretions.
d. a and c
e. b and c
58. Which of the following is an indication for brimonidine?
a. Benign prostatic hypertrophy
b. Epilepsy
c. Glaucoma
d. Increased intracranial pressure
e. Metabolic alkalosis
59. Which of the following is the correct dose of finasteride for benign prostatic hypertrophy?
a. 0.1 mg daily
b. 0.5 mg daily
c. 1 mg daily
d. 5 mg daily
e. 10 mg daily
60. Which of the following is the correct dosage of naproxen?
a. 750 mg as initial dose for acute gout
b. 500 mg twice daily for acute migraine
c. 500 mg twice daily for rheumatoid arthritis
d. All of the above
e. None of the above
61. What is the most appropriate initial treatment for status epilepticus?

- a. Phenytoin
 - b. Diazepam
 - c. Ethosuximide
 - d. Glutethimide
 - e. Paraldehyde
62. Which of the following may cause a lupus-like reaction?
- a. Guanethidine
 - b. Methyldopa
 - c. Hydralazine
 - d. Diazoxide
 - e. Reserpine
63. All of the following are calcium channel blockers EXCEPT?
- a. Amlodipine
 - b. Ibutilide
 - c. Nifedipine
 - d. Verapamil
 - e. Diltiazem
64. A 70-year-old man with renal insufficiency is to be treated with a tetracycline. Which of the following will not accumulate to a great degree in this patient's blood?
- a. Minocycline
 - b. Demeclocycline
 - c. Oxytetracycline
 - d. Tetracycline
 - e. Doxycycline
65. Which of the following may cause orthostatic hypotension?
- I. Prazosin
 - II. Sildenafil
 - III. Amitriptyline
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
66. Vyvanse is indicated for:
- a. Insomnia
 - b. ADHD
 - c. Depression
 - d. Hyperlipidemia
 - e. Migraine headaches
67. How many milligrams of oxycodone HCl are in the lowest strength of Percocet®?
- a. 1 mg
 - b. 2.5 mg
 - c. 5 mg
 - d. 7.5 mg
 - e. 10 mg
68. Cholestyramine interferes with the oral absorption of:
- a. phenobarbital.
 - b. chlorothiazide.
 - c. warfarin.
 - d. a and b
 - e. a, b, and c
69. All of the following are brands of Amoxicillin EXCEPT:
- a. Moxatag
 - b. Trimox
 - c. Kantrex
 - d. Amoxil
 - e. Wymox
70. Anticonvulsants interfere with the metabolism of:
- a. riboflavin
 - b. tyrosine
 - c. renin
 - d. folic acid
 - e. pyridoxine
71. Zyvox is available as:
- I. IV injection
 - II. Tablets
 - III. Oral suspension
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
72. Which of the following species is most likely to cause purulent boils on the skin?
- a. *Streptococcus*
 - b. *Staphylococcus*
 - c. *Candida*
 - d. *Aspergillus*
 - e. *Pseudomonas*
73. Which of the following is the most appropriate treatment for conjunctival herpes simplex virus (HSV) infection?
- a. Mupirocin
 - b. Idoxuridine
 - c. Bacitracin
 - d. Amphotericin B
 - e. Thiabendazole
74. Which of the following should NOT be used to treat candidal infections?
- a. Terconazole
 - b. Miconazole
 - c. Nystatin
 - d. Tolnaftate
 - e. Clotrimazole
75. Which of the following is an indication for methotrexate?
- a. Warts
 - b. Tinea infection
 - c. Psoriasis
 - d. Acne
 - e. Seborrhea

76. Which of the following may occur with corticosteroid ingestion?
- Disseminated infection
 - Immunosuppression
 - Increased risk of infection
 - Masking of infectious symptoms
 - All of the above
77. Compared with other NSAIDs, which of the following is a benefit associated with the use of piroxicam?
- Once-daily dosing
 - No gastric side effects
 - Cytoprotective effects
 - Inexpensive
 - Different mechanism of action
78. Which of the following is an indication for clomiphene citrate?
- Dysmenorrhea
 - Nausea
 - Depression
 - Infertility
 - Psoriasis
79. Which of the following is detected by the e.p.t. home pregnancy test?
- Human chorionic gonadotropin
 - Prolactin
 - Progestin
 - Progesterone
 - Estradiol
80. Which of the following is/are the mechanism of action of nitric oxide (NO)?
- Increased smooth muscle activity
 - Stimulation of nucleotide c-GMP
 - Smooth muscle relaxation
 - a and b
 - b and c
81. Which of the following drug combinations are found in Advair?
- Flunisolide and salmeterol
 - Fluticasone and salmeterol
 - Beclomethasone and formoterol
 - Fluticasone and formoterol
 - None of the above
82. Which of the following is the preferred method to evaluate the efficacy of warfarin therapy?
- Prothrombin time (PT)
 - Partial Thromboplastin Time (PTT)
 - Bleeding time
 - International Normalized Ratio (INR)
 - a, b, and d
83. InnoPran XLTM is available as:
- 80 mg
 - 120 mg
 - 180 mg
 - a and b
 - b and c
84. Which of the following is NOT a common symptom of antipsychotic medications?
- Akathisia
 - Anhedonia
 - Diabetes
 - Weight gain
 - Tardive dyskinesia
85. A 65-year-old woman with congestive heart failure and atrial fibrillation is diagnosed with glaucoma. What is the most appropriate topical treatment?
- Timolol
 - Timolol plus dorzolamide
 - Latanoprost
 - Epinephrine
 - Any of the above
86. What is the rationale for the preferred use of inhaled corticosteroids over oral corticosteroids in the treatment of asthma?
- Increased efficacy
 - Decreased systemic side effects
 - Increased ease of use
 - a and b
 - b and c
87. Lisinopril is a:
- β blocker.
 - α_1 blocker.
 - angiotensin-receptor blocker.
 - angiotensin-converting enzyme inhibitor.
 - diuretic.
88. True or False: It takes 2 to 6 weeks after initiation of cromolyn sodium to see therapeutic effects for the maintenance treatment of asthma.
- True
 - False
89. True or False: Angiotensin-converting enzyme (ACE) inhibitors combined with angiotensin-receptor blocker (ARB) provide greater efficacy than either alone.
- True
 - False
90. True or False: Antihypertensive agents of different classes may be combined in patients refractory to single-drug treatment.
- True
 - False
91. Bicitra[®] is the U.S. brand name for:
- Sodium citrate and citric acid
 - Dibasic sodium phosphate
 - Bismuth subsalicylate
 - Magaldrate and simethicone
 - Calcium carbonate
92. Aprepitant (Emend) is:
- Available as capsules
 - A substance P antagonist
 - Used to prevent acute and delayed nausea and vomiting associated with cancer chemotherapy

- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
93. Which of the following is the most appropriate initial treatment for a patient with newly diagnosed type 2 diabetes?
- a. Glyburide
 - b. Insulin
 - c. Metformin
 - d. Acarboze
 - e. Pioglitazone
94. Which of the following agent(s) is/are classified as a sulfonylurea?
- I. Chlorpropamide
 - II. Glipizide
 - III. Tolterodine
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
95. Type 1 diabetes mellitus:
- a. may be due to autoimmune phenomena.
 - b. usually presents before puberty.
 - c. must be treated with insulin.
 - d. commonly presents with polyuria, polydypsia, and polyphagia.
 - e. All of the above
96. Type 2 diabetes mellitus:
- a. does not have a genetic component.
 - b. requires insulin therapy.
 - c. is most likely to occur in thin, malnourished patients.
 - d. is a relative, not complete, lack of insulin.
 - e. All of the above
97. Diabetes mellitus can be diagnosed in which of the following situations?
- a. Fasting blood glucose greater than 126 mg/dL
 - b. Random plasma glucose greater than 200 mg/dL
 - c. Oral glucose challenge 2-hour plasma level greater than 200 mg/dL
 - d. Any of the above
 - e. a or b
98. Which of the following is classified as an NSAID?
- I. Celecoxib
 - II. Ketorolac
 - III. Acetaminophen
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
99. True or False: Insulin glargine is ultra fast acting.
- a. True
 - b. False
100. What are the active ingredients in Prempro®?
- a. Conjugated estrogen and methyltestosterone
 - b. Conjugated estrogen and medroxyprogesterone
 - c. Ethinylestradiol and medroxyprogesterone
 - d. Drospirenone and ethinyl estradiol
 - e. None of the above
101. All of the following medications are protease inhibitors EXCEPT:
- a. Reyataz®
 - b. Lexiva®
 - c. Viramune®
 - d. Agenerase®
 - e. Viracept®
102. Which of the following antiretroviral drugs are available as syrup or oral solution?
- a. Epivir
 - b. Ziagen
 - c. Videx
 - d. Norvir
 - e. All of the above
103. Which of the following is/are considered rapid-acting insulin?
- I. Apidra
 - II. Humalog
 - III. Novolog
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
104. All of the following drugs are prostaglandin analogs EXCEPT:
- a. Xalatan
 - b. Lumigan
 - c. Azopt
 - d. Travatan
 - e. Rescula
105. Which HMG-CoA reductase inhibitor is least likely to have drug interactions?
- a. Pravastatin
 - b. Lovastatin
 - c. Fluvastatin
 - d. Atorvastatin
 - e. Simvastatin
106. What is the brand name for levalbuterol?
- a. Ventolin®
 - b. Serevent®
 - c. Xopenex®
 - d. Flovent®
 - e. None of the above

107. What is the dose of trazodone for depression?
- 10 mg per day
 - 25-50 mg per day
 - 1-2 grams per day
 - 150 mg per day
 - 5 grams per day
108. Axert® is available as:
- 6.25 mg
 - 12.5 mg
 - 30 mg
- I only
 - III only
 - I and II only
 - II and III only
 - I, II and III
109. Imitrex® is available as:
- Nasal spray
 - Tablets
 - Injection
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
110. Ketorolac is a(n):
- salicylate.
 - NSAID.
 - corticosteroid.
 - opioid.
 - benzodiazepine.
111. What is the maximum oral daily dose of ketorolac?
- 20 mg
 - 40 mg
 - 50 mg
 - 100 mg
 - 250 mg
112. Which of the following conditions is NOT a contraindication for ketorolac?
- Hemorrhagic diathesis
 - Gastrointestinal perforation
 - Epilepsy
 - Renal failure
 - Breast-feeding
113. What is the brand name for latanoprost?
- Toradol®
 - Accuset®
 - Xalatan®
 - Conista®
 - Zerolast®
114. What is the correct daily topical dose of latanoprost for the treatment of glaucoma?
- 15 mcg
 - 15 mg
 - 1.5 mcg
 - 1.5 mg
 - 0.5 mcg
115. Latanoprost:
- has an onset of action of 1-2 hours.
 - has a peak effect at 8-12 hours.
 - has a volume of distribution of 1 L/kg.
 - is excreted unchanged in the urine.
 - has a half-life of elimination of 60 minutes.
116. Moduretic® contains:
- atenolol and chlorthalidone.
 - triamterene and hydrochlorothiazide.
 - amiloride and hydrochlorothiazide.
 - losartan and hydrochlorothiazide.
 - clonidine and chlorthalidone.
117. Combipres® contains:
- atenolol and chlorthalidone.
 - triamterene and hydrochlorothiazide.
 - amiloride and hydrochlorothiazide.
 - losartan and hydrochlorothiazide.
 - clonidine and chlorthalidone.
118. Tenoretic® contains:
- atenolol and chlorthalidone.
 - triamterene and hydrochlorothiazide.
 - amiloride and hydrochlorothiazide.
 - losartan and hydrochlorothiazide.
 - clonidine and chlorthalidone.
119. Dyazide® contains:
- atenolol and chlorthalidone.
 - triamterene and hydrochlorothiazide.
 - amiloride and hydrochlorothiazide.
 - losartan and hydrochlorothiazide.
 - clonidine and chlorthalidone.
120. Zosyn® contains:
- piperacillin and tazobactam.
 - ampicillin and sulbactam.
 - dalfopristin and quinupristin.
 - imipenem and cilastatin.
 - panipenem and betamipron.
121. What is the generic name for Crestor®?
- Carvedilol
 - Rosuvastatin
 - Venlafaxine
 - Pioglitazone
 - None of the above
122. Primaxin® contains:
- piperacillin and tazobactam.
 - ampicillin and sulbactam.
 - quinupristin and dalfopristin.
 - imipenem and cilastatin.
 - panipenem and betamipron.
123. Unasyn® contains:
- piperacillin and tazobactam.
 - ampicillin and sulbactam.
 - quinipristin and dalfopristin.
 - imipenem and cilastatin.
 - panipenem and betamipron.

124. Cyclobenzaprine is a:
- benzodiazepine.
 - skeletal muscle relaxant.
 - tricyclic antidepressant.
 - GABA receptor agonist.
 - barbiturate.
125. What is the correct dose of cyclobenzaprine for the treatment of pain associated with muscle spasms?
- 15–30 mg daily
 - 5–10 mg daily
 - 25–100 mg daily
 - 100–250 mg daily
 - 100–800 mg daily
126. What is the maximum length of time that cyclobenzaprine should be used?
- 7 days
 - 3 weeks
 - 2 months
 - 6 months
 - Indefinitely
127. Cyclobenzaprine:
- has an onset of action of 1 hour.
 - has a duration of action of 12–24 hours.
 - has a half-life of elimination of 8–37 hours.
 - a and b
 - a, b, and c
128. What is the correct dose of methocarbamol?
- 1.5 g PO 4 times per day
 - 1 g IM every 8 hours
 - 1–3 g IV every 6 hours
 - All of the above
 - a and b
129. Side effects associated with methocarbamol include all of the following EXCEPT:
- bradycardia
 - urticaria
 - vertigo
 - jaundice
 - leukocytosis
130. What is the correct initial dose of amlodipine?
- 0.5 mg bid
 - 5 mg bid
 - 10 mg bid
 - 5 mg qd
 - 10 mg qd
131. What is the maximum daily dose of amlodipine?
- 1 mg
 - 5 mg
 - 10 mg
 - 25 mg
 - 20 mg
132. Zolpidem is a(n):
- opiate.
 - selective serotonin reuptake inhibitor.
 - hypnotic.
 - barbiturate.
 - monoamine oxidase inhibitor.
133. What is the correct dosage of zolpidem?
- 10 mg
 - 0.1 mg
 - 10 mcg
 - 0.1 mcg
 - 25 mg
134. What is the maximum daily dose of zolpidem?
- 10 mg
 - 20 mg
 - 10 mcg
 - 20 mcg
 - 25 mg
135. Eszopiclone may cause all of the following adverse effects EXCEPT:
- unpleasant taste.
 - diplopia.
 - gynecomastia.
 - hallucinations.
 - headache.
136. Eszopiclone is used to treat:
- depression.
 - bipolar disorder.
 - generalized anxiety disorder.
 - ataxia.
 - insomnia.
137. True or False: Terbutaline may cause hypokalemia.
- True
 - False
138. True or False: Methylphenidate can be used to treat narcolepsy.
- True
 - False
139. True or False: Aspirin is safe to use during pregnancy.
- True
 - False
140. What is the correct initial dose of sulfasalazine in the treatment of ulcerative colitis?
- 0.5 g 3–4 times per day
 - 0.5 g once per day
 - 1 g 3–4 times per day
 - 10 g once per day
 - 25 g twice per day
141. What is the brand name of sulfasalazine?
- Azulfidine
 - Asosulfide
 - Sulfasalicide
 - Sulfocyte
 - Sulfonate

142. What is the generic name of Seroquel®?
- Amitriptyline
 - Aripiprazole
 - Quetiapine
 - Clozapine
 - Risperidone
143. What is the generic name of Abilify®?
- Amitriptyline
 - Aripiprazole
 - Quetiapine
 - Clozapine
 - Risperidone
144. What is the correct daily maintenance dose of quetiapine for depression?
- 100 mg
 - 150 mg
 - 300 mg
 - 500 mg
 - 600 mg
145. Of the following, which amount best represents an initial total daily target for quetiapine in the treatment of schizophrenia?
- 100 mg
 - 150 mg
 - 300 mg
 - 500 mg
 - 600 mg
146. Side effects of quetiapine include all of the following EXCEPT:
- hypotension.
 - somnolence.
 - hypercholesterolemia.
 - bradycardia.
 - fever.
147. Carisoprodol is metabolized to which of the following?
- Meprobamate
 - Dopamine
 - Morphine
 - Phenobarbital
 - None of the above
148. What is a correct initial daily dose of aripiprazole for the treatment of schizophrenia?
- 15 mg per day
 - 30 mg per day
 - 45 mg per day
 - 90 mg per day
 - 200 mg per day
149. What is the correct initial daily dose of aripiprazole for the treatment of bipolar disorder?
- 15 mg per day
 - 30 mg per day
 - 45 mg per day
 - 90 mg per day
 - 200 mg per day
150. True or False: Aripiprazole has an onset of action of 1–3 days.
- True
 - False
151. True or False: Olanzapine is approved for monotherapy of major depressive disorder.
- True
 - False
152. Olanzapine:
- may cause postural hypotension.
 - is available for oral, IM, and IV administration.
 - is a serotonin agonist.
 - is <50% protein bound in circulation.
 - has a half life of elimination of 12–16 hours.
153. What is the correct initial dosage of clonidine for the treatment of hypertension?
- 0.1 mcg PO
 - 0.1 mg PO
 - 1 mg PO
 - 5 mg PO
 - 10 mg PO
154. True or False: Clonidine commonly causes drowsiness.
- True
 - False
155. Which of the following is FALSE concerning rituximab?
- It is an anti-CD20 monoclonal antibody.
 - It increases antibody-dependent cellular toxicity.
 - It can be used to treat rheumatoid arthritis.
 - B-cell levels return to normal 2 weeks after treatment.
 - It may cause angioedema.
156. Memantine is a(n):
- dopamine agonist.
 - norepinephrine antagonist.
 - acetylcholinesterase inhibitor.
 - N-methyl-d-aspartate receptor antagonist.
 - serotonin agonist.
157. What is the correct initial dose of memantine?
- 0.5 mg per day
 - 2 mg per day
 - 2 mg three times per day
 - 5 mg per day
 - 5 mg two times per day
158. Paroxetine is used for:
- Depression
 - Obsessive compulsive disorder
 - Parkinson disease
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III

159. Singulair® is available in which of the following strength(s)?
- 5 mg
 - 10 mg
 - 4 mg
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
160. OTC products containing minoxidil include:
- solutions.
 - gel.
 - tablets.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
161. All of the following drugs are classified as DMARDs EXCEPT:
- Diflunisal
 - Penicillamine
 - Hydroxychloroquine
 - Methotrexate
 - Sulfasalazine
162. What is the correct initial dosage of transdermal selegiline?
- 6 mg per 12 hours
 - 6 mg per 24 hours
 - 6 mg per 48 hours
 - 3 mg per 24 hours
 - 10 mg per 48 hours
163. Donepezil is a(n):
- acetylcholinesterase inhibitor.
 - dopamine antagonist.
 - GABA agonist.
 - GABA antagonist.
 - serotonin reuptake inhibitor.
164. How is donepezil supplied?
- 5 or 10 mg
 - 10 or 20 mg
 - 5 or 15 mg
 - 100 or 250 mg
 - 250 or 500 mg
165. For the treatment of what condition(s) is/are donepezil approved?
- Major depression
 - Bipolar disorder
 - Dementia
 - a and b
 - a and c
166. True or False: Chloroquine is approved for the treatment of extraintestinal amebiasis.
- True
 - False
167. Chloroquine is a:
- peroxidase inhibitor.
 - aminoquinidine.
 - n*-alpha-quinine.
 - chlorhexadine.
 - aminoquinoline.
168. What is the correct dose of chloroquine for malaria prophylaxis?
- 500 mg per day
 - 500 mg bid
 - 500 mg tid
 - 500 mg per week
 - 500 mg one-time dose
169. Anturane® is the U.S. brand name for:
- Sulfinpyrazone
 - Allopurinol
 - Fenofibrate
 - Dolasetron
 - Auralgan
170. What is the correct dose of omeprazole for the treatment of GERD?
- 2 mg per day
 - 4 mg per day
 - 20 mg per day
 - 50 mg per day
 - 50 mcg per day
171. True or False: Omeprazole does NOT require dosage adjustment in patient with renal impairment.
- True
 - False
172. Tinidazole is a:
- nitroimidazole.
 - chloroquinolone.
 - amebicide.
 - a and b
 - a and c
173. What is the correct dosage of tinidazole for the treatment of bacterial vaginosis?
- 2 g per day for 5 days
 - 2 g per day for 2 days
 - 20 g per day for 5 days
 - 200 g per day for 2 days
 - 200 mg per day for 5 days
174. Side effects of amphotericin B include all of the following EXCEPT:
- hypotension.
 - tachypnea.
 - polycythemia.
 - hypomagnesemia.
 - hypokalemia.
175. What is the correct dose of clotrimazole for oropharyngeal candidiasis prophylaxis?
- 10-mg troche once per day
 - 10-mg troche three times per day

- c. 10-mg troche five times per day
 - d. 10-mg troche six times per day
 - e. 10-mg troche single dose
176. What is the correct dose of clotrimazole for treatment of active oropharyngeal candidiasis?
- a. 10-mg troche once per day
 - b. 10-mg troche three times per day
 - c. 10-mg troche five times per day
 - d. 10-mg troche six times per day
 - e. 10-mg troche single dose
177. True or False: Clotrimazole is available for administration as an oral troche, topical cream, topical solution, and vaginal cream.
- a. True
 - b. False
178. Clotrimazole:
- a. is excreted predominantly in the feces.
 - b. is absorbed into systemic circulation following topical application.
 - c. has a time to peak serum concentration of 1–2 days following oral troche.
 - d. a and b
 - e. a, b, and c
179. The federal transfer auxiliary label is required for what schedule of medication?
- a. Schedule II to IV
 - b. Schedule II only
 - c. All schedule drugs
 - d. Schedule II and III only
180. Pregabalin is structurally related to which of the following?
- a. Gabapentin
 - b. Carbamazepine
 - c. Felbamate
 - d. Tiagabine
 - e. Levetiracetam
181. Thiopental:
- a. is a potent analgesic.
 - b. increases cerebral activity as measured by EEG.
 - c. produces respiratory depression dose-dependently.
 - d. is only useful as a skeletal muscle relaxant.
 - e. should not be used in patients with epilepsy.
182. What are the active ingredients in Lotrel®?
- a. Amlodipine and atorvastatin
 - b. Lisinopril and hydrochlorothiazide
 - c. Amlodipine and benazepril
 - d. Hydralazine and isosorbide dinitrate
183. Prevpac® contains which of the following drugs?
- a. Amoxicillin, clarithromycin, and lansoprazole
 - b. Ampicillin, clarithromycin, and omeprazole
 - c. Amoxicillin, azithromycin, and lansoprazole
 - d. Amoxicillin, clarithromycin, and omeprazole
 - e. Ampicillin, azithromycin, and lansoprazole
184. What is a brand name for tacrolimus?
- a. Prograf®
 - b. Propecia®
 - c. Proscar®
 - d. Protonix®
185. Which of the following is (are) classified as an antiepileptic agent?
- I. Kaletra
 - II. Lamictal
 - III. Mysoline
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
186. Which of the following is a contraindication for alosetron use?
- a. Diarrhea
 - b. Constipation
 - c. Renal impairment
 - d. Asthma
 - e. Diabetes
187. Which of the following are the correct contents and quantity of medication contained in each teaspoonful of Tussionex®?
- a. Hydrocodone 2.5 mg and diphenhydramine 25 mg
 - b. Hydromorphone 2.5 mg and diphenhydramine 25 mg
 - c. Hydromorphone 5 mg and chlordiazepoxide 2.5 mcg
 - d. Hydrocodone 10 mg and diphenhydramine 50 mg
 - e. Hydrocodone 10 mg and chlorpheniramine 8 mg
188. What percent chlorhexidine concentration is in the antimicrobial agent Hibiclens®?
- a. 4%
 - b. 10%
 - c. 14%
 - d. 15%
 - e. 25%
189. What is the generic name of Bactroban®?
- a. Vistaril
 - b. Cetirizine
 - c. Hydroxyzine
 - d. Mupirocin
 - e. Homatropine
190. What is the generic name for Detrol®?
- a. Torsemide
 - b. Tolterodine
 - c. Tolazamide
 - d. Topiramate
 - e. Tolmetin

191. Which of the following statements are true regarding metformin?
- It may cause renal failure.
 - It is a hypoglycemic agent.
 - The maximum daily dose is 2550 mg/day.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and II
192. What is the generic name for Glynase®?
- Glyburide
 - Acarbose
 - Rosiglitazone
 - Glimepiride
 - Chlorpropamide
193. Cosopt® is made of which of the following ingredients?
- Brimonidine and timolol
 - Dorzolamide and timolol
 - Epinephrine and pilocarpine
 - Carbachol and dorzolamide
 - None of the above
194. True or False: Oxymetazoline nasal spray should be used for at least 2 weeks for the patient to experience relief.
- True
 - False
195. Timolol:
- may cause conjunctivitis.
 - has a duration of action of 12 hours.
 - has a peak effect 6 hours after topical application.
 - a and b
 - a and c
196. Which of the following medication suspensions do not need to be refrigerated?
- Zithromax®
 - Augmentin®
 - Biaxin®
- I only
 - III only
 - I and III
 - II and III
 - I, II, and III
197. Home ovulation test kits detect which of the following hormones?
- LH
 - FSH
 - hCG
 - TSH
 - None of the above
198. Which of the following medications should be avoided in pregnant women due to its properties as an abortifacient?
- Misoprostol
 - Piroxicam
 - Aspirin
 - Tetracycline
 - Phenytoin
199. Intermittent claudication is treated with which of the following?
- Diovan
 - Trental
 - Pletal
- I only
 - III only
 - I and III
 - II and III
 - I, II, and III
200. What is the generic name for Cozaar®?
- Hydrochlorothiazide
 - Lisinopril
 - Losartan
 - Enalapril
 - a and c
201. What are the active ingredients of Symbyax®?
- Fluoxetine and olanzapine
 - Duloxetine and venlafaxine
 - Paroxetine and quetiapine
 - Citalopram and olanzapine
 - Fluoxetine and clozapine
202. Enbrel® works by:
- T-cell deactivation.
 - TNF antagonism.
 - stimulation of red blood cell production.
 - gene fusion.
 - None of the above
203. Azithromycin is available in which of the following formulations?
- Oral tablets
 - Injection
 - Oral suspension
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
204. How frequent should the tetanus booster vaccine be administered?
- Every 2 years
 - Every 5 years
 - Every 10 years
 - Every 20 years
 - Every 30 years
205. How many mg of medication are in one teaspoonful of Naprosyn suspension?
- 125 mg/5 mL
 - 100 mg/5 mL
 - 50 mg/5 mL
 - 25 mg/5 mL
 - None of the above

206. Which is the generic name for Norflex?
- Diclofenac
 - Ibuprofen
 - Orphenadrine
 - Cyclobenzaprine
 - Oxaprozin
207. Atacand can best be described as an:
- ACE inhibitor
 - Diuretic
 - Alpha-1 adrenergic blocker
 - Beta blocker
 - Angiotensin II receptor blocker
208. Which of the following drug(s) is (are) an MAO inhibitor?
- Parnate
 - Eldepryl
 - Mobic
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
209. Select the available dosage strength(s) of oral Actos:
- 30 mg
 - 45 mg
 - 60 mg
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
210. Which of the following drug(s) is/are available as metered dose inhalers (MDIs)?
- Aerobid[®]
 - Serevent[®]
 - Pulmicort[®]
 - Advair[®]
 - Foradil[®]
211. The dose of Accolate[®] for asthma is:
- 2 mg BID
 - 20 mg BID
 - 200 mg QD
 - 200 mg BID
 - 2g QD

Patient Education

6

CHAPTER

- I. Provide health care information regarding the prevention and treatment of diseases and medical conditions, including emergency patient care.
 - A. Educate patients regarding their disease states and conditions.
 1. Patient-appropriate terms: Medical terminology should be translated to plain (simple) language to simplify concepts for the patient and to promote understanding. See Table 6-1 for common examples.

Table 6-1 Examples of Consumer Terms to be used in Patient Education

Medical Term	Consumer Term
Analgescic	pain reliever
Arrhythmia	irregular heartbeat
Buccal	between the cheek and the gum
Diuretic	water pill
Hepatic	liver
Hypercholesterolemia	high cholesterol
Hyperglycemia	high blood sugar
Hypertension	high blood pressure
Hypoglycemia	low blood sugar
Inflammation	swelling
Metabolism	(drug) breakdown
Ophthalmic	for the eye
Otic	for the ear
Postural hypotension	fainting
Prophylaxis	preventative
Pruritus	itching
Renal	kidney
Saline	salt solution
Sublingual	under the tongue
Subcutaneous	under the skin
Topical	applied to the skin
Transdermal	absorbed through the skin

- B. Steps in counseling patients regarding medication use
 1. Establish relationship, show interest in patient (verbal and nonverbal).
 2. Use two patient identifiers for verification (e.g., address and date of birth).

3. Ask about allergies (e.g., drug, food, contact, and environmental).
4. Ask what over-the-counter (OTC), herbals/supplements, and other prescriptions the patient is taking (patients may not fill all prescriptions at the same pharmacy). Additional medical conditions may also be considered as needed (i.e., a patient with asthma receiving a beta blocker with beta-2 action).
5. Ask the patient what they know about their medications and why they are being prescribed (i.e., the medication's use, expected benefits, and action).
6. Discuss with the patient what their doctors told them regarding their medications, how to use them, and what to expect.
7. Open the medication container and show the patient what the medication looks like or demonstrate use; the patient may not be expecting a generic substitution, and they can also verify correct product.
8. Discuss how to take the medication.
9. Discuss when to take and how long to take the medication.
10. Discuss what to do if a dose is missed (take missed dose immediately or skip the missed dose and wait until new administration time).
11. Discuss any special precautions to follow.
12. Discuss foods, alcoholic beverages, OTC, drugs, or supplements to be avoided.
13. Discuss how the patient will know the medication is working.
14. Discuss how to store the medication.
15. Discuss if the prescription can be refilled, and if so, when.
16. Instruct on beneficial nondrug activities as appropriate.
17. Verify the patient's knowledge and understanding by asking the patient to repeat the given information.
18. Ask patients what questions they have.
19. End the counseling session by repeating your name and the pharmacy's telephone number.
20. Document the counseling session.
- C. Important patient considerations for counseling
 1. New patients or those receiving a medication for the first time (including transfer prescriptions)
 2. Confused patients and their caregivers
 3. Patients who are vision or hearing impaired, handicapped, or in need of special assistance

4. Patients with low functional health literacy
 5. Patients whose profile shows a change in medications or dosing
 6. Patients whose overall appearance has worsened due to their condition(s)
 7. Patients who appear to be in distress
 8. Patients who speak a different language
 9. Elderly patients
 10. Children and their parents
 11. Patients receiving medication with special storage requirements, complicated directions, significant side effects, or narrow therapeutic ranges [e.g., digoxin and anti-epileptic drugs (AED)].
 12. Patients who cannot afford their medications
 13. Patients receiving oral contraception regarding the risk of cardiovascular disease (CVD) if they smoke or are older than 35 years
 14. Patients receiving oral contraception and select antibiotic medications (contraception failure may occur)
 15. Patients receiving warfarin should be aware of the signs and symptoms of bleeding and blood clotting.
 16. Patients using OTC medications that contain the same ingredients as their prescription medications (e.g., Vicodin® and Tylenol® [acetaminophen])
- D. Other Concepts to discuss with patients and health care professionals
1. Adverse reaction concerns:
 - a. An adverse drug event (ADE) is any undesirable experience associated with the use of a medical product in a patient. Most potential adverse drug events can be prevented; however, an unpreventable adverse drug event is considered an adverse drug reaction.
 - b. Most adverse drug reactions (ADR) are common, relatively mild, and disappear when the drug is discontinued or the dose is changed. Common mild drug reactions include loss of appetite, bloating, nausea, and constipation. Serious drug reactions are those that cause death, disability or congenital anomaly or that require hospitalization. Serious ADR may require medical intervention to prevent further damage or impairment.
 - c. The following examples illustrate various adverse drug events:
 - (a) Sulfonamide antibiotics versus other sulfa-containing products (i.e., cross-sensitivity reactions rather than sulfa-allergy)
 - (b) Risk of Reye syndrome in children taking salicylate containing medications and with concurrent viral illness
 - (c) Cross-sensitivity reaction potential between penicillins and cephalosporins
 - (d) Cross tolerance (or lack of tolerance) within drug classes (e.g., statins, angiotensin-converting enzyme [ACE] inhibitors, and triptans)
 - d. Adverse events that are common that require minimal intervention (e.g., postural hypotension when starting beta blockers; constipation for opioid analgesics), and that require immediate attention (e.g., Stevens-Johnson syndrome for sulfonamide antibiotics; tendinitis/tendon rupture for quinolones).
 - e. True allergy (e.g., anaphylaxis) versus ADR (nausea with opioid analgesics or oral penicillins); including what reactions allow a rechallenge or desensitization of the drug
 - 1) Types of allergic reactions:
 - a) Type I reaction (immediate): anaphylaxis, Immunoglobulin E (IgE) mediated (penicillin)
 - b) Type II reaction: cytotoxic, Immunoglobulin M (IgM) or Immunoglobulin G (IgG) mediated (penicillin, quinidine)
 - c) Type III reaction: immune complex mediated, IgG mediated (phenytoin, sulfonamides, radiocontrast)
 - d) Type IV reaction: delayed hypersensitivity, T-cell mediated (tuberculosis skin test)
2. Examples of appropriate drug use
- a. Spacing antacids and calcium containing products from certain medications (e.g., select antibiotics, such as tetracyclines, quinolones)
 - b. Taking drugs at appropriate times
 - c. Spacing of medication administration times for peak effects or to avoid toxic effects (e.g., aspirin shortly before or long after a nonsteroidal anti-inflammatory drug)
 - d. Dietary restrictions for monoamine oxidase inhibitor (MAOI), warfarin, or quinolones (no tyramine-containing products [cheese, wine, red meats], do not alter the intake of the amounts of vitamin K containing products, and separate dairy intake from the time of administration, respectively)
 - e. Understanding “Two tabs twice daily” = 4 tablets a day total not 2 tablets each day; and similar multiplying concepts
 - f. Importance of finishing an antibiotic course of treatment to ensure therapeutic response and avoid recurrence of infection
 - g. Not using corticosteroid and long-acting beta-agonist medication for acute asthma symptoms
 - h. How to use inhalers, nebulizers, injectable medications, insulin pens, blood glucose monitors, and other devices
 - i. Not to discontinue medications; consult the prescriber first.
 - j. Understand cautions needed with the use of medications in special populations (e.g., pediatric, geriatric, patients with organ failure, patients with immunosuppression, pregnant or lactating women)
 - k. Use of insulin products

- l. Proper disposal of needles and expired medications and other safety measures such as storage that are related to accidental exposure or poison prevention
- m. Compliance improvement strategies (dose timing, pill boxes, and reminder timers)
- n. Importance of reporting adverse drug reactions (e.g., MedWatch)
3. Product selection for patients
 - a. Brand and generic drugs
 - b. Over-the-counter (OTC) and dietary supplements
4. Possibly confusing concepts for patients
 - a. Brand versus generic drugs
 - b. The difference among drug tolerance, substance dependency, and addiction (including the upregulation and downregulation related to nonaddictive substances such as beta blockers)
 - c. Evidence-based medicine versus faith-based medicine (see also Section III)
 - d. Potassium (K^+) versus Vitamin K
 - e. Avoiding versus limiting intake
 - f. Vaccinations: Which populations/ages/international travelers require what vaccines; concerns about autism in conjunction with routine immunizations

E. Emergency/non-self-care considerations
Patients who present to the pharmacy on an ambulatory basis may need medical treatment versus pharmacist intervention. Here are some considerations when self-treatment is no longer acceptable and when patients should contact their primary care physician or go to the emergency department.

1. Generally managed by primary care physician
 - a. Mild-to-moderate side effects including constipation, sedation, headache
2. Example emergency situations
 - a. Uncontrolled bleeding (possibly from trauma or antiplatelet therapy)
 - b. Hypersensitivity reaction to any drug
 - c. Fainting (related to antihypertensives, erectile dysfunction medications, etc.)
 - d. Hypoglycemia (low blood sugar, too much insulin, or hypoglycemic use)
 - e. Diabetic ketoacidosis (DKA)
 - f. Acute asthma exacerbation not responsive to rescue inhaler
 - g. Angina not responsive to nitroglycerin after 5 minutes of first administration
 - h. Accidental ingestion of toxic substances
 - i. Sudden unilateral neurologic symptoms consistent with stroke
 - j. Symptoms consistent with serious local (e.g., cellulitis or gangrene) or systemic infection (e.g., excessive purulent cough - potential pneumonia)
- II. Provide health care information regarding nutrition, lifestyle, and other nondrug measures that are effective in promoting health or preventing or minimizing the progression of a disease or medical condition

A. Patient monitoring based on drug or disease state

1. Hypertension
 - a. Blood pressure; note different ranges and goals for patients with compelling indications (e.g., diabetes, chronic kidney disease, stroke, heart failure, coronary artery disease, or post-myocardial infarction)
 - b. Recording of blood pressure (self-monitoring)
 - c. Therapeutic lifestyle changes; diet (e.g., limit salt intake) and exercise
2. Diabetes
 - a. Control parameters (blood sugar 90–130 mg/dL, HbA1c < 7%)
 - b. Recording of blood glucose (self-monitoring)
 - c. Foot inspection
 - d. Vision exams
 - e. Blood pressure
 - f. Influenza vaccination
3. Asthma/COPD
 - a. Rescue inhaler use frequency (when to seek professional care for exacerbations)
 - b. Pulmonary function testing
 - c. Annual influenza vaccination
4. Headache/epilepsy
 - a. Headache/seizure frequency
 - b. Patient documentation and avoidance of precipitating factors (light/sound/mood/surroundings)
5. Antiretroviral therapy for HIV/AIDS
 - a. Nutritional status
 - b. Laboratory testing (CD4 cell count/RNA copies)
 - c. Transmission reduction (abstinence, condoms, no needle sharing), also applicable for hepatitis viruses, HBV and HCV
 - d. Refill verification/medication compliance
 - e. Drug toxicity monitoring
6. Mental disorders
 - a. Movement disorders (antipsychotics)
 - b. Glucose control (antipsychotics)
 - c. Triglyceride levels (antipsychotics)
 - d. Drug serum levels or recommended laboratory testing (e.g., antiepileptic drugs [AED], lithium, clozapine)
 - e. Suicide risk (AED, lithium, antidepressants, antipsychotics)
 - f. Appropriate psychotherapy
 - g. Healthy activities: meditation, yoga, etc.
7. Anticoagulation therapy
 - a. Dietary considerations (consistency with foods containing vitamin K)
 - b. Interactions with herbal supplements (e.g., garlic)
 - c. Anticoagulation clinic
 - d. Monitoring for unusual bleeding (e.g., bleeding gums, unusual bruising, blood in urine or stool)
8. Osteoporosis
 - a. How to take bisphosphonates, which can cause serious problems in the stomach or esophagus

- b. Take each dose with a full (8 oz) glass of water (plain water, not mineral water)
 - c. Patient must stay upright for at least 30 minutes after taking this medication.
 - d. Take the medication first thing in the morning, at least 30 minutes before eating or drinking other substances or before taking any other medication.
 - e. Importance of calcium and vitamin D supplementation
- 9. Hyperlipidemia
 - a. Report any muscle pain or weakness
 - b. Take statins at appropriate time (some taken at bedtime or at evening meal for maximal physiologic effect on cholesterol synthesis)
- 10. Smoking cessation counseling
 - a. Nonpharmacologic treatment – is a five-step process that includes:
 - 1) Asking every patient about tobacco use
 - 2) Advising all smokers to quit
 - 3) Assessing smokers' willingness to make an attempt to quit
 - 4) Assisting smokers with treatment and referrals
 - 5) Arranging follow-up contacts
 - b. Pharmacologic treatments (prescription and OTC)
- B. Preventative health measures
 - 1. Preventive and protective sexual behaviors
 - a) Birth control
 - b) Prevention of sexually transmitted disease (STD)
 - 2. Immunization against communicable diseases:
 - a) Mumps
 - b) Measles
 - c) Rubella
 - d) Tetanus and/or pertussis
 - e) Diphtheria
 - f) Rotavirus
 - g) Human papilloma virus (HPV), causing cervical cancer and genital warts)
 - h) Polio
 - i) Haemophilus influenzae Type b (Hib)
 - j) Varicella zoster virus, (VZV) (chicken pox and shingles)
 - k) Hepatitis A virus (HAV)
 - l) Hepatitis B virus (HBV)
 - m) Meningococcal infection
 - n) Influenza
 - o) Pneumococcal infection
- III. Provide information regarding the documented uses, adverse effects, and toxicities of dietary supplements.
 - A. Explaining basic differences between modern medicine (allopathic) and complementary (homeopathic, Chinese medicine, etc.)
 - 1. Allopathic medicine refers to modern conventional Western medicine.
 - 2. The term *complementary and alternative medicine* (CAM) is generally regarded as encompassing a broad group of healing philosophies, diagnostic approaches, and therapeutic interventions that do not belong to the dominant (conventional) Western health system.
 - a. CAM therapies are divided into five categories, or domains:
 - 1) Alternative medical strategies (e.g., homeopathic medicine, traditional Chinese medicine)
 - 2) Mind-body interventions (e.g., meditation, prayer)
 - 3) Biologically based therapies (e.g., dietary supplements, herbal products)
 - 4) Manipulative and body-based methods (e.g., chiropractic manipulation, massage)
 - 5) Energy therapies (e.g., qi gong, reiki)
 - B. Selecting dietary supplements
 - 1. Not all products have the stated doses or purity that the label may suggest. The manufacturers of herbals/supplements (products that have "Supplement Facts" on the back) decide if they are willing to be inspected by the FDA to reach Good Manufacturing Practice (GMP) standards. Not all companies are willing to do this, but those who pass inspections are granted USP status. Alternatively, all medications labeled as drugs (prescription and OTC medications containing "Drug Facts" on the back) must pass GMP standards. Products are assessed for purity, potency, and the stated strength.
 - C. Deciding if therapy is appropriate
 - 1. Patients should be evaluated by their physician to decide if supplemental therapy is necessary. Most patients with an adequate diet do not need supplements added to their diet. Patients should be aware of multisourcing their vitamins (dietary intake and supplements) to avoid exceeding the recommended dietary intakes (RDI).
 - 2. Certain patients, however, may need supplements added to their diets based on well documented conditions and drug use:
 - a. Folic acid for pregnant women to prevent neural tube defects
 - b. Pyridoxine (vitamin B₆) for patients on isoniazid to prevent peripheral neuropathy
 - c. Thiamine (vitamin B₁) in alcoholics to prevent encephalopathy
 - d. Vitamin D requirements in patients with select bone diseases
- IV. Provide information regarding the selection, use, and care of medical/surgical appliances and devices, self-care products, and durable medical equipment, as well as products and techniques for self-monitoring of health status and medical conditions.
 - A. Drug administration considerations
 - 1. Description of inhaler use (which is brand specific), with and without a spacer
 - a. Shake suspensions/aerosol solutions (not tablets or powders) before use
 - b. Prime suspensions/aerosol solutions before first use, and if they have not been used for a period of time (actual length of time where product requires re-priming is product/manufacturer specific)

- c. Hold the inhalation for an appropriate amount of time and the appropriate spacing between multiple inhalations
- d. Rinse the mouth after inhalation to prevent oral thrush and hoarseness from corticosteroids
- e. Routinely clean the device (not for powders or tablet formulations and not the canister) as directed
- f. Do not share: for individual use only
2. Description of eye drop or ointment administration
 - a. Washing hands before and after use
 - b. Gently holding open the lower eyelid creating a pocket where the drop should be inserted
 - c. Not touching the dropper to the eye or tube to the eyelid
 - d. Keeping the head tilted
 - e. After administration, with a tissue gently wiping away excess moisture or ointment from around the eye(s)
 - f. Separation of drops for multiple drops per dose and between different medication eye drops; use of lacrimal occlusion during administration to prevent systemic absorption (e.g., ophthalmic beta-blockers)
 - g. Do not share: for individual use only
 - h. Temporarily removing or disposing contacts before administration
 - i. Use of eye dropper aids
3. Description of ear drop administration
 - a. Washing hands before and after use
 - b. Warming drops by rolling between the hands, not a heating device; shake suspensions well before each use.
 - c. Not touching the dropper to the ear
 - d. Keeping the head in a tilted position for adequate entry into the ear canal
 - e. Gently pulling the ear up and back (adults) or down and back (children 8 and younger)
 - f. Covering the ear with the tragus (small portion of cartilage, just outside the opening) for about 5 minutes after administration
 - g. Do not share: for individual use
4. Description of nasal spray administration
 - a. Washing hands before and after use
 - b. Prime spray pump (if required) before first use, and if they have not been used for a period of time (actual length of time elapsed when product requires re-priming is product/manufacturer specific)
 - c. Blowing nose gently before spray and not blowing nose immediately after use
 - d. Direct spray back and away from nasal septum
 - e. Wiping nozzle after use
 - f. Do not share: for individual use only
5. Insulin administration
 - a. Wash hands before and after administration
 - b. Roll insulin vial between hands; preparation of insulin pen or other insulin devices
 - c. Inject insulin in the subcutaneous fat (the layer of fat just below the skin)
 - d. Pinch up a fold of skin and insert the needle at 90° to the skin fold. Inject at 45° in areas that have less fat
 - e. Rotate injection sites to maximize rate absorption and prevent lipohypertrophy (enlargement of subcutaneous fat)
 - f. Differences between products (basal/bolus) and timing (daily/before meals)
 - g. Mixing insulins
 - h. Insulin of NPH type may be mixed with rapid-acting insulin aspart (Novo-Log®) and insulin lispro (Humalog®) and regular insulin
 - 1) Mixing insulin of Lente type (e.g., Humulin® L) with regular insulin may result in loss of short-acting effect
 - 2) Order for mixing insulins is “clear before cloudy” (regular insulin drawn first, followed by intermediate-acting insulin)
 - i. Syringe disposal
 - j. Glucose meter device differences and use
 - 1) Testing frequency
 - 2) Required drop size
 - 3) Alternate site testing
 - 4) Display size
 - 5) Coding
 - 6) Memory and ability to connect with a personal computer (PC)
6. Epinephrine and glucagon pen/rescue device use
 - a. Carry at least two EpiPens at all times
 - b. Proper use of glucagon for emergency hypoglycemia typically requires training of companion, family, or other caregiver
7. Transdermal patch use
 - a. Application sites and site rotation (application sites are product specific)
 - b. Hair-free areas (which are not recently shaved)
 - c. Avoiding areas with broken or irritated skin
 - d. Removal and safe disposal
 - e. Application frequency
 - f. Avoiding tight clothing and heat application
8. Administration of rectal enemas and suppositories
 - a. Lying on the left side for product administration
 - b. Removal of suppository from the wrapper
 - c. Lubrication of enema applicators, not suppositories
 - d. Wait times after administration
9. Product specific considerations. Examples:
 - a. Nuva-Ring®: product-switching considerations (i.e., if a back-up method is necessary, how soon should the new product be initiated)
 - b. Nitroglycerin ointment: apply measured dose only to a 2" × 3" area using the provided ruler; application only to chest or back
 - c. Sublingual nitroglycerin (*Note:* patients may not experience a tingling sensation with newer products; if no relief after first dose, get emergency help and continue acute relief instructions.)
 - d. Nicorette® gum (“place” the chewing gum between the cheek and gum once peppery

- taste is noted, do not continue to chew it; resume chewing when tingle diminishes)
- e. EpiPen® (single use, carry extra device for emergency purpose)

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REVIEW QUESTIONS

(Answers and Rationales on page 333.)

- A person with type 1 diabetes is currently using insulin. What should the pharmacist advise?
 - Insulin may be unrefrigerated for 28 days.
 - Avoid smoking.
 - Do not shake cloudy insulin; roll in hands.
 - I only
 - III only
 - I and II
 - II and III
 - I, II, and III
- When a patient is being counseling on the use of Nexium®, which of the following is most appropriate for the pharmacist to state?
 - Take this medication once daily, 1 hour before a meal.
 - This medication may cause sedation.
 - This medication is used to treat your toenail infection.
 - This medication is used for your high blood pressure condition.
- An asymptomatic patient who started taking atenolol goes to the pharmacy with a blood pressure of 132/78 and pulse of 54 beats per minute? Which of the following is the most appropriate action?
 - Advising the patient that these are normal values and not to worry
 - Calling the physician and suggesting that metoprolol might have a less pronounced effect on the patient's heart rate
 - Asking the patient if he has noted any dizziness on standing or decreased exercise tolerance
 - Advising the patient to discontinue atenolol immediately
- Which "show-and-tell" question(s) should a pharmacist ask when dispensing a refill?
 - What do you take this medication for?
 - How do you take this medication?
 - What kind of problems have you been experiencing while taking this medication?
 - I only
 - III only
 - I and III
 - II and III
 - I, II, and III
- Which of the following counseling points should be made regarding the administration of Metamucil®?
 - Mix the granules with one gallon of water, stir, and store in the refrigerator; drink when needed.
 - Mix the granules with eight ounces of water, stir, and let stand for an hour; then drink.
 - Mix the granules with eight ounces of water, stir, and drink immediately.
 - Swallow a teaspoonful of granules with an eight-ounce glass of water.
- What are the possible side effects of Ritampin about which the pharmacist should counsel the patient?
 - This medication can cause stiffness in joints.
 - This medication can cause the urine to appear dark.
 - Wear sunscreen outside while taking this drug.
 - Report flu-like symptoms to your doctor.
- A 57-year-old patient with long-standing COPD takes a new prescription for an ipratropium (Atrovent®) inhaler to the pharmacy. The pharmacist's medication record shows that the patient is also using an albuterol inhaler as needed. Which of the following indicates that the patient understands how to incorporate the Atrovent® into her regimen?
 - She substitutes the Atrovent® for the albuterol.
 - She uses the Atrovent® inhaler as needed for wheezing.
 - She uses the Atrovent® inhaler four times a day.
 - For acute attacks, she should use the albuterol inhaler initially, then the Atrovent®, as needed for wheezing.
- A 48-year-old patient with stable COPD has a refill prescription for Combivent® and a new prescription for Spiriva®. Which of the following actions indicates that the patient understands the COPD regimen?
 - She uses the Combivent® inhaler every morning and evening.
 - She uses the Spiriva® as needed for wheezing.
 - She uses the Combivent® inhaler as needed for wheezing.
 - She takes the Spiriva® capsules by mouth.
- During medication counseling for Diovan® tablets, which of the following statements would verify that the patient has a good understanding of the possible side effects of the drug?
 - I might have bladder spasms with this medication.

- b. I might get dizzy with this medication.
 - c. I might get constipated while taking this medication.
 - d. My vision might turn yellow with this medication.
10. Which of the following would show that a patient understands why he is taking Abilify®?
- a. I have bipolar disorder.
 - b. I have obsessive compulsive disorder.
 - c. I have postherpetic neuralgia.
 - d. I have severe diabetic peripheral neuropathy.
11. Which questions should a pharmacist ask a patient when verifying the medication at pick-up?
- a. What OTC medicines do you take?
 - b. What doctor prescribed you this medication?
 - c. To make sure your medication is effective, how it should be taken?
 - d. Do you have any allergies?
 - e. None of the above
12. When counseling a patient, it is important to include “take on an empty stomach” for which of the following medications?
- I. Saquinavir
 - II. Alendronate
 - III. Levothyroxine
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
13. A mother comes to the pharmacy with questions about diaper rash. What counseling points would a pharmacist provide?
- a. Make frequent diaper changes.
 - b. Use breathable disposable diapers.
 - c. Expose skin under diaper to open air.
 - d. Use barrier creams such as zinc oxide.
 - e. All of the above
14. Which of the following questions should a pharmacist ask a patient when dispensing a new prescription?
- I. What did the doctor tell you the medication is for?
 - II. How did the doctor tell you to take this medication?
 - III. What did the doctor tell you to expect when taking this medication?
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
15. What should you advise a patient with diabetes to do if he/she feels symptoms of low blood sugar?
- I. Drink $\frac{1}{2}$ a glass of orange juice.
 - II. Test blood glucose.
 - III. Within 30 minutes after symptoms subside, eat a light snack.
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
16. A patient goes to the pharmacy with a prescription for Prandin®. What should the pharmacist tell the patient when dispensing the filled prescription?
- a. Take on an empty stomach.
 - b. Take before meals.
 - c. It may cause drowsiness.
 - d. If you miss a meal, take between meals.
17. Which of the following are counseling points regarding the use of metered-dose inhalers?
- a. Shake the canister or inhaler in place for 5–10 seconds before use.
 - b. Hold breath for 10 seconds to allow medicine to reach the lungs.
 - c. Tilt head back slightly and begin to inhale slowly.
 - d. Close your lips around the mouthpiece.
 - e. All of the above
18. Which of following describes proper technique for administering eye drops?
- I. With the forefinger, pull down the lower eyelid to form a pocket.
 - II. Touch the tip of the dropper against the eye when administering the drops.
 - III. Immediately after administering the drops, press a forefinger against the inside corner of the eye.
- a. I only
 - b. III only
 - c. I and II
 - d. I and III
 - e. I, II, and III
19. Which of following describes proper technique for using a peak flow meter?
- I. Before using the peak flow meter, fully inflate the lungs by taking a deep breath.
 - II. Do not put the mouthpiece of the peak flow meter into the mouth.
 - III. With as much force as possible, blow out as quickly as possible.
- a. I only
 - b. III only
 - c. I and II
 - d. I and III
 - e. I, II, and III
20. A 40-year-old man is going to a wedding this weekend. He is afraid he may experience heartburn and wants to try Gaviscon®. Which of the following should a pharmacist tell him?
- I. If you have milk or dairy allergies, you should avoid this medication.
 - II. Do not take more than 10 mg.
 - III. Do not use for more than 2 weeks.

- a. I only
 - b. III only
 - c. I and II
 - d. I and III
 - e. I, II, and III
21. A patient is thinking about trying the EZ Detect® fecal occult blood test. What should the pharmacist tell him about using the test?
- I. Avoid aspirin 2 days before use.
 - II. Urine may alter the results.
 - III. Toilet bowl cleaners may cause false positive results.
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
22. A 58-year-old man recently started using Niaspan®. He complains that he is experiencing flushing. What should a pharmacist recommend for this patient?
- I. Take Niaspan® first thing in the morning on an empty stomach to avoid flushing.
 - II. Take aspirin 325 mg 30 minutes before taking Niaspan®.
 - III. Avoid alcohol or hot drinks around the time of Niaspan® administration.
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
23. A 50-year-old woman asks a pharmacist about what she can do to prevent osteoporosis. What should the pharmacist recommend?
- I. Avoid weight-bearing exercises.
 - II. Consume at least 1200 mg per day of calcium and 800–1000 IU of vitamin D.
 - III. Limit alcohol intake.
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
24. A 62-year-old woman goes to the pharmacy with a prescription for Fosamax®. What should the pharmacist tell her about its use?
- I. Take the medication with food and a full glass of water.
 - II. Lie down for at least 30 minutes after swallowing the tablet.
 - III. Swallow the tablet whole.
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
25. A patient goes to the pharmacy with a new prescription for Miacalcin® nasal spray. What should the pharmacist tell the patient when dispensing the medication?
- I. After 30 doses, each spray may not deliver the correct amount.
 - II. The pump should be primed before each daily dose only.
 - III. Store unopened bottles in refrigerator.
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
26. A 16-year-old girl has a prescription for Servent® Diskus. What should the pharmacist tell her?
- I. The dose indicator shows how many doses are left.
 - II. Do not breathe out into the mouthpiece.
 - III. Close the Diskus after use so it is ready for the next dose.
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
27. When counseling a patient about emergency contraception, which of the following is an accurate statement to make?
- a. Emergency contraception may be used as a primary means of contraception.
 - b. Plan B® emergency contraception is no longer sold in the United States.
 - c. Emergency contraceptive pills can delay ovulation.
 - d. Emergency contraceptive pills take at least 72 hours to work.
 - e. Progestin only formulations, like plan B, are not better tolerated than estrogen/progestin combination regimens.
28. A patient has been counseled on the appropriate use of his new prescription for risedronate. Which of the following statements would verify that the patient has a good understanding of the consultation information that the pharmacist has provided?
- I. This medication will help with my Parkinson symptoms.
 - II. This medication will help with my osteoporosis.
 - III. I need to take this medication at least 30 minutes before the first food or drink of the day other than water, in an upright position, and should not lie down for at least 30 minutes after taking it.
 - IV. I need to take one tablet every other day.
- a. I and III only
 - b. II and III only
 - c. II and IV only
 - d. I and IV only

29. A patient is counseled on the appropriate use of his new prescription for Betaseron®. Which of the following statements would verify that the patient has a good understanding of the information that the pharmacist provided?
- This medication will help with my Parkinson symptoms.
 - This medication will help with my depression.
 - I need to tell my doctor if I get fevers or a sore throat.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
30. Which of the following statements demonstrates that a female patient understands the risks associated with cytarabine therapy?
- I should avoid pregnancy and breast-feeding.
 - I may become constipated while on this medication.
 - I need to make sure to keep current on my vaccinations while on this medication.
 - I will have permanent hair loss.
31. A pharmacist has counseled a patient on a new prescription for the Levemir® FlexPen. Which of the following demonstrates that the patient understands the storage requirements?
- I should store the in-use pen with a needle in place.
 - To avoid injecting myself with cold insulin, I should keep my pen in a warm place.
 - Once opened, the pen should be stored at room temperature, but I should keep the rest of the pens in the refrigerator.
 - Once opened, I should discard the pen after 28 days.
32. Which of the following factors would not be considered potential barriers to providing a thorough oral consultation to a patient?
- Education level
 - Physical impairment
 - Insurance coverage
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
33. Peak flow meters are often classified into three zones. Which of the following describes this system?
- Red zone is 80%–100%; blue zone is 50%–80%; yellow zone is less than 50%.
 - Green zone is 80%–100%; yellow zone is 50%–80%; red zone is less than 50%.
 - Green zone is 50%–100%; yellow zone is 30%–50%; red zone is less than 30%.
 - Red zone is 50%–100%; blue zone is 30%–50%; yellow zone is less than 30%.
 - None of the above
34. Which counseling point(s) should be made regarding the use of oral ketorolac?
- It is for short-term use only (up to 5 days).
 - Take with food or milk.
 - Do not break, chew, or crush the tablets.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
35. Which of the following counseling points should be mentioned to a person wanting to take Xenical®?
- It may cause oily spotting.
 - Take three times daily with each meal containing fat.
 - Take a multivitamin containing vitamins A, D, E, and K at the same time as Xenical®.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
36. Which of the following counseling points should be made to the patient taking felodipine (Plendil®)?
- Avoid grapefruit juice while using this medication.
 - It may cause headache.
 - Take the medication with a high-fat meal.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
37. A patient has a prescription for tranylcypromine (a MAO inhibitor). Which of the following foods should the pharmacist advise the patient to avoid?
- Chianti wine
 - Sauerkraut
 - Aged cheese
 - Pickled fish
 - All of the above
38. A patient with a prescription for simvastatin should be told which of the following statements?
- Report any unusual muscle pain or weakness.
 - Avoid large amounts of grapefruit juice.
 - Take the dose first thing in the morning.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III

39. A patient has a prescription for Tri-Levlen®. Which of the following counseling points should be made to the patient?
- If nausea occurs take with food or at bedtime.
 - Use an additional method of contraception when taking antibiotics.
 - It may cause weight gain, headaches, and breakthrough bleeding.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
40. Patients taking ibandronate should be advised to:
- take it on an empty stomach.
 - swallow tablets whole.
 - lie down for 60 minutes after taking the medication.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
41. A 52-year-old woman complains about menopausal hot flashes. She wants to avoid using any medication. She asks the pharmacist if there are any nonpharmaceutical therapies she can try. What could the pharmacist suggest?
- Sip a cold drink if a hot flash is coming on.
 - Exercise regularly.
 - Avoid hot and spicy foods and caffeinated beverages.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
42. A patient is planning on using a bismuth subsalicylate preparation. What should the pharmacist tell the patient?
- It may discolor stools black.
 - Salicylism is a possible complication with bismuth subsalicylate if too much is ingested.
 - It may cause severe constipation.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
43. A patient has a prescription for cimetidine for GERD. Which of the following counseling points should the pharmacist make to this patient?
- Elevate the head of the bed.
 - Eat no later than 30 minutes before going to bed.
 - Avoid foods that aggravate symptoms.
 - Avoid smoking.
 - All of the above
44. A pharmacist is counseling a new patient in the anticoagulant clinic who is beginning warfarin therapy. Which of the following should he avoid?
- Non-alcoholic wine
 - Vitamin K
 - Vitamin E
 - High-cholesterol foods
 - All of the above
45. Patients taking chlorpropamide should be counseled to avoid which of the following?
- Cheese
 - Vitamin K
 - Milk
 - Alcohol
 - Acetaminophen
46. A patient asks a pharmacist for advice on how to quit smoking and what products to use. Which of the following statements regarding nicotine replacement therapy are true?
- Do not eat or drink 15 minutes before using the Nicotine lozenge.
 - Nicotine gum works faster than the patch.
 - The patch should not be worn all day; it is used as a substitute for a cigarette.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
47. A patient asks a pharmacist about the DASH diet. Which of the following statements about the diet are true?
- It limits intake of salt, saturated fat and cholesterol.
 - It emphasizes fruits and vegetables.
 - It includes no red meat.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
48. Which of the following are symptoms of high blood sugar that should be mentioned when a pharmacist is counseling a patient with diabetes?
- Increased thirst
 - Headache
 - Fatigue
- I only
 - III only
 - I and III
 - II and III
 - I, II, and III
49. With which of the following medications should a pharmacist counsel the patient to avoid alcohol consumption?
- Metronidazole
 - Diphenhydramine
 - Warfarin

- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
50. A patient goes to the pharmacy counter looking to purchase Feosol®. Which of the following statements regarding iron supplements is true?
- I. It may discolor stool.
 - II. Taking it with food may increase absorption.
 - III. Enteric-coated products are preferred over nonenteric-coated preparations.
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III

Herbs and Dietary Supplements

7

CHAPTER

- I. Complementary and Alternative Medicine (CAM) and Integrative Medicine
 - A. CAM is variably defined, but the National Center for Complementary and Alternative Medicine (NCCAM) defines CAM as a group of diverse medical and health care systems, practices, and products that are not normally considered to be conventional or allopathic medicine.
 - B. The Consortium of Academic Health Centers for Integrative Medicine defines integrative medicine as the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, providers, and disciplines to achieve optimal health and healing.
 - C. Why do patients use CAM and integrative medicine?
 1. More active participation in care
 2. Perceived safety and lower cost
 3. Conventional medicine options are exhausted
- II. Formulation and Regulation of Dietary Supplements
 - A. A dietary supplement may include vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, and metabolites taken in addition to a normal dietary intake. Supplements are available in many dosage forms including extracts, concentrates, tablets, capsules, gel caps, liquids, teas, and powders. Herbs used for medicinal purposes are sold in many different forms, including capsules, tablets, tinctures, teas, powders, whole herbs, and creams.
 1. Examples of dietary supplements
 - a) Herbals: Gingko, saw palmetto
 - b) Supplements: Glucosamine, coenzyme Q10
 - c) Trace minerals: Selenium, chromium, zinc
 - d) Vitamins: B₆, A, C, E, folic acid
 - e) Hormones: melatonin, Dehydroepiandrosterone (DHEA)
 - f) Amino acids: L-tryptophan
 2. Decoction: A decoction is the product of boiling the roots or tough plant material in water to extract the “active principle.”
 3. Extracts: Pills, powders, liquids, or other forms of herbs that contain a concentrated and usually standard amount of therapeutic ingredients. The most commonly used extracts are fluid extracts (tinctures), solid extracts, powdered extracts, and essential oils.
 4. Essential oil: Highly volatile, aromatic, concentrated oil extracted from plants made by steam distilling volatile compounds from plant material. Also known as volatile oils, ethereal oils, or essences, they are usually complex mixtures of a wide variety of organic compounds, mostly volatile terpene derivatives that evaporate when exposed to air.
 5. Fluid extracts (tinctures): A concentrated solution of the soluble constituents of plant drugs, containing alcohol as both a solvent and a preservative. Fluid extracts are typically hydroalcoholic solutions, but they can also have a glycerin, nonalcoholic base. Alcohol content varies with each product.
 6. Infusion (tea): An herbal product or tea made by steeping (soaking) herbs in hot water (water of any temperature) to extract the herbal qualities. Delicate parts of the plant, like flowers or leaves, are most often used.
 7. Poultices: Topical application of a thick paste of hot, moist herb or a soft mush, prepared by wetting powders or other absorbent substances with oils or water for the purpose of alleviating pain, reducing inflammation, and promoting healing.
 8. Powdered extracts: Prepared from native extracts by diluting to the specified strengths with diluents (e.g., starch, lactose) with or without anticaking agents (e.g., magnesium carbonate) followed by drying, usually under vacuum, to yield dry solids. These are ground into powders to yield powdered extracts or are granulated to produce granular extracts.
 9. Solid extracts: A highly concentrated herbal product with a thick syrup-like consistency.
 - B. Regulation of health claims is largely monitored by the Dietary Supplement Health and Education Act (DSHEA), although the Food and Drug Administration (FDA) and other health alliances play minor roles.
 1. The Dietary Supplement Health and Education Act (DSHEA) was passed by the US Congress in October 1994. Topics discussed in DSHEA include product labeling and content, structure and function, and health claims. Health claims describe a relationship between food, food component, or dietary supplement ingredient,

Table 7-1 Health Claims Approved by the FDA

Supplement	Health Claim
Calcium	Reduced risk of Osteoporosis
Dietary sugar alcohol (polyols)	Does not promote tooth decay
Dietary fats	Increased risk of Cancer
Dietary saturated fat and cholesterol	Increased risk of coronary heart disease
Fiber-containing grain products, fruits, and vegetables	Reduced risk of coronary heart disease
Folate	Prevention of Neural tube defects (in pregnancy)
Fruits and vegetables	Reduced risk of Cancer
Plant sterol/stanol esters	Reduced risk of coronary heart disease
Potassium	Reduced risk of high blood pressure and stroke
Sodium	Increases Hypertension
Soy protein	Reduced risk of coronary heart disease
Vitamin B ₃	Treatment of Pellagra
Vitamin C	Treatment of Scurvy
Whole grain foods	Reduced risk of heart disease and certain cancers

or health-related condition, and are not about treating, mitigating, or curing diseases (Table 7-1).

- a) Product labeling: Labels must contain a descriptive name of the product stating that it is a “supplement”; the name and place of business of the manufacturer, packer, or distributor; a complete list of ingredients; and the net contents of the product. Additionally, each dietary supplement must have nutrition labeling in the form of a “supplement facts” panel and identify each dietary ingredient contained in the product in order of abundance in the product (Figure 7-1).

Supplement Facts	
Serving Size 1 Capsule	
Amount Per Capsule	% Daily Value
Calories 20	
Calories from Fat 20	
Total Fat 2 g	3%*
Saturated Fat 0.5 g	3%*
Polyunsaturated Fat 1 g	†
Monounsaturated Fat 0.5 g	†
Vitamin A 4250 IU	85%
Vitamin D 425 IU	106%
Omega-3 fatty acids 0.5 g	†
* Percent Daily Values are based on a 2,000 calorie diet.	
† Daily Value not established.	

Ingredients: Cod liver oil, gelatin, water, and glycerin.

Figure 7-1 — **Dietary supplement label.** Requirements of the label are found at: <http://ods.od.nih.gov/factsheets/dietarysupplements.asp#h6>
A fictitious example of a supplement label is available at: <http://vm.cfsan.fda.gov/~acrobot/fdsuppla.pdf> (Courtesy of U.S. Food and Drug Administration.)

- b) Nutrient content claims: Nutrient content claims characterize the level of a nutrient in a food. These types of claims describe the level of a nutrient or dietary substance in the product using terms like *free*, *high*, and *low*, or they compare the level of a nutrient in a food to that of another food using terms such as *more*, *reduced*, and *light*. For example, a product containing 500 mg of calcium may claim “high in calcium.”
- c) If a dietary supplement label includes such a claim, this following statement must appear on labels: “THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FDA. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE OR PREVENT ANY DISEASE.” The content of the label must be provided to the FDA 30 days before labeling.
- d) Structure and function claims explain the role of a nutrient or dietary ingredient intended to affect normal structure or function in humans, for example, “calcium builds strong bones” or “fiber maintains bowel regularity.” Structure and function claims may also describe a benefit related to a nutrient deficiency disease (e.g., vitamin C and scurvy), as long as the statement also tells how widespread such a disease is in the United States. The manufacturer is responsible for ensuring the accuracy and truthfulness of these claims; they are not preapproved by the FDA, but they must be truthful and not misleading.

2. The FDA has a limited role in regulating the quality of individual products.
- a) The 1990 Nutrition Labeling and Education Act (NLEA) provides for the FDA to issue regulations authorizing health claims for foods and dietary supplements after the FDA’s careful review of the scientific evidence submitted in health claim petitions.

- b) The 1997 Food and Drug Administration Modernization Act (FDAMA) provides for health claims based on an authoritative statement of a scientific body of the United States government or the National Academy of Sciences; such claims may be used after submission of a health claim notification to FDA.
 - c) The 2003 FDA Consumer Health Information for Better Nutrition Initiative provides for qualified health claims for which the quality and strength of the scientific evidence falls below that required for FDA to issue an authorizing regulation. Such health claims must be qualified to ensure accuracy of presentation to consumers.
3. In the United States, the FDA does not function to guarantee the strength, purity, or safety of dietary supplements. Companies are expected to prove the efficacy and safety of their products.
- a) The Office of Dietary Supplements (ODS) at the National Institutes of Health (NIH) was designed to strengthen knowledge and understanding of dietary supplements by evaluating scientific information, stimulating and supporting research, disseminating research results, and educating the public to foster an enhanced quality of life and health for the United States population.
 - b) The United States Department of Agriculture (USDA) provides leadership on food, agriculture, natural resources, and related issues based on sound public policy, the best available science, and efficient management. The USDA developed a Dietary Supplement Ingredient Database, which monitors the levels of ingredients in dietary supplement products.
4. Third party testing: Independent laboratories that test products to ensure that the label matches the product include Consumer Lab, Consumer Reports, Natural Products Association, NSF International, and the United States Pharmacopeia (USP). Quantitative and qualitative testing often finds that brand-to-brand and batch-to-batch variation exists in products.
- III. Common uses, adverse effects, and potential interactions of popular herbs and supplements, as well as manual therapies
- A. Clinicians are encouraged to recommend doses of herbs and supplements based on those most commonly used in human trials and clinical experience. However, with natural products it is often not clear what the optimal doses are to balance effectiveness and safety due to a lack of scientific data and the lack of standardization.
 - B. Why is this knowledge important for patient counseling?
 - 1. Many patients do not reveal their use of herbal remedies because they are in fear of being judged or criticized.
 - 2. Clinicians can provide information about recommended doses, frequencies, and specific brand-name products used in clinical trials.
 - C. Table 7-2 summarizes common herbs and supplements used in the United States, adverse effects, and potential interactions based on mechanism of action and laboratory, animal, or human evidence.
 - D. Manual therapies are also part of integrative medicine, and are often financially covered under health insurance plans. The risks of side effects should be noted (Table 7-3).

Table 7-2 Top Herbs and Supplements in the United States

Common Name	Common Uses	Special Considerations, Adverse Effects	Possible Interactions
Barley	Coronary heart disease	Use cautiously with diabetes, asthma, or arrhythmia	Oral agents, cholesterol-lowering drugs, and herbs or supplements with similar effects
Coenzyme Q10 (Co Q-10)	CoQ-10 deficiency, heart disease, antioxidant, high blood pressure	May reduce blood pressure; may reduce blood sugar	Alzheimer drugs, anticoagulants/ antiplatelets, antiretrovirals, antivirals, beta blockers, cancer drugs, clonidine, methyldopa, hydralazine, antidepressants, antipsychotics, blood pressure drugs, blood sugar medications, cholesterol-lowering drugs (statins), some diuretics, heart drugs, immune system-altering drugs, ginkgo, garlic, horsetail, red yeast, vitamin E, vitamin K, and other herbs or supplements with similar effects

Continued

Table 7-2 Top Herbs and Supplements in the United States—cont'd

Common Name	Common Uses	Special Considerations, Adverse Effects	Possible Interactions
Echinacea	Common cold, influenza, respiratory infections, immune system stimulant	May cause allergic reactions; to be avoided if allergic to plants in the daisy family including ragweed, chrysanthemums, and marigolds	Amoxicillin, anesthetics, antineoplastic agents, caffeine, corticosteroids, cytochrome P450 metabolized agents, disulfiram (Antabuse), econazole nitrate (Spectazole), hydrophilic agents, immunosuppressants, liver-damaging agents, metronidazole (Flagyl), and herbs and supplements with similar effects
Garlic	Cardiovascular disease (high cholesterol, high blood pressure)	May cause bad breath, body odor, and allergic reactions; may increase the risk of bleeding; avoid use with anticoagulants/antiplatelets; may lower blood sugar levels	Drugs that increase bleeding, anticoagulants/antiplatelets, antihypertensives, cholesterol-lowering drugs, thyroid drugs, human growth hormone, vitamin E, fish oils, and herbs or supplements with similar effects
Ginkgo biloba	Improve memory, prevent dementia, Alzheimer disease, cognitive function	May cause headache, nausea, gastrointestinal upset, diarrhea, and dizziness; may increase bleeding risk	Antidepressants, antipsychotic drugs, drugs that increase risk of bleeding, drugs used for erectile dysfunction (e.g., Viagra), blood pressure drugs, drugs that alter blood sugar levels, drugs metabolized by the liver, seizure drugs, aged foods (wine and cheese), St. John's wort, garlic, bitter melon, and herbs or supplements with similar effects
Ginseng	Diabetes, energy enhancement, erectile dysfunction	May cause headaches as well as sleep and gastrointestinal problems; may lower blood sugar	Anticoagulants/blood thinners, drugs that are broken down by the liver, HIV drugs such as protease inhibitors, drugs that lower blood sugar levels, digoxin (Lanoxin), nifedipine (Procardia), blood pressure drugs, over-the-counter drugs for treating cold symptoms (e.g., pseudoephedrine), diuretics, central nervous system stimulants such as methylphenidate (Ritalin), corticosteroids, hormonal drugs, antipsychotics, opioids such as morphine, phenelzine (Nardil), alcohol, metronidazole (Flagyl), disulfiram (Antabuse), and herbs or supplements with similar effects
Glucosamine/chondroitin	Osteoarthritis	May increase intestinal gas and soften stool; patients with diabetes should monitor glucose; may increase anticoagulant effects of warfarin	Drugs that alter blood sugar levels, diuretics, drugs that increase the risk of bleeding such as aspirin, anticoagulants/antiplatelet drugs, NSAID, herbs or supplements with similar effects (e.g., arginine, cocoa, ephedra, juniper berry, kava, shepherd's purse, sweet clover, turmeric, vitamin E)

Table 7-2 Top Herbs and Supplements in the United States—cont'd

Common Name	Common Uses	Special Considerations, Adverse Effects	Possible Interactions
Kava	Anxiety	May cause liver damage	ACE inhibitors, alcohol, antianxiety drugs, anticoagulants/antiplatelets, antidepressant agents, antineoplastic agents, anxiety medications, CNS depressants, contraceptives, cytochrome P450 metabolized agents, diuretics, dopamine agonists, dopamine antagonists, drugs eliminated by the kidneys, gastrointestinal agents, hepatotoxic (liver-damaging) agents, hormonal agents, mood stabilizers, neurologic agents, pain relievers, pain-numbing agents, sedatives, tranquilizers, and herbs and supplements with similar effects
Melatonin	Sleep disorders	May cause daytime drowsiness, dizziness, gastrointestinal cramps and headache; may cause additive sedation when used with CNS depressants	Drugs broken down by the liver, sedative drugs (e.g., Ambien), barbiturates, narcotics, antidepressants, alcohol, drugs that increase the risk of bleeding such as warfarin (Coumadin), anticoagulants (e.g., aspirin or heparin), nonsteroidal antiinflammatories (e.g., ibuprofen), naproxen (Naprosyn, Aleve), drugs that affect blood pressure (e.g., atenolol), drugs that lower levels of vitamin B ₆ in the body (e.g., birth control pills, hormone replacement therapy, or loop diuretics), diazepam, verapamil, temazepam, somatostatin, drugs that alter blood sugar levels (e.g., insulin), caffeine, succinylcholine, methamphetamine, isoniazid, herbs or supplements with similar effects (e.g., 5-HTP, ginkgo biloba, garlic, saw palmetto, vitamin B ₁₂ , chasteberry, arginine, DHEA, echinacea)
Saw palmetto	Benign prostatic hyperplasia (BPH)	May increase risk of bleeding	Androgenic drugs, antiandrogenic drugs, antibiotics, antiinflammatory agents, antineoplastic agents, blood pressure-altering agents, blood thinning agents, disulfiram (Antabuse), drugs that may lower seizure threshold, hormonal agents, immunomodulators, and herbs and supplements with similar effects
Soy	Menopause, breast cancer, osteoporosis	May cause gastrointestinal upset; may have estrogenic effects	Birth control pills containing estrogen, selective estrogen receptor modulators (e.g., tamoxifen), aromatase inhibitors (e.g., anastrozole [Arimidex], exemestane [Aromasin], or letrozole [Femara]), blood-thinning drugs (e.g., warfarin), calcium, iron, phosphate, panax ginseng, and herbs and supplements with similar effects

Continued

Table 7-2 Top Herbs and Supplements in the United States—cont'd

Common Name	Common Uses	Special Considerations, Adverse Effects	Possible Interactions
St. John's wort	Depression (mild to moderate)	May increase sensitivity to sunlight; may cause headache, sexual dysfunction, and dizziness; induces CYP450 2C9 and 3A4; increases risk of serotonin syndrome when used with certain antidepressants or other drugs increasing serotonin levels	Drugs that are broken down by the liver such as birth control pills, warfarin, cyclosporine, carbamazepine, digoxin, antidepressants, antibiotics, loperamide (Imodium), migraine drugs, irinotecan (CPT-11), HIV drugs such as nonnucleoside reverse transcriptase inhibitors or protease inhibitors, theophylline, drugs that affect thyroid activity, antiinflammatories, 5-HT ₁ receptor agonists (triptans), alcohol, anesthetic drugs, antifungals, antineoplastic drugs, benzodiazepine, calcium channel blocking drugs (verapamil), dextromethorphan, histamine H ₁ antagonist (MDRI), HMG CoA reductase inhibitors (statins), imatinib (Gleevac), irinotecan (CPT-11, Camptosar), loperamide (Imodium), methadone, monoamine oxidase inhibitors (MAOI), mycophenolic acid, nifedipine (e.g., Procardia, Adalat), P-glycoprotein-regulated drugs, drugs that increase sun sensitivity, omeprazole, selective serotonin reuptake inhibitors (SSRI), tacrolimus (Prograf), theophylline, drugs for thyroid disorders, cardiac glycoside herbs and supplements, iron, red yeast rice, valerian, foods containing tyramine/tryptophan (e.g., cheese, wine, yogurt, caffeine, soy sauce, and chocolate), and herbs and supplements with similar effects (e.g., hops, oleander, fenugreek)
Fish oil/ omega-3 fatty acids	Cardiovascular disease (high blood pressure, high cholesterol), rheumatoid arthritis	May cause gastrointestinal upset; may increase bleeding; may increase blood sugar	Drugs that increase the risk of bleeding (anticoagulants) such as warfarin or heparin, antiplatelet drugs, antiinflammatories such as ibuprofen (Motrin, Advil), drugs that lower blood pressure, drugs that may alter blood sugar levels (e.g., insulin), drugs that lower cholesterol such as atorvastatin (Lipitor), vitamins A, E and D, and other herbs and supplements with similar effects
Milk thistle	Liver disease, liver protection	May cause gastrointestinal upset; may lower blood sugar levels	Drugs broken down by the liver, drugs used to control blood sugar levels, phenytoin (Dilantin), cancer drugs (doxorubicin, cisplatin, and carboplatin), and herbs or supplements with similar effects (e.g., aloe vera, American ginseng, bilberry, bitter melon, burdock, fenugreek, fish oil, gymnema, horse chestnut/horse chestnut seed extract, marshmallow, milk thistle, panax ginseng, rosemary, Siberian ginseng, stinging nettle, vitamin E)

Table 7-2 Top Herbs and Supplements in the United States—cont'd

Common Name	Common Uses	Special Considerations, Adverse Effects	Possible Interactions
Black cohosh	Menopause	May cause liver damage	Alcohol, anesthetics, antiestrogen drugs (e.g., Tamoxifen), antiseizure drugs, aspirin or nonsteroidal antiinflammatories/pain relievers, blood pressure drugs, drugs broken down by the liver, cholesterol-lowering drugs, drugs for depression (MAOI or SSRI), drugs for seizures, drugs (e.g., raloxifene), drugs that increase the risk of bleeding (e.g., warfarin [Coumadin]), estrogens (e.g., hormone replacement therapy drugs, birth control pills), and herbs and supplements with similar effects
Ginger	Nausea	May increase the risk of bleeding	Antacids, antiinflammatory agents, antiarrhythmic agents, antiarthritic agents, antidiabetic agents, antiemetics, antihistamines, antineoplastic agents, antiobesity agents, antitussives, beta blockers, blood pressure medications, blood thinners, cardiac glycosides, cardiovascular agents, cholesterol medications, CNS depressants, cytochrome P450 metabolized agents, xanthine oxidase, dexamethasone, gastrointestinal agents, H ₂ blockers, immunosuppressants, nifedipine, nonsteroidal antiinflammatory agents, COX 2 inhibitors, P-glycoprotein-regulated drugs, proton pump inhibitors, sedatives, vasodilators, warfarin, and herbs and supplements with similar effects
Calcium	Antacid, bone loss prevention, osteoporosis	May cause kidney stones in high doses; to be avoided with hypercalcaemia, hypercalciuria, hyperparathyroidism, bone tumors, digitalis toxicity, ventricular fibrillation, or sarcoidosis	Alcohol, aluminum-containing compounds, antacids, anticonvulsants, anti-inflammatories, antibiotics, bisphosphonates, blood pressure medications, caffeine, calcium channel blockers, cholesterol medications, corticosteroids, diuretics, estrogen, heart medications, hormone replacement therapy, levothyroxine, mineral oil, orlistat (Xenical, Alli), phosphorus, potassium, proton pump inhibitors, stimulant laxatives, tetracycline, vitamin D, and herbs and supplements with similar effects
Vitamin D	Rickets, osteoporosis	Use cautiously with hyperparathyroidism (overactive thyroid), kidney disease, sarcoidosis, tuberculosis, and histoplasmosis	Antiseizure drugs, calcium, cholestyramine or colestipol, corticosteroids, digoxin, magnesium-containing antacids, mineral oil, orlistat (an obesity drug), rifampin, stimulant laxatives, thiazide diuretics including chlorothiazide (Diuril), chlorthalidone (Hygroton, Thalitone), hydrochlorothiazide (HCTZ, Esidrix, HydroDIURIL, Ortec, Microzide), indapamide (Lozol), and metolazone (Zaroxolyn), and herbs and supplements with similar effects

Continued

Table 7-2 Top Herbs and Supplements in the United States—cont'd

Common Name	Common Uses	Special Considerations, Adverse Effects	Possible Interactions
Vitamin E	Vitamin E deficiency	May cause abdominal pain/GI upset, blurred vision/dizziness (particularly when used in high doses), diminished kidney function, increased rate of hemorrhagic (bleeding) stroke and gum bleeding, increased risk of bleeding, and weakness	Anticoagulants, anticonvulsants, antioxidants, antiplatelet drugs, blood-thinning drugs, chemotherapy agents, cholesterol-lowering medications, cholestyramine (Questran), colestipol (Colestid), orlistat (Xenical, Alli), isoniazid (INH, Lanizid, Nydrazid), olestra (Olean fat substitute), and sucralfate (Carafate), cyclosporine, gemfibrozil (Lopid), nonsteroidal antiinflammatory drugs such as ibuprofen (Motrin, Advil) or naproxen (Naprosyn, Aleve), and herbs and supplements with similar effects

From Natural Standard, www.naturalstandard.com, ©2008.

Table 7-3 Manual Therapies and Adverse Effects

Manual Therapy	Special Considerations, Adverse Effects
Acupuncture	Needles must be sterile to avoid disease transmission. Avoid with valvular heart disease, infections, bleeding disorders or with drugs that increase the risk of bleeding (anticoagulants), medical conditions of unknown origin, neurological disorders. Avoid on areas that have received radiation therapy and during pregnancy. Use cautiously with pulmonary disease (e.g., asthma or emphysema). Use cautiously in elderly or medically compromised patients and in those with diabetes or with history of seizures. Avoid electroacupuncture with arrhythmia (irregular heartbeat) or in patients with pacemakers.
Acupressure	Forceful acupressure may cause bruising.
Chiropractic (manual adjustments)	Use extra caution during cervical adjustments. Use cautiously with acute arthritis, conditions that cause decreased bone mineralization, brittle bone disease, bone softening conditions, bleeding disorders, or migraines. Use cautiously with the risk of tumors or cancers. Avoid with symptoms of vertebrobasilar vascular insufficiency, aneurysms, unstable spondylolisthesis or arthritis. Avoid with agents that increase the risk of bleeding. Avoid in areas of paraspinal tissue after surgery.
Yoga	Avoid some inverted poses with disc disease of the spine, fragile, or atherosclerotic neck arteries, risk for blood clots, extremely high or low blood pressure, glaucoma, detachment of the retina, ear problems, severe osteoporosis, or cervical spondylitis. Certain yoga breathing techniques should be avoided by people with heart or lung disease.

Examples of Resources for the Clinician

Natural Standard: www.naturalstandard.com.

National Center for Complementary and Alternative Medicine: www.nccam.nih.gov.

Consumer Lab: www.consumerlab.com.

- c. It requires ingredient and nutrition labeling.
- d. It establishes good manufacturing practice (GMP) regulations.
- e. All of the above

REVIEW QUESTIONS

(Answers and Rationales on page 335.)

1. Which of the following statements about DSHEA is true?
 - a. It defines dietary supplements and dietary ingredients.
 - b. It provides for use of claims and nutritional support statements.

2. Which of the following statements about kava is true?
 - I. It may cause nephrotoxicity.
 - II. It may be used to increase cognition.
 - III. Alcohol consumption increases toxicity.
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III

3. Which is NOT an example of a government resource on CAM?
 - a. NCCAM
 - b. ODS
 - c. CFSAN
 - d. ASHP Essentials
4. Which of the following is popularly used to stimulate the immune system?
 - a. Valerian
 - b. Chamomile
 - c. Chasteberry
 - d. Echinacea
 - e. Kava
5. A patient with poison ivy asks the pharmacist if she can use a skin lotion that contains comfrey. What should the pharmacist tell the patient?
 - a. Comfrey-containing products are not recommended for use in any form due to possible toxicity.
 - b. Comfrey-containing lotions should help to dry weeping lesions.
 - c. An oral comfrey supplement will be more effective.
 - d. Apply comfrey-containing products to the open lesions.
6. Which of the following are considered fat-soluble vitamins?
 - a. Vitamin K
 - b. Vitamin A
 - c. Vitamin D
 - d. Vitamin E
 - e. All of the above
7. Licorice is commonly used for which of the following?
 - a. Peptic ulcers
 - b. Depression
 - c. Benign Prostatic Hypertrophy (BPH)
 - d. Osteoarthritis
 - e. Diabetes
8. Which of the following has been shown to interact with medications by inhibition of cytochrome P450 3A4 in the intestinal wall?
 - a. Kava
 - b. Ginkgo
 - c. Grapefruit
 - d. St. John's wort
9. The mechanism of grapefruit's interaction with medications is through:
 - a. induction of CYP 3A4.
 - b. inhibition of CYP 3A4.
 - c. induction of CYP 2D6.
 - d. inhibition of CYP 2D6.
10. Saw palmetto is commonly taken to improve:
 - a. vasomotor symptoms associated with menopause.
 - b. sleep patterns in shift workers.
 - c. urinary symptoms associated with Benign Prostatic Hypertrophy (BPH).
 - d. mental alertness.
11. There is good evidence to suggest that which of the following is effective in treating Benign Prostatic Hyperplasia (BPH)?
 - a. Yohimbine
 - b. Valerian
 - c. Horsetail
 - d. Saw palmetto
12. Which of the following statements about black cohosh is true?
 - I. It may cause hepatotoxicity.
 - II. It is popularly used for menopausal hot flashes.
 - III. It is a strong CYP450 2C9 inducer.
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
13. Which of the following statements about yohimbine is true?
 - a. Yohimbine is used to treat impotence although there is not enough scientific evidence to form a firm conclusion in this area.
 - b. Yohimbine is used as a stimulant to increase cognition.
 - c. Yohimbine is a MAO inhibitor and should be avoided with foods containing tyramine.
 - d. a and c
 - e. None of the above
14. What are compounds produced by plants for their protection?
 - a. Botanochemicals
 - b. Phytochemicals
 - c. Phytomedicinals
 - d. Aetheroleum
15. Which of the following are examples of phytochemicals?
 - A. Flavonoids
 - B. Phytoestrogens
 - C. Tannins
 - D. All of the above
16. What phytochemicals have estrogenic activity?
 - a. Antiandrogens
 - b. Isoestrogens
 - c. Benzylic estrogens
 - d. Phytoestrogens
17. Which of the following may be used to decrease homocysteine levels?
 - I. Vitamin B₆
 - II. Vitamin B₁₂
 - III. Folic acid
 - a. I only
 - b. III only
 - c. I and II
 - d. I and III
 - e. I, II, and III

18. What is the mechanism by which glucosamine and chondroitin are suggested to treat osteoarthritis?
- Immunomodulatory
 - Anti-inflammatory
 - Analgesic
 - Production and maintenance of healthy cartilage
19. True or False: Calcium carbonate should be taken with meals to enhance absorption.
- True
 - False
20. Patients with which of the following food allergies should use caution when choosing glucosamine supplements?
- Peanut
 - Tree nuts
 - Dairy
 - Shellfish
21. Hypericum perforatum is also known as:
- bitter orange
 - hydrangea
 - St. John's wort
 - hyoscine
22. What cytochrome P450 enzyme is primarily induced by St. John's wort?
- 2C8
 - 2C9
 - 2D6
 - 3A4
23. Pyridoxine may interact with which of the following?
- Isoniazid
 - Oral contraceptives
 - Levodopa
- I only
 - III only
 - I and II
 - I and III
 - I, II, and III
24. Which of the following herbs/supplements is used for erectile dysfunction?
- Saw palmetto
 - Yohimbine
 - Kava
 - Black cohosh
 - None of the above
25. Garlic use has been reported to cause:
- bleeding
 - muscle pain
 - blurred vision
 - increased blood pressure
 - None of the above
26. True or False: The DSHEA is an organization that regulates good manufacturing practice for dietary supplements.
- True
 - False
27. Which of the following herbs is used to increase milk supply in breastfeeding women?
- Fenugreek
 - Yarrow
 - Cascara sagrada
 - Garlic
 - None of the above
28. Patients with which of the following conditions may be thiamine deficient?
- Alcoholism
 - Chronic diarrhea
 - Korsakoff psychosis
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
29. Which of the following statements is FALSE?
- DSHEA places dietary supplements under the category of food, not drugs.
 - Third-party testers like Consumer Lab test the chemical ingredients of products.
 - Each dietary supplement must have nutrition labeling with the panel title "Nutritional Facts" like other products sold on store shelves.
 - It is required that every supplement be labeled a dietary supplement.
30. What is a common herb used in sleep remedies?
- Kava
 - Hypericum
 - Valerian
 - Ginkgo
 - Ginseng
31. The mechanism by which cranberries prevent urinary tract infections (UTI) is thought to be:
- inhibition of bacterial adherence to uroepithelial cells.
 - acidifying the urine.
 - restoring the urogenital flora.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
32. Which of the following herbs is used to stimulate the immune system?
- Echinacea
 - Ginseng
 - Melatonin
 - Saw palmetto
 - All of the above
33. The use of which of the following herbs has been reported to cause liver damage?
- Kava
 - Black cohosh
 - Saw palmetto

- d. Hypericum perforatum
 - e. Both a and b
34. Which of the following is commonly used to support mental energy?
- a. Ginseng
 - b. Melatonin
 - c. Echinacea
 - d. Grapefruit
 - e. Garlic
35. Which of the following is a common side effect of St. John's wort?
- a. Photosensitivity
 - b. Diarrhea
 - c. Breath odor
 - d. Heartburn
 - e. Hepatotoxicity
36. For what may feverfew be used?
- a. Diabetes
 - b. Common cold
 - c. Migraine prevention
 - d. Depression
 - e. None of the above
37. All of the following statements are true about the Dietary Supplement Health and Education Act of 1994 (DSHEA) EXCEPT:
- a. Dietary supplements must undergo FDA approval after clinical studies to determine effectiveness and safety.
 - b. The manufacturer is responsible for safety evaluation.
 - c. Authorized use of FDA approved health claims on label.
 - d. Products must be labelled as "Dietary Supplements".
38. Which of the following is considered a mineral supplement?
- I. Biotin
 - II. Choline
 - III. Calcium
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
39. Which of the following products contains calcium?
- I. Tums EX
 - II. VIActiv
 - III. Os-Cal
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
40. True or False: Ferrous salts are more efficiently absorbed than ferric salts.
- a. True
 - b. False
41. Which of the following products does NOT contain vitamin K?
- I. Centrum®
 - II. Centrum Silver®
 - III. Unicap® Senior Multivitamin
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
42. Topical capsicum may be used for which of the following?
- a. Neuropathic pain
 - b. Shingles
 - c. Osteoarthritis
 - d. All of the above
43. Which of the following statements about ephedra is true?
- I. It is used for weight loss.
 - II. It may interact with MAOI.
 - III. It was removed from the market by the FDA due to safety concerns.
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
44. True or False: Iodine is used to synthesize thyroxine (T₄) and triiodothyronine (T₃).
- a. True
 - b. False
45. Chasteberry is commonly used for:
- a. Premenstrual syndrome (PMS)
 - b. blood pressure
 - c. tinnitus
 - d. migraine
 - e. None of the above
46. Which of the following herbs will likely cause drowsiness?
- a. Yohimbine
 - b. Valerian
 - c. Ma huang
 - d. Guarana
 - e. Kola nut
47. Which of the following herbs is commonly found in teas?
- a. Garlic
 - b. Ginkgo
 - c. Capsicum
 - d. Chamomile
 - e. None of the above

48. Which of the following common cold products contain(s) zinc?

- I. Airborne[®]
- II. Zicam[®]
- III. Cold-eeze[®]

- a. I only
- b. III only
- c. I and II
- d. II and III
- e. I, II, and III

49. Which of the following may cause discoloration of skin or urine?

- a. Pyridoxine
- b. Riboflavin
- c. Thiamine
- d. Cyanocobalamin
- e. None of the above

Laboratory Tests

8

CHAPTER

I. Introduction

Laboratory tests are an essential tool in clinical medicine. They are used to help identify, diagnose, or confirm a disease or health problem. They are also used for differential diagnosis, to stage disease, and to monitor disease progression or responsiveness to a given treatment. Laboratory testing is most beneficial when the test influences a course of treatment or decision making with regard to a patient's health.

A. Laboratory tests are of two main types:

1. Screening tests: used in patients with no active symptoms or signs of a health problem or disease, usually for purposes of early detection or mitigation of health risk factors for serious disease.
2. Diagnostic tests: used to analyze an abnormal screening test or to establish additional information in patients with signs and symptoms of a health problem or disease.

B. It is important for the pharmacist to have a strong knowledge of the more common laboratory tests used to guide patient diagnosis and treatment. Pharmacists are likely to review laboratory tests to assess the efficacy and the safety of medications. They may recommend testing when necessary or may be called to help interpret the results obtained from such tests. A pharmacist may be asked to help a patient understand the results of a particular test.

II. The International System of Units (SI), Conventional Units of Measure, and the Reporting of Laboratory Results

A. Around the world, laboratory tests are reported in the SI units, which are based on standard metric measurements. The United States has yet to fully adopt this system, and laboratories typically report results in traditional, customary units as well as the SI units. The reporting of both types of units typically aids communication among health care professionals of different training backgrounds or nationalities.

B. "Normal" laboratory results usually fall within a reference range of values determined by taking the usual measurements of that test found within a set and defined population of healthy individuals. For qualitative tests, results are often reported as either positive or negative for a specific finding. Quantitative tests are usually reported in terms of a reference range. For most tests, the reference range is statistically determined by the mean value plus two standard deviations. Values that fall out of the reference range or expected result are sometimes labeled "abnormal." A value that falls outside an accepted range does not necessarily indicate the need for treatment or a need to make the value "normal." An "abnormal" result requires interpretation in the context of the patient's demographics, overall health status, medical examination findings, symptoms, timing and conditions of the test, and other relevant factors. A test may not produce results consistent with the results expected, and a repeat test may be needed to rule out errors in collection or processing of the test.

III. The Most Common Laboratory Tests Pharmacists Should Know (Tables 8-1 through 8-6)

- A. The following sections will provide a brief synopsis and review of laboratory testing familiar to the pharmacist, including the common medical reasons the tests are monitored. The lists are not inclusive, but are representative of the tests pharmacists are most likely to encounter in their general clinical practices.
- B. For greater details regarding how the test is used, please refer to the specific therapeutic chapter in this review. For example, a more complete discussion of the use of HbA1c for the monitoring of diabetes mellitus would be found in the chapter discussing diabetes treatments.
- C. Ranges are given in conventional reporting units in the United States.

Table 8-1 Electrolytes and Minerals/Acid Base; Common Serum Enzymes

Substance	Reference Range (Typical Adult Range)	Comments	Commonly Used to Detect
Sodium	135–146 mEq/L		Hypo- or hypernatremia, aid in determining osmolality
Potassium	3.5–5.3 mEq/L		Hypo- or hyperkalemia; monitoring renal function; effects of medications
Chloride	98–110 mEq/L		Acid-base balance (e.g., from vomiting, diarrhea)
Bicarbonate (venous)	22–33 mEq/L		Acid-base balance
Magnesium	1.6–2.6 mg/dL		Hypo- or hypermagnesemia; hypomagnesemia is more common
Calcium	8.6–10.2 mg/dL		Hypo- or hypercalcemia; renal osteodystrophy; metastatic malignancy; parathyroid hormone (PTH) abnormalities
Phosphorous	2.4–4.4 mg/dL		Hypo- or hyperphosphatemia; renal insufficiency
Uric acid	2.6–6 mg/dL		Gout or hyperuricemia due to medications (e.g., cytolytic chemotherapies)
Low-density lipoprotein (LDL) cholesterol	<130 mg/dL	<100 is better for many adults to reduce heart disease risk	Hypercholesterolemia and heart disease risk
High-density lipoprotein (HDL) cholesterol	≥46 mg/dL		Hypercholesterolemia and heart disease risk
Total cholesterol	<200 mg/dL		Hypercholesterolemia and heart disease risk
Alkaline phosphatase (ALP)	33–115 units/L	Produced by liver and bones	Increase in osteoblastic activity (e.g., Paget disease); biliary obstruction
Creatinine kinase (CK)	20–200 units/L	Isoenzymes of CK found primarily in heart, brain, and skeletal muscle; elevations indicate tissue damage	Acute myocardial infarction
Lactate dehydrogenase (LDH)	100–200 units/L	Isoenzymes found primarily in heart, lungs, liver, and skeletal muscle	Pattern of elevations to help in diagnosis of myocardial infarction, liver or lung disease

Table 8-2 Renal Tests

Test	Reference Range (Typical Adult Range)	Comments	Commonly Used To Detect
Serum creatinine (SCr)	0.5–1.2 mg/dL	Decreased muscle mass in elderly may give “low” result and may be misleading; creatinine clearance (CrCl) should be calculated or estimated to more reliably estimate renal function	Elevated in renal impairment, indicating decreased glomerular filtration rate (GFR)
Blood urea nitrogen (BUN)	6–25 mg/dL		Decreased when liver disease is significant; increased with dehydration, overdiuresis, decreased renal function, protein intake
Creatinine clearance (CrCl)	59–137 mL/min/ 1.73 m ²	Estimates GFR Can be measured formally by 24-hour urine collection; most commonly calculated using Cockcroft-Gault method to estimate, using SCr, ideal body weight, and age; renal dosing of medications is primarily based on adjustments according to CrCl	Lowered CrCl indicates a decline in renal function
BUN:SCr ratio	6–22		When elevated, commonly indicates dehydration or overdiuresis
Modified diet in renal disease (MDRD) estimation of GFR	≥60 mL/min/ 1.73 m ²	Another way to validate GFR; has not been used to determine drug dosing	Used to determine staging of renal disease; the calculation is now commonly reported as part of a laboratory panel

Table 8-3 Urinalysis

Test	Reference Range (Typical Adult Range)	Comments	Commonly Used To Detect
Appearance or color	Clear, yellow (pale to gold)		Dark brown color may indicate excretion of bilirubin; other colors (e.g., red) may indicate blood or drug effect
pH	4.5–8		Alkaline pH may indicate alkalosis, use of carbonic anhydrase inhibitor, or infection by certain bacteria (e.g., <i>Proteus</i> sp)
Specific gravity	1.002–1.030	Indicates solute particles in urine	Increased with diabetes mellitus or nephrosis; decreased with diabetes insipidus; may indicate loss of kidneys' ability to dilute or concentrate urine

Continued

Table 8-3 Urinalysis—cont'd

Test	Reference Range (Typical Adult Range)	Comments	Commonly Used To Detect
Protein	1–14 mg/dL	Most proteins do NOT filter if the person is healthy	Proteinuria may indicate renal disease or diabetic nephropathy; urinary tract infection; specific proteins may indicate certain diseases. Albuminuria may indicate abnormal glomerular function
Glucose	Negative		Positive result occurs most commonly in diabetes mellitus
Ketones	Negative		Positive result occurs most commonly in uncontrolled diabetes mellitus; may also occur with starvation or low-carbohydrate diets
Microscopic evaluation	Negative to very few WBC or RBC, no crystals and only an occasional cast, no to few bacteria	Looks for crystals, red blood cells, protein casts from renal tubules, bacteria; urine collection, if not done properly, can contaminate the sample	Presence of specific elements indicates infection, trauma, kidney stones, etc.

Table 8-4 Hepatic Tests

Substance	Reference Range (Typical Adult Range)	Comments	Commonly Used To Detect
Aspartate aminotransferase (AST)	10–30 units/L		Elevated in acute hepatitis; milder elevations in cirrhosis, fatty liver, or acute congestion caused by heart failure
Alanine aminotransferase (ALT)	6–40 units/L		Elevated in liver dysfunction, hepatitis, cirrhosis, etc.
Albumin	3.6–5.1 g/dL	Decreased production in liver disease; important as a transport agent; maintains osmotic pressure	Nutritional status; liver function; useful in therapeutic drug monitoring (e.g., phenytoin monitoring)
Total serum protein	6.2–8.3 g/dL	Measures albumin plus globulins	Nutritional status and liver function
Serum bilirubin (total bilirubin)	0.2–1.2 mg/dL	Clinical result of increased bilirubin is jaundice	Without an associated increase in direct bilirubin, elevation may indicate hemolysis; also increased with biliary obstruction or liver disease
Direct bilirubin	<0.2 mg/dL	Conjugated form of bilirubin	Elevated in biliary obstruction or liver necrosis
Ammonia	10–80 mcg/dL	A by-product of protein metabolism that is removed by the liver	Elevated in hepatic encephalopathy/ hepatic failure

Table 8-5 Hematologic Tests

Substance	Reference Range (Typical Adult Range)	Comments	Commonly Used To Detect
Red blood cell (RBC) count	3.5–5.9 million/mm ³		Anemia, hydration status, blood volume
Hemoglobin (Hb)	12–18 g/dL	Estimates RBC oxygen-carrying capacity/function	Low values mean anemia
Hematocrit (Hct)	37%–52%	Numerically usually three times the Hb value; also called the packed cell volume; measures the percentage by volume of RBC in whole blood after use of centrifuge	Low Hct = anemia, overhydrated, blood loss/bleeding High Hct = dehydration or unusual blood conditions
Mean corpuscular volume (MCV)	80–100	Ratio of the Hct to the RBC count	Low MCV = microcytic anemia (e.g., iron deficiency) High MCV = macrocytic anemia (e.g., folate or vitamin B ₁₂ deficiency)
Reticulocyte count	0.1%–2.4% of the total RBC count	Immature RBC; helps quantify bone marrow production of RBC	Percentage is decreased with aplastic anemia Increased in response to acute blood loss, hemolysis, or treatments for anemia
Erythrocyte sedimentation rate (ESR)	0–30 mm/hr	Measures the rate at which RBC settle in uncoagulated blood over time; alterations in plasma proteins alter the ESR	Increases with inflammation such as infection, tissue infarction (e.g., myocardial infarction), rheumatoid or collagen diseases
WBC count	4000–11,000/mm ³		Increased values usually mean infection; leukemia and administration of corticosteroids can cause a WBC increase too
WBC differential	See below for specific components of differential	Distribution and morphology of the WBC count consisting of neutrophils, lymphocytes, monocytes, eosinophils, basophils	Changes in the normal distribution can indicate certain disease, environmental, or inflammatory responses
Neutrophils	60% PML 3% bands	Phagocytic cells (mature neutrophils) are polymorphonuclear leukocytes (PML) (“segs”) Immature neutrophils are called bands (“stabs”)	When an increase in WBC occurs with an increase in the percentage of bands, this is called a “left shift”; bandemia often occurs in systemic bacterial infection; can also occur with certain viruses, fungi, and serious stress such as acute trauma with hemorrhage. Inflammatory responses and leukemia may also cause leukocytosis Neutropenia may be caused by chemotherapy, drug reactions, overwhelming infections
Lymphocytes	30%	Produce antibodies and important in immune activity	Increased counts occur with viral infections; decreased counts occur with immunodeficiency, such as AIDS; atypical lymphocytes appear during infectious mononucleosis

Continued

Table 8-5 Hematologic Tests—cont'd

Substance	Reference Range (Typical Adult Range)	Comments	Commonly Used To Detect
Monocytes	4%	Phagocytic cells	May be increased during certain infections, such as tuberculosis or endocarditis
Eosinophils	2%	Play a part in immune reactions	Increased in acute allergy (pollen, drug, asthma) and in some parasitic infections
Basophils	1%	Also called mast cells; complete function not understood	Increased counts may occur in chronic myelogenous leukemia (CML)
Platelet count	150,000–300,000/ mm ³	Formed elements in the blood, vital to blood clotting	Thrombocytopenia is notable when counts are <100,000/mm ³ and severe if <50,000/mm ³

Table 8-6 Endocrine Tests

Substance	Reference Range (Typical Adult Range)	Comments	Commonly Used to Detect
Glucose (2-hour postprandial)	80–140 mg/dL		High result indicates glucose intolerance and diabetes. Used after glucose tolerance test in pregnancy and to self-monitor diabetes at home
Fasting glucose	70–100 mg/dL		High result indicates impaired glucose tolerance or diabetes. Most commonly used test for diagnosing diabetes mellitus (value >200) or prediabetes (impaired glucose tolerance, value >110 in nonpregnant or >125 if pregnant); also used to self-monitor diabetes at home
HbA1c	4%–6%	For patients with known diabetes, a “good” result is usually 7%; in some patients, a HbA1c up to 7.5% may be acceptable. Trying to achieve “normal” levels may increase risk of hypoglycemia.	Reflects average glucose level over previous 2 to 3 months, a good indicator of glycemic control Percentage of HbA1c found to correlate with average blood glucose concentrations; a result of >7% correlates with mean plasma glucose >200 mg/dL
Thyroid stimulating hormone (TSH)		Low result indicates hyperthyroid status; high result indicates hypothyroid status	Most common test to screen for hypo- or hypothyroidism; may be used in conjunction with free thyroxine (T ₄) or other thyroid function tests; also used to monitor the effectiveness of thyroid treatment regimens or replacement hormones

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REVIEW QUESTIONS

(Answers and Rationales on page 337.)

- A clinical coordinator at the local hospital is looking for appropriateness of tobramycin therapy in her institution via drug utilization review (DUR). In addition to the serum drug concentration trends in the reviewed patient records, what other laboratory tests would be helpful?

 - Serum creatinine
 - Alkaline phosphatase
 - AST/ALT
 - Cultures and sensitivities
 - I and II only
 - I and IV only
 - II and III only
 - All of the above
- A 56-year-old man with type 2 diabetes mellitus goes to the pharmacy to refill prescriptions after his 6 month physician visit. He is grumbling about taking his medications and explains that his "A1c" was "too high." Now he has to take an additional medication. He asks the pharmacist "What is so important about that A1c anyway?" What is the best response?

 - Glucose in the urine indicates poor diabetes control.
 - Poorly controlled diabetes can result in eye, kidney, and vascular problems over time.
 - The HbA1c gives the doctor an indication of blood glucose control over several months, and if this test can be maintained at HbA1c value of 7% or lower, the complications of diabetes (eye, kidney, neuropathy, vascular) can be minimized.
 - It is important to prevent hypoglycemia.
- A young woman presents to the emergency department with fever, pain in her chest, and a purulent cough. She is a poor historian of health problems. She has a small cut on her lower leg that is red but not oozing. There are decreased breath sounds at the base of the right lung. A chest x-ray result is pending. Her white blood cell (WBC) differential reveals:

WBC count: 15,600
 PML neutrophils: 80%
 Bands: 6%
 Lymphocytes: 11%
 Monocytes: 1%
 Eosinophils: 1%
 Basophils: 1%

What is the most likely explanation for this WBC panel?

 - Bacterial infection of lung or blood
 - Neutropenia
 - A localized infection of the leg tissue
 - Acute allergic reaction to pollen
- Which of the following laboratory tests would be helpful in the diagnosis of myocardial infarction?

 - Hematocrit
 - Creatine kinase (CK)
 - Lactate dehydrogenase (LDH)
 - Albumin
 - Alkaline phosphatase
 - I and IV
 - II and V
 - II and III
 - II and IV
 - All of the above
- A 35-year-old woman has been maintained on 50 mcg per day of levothyroxine, with a normal TSH of 2 mIU/L; she is monitored every 6 months and has been stable for several years on this dosage. Recently, she is complaining of weight gain, fatigue, hair loss, and sensitivity to cold. A check of her TSH reveals a result of 10 mIU/L. She appears to have no other symptoms or findings on exam. A careful review of medications and recent changes in health habits reveals that she is now taking a multivitamin with minerals every morning, which she began 2 months ago. What is the best approach at this time?

 - The patient is now hyperthyroid and needs further testing.
 - Increase the dose of levothyroxine and recheck in 6 months.
 - Separate the administration of levothyroxine from the multivitamin with minerals by at least several hours and recheck the TSH in 1 month.
 - Try another brand of levothyroxine.

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Antiinfective Agents

9

CHAPTER

- I. Diagnosis
 - A. Identify the organism
 1. Gram stain differentiates bacteria based on structure and composition of the layers of the cell wall.
 - a) Gram positive = purple stain
 - b) Gram negative = pink stain
 2. Culture and sensitivity; serologic testing
 - B. Laboratory tests
 1. Nonspecific tests: white blood cell count with differential
- II. Initial treatment strategies
 - A. Empiric
 1. Empiric therapy must be initiated without delay.
 2. Empiric therapy is based on likely pathogens suspected but not specifically known.
 3. Empiric therapy is altered to more specific therapies based on culture and sensitivity and patient's disease state.
 - B. Definitive
 1. Microbiologic or serologic diagnosis with susceptibilities known
 - C. Prophylaxis
 1. Before surgery or procedure
 2. Immunocompromised patients
- III. Common infections
 - A. Bacteria
 - Classification
 - Gram-positive cocci (spherical)
 - *Staphylococcus aureus*
 - *Streptococcus pneumoniae*
 - *Enterococcus faecalis*, *Enterococcus faecium*
 - Gram-positive bacilli (rods)
 - *Clostridium perfringens*, *Clostridium difficile*
 - Gram-negative cocci (spherical)
 - *Neisseria meningitidis*, *Neisseria gonorrhoeae*
 - *Moraxella catarrhalis*
 - Gram-negative bacilli (rods)
 - *Escherichia coli*
 - *Klebsiella* spp.
 - *Enterobacter* spp.
 - *Pseudomonas aeruginosa*
 - *Bacteroides fragilis*
 - Atypical bacteria
 - *Chlamydia pneumoniae*
 - *Mycobacteria pneumoniae*
 - *Legionella* spp.
 - B. Fungal
 1. Superficial
 - Vulvovaginal candidiasis
 - Major pathogen: *Candida albicans*
 - Oropharyngeal and esophageal candidiasis
 - Major pathogen: *Candida albicans*
 - Mycotic infections of hair, skin, and nails
 - Tinea pedis ("athlete's foot")
 - Tinea cruris ("jock itch")
 - Tinea corporis ("ring worm")
 - Tinea capitis
 - Pityriasis versicolor
 - Onychomycosis
 2. Invasive
 - Candida
 - Caused by *Candida* spp. (*C. albicans*, *C. glabrata*, *C. tropicalis*, *C. krusei*)
 - Aspergillosis
 - Caused by *Aspergillus* spp.
 - Histoplasmosis
 - Caused by *H. capsulatum*
 - Cryptococcus
 - Caused by *C. neoformans*
 - Blastomycosis
 - Caused by *B. dermatitidis*
 - Coccidiomycosis
 - Caused by *C. immitis*
 - C. Virus
 - Types of virus that cause human infection:
 - Influenza virus
 - Cytomegalovirus (CMV)
 - Varicella zoster virus (chickenpox, shingles)
 - SARS coronavirus (severe acute respiratory syndrome [SARS])
 - Herpes simplex (HSV-1 and HSV-2)
 - Respiratory syncytial virus (RSV)
 - Adenovirus
 - Epstein-Barr virus (EBV)
 - Human immunodeficiency virus (HIV)
 - Hepatitis A, B, C, or others

Table 9-1 General Antibiotic Classes Used for Major Organism Categories

Gram positive	Penicillin, nafcillin or oxacillin First generation cephalosporins Macrolides Vancomycin
Gram negative	Extended penicillins or imipenem Second and third generation cephalosporins Quinolones Aminoglycosides
Anaerobes	Metronidazole Clindamycin

IV. Antimicrobial treatment (Table 9-1)

A. Penicillins

1. Mechanism of action (MOA): inhibits synthesis of bacterial cell walls; bactericidal
2. Penicillins are classified as β -lactam antibiotics because their structure consists of a β -lactam ring that joins to a thiazolidine ring
3. Highly active against gram-positive cocci (e.g., *Streptococcus*), gram-positive rods (e.g., *Listeria*), and gram-negative cocci (e.g., *Neisseria*)
 - a) Antistaphylococcal penicillins: nafcillin, oxacillin, cloxacillin, dicloxacillin
 - b) Broad-spectrum penicillins
 - (1) Second-generation (amoxicillin, ampicillin): active against most strains of *Escherichia coli*, *Proteus mirabilis*, *Salmonella* sp, *Shigella* sp, and *Haemophilus influenzae*
 - (2) Third- and fourth-generation (carbenicillin, ticarcillin, piperacillin, mezlocillin, azlocillin): *Pseudomonas aeruginosa* and indole-positive *Proteus* spp, *Enterobacter* spp
4. Adverse effects: anaphylaxis, interstitial nephritis, anemia, leukopenia, hepatitis (oxacillin and nafcillin)

B. β -lactamase inhibitors

1. Exhibit no or minimal antibacterial activity of their own
2. Used in combination products with certain penicillins to allow coverage of β -lactamase-producing organisms that would ordinarily not be covered by the particular penicillin (extends antimicrobial spectrum)
3. All agents are irreversible inhibitors of β -lactamases
4. Examples: clavulanic acid, sulbactam, tazobactam
 - a) Amoxicillin/clavulanic acid (Augmentin[®])
 - b) Ticarcillin/clavulanic acid (Timentin[®])
 - c) Ampicillin/sulbactam (Unasyn[®])
 - d) Piperacillin/tazobactam (Zosyn[®])

C. Cephalosporins (Table 9-2)

1. Mechanism of action (MOA): same as penicillins

Table 9-2 Cephalosporins

Generation	Drug name	Route
First	Cefazolin (Ancef, Kefzol)	IM, IV
	Cephalexin (Keflex, Keftab)	PO
	Cefadroxil (Duricef, Ultracef)	PO
Second	Cephadrine (Velosef)*	PO, IM, IV
	Cephapirin (Cefadyl)*	IM, IV
	Cefuroxime (Ceftin, Kefurox, Zinacef)	PO, IM, IV
	Cefoxitin (Mefoxin)	IM, IV
	Cefotetan (Cefotan)	IM, IV
	Cefprozil (Cefzil)	PO
	Cefaclor (Ceclor)	PO
	Loracarbef (Lorabid)	PO
	Cefdinir (Omnicef)	PO
	Ceftriaxone (Rocephin)	IM, IV
Third	Cefotaxime (Claforan)	IM, IV
	Ceftizoxime (Ceftizox)*	IM, IV
	Cefoperazone (Cefobid)*	IM, IV
	Cefixime (Suprax)	PO
Fourth	Ceftazidime (Fortaz, Tazicef, Tazidime)	IM, IV
	Cefepime (Maxipime)	IM, IV

*Discontinued from US market.

2. Also β -lactam antibiotics, but composed of a dihydrothiazine and a β -lactam ring
3. In general, each successive generation has broader gram-negative coverage.
4. First generation (cefazolin, cephadrine, cefadroxil, cephalexin, cephapirin): activity against staphylococci, streptococci, and community-acquired *Escherichia coli*, *Klebsiella*, and *Proteus* spp
5. Second generation (cefuroxime, cefoxitin, cefotetan, cefprozil, cefaclor, loracarbef): expanded coverage against enteric gram-negative rods
 - a) cefuroxime: useful against *Haemophilus influenzae*
 - b) cefoxitin, cefotetan: useful against *Bacteroides* spp
6. Third generation (ceftriaxone, cefotaxime, cefdinir, ceftizoxime, cefoperazone, cefixime, ceftazidime): broadest coverage for enteric, aerobic gram-negative rods, and retain good activity against streptococci other than enterococci; moderate anaerobic activity (not *B. fragilis*)
 - a) ceftazidime: useful against *Pseudomonas aeruginosa*
7. Fourth generation (cefepime): excellent aerobic gram-negative rod coverage including *P. aeruginosa*; aerobic and gram-positive coverage is similar to third generation
 - a) Used as empiric therapy for febrile patients with neutropenia

8. Adverse effects: anaphylaxis, interstitial nephritis, anemia, leukopenia
 - a) Patients should be asked about allergy to penicillins
 - D. Carbapenems
 1. Mechanism of action (MOA): interferes with cell-wall synthesis similar to penicillins and cephalosporins; bactericidal
 2. Active against most gram-positive and gram-negative bacteria including anaerobes
 - a) Unlike imipenem and meropenem, ertapenem is not effective against *Pseudomonas* and *Enterobacter*
 3. Useful for Fournier's gangrene, intra-abdominal infection
 - a) Do not use for CNS infections due to seizure risk
 4. Examples: imipenem, meropenem (Merrem®), ertapenem (Invanz®), doripenem (Doribax®)
 - a) Imipenem/cilastatin (Primaxin®): used IV and IM only; combined with cilastatin because the action of dehydropeptidase enzymes on imipenem rapidly produces a nephrotoxic and inactive metabolite; cilastatin prevents dehydropeptidase degradation
 5. Adverse effects: precipitate seizure activity or confusion particularly in elderly patients or those with seizure disorders; adjust dose in patients with renal impairment because risk is higher with high-dose exposure
 - a) Meropenem has a lower risk of seizures than imipenem
 - E. Monobactams (Aztreonam)
 1. Mechanism of action (MOA): interacts with penicillin binding proteins; induces formation of long filamentous bacteria; β -lactam ring is isolated; bacteriocidal
 2. Excellent activity against gram-negative aerobes including *Pseudomonas aeruginosa*; no activity against gram-positive aerobes; inactive against all anaerobes
 3. Should be reserved for serious gram-negative infections in the lung, bone, urinary tract, or blood
 4. Rarely exhibits cross-sensitivity with agents from other classes of β -lactam antibiotics
 5. Adverse effects: injection site reactions, nausea, vomiting, diarrhea, rash
 - F. Gram-positive antibiotics
 1. Vancomycin (Vancocin®, Vancoled®)
 - a) Mechanism of action (MOA): glycopeptides; binds a D-alanyl-D-alanine precursor that is critical for peptidoglycan crosslinking in most gram-positive bacterial cell walls; bacteriostatic for enterococci; bactericidal against other susceptible isolates
 - b) Active against staphylococci including methicillin-resistant staphylococcus aureus (MRSA), enterococci, streptococci, and *Clostridium* including *C. difficile* (when given orally)
 - (1) Drug of choice for MRSA/MRSE
 - (2) Enterococci may be vancomycin-resistant (e.g., vancomycin-resistant enterococci, also known as VRE)
 - c) Acts synergistically with aminoglycosides against susceptible enterococci
 - d) Usual adult intravenous dose: 1 g over 60 minutes every 12 hours
 - (1) Give by slow IV infusion
 - (2) Adjust dose for patients with renal impairment and in patients older than 65 years
 - (3) Monitor serum levels and adjust dose accordingly
 - (a) Therapeutic concentrations: peak 20–40 mg/L; trough 5–15 mg/L
 - e) Adverse effects
 - (1) Red man syndrome (flushing of the upper body) if given at infusion rates greater than 10 mg/min. Slow infusion over at least 1 hour is recommended to avoid this side effect.
 - (2) Nephrotoxicity and ototoxicity (often permanent): may be increased when used in combination with aminoglycosides
 2. Linezolid (Zyvox®)
 - a) Mechanism of action (MOA): interrupts bacterial growth by inhibiting the initiation of protein synthesis
 - b) Activity against gram-positive infections including certain drug-resistant enterococcus, staphylococcus (MRSA), and pneumococcus strains
 - c) IV and PO forms available
 - d) Adverse effects: myelosuppression (infrequent), thrombocytopenia, and hypertension (particularly with tyramine-containing foods)
 - e) Drug interactions: Avoid use with SSRIs due to risk of serotonin syndrome
 3. Quinupristin-dalfopristin (Synercid®)
 - a) Mechanism of action (MOA): dalfopristin blocks early step in protein synthesis; quinupristin blocks a later step; combination is synergistic; bactericidal
 - b) Active against antibiotic-resistant gram-positive organisms, particularly vancomycin-resistant *Enterococcus faecium* (VRE)
 - c) Adverse effects: reversible arthralgias, myalgias, and peripheral venous irritation
 - d) Drug interactions: significantly inhibits the cytochrome P-450 (CYP) 3A4 enzyme system
 4. Others: Daptomycin (Cubicin®)
- G. Fluoroquinolones
 1. Mechanism of action (MOA): inhibit bacterial DNA gyrase and topoisomerase, which are critical for DNA replication; bactericidal
 2. Variable gram-positive activity; extensive gram-negative activity; poor anaerobic coverage; variable atypical activity; all have high activity against *Legionella*; some are effective against anthrax
 - a) First generation (quinolones, nalidixic acid [NegGram®]): useful for UTI caused by gram-negative rods
 - b) Second generation (fluoroquinolones, ciprofloxacin [Cipro®], norfloxacin

- [Noroxin®], enoxacin [Penetrex®]*, ofloxacin [Floxin®]: active against gram-negative aerobes; ciprofloxacin most active against *P. aeruginosa*
- (1) Poor activity against gram-positive cocci and anaerobes
- c) Third generation (levofloxacin [Levaquin®], sparfloxacin [Zagam®]*, gatifloxacin [Tequin®]*, grepafloxacin [Raxar®]*): improved coverage of aerobic gram-positive bacteria including streptococci, staphylococci, and enterococci; less activity against gram-negative bacteria than ciprofloxacin; expanded activity against atypical pathogens
- d) Fourth generation (trovafloxacin [Trovan®]*, moxifloxacin [Avelox®]): same as third generation plus broad anaerobic coverage
3. Adverse effects: nausea, CNS disturbances, rash, phototoxicity, QTc prolongation
- a) Increased risk of developing tendinitis and tendon rupture (class effect)
- b) A longer course of treatment (more than 7 days) of gemifloxacin (Factive®) associated with serious rash, especially in post-menopausal women on hormone replacement therapy and in patients younger than 40 years.
- c) Many drugs in class no longer available*:
- (1) Grepafloxacin* withdrawn from the United States market by the manufacturer due to adverse cardiovascular events (QT prolongation)
- (2) Sparfloxacin* withdrawn due to lack of sales
- (3) Trovafloxacin* withdrawn due to risk of hepatic toxicity
- (4) Gatifloxacin* withdrawn because of an increased incidence of hypoglycemia and hyperglycemia
4. Drug interactions
- a) Antacids, calcium, mineral supplements (divalent cations), sucralfate, and select foods may impair the absorption of oral quinolones.
- b) Cimetidine and probenecid can inhibit renal tubular secretion of fluoroquinolones that are primarily eliminated through renal excretion (except trovafloxacin).
- c) Fluorquinolones can inhibit clearance of xanthine derivatives (e.g., theophylline).
- d) Some fluoroquinolones can raise cyclosporine levels (e.g., ciprofloxacin)
- e) Increase effect of warfarin
- H. Macrolides
1. Mechanism of action (MOA): inhibits protein by binding to 50S subunit of the bacterial ribosome; bacteriostatic
2. Examples: erythromycin (E-Mycin®, Ery-Tab®, Eryc®, Erythrocin® stearate, Ilosone®, Eryped®, EES®, Emgel®), dirithromycin (Dynabac®), clarithromycin (Biaxin®), azithromycin (Zithromax®), telithromycin (Ketek®)
3. Extensive gram-positive activity; drugs of choice for treating *Legionella*, *Chlamydia*, and *Mycoplasma* infections
- a) Azithromycin: more effective against *H. influenzae*, *Legionella* and *Toxoplasma gondii* than erythromycin; effective against mycobacterium avium-intercellulare complex (MAC); longer half-life than erythromycin
- b) Clarithromycin: more effective against *H. influenzae* than erythromycin; also effective against MAC; used with other drug for *Helicobacter pylori*; also useful in Lyme disease; renally eliminated
4. Adverse effects: GI disturbances (nausea, abdominal cramping), abnormalities in liver function tests (LFTs)
5. Drug interactions: metabolized by CYP3A4 (exception of azithromycin); erythromycin and clarithromycin are strong inhibitors of CYP3A4.
- I. Tetracyclines
1. Mechanism of action (MOA): binds to 30S ribosomal subunit blocking protein synthesis; bacteriostatic
2. May be used to treat *Rickettsia* (Rocky Mountain spotted fever), *Chlamydia*, *Mycoplasma*, and *Spirochete* infections (Lyme disease, syphilis); may be effective against anthrax; used for acne and rosacea
- a) Minocycline and doxycycline are more lipid soluble than other tetracycline antibiotics
3. Examples: tetracycline (Sumycin®, Panmycin®, Tetracycl®), doxycycline (Vibramycin®, Doryx®), minocycline (Minocin®)
4. Adverse effects: nausea, photosensitivity; tooth enamel discoloration in children, QTc prolongation
5. Drug interactions
- a) Concomitant administration of iron supplements or antacids may impair the oral absorption of tetracyclines.
- b) Tetracyclines (particularly doxycycline) may be less effective in patients receiving anticonvulsants like phenytoin and carbamazepine due to induction of hepatic microsomal enzymes.
- c) Tetracyclines may reduce the efficacy of oral contraceptives.
- d) Tetracyclines may enhance the anticoagulant effect of warfarin.
- J. Sulfonamides
1. Mechanism of action (MOA): inhibits folic acid metabolism by competitively inhibiting *p*-aminobenzoic acid (PABA) utilization; bacteriostatic
2. Commonly used for uncomplicated UTI, sinusitis, and otitis media
3. Adverse effects
- a) Hemolytic anemia in glucose-6-phosphate dehydrogenase (G6PDH) deficient patients
- b) Allergy (ask patient if allergic to sulfa drugs)
- c) Rash includes Stevens-Johnson syndrome
- d) Kernicterus in newborns

4. Examples
 - a) Silver sulfadiazine (topical)
 - b) Sulfadiazine
 - c) Sulfisoxazole
 - d) Sulfamethoxazole (SMZ)
 - e) Sulfacetamide
 - K. Trimethoprim (TMP; Proloprim®)
 1. Mechanism of action (MOA): competes with PABA for incorporation into the pteridine precursor molecule that leads to inhibition of dehydropteroate synthetase enzyme
 - L. SMZ/TMP (Bactrim®, Septra®)
 1. There is an increased risk of resistance when sulfonamide antibiotics are used alone.
 2. Used for *Nocardia* (rare pulmonary infection), *Chlamydia trachomatis*, uncomplicated UTI, burns, *Pneumocystis pneumonia* (PCP)
 3. Adverse effects
 - a) Rash includes Stevens-Johnson syndrome
 - b) Leukopenia
 - c) Granulocytopenia
 - d) Megaloblastic anemia
 - e) Thrombocytopenia
 - M. Aminoglycosides
 1. Mechanism of action (MOA): binds to bacterial ribosome causing misreading during translation of bacterial messenger RNA into proteins; bactericidal
 2. Active against aerobic, gram-negative bacteria; also active against staphylococci and certain mycobacteria. Good activity against *Pseudomonas* spp.
 3. Examples: gentamicin (Garamycin®), tobramycin (Nebcin®), amikacin (Amikin®), kanamycin (Kantrex®), neomycin (Mycifradin®), streptomycin
 4. Adverse effects: nephrotoxicity, ototoxicity, neuromuscular blockade (rare)
 5. Drug interactions: aminoglycosides must be used with extreme caution with other drugs that may cause nephrotoxicity
 - N. Miscellaneous
 1. Chloramphenicol (Chloromycetin®)
 - a) Mechanism of action (MOA): binds to 50S ribosomal subunit blocking protein synthesis; bacteriostatic
 - b) Broad activity against aerobic and anaerobic gram-positive and gram-negative bacteria including *S aureus*, enterococci, and enteric gram-negative rods; also has activity against *Rickettsia*, *Chlamydia*, *Mycoplasma*, and *Spirochetes*
 - c) Adverse effects: aplastic anemia and dose-related bone marrow suppression; gray baby syndrome
 - d) Drug interactions: inhibitory effect on CYP2C19, CYP3A4, and, to a lesser extent, CYP2D6
 2. Metronidazole (Flagyl®)
 - a) Mechanism of action (MOA): inhibits bacterial nucleic acid synthesis; bactericidal
 - b) Greater activity against gram-negative than gram-positive anaerobes but active against *Clostridium perfringens* and *Clostridium difficile*; also effective against amebae and protozoa
 - c) Adverse effects: nausea, headache, restlessness, disulfiram-like reactions to alcohol, seizures (rare), peripheral neuropathy (rare)
 - (1) To be used cautiously in patients with hepatic function impairment
- Antifungal agents
1. Amphotericin B desoxycholate (Fungizone®); amphotericin B lipid-based (AmBisome®, Abelcet®, Amphotec®)
 - a) Mechanism of action (MOA): binds with ergosterol to disrupt the fungal plasma membrane; fungicidal
 - b) Activity against *Aspergillus*, *Coccidioides*, *Cryptococcus*, *Histoplasma*, and *Candida*
 - c) Lipid complex formulations of amphotericin B (amphotericin B lipid complex, liposomal amphotericin B, and amphotericin B cholesterol sulfate complex) have reduced adverse effects, including less risk of nephrotoxicity, and less common infusion-related reactions (chills, fever, nausea).
 - d) Adverse effects: nephrotoxicity (more likely with conventional amphotericin B); increased LFT
 2. Caspofungin (Cancidas®)
 - a) Mechanism of action (MOA): irreversibly inhibits the enzyme 1,3- β -glucan synthase, thereby disrupting the integrity of the fungal cell wall; fungicidal
 - b) Activity against *Candida*, *Aspergillus*, and *Histoplasma*
 - c) Adverse effects: May increase LFT
 3. Flucytosine (Ancobon®)
 - a) Mechanism of action (MOA): interferes with DNA synthesis
 - b) Activity against *Candida* and *Cryptococcus*
 - c) Adverse effects: dose-related bone marrow suppression, hepatotoxicity
 - (1) Use with extreme caution in patients with renal dysfunction
 4. Griseofulvin (Frisactin®, Grifulvin V®, Fulvicin®)
 - a) Activity against *Trichophyton*, *Microsporum*, and *Epidermophyton*
 5. Azole antifungal (itraconazole [Sporanox®], ketoconazole [Nizoral®], fluconazole [Diflucan®])
 - a) Mechanism of action (MOA): inhibits ergosterol synthesis
 - b) Activity against *Candida albicans*
 - (1) Fluconazole is the drug of choice for localized candidal infections (e.g., UTI, thrush).
 - c) Interactions
 - (1) Ketoconazole: major substrate of CYP A4; strong inhibitor of CYP 3A4, CYP 1A2, and CYP 2C8, CYP 2C9; moderate inhibitor of CYP 2A6, CYP 2C19, and CYP 2D6
 - (2) Itraconazole: major substrate of CYP 3A4; major inhibitor of CYP 3A4
 - (3) Fluconazole: strong inhibitor of CYP 2C19 and 2C9; moderate inhibitor of 3A4

- (4) To be avoided with cisapride due to life-threatening arrhythmias
 - (5) To be used with extreme caution with digoxin (decreased clearance of digoxin)
 - (6) Oral absorption of itraconazole and ketoconazole is impaired by concomitant antacids, H₂ blockers, or proton-pump inhibitors (PPI)
 6. Terbinafine (Lamisil®)
 - a) Mechanism of action (MOA): inhibits ergosterol synthesis
 - b) Used for fungal infections of fingernail or toenail
 - c) Adverse effects: LFT abnormalities, rash, headache, GI disturbance, neutropenia (rare)
 - d) Interactions: strong inhibitor of CYP 2D6
 7. Nystatin
 - a) MOA: binds to sterols on cell membrane
 - b) Most commonly used orally as swish/swallow for thrush, or topically for fungal rashes
 - P. Antitubercular agents
 1. Effective against *Mycobacterium tuberculosis* infections
 - a) Isoniazid (Nydrazid®)
 - (1) Mechanism of action (MOA): kills susceptible mycobacteria by interfering with synthesis of lipid components of cell wall
 - (2) Adverse effects: LFT elevations
 - (3) Interactions: major CYP 2E1 substrate; strong inhibitor of CYP 2C19 and 3A4; may also inhibit 1A2, 2A6, 2C9, 2D6, 2E1
 - b) Rifamycins (rifampin [Rifadin®], Rimactane®, rifabutin [Mycobutin®], rifapentine [Priftin®]): inhibits DNA-dependent RNA polymerase, blocks RNA transcription
 - (1) Rifampin also active against gram-positive and gram-negative bacteria
 - (2) Adverse effects: reddish-orange discoloration of body fluids, rash, GI disturbances, increased LFT
 - (3) Interactions: strong inducer of CYP 3A4, 1A2, 2A6, 2B6, 2C8, 2C9, and 2C19
 - c) Pyrazinamide
 - (1) Mechanism of action (MOA): unknown
 - (2) Adverse effects: increased LFT; may inhibit uric acid
 - d) Ethambutol (Myambutol®)
 - (1) Mechanism of action (MOA): interferes with RNA synthesis
 - (2) Adverse effects: optic neuritis (decreased red-green color perception, decreased visual acuity); hepatotoxicity
 - e) Capreomycin (Capastat® sulfate)
 - (1) Mechanism of action (MOA): unknown
 - (2) Adverse effects: ototoxicity, nephrotoxicity, hepatotoxicity
 - f) Cycloserine (Seromycin®)
 - (1) Mechanism of action (MOA): inhibits bacterial cell wall synthesis by competing with D-alanine (amino acid)
 - (2) Adverse effects: CNS effects (drowsiness, headache, vertigo)
 - g) Para-aminosalicylic acid (PAS, Paser® granules)
 - (1) Mechanism of action (MOA): inhibits folic acid synthesis
 - (2) Adverse effects: GI upset, loose stools during initial days of treatment, hypersensitivity reactions, vitamin and mineral malabsorption (rare)
 - (a) Patients with sensitivity to tartrazine dyes have increased risk of salicylate sensitivity.
- Antiviral agents
 1. Most block viral entry into the cell or must work inside the cell
 2. Most agents are pyrimidine or purine nucleoside analogs
 3. Antiinfluenza agents
 - a) Amantadine (Symmetrel®) and rimantadine (Flumadine®)
 - (1) Mechanism of action (MOA): inhibits the uncoating of viral RNA, inhibiting replication
 - (2) Used in the prevention and treatment of influenza A (no effect on influenza B)
 - (3) Effective when initiated within 48 hours of initial symptoms
 - (4) Fewer drug interactions with rimantadine
 - (5) Use of agents limited due to viral resistance
 - b) Zanamavir (Relenza®) and oseltamivir (Tamiflu®)
 - (1) Mechanism of action (MOA): inhibits the enzyme neuraminidase; inhibits replication of influenza A and influenza B
 - (2) Treats uncomplicated influenza infections
 - (3) Relenza is administered by oral inhalation; Tamiflu is given orally. Both are to be initiated within 48 hours of onset of symptoms
 4. Antiherpes agents
 - a) Acyclovir (Zovirax®): a prototype antiviral agent
 - (1) Mechanism of action (MOA): inhibits viral DNA synthesis by competition with dGTP for viral DNA polymerase and chain termination
 - (2) Used for herpes simplex virus 1 and 2 (HSV) and varicella-zoster virus (VZV)
 - (3) Available IV, topical, and oral
 - (4) Adverse effects: nausea, headache, dizziness, reversible crystalline nephropathy; CNS disturbances (rare)
 - b) Valacyclovir (Valtrex®)
 - (1) Converted to acyclovir when ingested; MOA same as acyclovir
 - (2) Used for recurrent genital herpes and herpes zoster infection
 - (3) Adverse effects: nausea, CNS disturbances (rare)
 - c) Penciclovir (Denavir®)
 - (1) Mechanism of action (MOA): same as acyclovir
 - (2) Used for HSV-1, HSV-2 (topical)

- d) Famciclovir (Famvir®)
 - (1) Prodrug of penciclovir
 - (2) Mechanism of action (MOA): same as acyclovir
 - (3) Used for HSV-1, HSV-2, VZV, Epstein-Barr virus (EBV), and hepatitis B
- e) Trifluridine (Viroptic®)
 - (1) Mechanism of action (MOA): inhibits viral DNA synthesis similar to acyclovir; incorporates viral and cellular DNA
 - (2) Used for HSV-1 and HSV-2 (ophthalmic drops)
- f) Vidarabine (Vira-A® ophthalmic)
 - (1) Mechanism of action (MOA): inhibits viral DNA polymerase; incorporated into viral and cellular DNA; adenosine analog
 - (2) Adverse effects: tearing, mild eye irritation
- 5. Anticytomegalovirus agents
 - a) Ganciclovir (Cytovene®)
 - (1) Mechanism of action (MOA): similar to acyclovir; requires triphosphorylation for activation
 - (2) Used for cytomegalovirus (CMV), HSV, VZV, and EBV
 - (3) Adverse effects: neutropenia
 - b) Valganciclovir (Valcyte®)
 - (1) Mechanism of action (MOA): same as ganciclovir
 - (2) Prodrug of ganciclovir
 - (3) Used for CMV
 - c) Foscarnet (Foscavir®)
 - (1) Mechanism of action (MOA): inhibits viral DNA polymerase, RNA polymerase, and HIV reverse transcriptase
 - (2) Used for HSV, VZV, CMV, EBV, human herpesvirus six (HHV-6), hepatitis B (HBV), and HIV
 - (3) Adverse effect: nephrotoxicity (avoid with other nephrotoxic agents)
 - d) Cidofovir (Vistide®)
 - (1) Mechanism of action (MOA): cytosine analog; phosphorylation not dependent on viral enzymes
 - (2) Used for CMV, HSV-1, HSV-2, VZV, EBV, HHV-6, adenovirus, and human papillomavirus
 - (3) Adverse effect: nephrotoxicity (prevented with the administration of probenecid)
- 6. Antihepatitis agents
 - a) Lamivudine (nucleoside reverse transcriptase inhibitor [NRTI]), for hepatitis B
 - b) Adefovir (NRTI), for chronic hepatitis B
 - c) Interferon-alfa (Pegasys®, Peg-intron®) and ribavirin (Virazole®, Rebetol®, Copegus®), for chronic hepatitis C
 - d) Prevention (see Chapter 24, Immunology and Vaccines)

REVIEW QUESTIONS

(Answers and Rationales on page 338.)

1. Which of the following antibiotics is most appropriate for empiric treatment of bacterial meningitis?
 - a. Erythromycin
 - b. Gatifloxacin
 - c. Vancomycin
 - d. Ceftriaxone
 - e. Gentamicin
2. Which of the following drugs is considered a drug of choice for Legionnaires' disease?
 - a. Gentamicin
 - b. Azithromycin
 - c. Tetracycline
 - d. Oseltamivir
 - e. Cephalexin
3. Which of the following statements about hepatitis A is true?
 - I. It is commonly spread through sharing needles.
 - II. It can lead to chronic hepatitis in 80% of cases.
 - III. A vaccine is available that will prevent infection.
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
4. Aminoglycosides are used to treat all of the following pathogens EXCEPT:
 - a. *Escherichia coli*
 - b. *Neisseria meningitidis*
 - c. *Proteus mirabilis*
 - d. *Enterobacter aerogenes*
 - e. *Klebsiella pneumoniae*
5. A young female patient begins treatment with metronidazole for a *Trichomonas* infection. Which of the following are important to monitor during her therapy?
 - a. Pregnancy status
 - b. Alcohol use
 - c. Protein intake
 - d. a and b
 - e. b and c
6. Which of the following measurements should be evaluated before implementing tobramycin therapy?
 - a. Serum calcium
 - b. Serum creatinine (SCr)
 - c. Urine protein
 - d. Serum protein
 - e. Serum alanine aminotransferase (ALT)
7. Which of the following pathogens is the most commonly isolated organism in community-acquired urinary tract infections?
 - a. *Escherichia coli*
 - b. *Klebsiella pneumoniae*
 - c. *Staphylococcus aureus*
 - d. *Pseudomonas aeruginosa*
 - e. None of the above

References

- DiPiro JT, et al: *Pharmacotherapy: a pathophysiologic approach*, ed 7. McGraw-Hill Medical, 2008.
- Sanford JP, et al: *The Sanford guide to antimicrobial therapy*, ed 38. Antimicrobial Therapy, 2008.

8. Cold sores are typically caused by:
 - a. HSV-1
 - b. HSV-2
 - c. Varicella zoster
 - d. HIV
 - e. None of the above
9. A 60-year-old man is referred to the infectious disease clinic with a diagnosis of tuberculosis (TB). He was diagnosed 3 months ago and has been treated subsequently with isoniazid, rifampin, ethambutol, and streptomycin. However, his sputum continues to be positive for acid-fast bacillus (AFB). What is the most appropriate next step?
 - a. Changing rifampin to rifabutin and repeating sputum culture and sensitivity
 - b. Changing streptomycin to levofloxacin and repeating sputum culture and sensitivity
 - c. Continuing current regimen, adding levofloxacin and ethionamide, and repeating sputum culture and sensitivity
 - d. Performing bronchoscopic lavage and biopsy for histological analysis
 - e. Continuing current regimen and rechecking sputum in 2 months
10. Trachoma is typically caused by:
 - a. Tinea cruris
 - b. *Chlamydia trachomatis*
 - c. CMV
 - d. A herpes virus
 - e. None of the above
11. Which of the following is the correct adult dose of azithromycin for the treatment of CAP?
 - a. Single 500 mg dose
 - b. Single 2 g dose
 - c. 2 g per day for 3 days
 - d. 500 mg per day for 10 days
 - e. 500 mcg/kg per day for 5 days
12. All of the following are true about Vibramycin EXCEPT:
 - a. indicated for the treatment of uncomplicated gonococcal infections and syphilis
 - b. may cause photosensitivity
 - c. is indicated for secretion of inappropriate antidiuretic hormone (SIADH)
 - d. can impair the effectiveness of hormone contraception
 - e. a and c
13. A 6-year-old boy is taken to the pediatrician's office with complaint of a face rash. On examination, the patient has crusted bullae on the chin and jaw. The physician diagnoses bullous impetigo. What is the most appropriate treatment?
 - a. Cephalexin 50 mg/kg per day PO
 - b. Erythromycin 10 mg/kg per dose PO q6h
 - c. Dicloxacillin 50 mg/kg per day PO, in divided doses
 - d. Azithromycin 10 mg/kg per day PO, given once daily
 - e. a and b
14. A shingles infection most commonly appears in which of the following areas of the body?
 - a. Hands and feet
 - b. Trunk
 - c. Gums
 - d. Mucosa
 - e. None of the above
15. A 40-year-old man admitted to the hospital for community acquired pneumonia develops blood cultures positive for *Streptococcus pneumoniae*. Sensitivity testing shows intermediate susceptibility to penicillin. What is the most appropriate treatment?
 - a. Ciprofloxacin 500 mg PO bid
 - b. Amoxicillin 875 mg PO bid
 - c. Levofloxacin 500 mg PO qd
 - d. Erythromycin 500 mg PO qid
 - e. Imipenem 500 mg IV q8h
16. A 50-year-old male with a history of poorly controlled diabetes complains of lower extremity swelling, erythema, and tenderness. His temperature is 39° C. The attending physician believes the patient has a superficial diabetic foot infection involving a limited area of the ankle and lower leg. Which of the following is the appropriate therapy?
 - a. Ciprofloxacin 500 mg bid
 - b. Doxycycline 100 mg bid
 - c. Clindamycin 300 mg po qid
 - d. a and c
 - e. Admit to the in-patient ward and treat with Levaquin 750 mg IV qd.
17. A 50-year-old woman with a history of hypertension and a 40 pack-year smoking history presents to her doctor with a chronic cough for the past 4 months. She states that the cough is worse in the morning and is occasionally productive of sputum, and she denies fever or chills. Which of the following is the most appropriate next step in the management of this patient?
 - a. Amoxicillin/clavulanate 875 mg PO qd
 - b. Ciprofloxacin 500 mg PO bid
 - c. Sputum cultures to determine sensitivity and specificity
 - d. a and c
 - e. No antibiotic treatment is warranted at this time
18. A 28-year-old woman presents with symptoms of sinusitis, including mucopurulent nasal discharge, sinus congestion, headache, and sinus pain. She began taking amoxicillin she found in her medicine cabinet 3 days ago, but has had no relief. What is the most appropriate treatment for this patient?
 - a. Ciprofloxacin 500 mg PO qd
 - b. Erythromycin base 500 mg PO qid
 - c. Levofloxacin 500 mg PO qd
 - d. Amoxicillin/clavulanate 875 mg PO bid
 - e. No treatment is warranted at this time

19. An 18-year-old man presents with symptoms of pharyngitis. A rapid strep test is positive. He reports severe hives with penicillin. What is the most appropriate treatment for this patient?
 - a. Penicillin V 500 mg PO bid
 - b. Ceftriaxone 125 mg IM for one dose
 - c. Azithromycin 500 mg PO for one dose
 - d. Azithromycin 250 mg PO qd for three days
 - e. Azithromycin 500 mg PO for one dose, followed by 250 mg po qd for four days
 20. A 12-month-old child infant is taken to the pediatric clinic with complaints of nonhealing otitis media. The mother states that she took the patient to an urgent care clinic 2 weeks ago for fever, irritability, and anorexia, and the physician diagnosed otitis media and prescribed erythromycin. One week later, he did not show any improvement; she returned to the urgent care clinic, and his prescription was replaced with amoxicillin. Now she reports that his symptoms have not changed. The pediatrician confirms the diagnosis of acute otitis media. What is the most appropriate treatment for this patient?
 - a. Continuing amoxicillin for another 7 days
 - b. Continuing amoxicillin for another 14 days
 - c. Replacing amoxicillin with cefuroxime 80 mg/kg/day PO divided BID
 - d. Replacing amoxicillin with ceftriaxone 500 mg/kg per day IM
 - e. Replacing amoxicillin with ceftriaxone 50 mg/kg per day IM
 21. A 74-year-old male nursing home resident is taken to the emergency department for mental status changes, poor oral intake, and lethargy. Physical examination is essentially normal. Lumbar puncture is performed and reveals the following:
 WBC: 1200, 90% PMN
 protein: 150 mg/dL
 glucose: 25 mg/dL
 Gram stain: gram-positive bacilli
 What is the most appropriate treatment for this patient?
 - a. Cefotaxime
 - b. Gentamycin
 - c. Ampicillin
 - d. a and b
 - e. b and c
 22. A 70-year-old woman was hospitalized for 3 weeks after a femoral fracture and develops a urinary tract infection. Urinalysis reveals the following:
 WBC: 20
 RBC: Scant
 Leukocyte esterase: positive
 Bacteria: many
 Urine culture is positive for *P aeruginosa*. What is the most appropriate antibiotic therapy at this time?
 - a. Moxifloxacin 400 mg PO qd for 2 weeks
 - b. Ampicillin 500 mg PO qd for 4 weeks
 - c. Ciprofloxacin 500 mg PO bid for 2 weeks
 - d. 160 mg trimethoprim/800 mg sulfamethoxazole PO every 12 hours for 14 days
 - e. Remove the Foley catheter and repeat culture in 1 week
 23. A 23-year-old woman presents with symptoms of urinary tract infection. She is prescribed trimethoprim/sulfamethoxazole, but returns to the clinic in 1 week reporting no improvement. In addition to obtaining a urine culture and sensitivity, what is the most appropriate initial treatment?
 - a. Continuing trimethoprim/sulfamethoxazole for an additional week
 - b. Nitrofurantoin 100 mg PO qid for 3 days
 - c. Ciprofloxacin 500 mg PO bid for 7 days
 - d. Ciprofloxacin 250 mg PO bid for 3 days
 - e. Gatifloxacin 400 mg PO qid for 7 days
 24. Which of the following is true about azithromycin?
 - I. It is classified as a macrolide antibiotic
 - II. It has a long duration of action
 - III. It is indicated for mild-to-moderate pneumonia associated with AIDS
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
- Read the case study and then answer the questions that follow:
- A 40-year-old open water fisherman comes to the ER with a sore wrist. He reports suffering a laceration while on the job 5 days prior. Since that time, the wound has failed to close and has continued to swell. On examination, his right wrist has a 1 cm superficial wound with 5 cm surrounding area of brown discoloration, erythema, edema, and subcutaneous emphysema. There are several ruptured bullae, which are leaking significant amounts of grey watery fluid. The patient reports that the swelling is rapidly increasing in size. He is diagnosed with cellulitis.
25. Clostridial cellulitis:
 - a. Does not require surgical debridement
 - b. Is usually preceded by local trauma
 - c. Can be treated on an outpatient basis
 - d. Is penicillin-resistant
 - e. All of the above
 26. Which of the following are the most common cause of cellulitis?
 - a. *E. coli*
 - b. *Staph. epidermidis*
 - c. *Beta-hemolytic Streptococcus*
 - d. *Clostridium*
 - e. *Pasteurella multocida*
 27. Which of the following is an appropriate treatment for Clostridial cellulitis?
 - a. Penicillin
 - b. Clindamycin
 - c. Chloramphenicol
 - d. a and b
 - e. a, b and c

28. Which of the following is a risk factor for cellulitis?
- Tinea pedis
 - Venous insufficiency
 - High carbohydrate diet
 - a and b
 - a, b and c
29. Which of the following does NOT increase the risk of nephrotoxicity associated with gentamicin treatment?
- Cisplatin therapy
 - Age > 75 years
 - Amphotericin B therapy
 - Chronic renal insufficiency
 - All of the above increase the risk of nephrotoxicity.
30. Which of the following medications is NOT effective for the treatment of *P aeruginosa* urinary tract infection?
- Trimethoprim-sulfamethoxazole
 - Norfloxacin
 - Ciprofloxacin
 - Methenamine mandelate
 - All of the above are effective.
31. Which of the following supplements should be prescribed to patients treated with four-drug regimen for active TB, and what is the symptom associated with drug-induced deficiency?
- Folic acid, anemia
 - Calcitriol, muscle spasms
 - Iron, anemia
 - Pyridoxine, paresthesia
 - Cyanocobalamin, anemia
32. Bactroban® nasal ointment should be applied intranasally to eradicate which of the following pathogens?
- N. gonorrhea*
 - S. aureus*
 - S. pneumonia*
 - H. influenzae*
 - Any of the above
33. Flagyl may be used to treat:
- giardiasis
 - trichomonas
 - bacterial vaginosis
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
34. Which of the following is appropriate therapy for *P. aeruginosa* infection?
- Cefepime
 - Aztreonam
 - Cefotaxime
 - a or b
 - a or c
35. Which of the following is the active ingredient in Abelcet®?
- Amphotericin B
 - Ketoconazole
 - Isradipine
 - Rifampin
 - Tetracycline
36. Which of the following statements is (are) true?
- Clarithromycin and azithromycin are chemically related to erythromycin.
 - Clarithromycin and azithromycin have less incidence of gastrointestinal adverse effects.
 - Azithromycin has less drug interactions than erythromycin.
 - All of the above.
37. Famciclovir:
- is not useful in the prevention of recurrent genital herpes simplex.
 - does not require dose adjustment for renal impairment.
 - may cause dysmenorrhea.
 - is excreted predominately in the feces.
 - is rapidly metabolized to penciclovir.
38. Vision should be monitored in patients taking which drug?
- Aspirin
 - Hydroxychloroquine
 - Indomethacin
 - Cyclophosphamide
 - Auranofin
39. Which of the following is true about amikacin?
- classified as a penicillin antibiotic
 - normal trough is 10 mcg/mL
 - may cause nephrotoxicity and ototoxicity
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
40. Which of the following pathogens are normally responsible for causing otitis media?
- H. influenzae*
 - S. pneumoniae*
 - P. aeruginosa*
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
41. Which of the following antibiotics may inhibit aggregation of platelets and worsen bleeding?
- cefoperazone
 - cefamandole
 - ceftriaxone
 - cefotetan
 - all of the above

42. A 35-year-old man with asthma presents to an urgent care clinic with complaints of dry cough, fever, headache, malaise, and myalgia. A rapid influenza test is positive for influenza B. What is the most appropriate therapy?
- Amantadine, oral
 - Rimantadine, oral
 - Oseltamivir, oral
 - Zanamavir, inhaled
 - c and d
43. A 22-year-old woman presents to her primary care physician with complaints of purulent vaginal discharge, pain with intercourse, and lower pelvic tenderness. She is admitted directly for treatment of suspected pelvic inflammatory disease. What is the most appropriate empiric treatment?
- Clindamycin 900 mg IV q8h
 - Cefotetan 2 g IV q12h
 - Doxycycline 100 mg IV bid
 - a and b
 - b and c
44. Which of the following cephalosporins is most useful in the treatment of bacterial meningitis?
- cefprozil
 - ceftriaxone
 - cefaclor
 - cephalexin
 - cefadroxil
45. Which of the following antibiotics has the longest duration of action?
- azithromycin
 - gentamicin
 - amoxicillin
 - cephalexin
 - streptomycin
46. Which of the following cephalosporins can be given without dose adjustment to a patient with impaired renal function?
- cephalexin
 - cefaclor
 - cefoperazone
 - cefadroxil
 - cephaloridine
47. Which of the following erythromycin formulations is/are parenterally available?
- Erythrocin
 - Ilotycin
 - Erycin
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
48. Which of the following drugs is/are used topically in the treatment of vaginal infections caused by yeast?
- Femstat
 - Monistat
 - Gyne-Lotrimin
 - Mycelex G
 - All of the above.
49. Which of the following cephalosporin suspensions should be avoided in patients with phenylketonuria?
- cefprozil
 - cefaclor
 - cefazolin
 - cefixime
 - cephalexin
50. Diflucan is/are available in which of the following form(s)?
- oral tablet
 - injection
 - suspension
- I only
 - III only
 - I and II only
 - II and III only
 - I, II and III
51. All of the following are indicated for the treatment of *Pneumocystis* pneumonia (PCP) EXCEPT?
- Bactrim
 - Pentam
 - Mepron
 - Clindamycin
 - Erythromycin
52. Which of the following agents are useful in the treatment of mycobacterium avium complex (MAC)?
- Zithromax
 - Biaxin
 - Lamprene
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
53. Mycobutin is used to prevent infections caused by:
- E. coli*
 - Herpes zoster
 - N. gonorrhoea*
 - Mycobacterium avium complex
 - CMV
54. Rifampin is contraindicated in patients suffering from:
- migraines
 - jaundice
 - seizures
 - gout
 - CHF
55. Denavir® is indicated for:
- cold sores
 - HIV
 - genital herpes
 - influenza
 - CMV

56. Which of the following antibiotic regimens is optimal for endocarditis due to enterococcal infection?
- gentamicin alone
 - ampicillin alone
 - ampicillin with gentamicin
 - ampicillin with vancomycin
 - None of the above
57. Seromycin is classified as a(n):
- Antitubercular
 - Antibacterial
 - Antiviral
 - Antifungal
 - Antiparasitic
58. Which of the following organisms is typically responsible for causing otitis externa?
- Haemophilus influenza*
 - Streptococcus pneumonia*
 - Pseudomonas aeruginosa*
 - Klebsiella pneumoniae*
 - Escherichia coli*
59. Doxycycline:
- is the drug of choice for pneumonia
 - is used for the treatment and prevention of leprosy
 - is used for the prevention of malaria
 - is used to treat sexually transmitted diseases
 - c and d
60. KT has watery stools and amebic dysentery. The drug he is prescribed is causing a metallic taste. Which of the following drugs was he most likely given?
- metronidazole
 - nitrofurantoin
 - ciprofloxacin
 - ceftriaxone
 - amoxicillin
61. Which of the following antibiotics should be avoided in patients with G6PD deficiency?
- Penicillins
 - Tetracyclines
 - Cephalosporins
 - Sulfonamides
 - None of the above
62. Liver enzymes should be monitored in patients taking:
- isoniazid
 - tetracycline
 - rifampin
 - All of the above
 - None of the above
63. Erythromycin is the preferred agent for the treatment of:
- Mycoplasma pneumoniae*
 - Legionnaire's disease
 - Streptococcus pyogenes*
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
64. True or false: Aminoglycosides are effective monotherapy against *Streptococcus pneumoniae*.
- True
 - False
65. Telithromycin:
- is a ketolide structurally related to macrolides
 - inhibits cell wall synthesis
 - is the drug of choice for Lyme disease
 - All of the above
 - None of the above
66. Which of the following statements about imipenem is true?
- It is contraindicated in patients with penicillin allergy.
 - It is active against gram-negative rods.
 - It has broad antimicrobial activity.
 - Pseudomonas* resistance has been reported.
 - All of the above
67. Which of the following demonstrate bactericidal activity in vitro?
- Penicillins
 - Cephalosporins
 - Clindamycin
 - a and b
 - a and c
68. Which of the following statements is FALSE regarding cephalosporins?
- Enterococcus is sensitive to cephalosporins.
 - Cephalosporins depress beta-lactamase activity in some organisms.
 - Beta-lactamase binds cephalosporins.
 - Third-generation cephalosporins have more activity against gram-negative organisms.
 - All of the above are true.
69. Which of the following could be used to treat methicillin-resistant *Staph. aureus*?
- Piperacillin
 - Gentamicin
 - Oxacillin
 - Streptomycin
 - Vancomycin
70. Which of the following statements regarding cefazolin is true?
- It may be administered at 8-hour dosing intervals.
 - It has a favorable pharmacokinetic profile.
 - It has a relatively long half-life.
 - It has a lower overall cost.
 - All of the above
71. Tetracyclines:
- can be used to treat rickettsial infections.
 - are bactericidal in vitro.

- c. interfere with cell wall synthesis.
 - d. a and b
 - e. a and c
72. Which of the following antimicrobials has little activity against anaerobes?
- a. Metronidazole
 - b. Clindamycin
 - c. Imipenem
 - d. Ceftriaxone
 - e. Amoxicillin/clavulanate
73. Penicillin:
- a. penetrates the blood-brain barrier well.
 - b. has a 30-minute half-life.
 - c. is excreted by the kidneys.
 - d. a and b
 - e. b and c
74. A patient with a severe penicillin allergy may:
- a. have a reaction to any cephalosporin.
 - b. have a reaction to broad-spectrum antipseudomonal penicillin.
 - c. take cephalosporins without worry of a reaction.
 - d. a and b
 - e. b and c
75. Which of the following may occur with chloramphenicol administration?
- a. Pancytopenia
 - b. Erythroid suppression of bone marrow
 - c. Gray baby syndrome
 - d. All of the above
 - e. None of the above
76. Vancomycin:
- a. can be used to treat MRSA.
 - b. can be used to treat *C. difficile* colitis.
 - c. is ototoxic.
 - d. requires dose adjustment in renal impairment.
 - e. All of the above
77. Inappropriate and poorly planned antibiotic use may:
- a. increase infection rate.
 - b. increase adverse effects.
 - c. affect normal hospital flora.
 - d. increase cost.
 - e. All of the above
78. What is the first line therapy for *Strep. pneumoniae*?
- a. Penicillin
 - b. Ceftriaxone
 - c. Vancomycin
 - d. Gentamicin
 - e. Erythromycin
79. Aminoglycosides are:
- a. bactericidal.
 - b. nephrotoxic.
 - c. renally excreted.
 - d. toxic to the vestibulocochlear nerve.
 - e. All of the above
80. Clindamycin can be used against:
- a. gram-negative organisms.
 - b. gram-positive organisms.
 - c. anaerobes.
 - d. a and b
 - e. b and c
81. Amphotericin B:
- a. is nephrotoxic.
 - b. is hydro- and lipophilic.
 - c. should first be administered in a test dose.
 - d. binds sterols in fungal membranes.
 - e. All of the above
82. Sulfonamides:
- a. should not be used with para-amino benzoic acid (PABA).
 - b. prevent bacterial folic acid synthesis.
 - c. do not affect mammalian cells.
 - d. act synergistically with trimethoprim.
 - e. All of the above
83. Which of the following is a common early side effect of penicillin?
- a. Skin rash
 - b. Constipation
 - c. Loss of concentration
 - d. Orthostatic hypotension
 - e. Drowsiness
84. Aminoglycosides:
- a. require dose adjustment in renal insufficiency.
 - b. may act synergistically with penicillin.
 - c. should not be used for anaerobic infections.
 - d. can be used in gram-negative aerobic infections.
 - e. All of the above
85. Ciprofloxacin is available in which of the following form(s)?
- I. oral tablets
 - II. intravenous solutions
 - III. topical ointment
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
86. Which of the following is NOT a beta-lactam or related antibiotic?
- a. meropenem
 - b. aztreonam
 - c. vancomycin
 - d. ceftriaxone
 - e. ampicillin
87. Which of the following agents does NOT have activity against vancomycin-resistant *Enterococcus faecium*?
- a. linezolid
 - b. daptomycin
 - c. tigecycline
 - d. doxycycline
 - e. quinupristin/dalfopristin

88. Which of the following quinolone antibiotics has the greatest activity against *Pseudomonas aeruginosa*?
- Moxifloxacin
 - Levofloxacin
 - Gatifloxacin
 - Ciprofloxacin
 - Gemifloxacin
89. Which of the following bacteria alters the composition of the peptide side chain of peptidoglycan to cause resistance to vancomycin?
- Neisseria meningitidis*
 - Streptococcus pneumoniae*
 - Haemophilus influenzae*
 - Enterococcus faecalis*
 - Borrelia burgdorferi*
90. Which of the following agents is NOT useful in the treatment of enterococcal infections?
- cefazolin
 - penicillin
 - vancomycin
 - ampicillin
 - linezolid
91. Which of the following carries a risk of ophthalmic toxicity?
- Ethambutol
 - Isoniazid
 - Streptomycin
 - Rifampin
 - All of the above
92. Which of the following agents targets the bacterial ribosome?
- isoniazid
 - vancomycin
 - tetracycline
 - levofloxacin
 - all of the above
93. Which of the following may cause drug-induced hepatitis?
- Ethambutol
 - Isoniazid
 - Tetracycline
 - Penicillin G
 - Kanamycin
94. Which of the following may cause both renal and ototoxicity?
- Ethambutol
 - Isoniazid
 - Tetracycline
 - Penicillin G
 - Kanamycin
95. Which of the following may interfere with the ability to detect the color green?
- Ethambutol
 - Isoniazid
 - Tetracycline
 - Para-amino salicylic acid
 - Streptomycin
96. Which of the following may produce drug-induced lupus?
- Ethambutol
 - Isoniazid
 - Tetracycline
 - Para-amino salicylic acid
 - Streptomycin
97. Which of the following statements about isoniazid-induced hepatotoxicity is true?
- It is associated with fever, rash, and eosinophilia.
 - It is more common in patients concomitantly receiving ethambutol.
 - It is more common in patients younger than 20 years.
 - It is due to a hydrazine metabolite.
 - All of the above
98. Pyrazinamide is used to treat infections caused by?
- Mycobacterium tuberculosis*
 - Mycobacterium leprae*
 - Mycobacterium avium* complex
 - Legionella pneumophila*
 - Rickettsia rickettsii*
99. Which of the following may cause hyperuricemia?
- Rifampin
 - Ethambutol
 - Isoniazid
 - Pyrazinamide
 - Streptomycin
100. Which of the following inhibits bacterial cell wall synthesis?
- Rifampin
 - Ethambutol
 - Isoniazid
 - Pyrazinamide
 - Streptomycin
101. Which of the following is the most significant side effect associated with ethambutol?
- Hepatitis
 - Retrobulbar neuritis
 - Renal tubular acidosis
 - Agranulocytosis
 - Stevens-Johnson syndrome
102. Which of the following is NOT a first-line agent in the treatment of tuberculosis?
- Rifampin
 - Ethionamide
 - Isoniazid
 - Pyrazinamide
 - Streptomycin
103. Which of the following drugs are bacteriostatic?
- Chloramphenicol
 - Tetracycline
 - Spectinomycin
 - a and c
 - a, b, and c

104. Which of the following is/are true about famciclovir?
- It is prodrug of penciclovir
 - It is available as oral tablet
 - It is commonly used for CMV
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
105. Ganciclovir is available in which of the following form(s):
- oral capsules
 - injection
 - implant
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
106. The mechanism of action of primaquine is to:
- disrupt mitochondria.
 - bind DNA.
 - eliminate exoerythrocytic malaria.
 - a and b
 - a, b and c
107. True or False: *Cryptococcus* is susceptible to amphotericin B.
- True
 - False
108. True or False: Clotrimazole acts via inhibition of fungal cell membrane synthesis.
- True
 - False
109. Which of the following can most commonly cause otitis media?
- Escherichia coli*
 - Legionella pneumophila*
 - Enterobacter aerogenes*
 - Haemophilus influenzae*
 - Pseudomonas aeruginosa*
110. The most common symptoms of acute lower urinary tract infections are:
- burning on urination, urgency, and frequency.
 - fever and chills.
 - numbness and flank pain.
 - headache.
111. Which of the following may be used for aspergillosis?
- Ketoconazole
 - Itraconazole
 - Amphotericin B
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
112. Which of the following drugs represent primary agents of treatment in patients with TB?
- Isoniazid and rifampin
 - Penicillin and ethambutol
 - PASA and cycloserine
 - Streptomycin and PASA
 - Ethambutol and ciprofloxacin
113. A 32-year-old woman with gonorrhea has a penicillin allergy. Which of the following may be used to treat her condition?
- Ceftriaxone
 - TMP/SMX
 - Streptomycin
 - Cefoxitin
 - None of the above
114. *Pneumocystis pneumonia* (PCP) is best treated with:
- trimethoprim/sulfamethoxazole
 - ciprofloxacin
 - ethambutol
 - penicillin
 - rifampin
115. *E coli* is best described as:
- a fungus
 - a gram-negative bacilli.
 - a gram-positive cocci.
 - a virus.
 - None of the above
116. Which of the following statements regarding penciclovir is true?
- It is a antiviral agent used for herpes labialis.
 - It is used at the first sign of fever blister.
 - It is applied every 2 hours.
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
117. Accepted regimens for the treatment of *H. pylori* may contain each of the following agents EXCEPT:
- Metronidazole
 - Ceftriaxone
 - Amoxicillin
 - Clarithromycin
 - Bismuth subsalicylate
118. Which of the following oral antibiotics is commonly associated with pseudomembranous colitis?
- Clindamycin
 - Ceftriaxone
 - Vancomycin
 - Linezolid
 - Ampicillin

119. Which of the following statements regarding tetracycline are true?
- It is effective against rickettsial species.
 - Phototoxic reactions are possible.
 - It should be taken with food to avoid gastrointestinal upset.
 - It is mainly bacteriostatic but can be bactericidal at high concentrations.
 - All of the above
120. Which of the following cephalosporins are associated with disulfiram-like reactions with ethanol?
- Cefoperazone
 - Cefamandole
 - Cefmetazole
 - Cefotetan
 - All of the above
121. All of the following are considered third-generation cephalosporins EXCEPT:
- cefdinir
 - cetrixaxone
 - cefepime
 - cefixime
 - cefibuten
122. A 21-year-old, HIV-positive man presents to the HIV clinic for examination. A tuberculosis skin test (PPD test) is placed, and when he returns to clinic 3 days later and is found to be positive. His LFTs are normal, and anti-TB therapy is started. In addition to clinical evaluation for adverse events, what is the most appropriate monitoring regiment?
- Only clinical examination and interviewing is needed
 - LFT monthly
 - LFT every 8 weeks
 - LFT at 2, 4, and 6 weeks
 - None of the above
123. All of the following are classified as gram-positive organisms EXCEPT?
- Staphylococcus aureus*
 - Streptococcus pyogenes*
 - Pseudomonas aeruginosa*
 - Bacillus anthracis*
 - Listeria monocytogenes*

Read the case study and then answer the questions that follow.

A 40-year-old man presents to his physician with a 3 day history of fever, productive cough, and chest pain. He reports shortness of breath with minimal exertion and generalized fatigue. He has no other medical problems. On examination, he is found to have a temperature of 101 °F and decreased breath sounds over the right lower lung lobe. Chest x-ray reveals consolidation of the right lower lobe. Laboratory testing shows a white blood cell count of 15,000.

124. Which of the following is a common cause of community-acquired pneumonia (CAP)?
- H. influenza*
 - E. coli*
 - Streptococcus bovis*
 - Pneumocystic carinii*
 - Toxoplasma gondii*
125. Which of the following is an indication to consider hospital admission in patients with CAP?
- Systolic blood pressure <120 mm Hg
 - Blood urea nitrogen >10 mg/dL
 - Mental status changes
 - Age <40 years
 - All of the above
126. Which of the following is appropriate empiric therapy for this patient?
- Azithromycin
 - Vancomycin
 - Rifampin
 - Trimethoprim
 - Amoxicillin
127. Azithromycin:
- inhibits bacterial cell wall synthesis.
 - inhibits RNA-dependent protein synthesis.
 - inhibits mitosis.
 - binds to the 30s ribosomal subunit.
 - Blocks transcription
128. Which of the following is an appropriate indication for vancomycin?
- Pseudomembranous colitis
 - Atypical community-acquired pneumonia
 - Staphylococcus enterocolitis
 - a and b
 - a and c

Cardiovascular Disorders

10 CHAPTER

- I. Introduction
 - A. Heart disease is the leading cause of death in the United States.
 - B. Common heart diseases
 - 1. Hypertension
 - 2. Coronary artery disease (CAD)
 - 3. Cardiac arrhythmias
 - 4. Lipid disorders
 - 5. Congestive heart failure
 - C. Diagnostic tests used to evaluate cardiovascular function
 - 1. Electrocardiogram (ECG)
 - 2. Blood tests
 - 3. Auscultation
 - 4. Exercise stress tests
 - 5. Chest x-ray
 - 6. Cardiac catheterization
 - 7. Angiography
 - 8. Doppler studies
 - D. Treatment
 - 1. Dietary modification
 - a) Dietary Approach to Stop Hypertension (DASH) diet—dietary plan to help reduce sodium intake
 - b) Low sodium intake
 - 2. Exercise
 - a) Moderately intense aerobic activity for at least 30 minutes on most days of the week
 - 3. Smoking cessation
 - 4. Alcohol modification
 - 5. Drug therapy
- II. Hypertension
 - A. Nearly one in three adults in the United States has hypertension.¹
 - B. Essential hypertension develops when blood pressure is consistently greater than 140/90 mm Hg.
 - 1. For patients with diabetes or chronic kidney disease, diagnosis of hypertension is made with blood pressure >130/80 mm Hg on at least two separate occasions (Table 10-1).
 - C. Risk factors
 - 1. Age (>45 years, men; >55 years, women)
 - 2. Obesity (body mass index [BMI] >30)
 - 3. Race (African American)
 - 4. Sex (men)
 - 5. Unhealthy lifestyle
 - a) Sedentary lifestyle
 - b) Smoking
 - c) Alcohol
 - d) High sodium intake
- 6. Stress
- 7. Family history
- D. Classes of antihypertensive drugs
 - 1. Diuretics
 - a) First-line therapy (e.g., thiazides)
 - (1) Notably, lower doses are demonstrated to be efficacious, with a lower incidence of side effects.
 - (2) Favorable cost
 - b) Examples
 - (1) Thiazide: hydrochlorothiazide (HCTZ)
 - (2) Loop: furosemide (Lasix), torsemide (Demadex), ethacrynic acid (Edecrin)
 - (3) Potassium-sparing: amiloride (Midamor), spironolactone (Aldactone), triamterene (Dyrenium), Eplerenone (Inspra)
 - c) Mechanism of action
 - (1) Initial reduction of total blood volume and thus cardiac output; peripheral vascular resistance may increase
 - (2) When cardiac output returns to normal, peripheral vascular resistance may increase
 - (3) Depletes sodium
 - d) Side effects
 - (1) Depletes potassium (except potassium-sparing diuretics)
 - (2) Increases uric acid
 - (3) Increases lipid concentrations
 - (4) Gynecomastia with spironolactone
 - 2. Calcium channel blockers
 - a) Examples
 - (1) Dihydropyridines
 - (a) Nifedipine (Procardia/Adalat), amlodipine (Norvasc), felodipine (Plendil), nicardipine (Cardene), nisoldipine (Sular)
 - (2) Nondihydropyridines
 - (a) Diphenylalkylamines: verapamil (Calan/Isoptin and many others)
 - (b) Benzothiazepines: diltiazem (Cardizem and many others)
 - b) Mechanism of action
 - (1) Blocks entry of calcium through L-type channels located on the vascular smooth muscle, cardiac myocytes, and cardiac nodal tissue (sinoatrial and atrioventricular nodes)

Table 10-1 Blood Pressure (BP) Classification

Category	Systolic BP/ Diastolic BP (mm Hg)	Lifestyle Modification	Drug Therapy
Normal	<120/<80	Encourage	Not needed
Prehypertension	120–139/80–89	Yes	No compelling evidence
Stage 1 hypertension	140–159/90–99	Yes	Thiazide diuretic, usually first line
Stage 2 hypertension	≥160/≥100	Yes	Two drug combo, usually thiazide diuretic plus angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, beta-blocker, or calcium channel blocker

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- (2) Causes vascular smooth muscle relaxation
- (3) Decreases systemic vascular resistance, which lowers arterial blood pressure
- c) Side effects
 - (1) Nifedipine: flushing, headache, hypotension, peripheral edema (due to vasodilation), nausea, heartburn, muscle cramps, nervousness, fatigue; immediate-acting nifedipine may cause severe hypotension; sustained-release form is recommended for maintenance dosing (due to vasodilation).
 - (2) Verapamil: constipation, dizziness, fatigue
 - (3) Diltiazem: well tolerated; may see hypotension, headache, dizziness
 - (4) Felodipine: headache
 - (5) All calcium channel blockers: use cautiously in patients with congestive heart failure (CHF); avoid dihydropyridines in patients with CHF
- d) Interactions
 - (1) Calcium channel blockers and other hypotensive medications may increase hypotension.
 - (2) The dihydropyridines are not inhibitors of the cytochrome P-450 (CYP) 3A4 isoenzyme; however, they are substrates and should be used cautiously in patients taking drugs such as ketoconazole, ritonavir, or erythromycin.
 - (3) Diltiazem and verapamil are potent CYP 3A4 inhibitors.
- 3. Angiotensin-converting enzyme (ACE) inhibitors
 - a) Examples
 - (1) Active molecules: lisinopril (Prinivil/Zestril), captopril (Capoten)
 - (2) Prodrugs: enalapril (Vasotec), benazepril (Lotensin), ramipril (Altace), quinapril (Accupril)
 - b) Mechanism of action
 - (1) Inhibits angiotensin II formation
 - (2) Competitive inhibition of ACE reduces circulating angiotensin II, thereby reducing vascular tone
- c) Drugs of choice in patients with diabetes mellitus or CHF
- d) More effective in white patients versus black patients
- e) Efficacy is enhanced by diuretics
- f) Side effects
 - (1) Dry cough, hyperkalemia, skin rash, proteinuria, angioedema
 - (2) Use cautiously in patients with renal insufficiency or renal artery stenosis
- 4. Angiotensin II receptor blockers (ARB)
 - a) Examples
 - (1) Losartan (Cozaar), valsartan (Diovan), telmisartan (Micardis), irbesartan (Avapro), olmesartan (Benicar), candesartan (Atacand), eprosartan (Teveten)
 - b) Mechanism of action
 - (1) Competitive inhibitor of AT₁ receptors
 - (2) Blocks the ability of angiotensins II and III to stimulate pressor and cell proliferative effects; does not affect bradykinin
 - c) Used in patients who cannot tolerate ACE inhibitors
- 5. Beta blockers
 - a) Examples
 - (1) Propranolol (Inderal): antagonizes beta-1 and beta-2; inhibits renin production
 - (2) Metoprolol (Lopressor/Toprol XL): less beta-2 antagonism; may be used in patients with asthma, diabetes, or peripheral vascular disease
 - (3) Nadolol (Corgard), carteolol (Cartrol), atenolol (Tenormin), betaxolol (Kerlone), bisoprolol (Zebeta): beta-1 selective antagonist; slower metabolism and longer half-life

- (4) Acebutolol (Sectral) and pindolol (Visken) have intrinsic sympathomimetic activity (ISA)
 - (5) Labetalol (Normodyne/Trandate), carvedilol (Coreg): alpha and beta blocker
 - (a) Labetalol has some beta-2 agonist activity; may be used in hypertensive emergencies
 - (b) Carvedilol used in CHF
 - b) Mechanism of action
 - (1) Reduces cardiac output
 - (2) Inhibits renin release
 - c) Side effects
 - (1) Fatigue, weakness, trouble sleeping; may increase triglycerides and decreases high-density lipoprotein (HDL) cholesterol; hypoglycemia
 - (2) Bronchoconstriction: highest risk in patients with obstructive pulmonary disease
 - (3) Arrhythmias: must taper medication when ending therapy
 - (4) Sexual impairment (men, exact mechanism unknown)
 - (5) Overdose: bradycardia, hypotension, bronchospasm, acute cardiac failure, death
 - (6) Use cautiously in patients with CHF, diabetes, or hyperthyroidism
 - d) Interactions
 - (1) Beta blockers and other hypotensive medications: possible increased hypotension
 - (2) Beta blockers and diabetes medications: possible increased risk of hypoglycemia
 - (3) Propranolol is a substrate of CYP1A2 and 2D6 (major); CYP1A2 inducers (e.g., carbamazepine, rifampin) may decrease the levels and effects of propranolol; CYP1A2 inhibitors (e.g., ciprofloxacin, amiodarone) may increase levels and effects of propranolol.
6. Peripheral alpha blockers
- a) Examples
 - (1) Prazosin (Minipress/Vasoflex), terazosin (Hytrin), doxazosin (Cardura)
 - b) Competitive antagonists for alpha-1
 - c) Side effects
 - (1) Reflex tachycardia
 - (2) First-dose syncope
7. Vasodilators
- a) Examples
 - (1) Hydralazine (Apresoline), minoxidil (Loniten), sodium nitroprusside (Nitropress)
 - b) Mechanism of action
 - (1) Relaxes smooth muscle of arterioles and some veins
 - c) Side effects
 - (1) Reflex tachycardia, sodium retention
 - (2) Nitroprusside may cause cyanide ion production
 - (3) Minoxidil causes excess hair growth
8. Central alpha-adrenergic agonists
- a) Clonidine, guanabenz, guanfacine: direct-acting alpha-2 agonists
 - b) Methyldopa: prodrug taken up by central adrenergic neurons and converted to alpha-2 adrenoceptor agonist α -methylnorepinephrine
 - c) Not generally used as monotherapy
 - d) Clonidine (Catapres)
 - (1) Also useful in diagnosis of pheochromocytoma
 - (2) Lipid soluble; readily enters the brain
 - (3) Available as a sustained-release transdermal patch
 - e) Side effects
 - (1) Sedation, dry mouth, sodium, and water retention
 - (2) Withdrawal syndrome (not with transdermal patch)
 - (3) Avoid in patients who are taking tricyclic antidepressants (TCAs)
- E. Special considerations regarding drug selection
1. Thiazide diuretics
 - a) Favorable: may slow demineralization in osteoporosis
 - b) Unfavorable: may worsen gout
 2. Beta blockers
 - a) Favorable: useful for migraine and essential tremor (propranolol)
 - b) Unfavorable: Should not be used in patients with asthma or heart block
 3. Alpha blockers
 - a) Favorable: useful in benign prostatic hyperplasia (BPH)
 4. Loop diuretics
 - a) Favorable: More effective in lowering blood pressure than thiazides in patients with renal insufficiency
- F. Special populations
1. African Americans
 - a) Typically associated with low renin, expanded volume, and sensitivity to salt
 - b) Drugs of choice: Thiazide diuretics and long-acting calcium channel blockers
 - c) ACE inhibitors, ARB, and beta blockers alone are less effective in lowering blood pressure in African Americans
 2. Pregnancy
 - a) Drug of choice: methyldopa (based on long-term data of safety)
 - b) ACE inhibitors and ARB contraindicated
- III. Coronary Artery Disease
- A. Coronary artery disease (CAD) includes
1. Angina pectoris (chest pain): occurs when there is a deficiency of oxygen for the heart muscle
 - a) Angina occurs when the blood or oxygen supply to the myocardium is impaired and/or the heart is working harder than usual to supply oxygen
 2. Myocardial infarction (MI) (heart attack): occurs when a coronary artery is obstructed, which leads to prolonged ischemia that results in death or damage to heart muscle tissue

- a) Characterized by persistent chest pain radiating down the left arm, weak pulse, pallor
- B. Drug therapy
1. Organic nitrates
- a) Examples
- (1) Nitroglycerin (e.g., Nitrolingual, Nitro-time, Nitrobid, Nitrol, Nitrostat, Nitroguard, Nitro-Dur) (Figure 10-1)
 - (2) Isosorbide mononitrate (Imdur, Ismo, Monoket)
 - (3) Isosorbide dinitrate (Isordil, Dilatrate SR)
- b) Mechanism of action: Exact mechanism not known
- (1) Relax vascular smooth muscle = vasodilation
 - (2) Metabolized to nitric oxide = vasodilation
 - (3) Vasodilation = venous pooling = ↓ preload
 - (4) ↓ peripheral venous return = venous pooling = ↓ venous return to heart = ↓ preload
 - (5) ↑ total coronary blood flow (coronary vasodilation)
- c) Indications
- (1) Acute relief of angina pectoris, prophylaxis of anginal attacks, long-term prophylaxis of angina pectoris

- (2) Nitroglycerin is the drug of choice for acute angina pectoris attacks
- d) Contraindications
- (1) Severe anemia
 - (2) Previous reaction to nitrates
 - (3) Caution: increased intracranial pressure, diuretic-induced fluid depletion, severe hypotension
- e) Interactions
- (1) Nitrates and alcohol: may increase hypotension
 - (2) IV nitroglycerin and heparin: may need to increase heparin dose
 - (3) Antihypertensive medications and nitrates: may increase hypotension
 - (4) CONTRAINDICATED: Concurrent use with sildenafil (Viagra, Revatio) or other phosphodiesterase-5 inhibitors (commonly used for erectile dysfunction): may increase hypotension, cause MI or death (severe cases)
- f) Toxicity and side effects
- (1) Headache is the most common side effect
 - (2) Postural hypotension
 - (3) Facial flushing
 - (4) Tachycardia (rapid heart rate)
 - (5) Tolerance: Patients should have a nitrate-free interval; Minimal time period not known, but can range 6–14 hours.

2. Beta blockers

- a) Mechanism of action
- (1) Block beta-1 receptors in the heart and vascular smooth muscle (some are not selective)
 - (a) Negative chronotropic activity = decreases rate of heart
 - (b) Negative inotropic activity = decreases work of heart

b) Indications

- (1) Chronic stable angina pectoris

3. Ischemic chest pain

- a) “MONA”—acronym for the primary emergency treatments recommended as follows:
- (1) Morphine
 - (a) Drug of choice to relieve pain associated with acute MI
 - (b) Dose: 2–4 mg IV push; repeat doses every 5 to 10 minutes until pain relief is obtained
 - (2) Oxygen
 - (a) Reduces ST elevation and limits ischemic myocardial injury
 - (b) May be administered by nasal cannula and mask
 - (c) Amount of oxygen is determined by oxygen saturation
 - (3) Nitroglycerin
 - (a) Preferred drug initially for treatment of ischemic pain
 - (b) Dose: 0.3–0.4 mg nitroglycerin sublingually given three times at

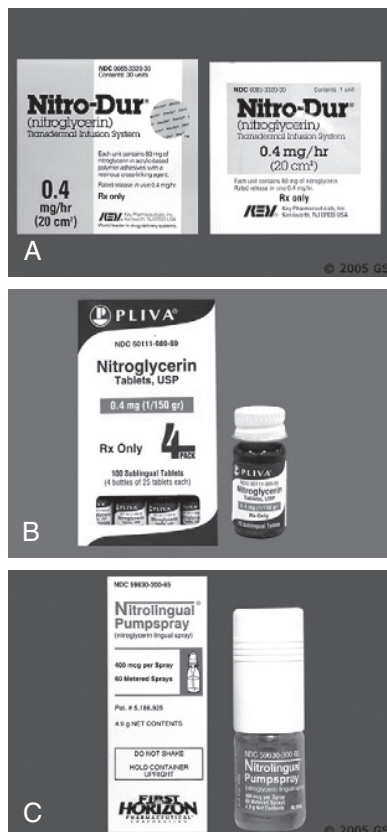


Figure 10-1 — Nitroglycerin dosage forms. (Drug photos provided by Gold Standard, Inc.)

- 5 minute intervals as long as blood pressure is stable
- (c) Contraindicated in patients with right ventricular infarction or when heart rate is <50 beats per minute
- (4) Aspirin
- (a) Antiplatelet effect, which prevents subsequent thrombus formation (Figure 10-2)
- (b) Dose: 160–325 mg given by mouth as soon as possible; chewable aspirin is preferred
4. Calcium channel blockers
- a) Mechanism of action
- (1) Inhibit movement of extracellular calcium ions across membranes of myocardial cells and vascular smooth muscle cells without changing serum calcium concentration
 - (2) Decreases myocardial contractility = decreased work of heart
 - (3) Relax vascular smooth muscle = decreased afterload
- b) Indications
- (1) Prinzmetal variant angina, chronic stable angina (not first choice)
5. Ranolazine (Ranexa)

IV. Arrhythmias

Arrhythmia is an abnormal conduction of the heart, may be an atrial or ventricular problem. Ventricular arrhythmias are more serious than atrial. Electrolytes should be checked and corrected if abnormal. Some patients require mechanical treatment: defibrillator; current models may have a pacemaker. Patients should

know which type of defibrillator they have and when it was placed in their body.

A. Atrial: arrhythmia occurring in the atria

1. Atrial fibrillation (Afib): most common supraventricular arrhythmia, overall incidence approximately 2% (older than 75 years old, incidence may be as high as 10%); extremely active and disorganized atrial activation leads to loss of atrial contraction and lower ventricular contraction and response.
 - a) Acute treatment: If the patient is considered hemodynamically unstable, give electrical cardioversion or medication; If the patient is considered hemodynamically stable, use electrical cardioversion or medication; may require chronic treatment
 - b) Chronic treatment: medication to maintain cardioversion; warfarin (Coumadin) to prevent potential coagulation problems
2. Atrial flutter (Aflutter): less frequent than Afib, similar in consequences and treatment; difference is that there are rapid beats, but atrial activation is normal; it is a disorder of atrial pulse formation, most commonly resulting from localized atrial reentry or ectopic focus in lower part of right atrium.

B. Ventricular: arrhythmia occurring in the ventricle

1. Ventricular tachycardia (Vtach): most commonly encountered life-threatening arrhythmia; episode usually constituted by at least three successive ventricular ectopic beats >100/min; QRS complex is wide. Usually a regular rhythm; conduction from ventricle to atria may occur, resulting in retrograde atrial

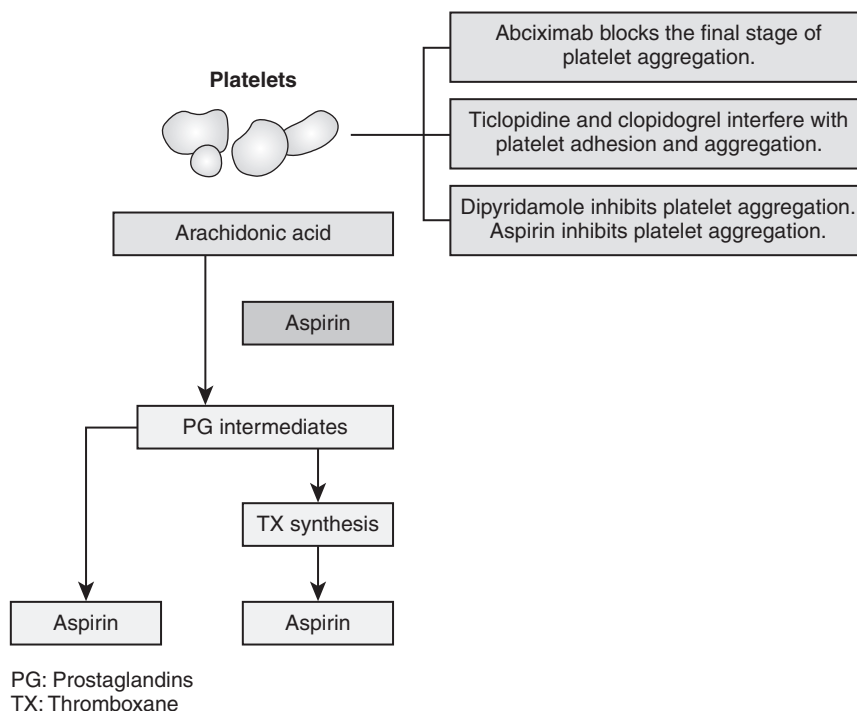


Figure 10-2—**Action for antiplatelet drugs.** (Modified from Lilley LL, Harrington S, Snyder JS: Pharmacology and the nursing process, ed. 5, St. Louis, 2007, Mosby. In Mosou K, Snipe K: Pharmacology for pharmacy technicians. St. Louis, 2009, Mosby.)

depolarization. Coronary artery disease with MI is the most common structural heart disease predisposing to Vtach; symptoms palpitations, breathlessness, lightheadedness, angina, syncope.

- a) Hemodynamically unstable: electrical cardioversion
 - b) Hemodynamically stable: chemical cardioversion; can start lidocaine, procainamide, bretylium, amiodarone
2. Ventricular fibrillation (Vfib): chaotic ventricular rhythm; no organized electrical activity, no ventricular contraction, patient requires immediate medical attention to prevent death; any structural, toxic, or metabolic derangement adversely affecting ventricular repolarization may predispose patient to Vfib; immediate electrical cardioversion necessary or use medical cardioversion
- a) Correct reversible causes (e.g., hypomagnesemia, hypokalemia). If occurring within the first 72 hours of an acute MI and not associated with increased risk of recurrence, chronic drug therapy is not required.
 - b) Other: mechanical defibrillator implanted and/or chemical prophylaxis
- C. Antiarrhythmic therapies (Vaughan Williams antiarrhythmic classification)
1. Class I: inhibit fast sodium channels
 - a) Class Ia: prolong ventricular refractoriness and QT interval
 - (1) Quinidine: suppress symptomatic atrial premature depolarizations and complex ventricular ectopy, convert Afib to sinus rhythm and prevent recurrence, terminate and prevent paroxysmal supraventricular tachycardia (PSVT), may prevent recurrence of sustained Vtach or Vfib in some patients.
 - (2) Procainamide: same effects as quinidine on automaticity, conduction, and refractoriness; major metabolite: *N*-acetylprocainamide (NAPA) has class III action; may be as effective as lidocaine in acute termination of sustained Vtach
 - (3) Disopyramide: slows conduction and prolongs refractoriness; similar to procainamide and quinidine
 - b) Class Ib: less potent sodium channel blockers; shorten action potential duration and refractoriness
 - (1) Lidocaine: effective in management of Vtach, especially in setting of acute MI, not to be used as prophylaxis when patient has an MI
 - (2) Mexiletine: similar to lidocaine, but has less-potent antiarrhythmic activity; can be used alone or with class Ia medication; has not been shown to be effective in preventing recurrence of sustained life-threatening ventricular arrhythmias when used alone

- (3) Tocainide: alone or with class Ia drugs for treatment of ventricular arrhythmias; not shown effective in preventing recurrences of sustained life-threatening ventricular arrhythmias
 - (4) Phenytoin: primarily used for treatment of digoxin-induced ventricular and supraventricular arrhythmias
 - (5) Moricizine: combined effect of class Ia/Ib; may be used to treat ventricular arrhythmias; not shown to be effective in preventing recurrences of sustained life-threatening ventricular arrhythmias
- c) Class Ic: potent sodium channel blockers; slow conduction with little effect on repolarization
- (1) Flecainide: may be more effective than other class I agents in management of Afib, flutter, and PSVT
 - (2) Propafenone: chemical structure is similar to flecainide's, but has type Ic and moderate beta-adrenergic antagonism; used similar to flecainide
2. Class II: blocks beta-adrenergic receptor sites
- a) Beta-adrenergic antagonists (beta blockers): bind at catecholamine receptor sites; decrease automaticity and prevent re-entrant arrhythmias involving the atrioventricular (AV) node; may favorably alter myocardial oxygen supply versus demand and by blunting tissue response to catecholamines
3. Class III: impact potassium channels and prolong repolarization; prolong action potential duration and repolarization to a greater extent than they depress conduction velocity
- a) Amiodarone: prolongs repolarization and refractoriness in atrial and ventricular tissue; slows sinus rate and prolongs AV nodal conduction; alpha and beta antagonist; can reduce systemic vascular resistance and mean arterial blood pressure (BP). Potent antiarrhythmic effective for a number of arrhythmias. Prevents recurrence of sustained Vtach or Vfib in <60% patients; full suppression takes 4–6 weeks
 - b) Bretylium: has important interactions with the autonomic nervous system; prolongs action potential duration and refractoriness in Purkinje fibers and ventricular muscle; affects peripheral adrenergic nerve terminals (initially causes abrupt release of norepinephrine, then prevents further release and reuptake); main use is in treatment of Vtach and Vfib
 - c) Sotalol: patients should stay in hospital for 3 days when initiating and if dose is changed; decreases frequency and duration of nonsustained Vtach in <40% of patients; prevents recurrence of sustained Vtach and Vfib in 70% of patients; prevents recurrence of symptomatic AFib and flutter

- d) Ibutilide: for chemical cardioversion of AFib and flutter; prolongs atrial and ventricular refractory period; minimal effect on conduction
- 4. Class IV: selectively blocks slow calcium channels; sinoatrial (SA) and AV nodes depend on slow channel activity; induces a concentration-dependent depression in phase 4 depolarization and prolonged refractoriness = depressed automaticity and slowed conduction
 - a) Calcium channel antagonists
 - (1) Verapamil: slows ventricular response in AFib and atrial flutter, slows or abolishes SVT using AV node for re-entrant circuit
 - (2) Diltiazem: similar to verapamil; shorter half-life.
 - b) Purinergic agonists
 - (1) Adenosine: inhibits sinus node automaticity, shortens atrial refractory period duration, depresses AV node conduction, prolongs AV node refractoriness; not effective in converting atrial flutter, AFib, or Vtach to sinus rhythm, but may allow diagnosis
 - c) Digitalis glycosides
 - Caution: antiarrhythmics may cause arrhythmias; agents may cause more than one action
 - (1) Digoxin: control resting ventricular rate in Afib or atrial flutter in the setting of left ventricular dysfunction and heart failure; may be useful as adjunctive therapy in combination with calcium-channel blocker (CCB) or beta blocker (BB) for rate control of chronic Afib
 - d) Warfarin (Coumadin)
 - (1) Anticoagulation: prevent potential clotting due to abnormal blood flow, aspirin may be used in patients at high risk of complications from warfarin therapy

V. Lipid Disorders

A. Lipoproteins

- 1. Clusters of lipids associated with proteins that serve as transport vehicles for lipids in the lymph and blood
- 2. Lipoproteins are distinguished by size and density. Each contains different amounts and kinds of lipids and proteins.
 - a) Chylomicrons are made by intestinal cells and transport fatty acids from intestines to muscle and other energy using tissues by lipoprotein lipase.
 - b) Very low-density lipoproteins (VLDLs) are made by the liver and contain large amounts of triglyceride. They are similar to chylomicrons because they transport fatty acids to cells.
 - c) Intermediate density lipoproteins (IDLs) result from the loss of fatty acids from VLDLs.

They are taken up by the liver or remain in the circulation and are converted to low-density lipoproteins (LDL).

- d) LDL the “bad” cholesterol that delivers cholesterol from liver to cells.
- e) HDL the “good” cholesterol that are made by the liver to scavenge or collect excess cholesterol from cells, including atherosclerotic plaques.
- B. Hyperlipidemias
 - 1. Primary hyperlipidemias: familial disease
 - 2. Suspected in people with very high levels of cholesterol (>300 mg/dL) or triglycerides (>1000 mg/dL)
 - 3. Secondary hyperlipidemias are due to other factors such as diet, exercise, medications, diabetes, alcohol intake, hypothyroidism, primary biliary cirrhosis.
- C. Laboratory tests to measure lipids
 - 1. Total cholesterol
 - 2. Triglycerides
 - 3. Glycerol kinase reaction assays
- D. Plasma lipid levels (mg/dL)
 - 1. Total cholesterol
 - a) < 200 desirable
 - b) 200–239 borderline
 - c) >240 high
 - 2. LDL
 - a) <130 desirable (lower levels of LDL are desirable in patients with select risk factors; see Guidelines [F])
 - b) 130–159 borderline
 - c) >160 high
 - 3. HDL
 - a) <35 low
- E. Risk factors for heart disease
 - 1. Age (men ≥ 45 years of age; women ≥ 55 years of age)
 - 2. Family history of premature heart disease
 - a) Heart disease in male first-degree relative <55 years
 - b) Heart disease in female first-degree relative <65 years
 - 3. Cigarette smoking
 - 4. Hypertension (BP = 140/90 mm Hg or on antihypertensive medication)
 - 5. Low HDL (<40 mg/dL)
 - 6. Obesity
 - 7. Diabetes mellitus
- F. National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) Guidelines
 - 1. High-risk patients
 - a) Heart disease or heart disease risk equivalents (10-year risk >20%)
 - (1) Heart disease plus
 - (a) Multiple risk factors
 - (b) Poorly controlled risk factors
 - (c) Multiple risk factors for metabolic syndrome
 - (d) High triglycerides
 - (e) Low HDL
 - b) Goal: LDL cholesterol <100 mg/dL

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Figure 10-3—**Algorithm for digoxin therapy for heart failure.** (Modified from Morris S, Hatcher HF, Reddy DK: Digoxin therapy for heart failure: An update, American Family Physician, August 15, 2006. Available at: <http://www.aafp.org/afp/20060815/613.html>.)

2. Moderately high risk patients
 - a) Two or more risk factors (10-year risk 10%–20%)
 - b) Goal: LDL cholesterol <130 mg/dL
3. Moderate-risk patients
 - a) Two or more risk factors (10-year risk <10%)
 - b) Goal: LDL cholesterol <160 mg/dL
4. Low-risk patients
 - a) None or one risk factor
 - b) Goal: LDL cholesterol <160 mg/dL
 - c) If LDL cholesterol is ≥ 160 mg/dL consider therapeutic lifestyle changes (TLC)
 - d) If LDL cholesterol is ≥ 190 mg/dL consider TLC and possible drug therapy
 - e) If LDL cholesterol is 160–189 mg/dL consider TLC and drug therapy
- G. Nondrug therapy
 1. Weight control
 2. Smoking cessation
 3. Limit intake of saturated fat
 4. Blood pressure control
- H. Drug therapy
 1. Hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors (statins)
 - a) Examples
 - (1) Lovastatin (Mevacor), pravastatin (Pravachol), simvastatin (Zocor), fluvastatin (Lescol), atorvastatin (Lipitor), rosuvastatin (Crestor)
 - b) Method of action
 - (1) Decrease LDL, triglyceride, and total cholesterol

- (2) Inhibits HMG-CoA reductase
 - (3) Selective, reversible, competitive inhibition
 - (4) HMG-CoA converts to mevalonic acid, a precursor of cholesterol
 - c) Indications
 - (1) Hyperlipoproteinemia
 - d) Caution
 - (1) Patients who consume substantial amounts of alcohol
 - (2) Patients with active liver disease
 - (3) Patients with unexplained persistent elevations in serum aminotransferase concentrations
 - (4) Contraindication: absolute liver disease, pregnancy, lactating women, women of childbearing age who may conceive during therapy, hypersensitivity to medication
 - e) Interactions
 - (1) Immunosuppressants such as cyclosporine may increase serum concentrations of atorvastatin, thereby increasing the risk of myopathy.
 - (2) Concurrent use of fibrates with HMG-CoA reductase inhibitors may increase the risk of myopathy and rhabdomyolysis.
 - (3) Systemic azole-derivative antifungals (e.g., itraconazole) may decrease the CYP 450 metabolism of HMG-CoA reductase inhibitors. If systemic antifungal treatment is needed, statin is usually discontinued during the course of antifungal treatment.
 - (4) Select systemic macrolides (e.g., erythromycin, clarithromycin) may decrease the CYP 450 metabolism isoenzymes of HMG-CoA reductase inhibitors. If systemic macrolide treatment is needed with one of these drugs, statin is usually discontinued during the course of the macrolide treatment.
 - (5) Simvastatin, lovastatin, and atorvastatin are major substrates of CYP 3A4.
 - (6) Fluvastatin is a major substrate of CYP 2C9.
 - (7) Grapefruit juice may inhibit metabolism of HMG-CoA reductase inhibitors by CYP3A4; therefore high dietary intakes of grapefruit juice should be avoided.
 - f) Toxicity and side effects
 - (1) Increased liver function tests (LFTs)
 - (2) Rhabdomyolysis
 - (3) Headache
 - (4) Myopathy (myalgia and/or muscle weakness)
 - (a) Risk factors
 - (i) Acute or chronic renal failure
 - (ii) Obstructive liver disease
 - (iii) Hypothyroidism
 - (iv) Concurrent drug therapy (e.g., fibrates, CYP3A4 inhibitors)
 - (v) Age
 - (vi) Sex (women more so than men)
 - (vii) Small body frame
 - (viii) Alcohol abuse
 - (ix) Grapefruit juice
2. Fibrates
- a) Examples
 - (1) Clofibrate (Atromid-S), gemfibrozil (Lopid), fenofibrate (TriCor, others)
 - b) Method of action
 - (1) Hydrolyze triacylglycerol and VLDL
 - (2) Causes increased removal of triacylglycerol and VLDL from plasma
 - (3) Triglycerides reduced
 - (4) Little to no change in LDL
 - (5) Possible increase in HDL
 - (6) Greater effect seen with gemfibrozil than clofibrate
 - c) Indications
 - (1) Hypertriglyceridemia
 - (2) Dyslipidemia (high triglycerides [TG], low HDL cholesterol)
 - d) Caution
 - (1) Should be discontinued if response is not observed within 3 months
 - (2) None has shown beneficial effect on cardiovascular mortality
 - (3) None is considered first-line choice
 - (4) Patients with a history of hepatic or renal dysfunction, peptic ulcer disease, or gallbladder disease
 - (5) Contraindicated: known hypersensitivity to medication, pregnancy, lactation
 - e) Interactions
 - (1) Fibrates may increase effects of coumanin anticoagulants; monitor international normalized ratio (INR)
 - (2) Gemfibrozil may increase the serum concentrations of repaglinide and cause severe hypoglycemia.
 - (3) Concurrent use with HMG-CoA reductase inhibitors may increase the risk of myopathy and rhabdomyolysis.
 - (4) Gemfibrozil is a strong inhibitor of CYP 2C8, 2C9, and 2C19.
 - f) Toxicity and side effects
 - (1) Leukopenia
 - (2) Acute muscular syndrome (acute flu-like syndrome)
 - (3) Cholelithiasis (increased cholesterol excretion in bile)
 - (4) Arrhythmias
 - (5) Reversible increased liver function tests
 - (6) Nausea, abdominal pain, epigastric pain, dyspepsia
3. Nicotinic acid
- a) Examples
 - (1) Niaspan, Niacor
 - b) Method of action
 - (1) Inhibits lipolysis in adipose tissue, decreasing free fatty acids

- (2) Prevents liver from forming VLDL
- (3) Prevents VLDL from forming LDL, the "bad cholesterol"
- (4) Increases HDL, the "good cholesterol"
- (5) May reverse some endothelial cell dysfunction
- c) Indications
 - (1) Hypercholesterolemia, niacin deficiency, pellagra
- d) Caution
 - (1) Patients with diabetes
 - (2) Liver dysfunction, history of jaundice
 - (3) Gallbladder disease
 - (4) Gout
 - (5) Peptic ulcer disease
 - (6) Hypersensitivity to niacin, niacinamide
- e) Interactions
 - (1) Nicotinic acid may increase the effects of ganglionic blocking drugs.
 - (2) May increase the adverse effects of HMG-CoA reductase inhibitors.
- f) Toxicity and side effects (not tolerated by many patients)
 - (1) Flushing: especially the face and neck (tolerance may build), may be less with sustained-release, may pretreat with aspirin
 - (2) Other: pruritus, sensation of burning, stinging or tingling of skin, nausea, bloating, flatulence, hunger pains, vomiting, heartburn, diarrhea, hypotension, dizziness, tachycardia, syncope, headache, hyperglycemia
 - (3) Long-term use: rash, hyperpigmentation, liver impairment
- 4. Bile acid binding resins
 - a) Examples
 - (1) Cholestyramine (Questran), colestipol (Colestid)
 - b) Method of action
 - (1) Bind bile acids and bile salts in small intestine
 - (2) Bound complex is excreted in feces
 - (3) Liver increases conversion of cholesterol to bile acids
 - (4) Intracellular cholesterol levels decrease
 - (5) Increased uptake of LDL in liver
 - (6) May see increase in HDL
 - c) Indications
 - (1) Hypercholesterolemia (adjunct)
 - d) Caution
 - (1) GI dysfunction (constipation)
 - (2) Patients with phenylketonuria: flavored Colestid granules contain aspartame, which is converted to phenylalanine
 - e) Interactions
 - (1) Bile acid resins may bind to numerous medications and reduce absorption; recommend separating 1 hour before or 4 hours after other medications
 - f) Toxicity and side effects
 - (1) GI: constipation, fecal impaction, hemorrhoids, abdominal pain, distention, bloating, flatulence, nausea, vomiting, diarrhea, anorexia, dyspepsia, heartburn, biliary colic, indigestion (tolerance may develop to flatulence and bloating)
- (2) Hyperchloremic acidosis or increased urinary calcium excretion
- 5. Ezetimibe
 - a) Examples
 - (1) Zetia, also found in combination with simvastatin (Vytorin)
 - b) Method of action
 - (1) Inhibits absorption of cholesterol at the brush border of the small intestine
 - (2) Decreases transport of cholesterol to liver
 - (3) Decreases total, LDL, and triglycerides
 - (4) Increases HDL
 - c) Indications
 - (1) Hypercholesterolemia (adjunct)
 - d) Caution
 - (1) Hepatic or renal impairment
 - (2) Contraindications: active liver disease
 - e) Interactions
 - (1) Concurrent use of ezetimibe with fibrates may increase risk of cholelithiasis
 - (2) Bile acid sequestrants may decrease ezetimibe bioavailability
 - f) Toxicity and side effects
 - (1) Upper respiratory tract infection, headache, myalgia
 - (2) Increased liver transaminases with HMG-CoA reductase inhibitors
 - (3) Possible association between the use of simvastatin and ezetimibe and increased incidence of cancer.
- 6. Probucol (no longer on U.S. market, listed for historic reference)
 - a) Method of action
 - (1) Increases fecal loss of bile acid-bound LDL
 - (2) Decreases synthesis of cholesterol
 - (3) Inhibits enteral cholesterol absorption
 - (4) Inhibits macrophages ingestion of oxidized LDL
 - (5) Inhibits plaque formation
 - b) Indications
 - (1) Hypercholesterolemia (adjunct)
 - c) Caution
 - (1) Patients with prolonged QT interval
 - (2) Contraindication: pregnancy (discontinue 6 months before pregnancy)
 - d) Interactions
 - (1) Increased risk of toxicity when used with medications that prolong QT interval
 - e) Toxicity and side effects
 - (1) Prolonged QT interval (market removal due to risk for proarrhythmia)
 - (2) Mild GI disturbance (tolerance should develop)

VI. Congestive Heart Failure

CHF represents a complex clinical syndrome characterized by abnormalities of left ventricular function and neurohormonal regulation. It may be caused by multiple underlying diseases such as CHD, atherosclerosis, rheumatic fever, cardiomyopathy, valve disorders, ventricular failure, left or right-sided failure, hypertension, prolonged drug or alcohol addiction, diabetes, or previous heart attack.

A. Types of heart failure

1. Left ventricular heart failure
 - a) Most common
 - b) Systolic failure: unable to contract
 - c) Diastolic failure: unable to relax
2. Right ventricular heart failure
 - a) Usually occurs after left failure
 - b) Less blood received causes right damage
 - c) Less pumping by right side
 - d) Venous pooling of blood in legs

B. New York Heart Association functional classification

1. Class I: Physical activity is not limited
2. Class II: Some limitation with physical activity; comfortable at rest
3. Class III: Marked limitation with physical activity
4. Class IV: Unable to be physically active without discomfort

C. Risk factors

1. Family history
2. Cigarette smoking
3. Obesity
4. Dyslipidemia
5. Hypertension
6. Sedentary lifestyle
7. High dietary sodium intake

D. Signs and symptoms

1. Tachycardia
2. Decreased exercise tolerance
3. Shortness of breath
 - a) Orthopnea (dyspnea that occurs from lying flat)
4. Peripheral and pulmonary edema
5. Cardiomegaly

E. Goals of therapy

1. Meet oxygen requirements of the body
2. Reduce symptoms and improve quality of life
3. Reduce hospitalization
4. Reduce mortality

F. Nondrug therapy

1. Rest
2. Salt restriction
3. Fluid restriction
4. Gradual exertion programs

G. Drug therapy (Figure 10-3)

1. Cardiac glycosides (e.g., digoxin)
 - a) Increases force of myocardial contractility
 - b) Increases cardiac output
 - c) Increases cardiac efficiency
 - d) Decreases heart rate
 - e) Decreases cardiac size
2. Diuretics
 - a) Controls fluid retention and improves symptoms rapidly
 - b) Should be prescribed to all patients with evidence of fluid retention
 - c) Do not use alone in patients with heart failure

3. Drugs

- a) Loop diuretics (e.g., furosemide)
- b) Aldosterone antagonists with spironolactone or eplerenone may be added to loop diuretics to enhance diuresis and minimize potassium loss
- c) Oral metolazone, spironolactone, or intravenous chlorothiazide can be added as a second diuretic agent when diuretic response is inadequate
 - (1) Metolazone is the drug of choice in refractory patients with advanced renal failure

4. Vasodilators

- a) Used in patients who remain symptomatic after administration of diuretics and digitalis
- b) Useful in patients with dilated left ventricle, normal or increase systemic blood pressure, increased systemic vascular resistance, or valvular regurgitation
- c) Venous dilators: nitrates
- d) Arterial vasodilators: hydralazine and minoxidil

5. Beta blockers (e.g., Carvedilol, metoprolol)

- a) Positive actions
 - (1) Decreases myocardial oxygen consumption demand by decreasing heart rate
 - (2) Decreases blood pressure, thereby decreasing afterload and preload
- b) Negative actions
 - (1) Decreases cardiac contractility

6. ACE inhibitors/ARB

- a) Reduces afterload and preload; reduces workload on the heart
- b) Generates positive cardiac inotropy
- c) Slows progression of left ventricular dysfunction in CHF (ACE inhibitors)
- d) Used for chronic CHF

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PATIENT PROFILE

Patient Initials: RM

Sex: Male

Age: 55 years

Height: 6'0"

Weight: 101 kg
 Race: White
 Allergies: No known drug allergies (NKDA)

Chief Complaint:

RM is a 55-year old man presenting to his family physician with increasing shortness of breath. In the past few days, he has had more difficulty breathing, and he complains of swelling of his ankles.

Recent History:

RM has recently been noncompliant with his reduced-salt diet due to the start of football season at his alma mater, including intake of salty chips and beer while tailgating with former college buddies. He has missed a few doses of his heart failure medications, specifically the “water pill.” His shortness of breath now occurs even at rest, and to sleep comfortably over the past several days he has elevated his head.

Social History:

Tobacco use: None now, quit 5 years ago, before then “smoked heavily”

Alcohol use: 1–2 drinks per week, usually in a social setting

Medications (before admission):

Enalapril 10 mg PO twice per day (recently started, physician is titrating dosage up to maximum recommended for heart failure, 20 mg PO twice daily, as tolerated)

Furosemide 20 mg PO once daily

Digoxin 0.25 mg PO qAM

Family History:

Father is alive but had a heart attack (myocardial infarction) at age 65 years.

Mother is alive and, other than mild arthritis, is fairly active and healthy.

Physical Exam:

Vitals: BP 139/93 mm Hg; respiratory rate 27 breathes per minute; temperature: afebrile.

Chest: Inspiratory rales, bilateral rhonchi, decreased breath sounds, decreased percussion

CV: Regular rate and rhythm, rate 98

Extremities: 2+ pitting edema

ECG: Pattern consistent with left ventricular hypertrophy (LVH)

CXR: Cardiomegaly, bilateral pleural effusion

Laboratories: All within normal limits.

Diagnosis: Decompensated heart failure; admit to hospital for acute management and to maximize and stabilize current medications.

PATIENT PROFILE QUESTIONS

- Upon discharge from the hospital, RM should be counseled on which of the following regarding his drug therapy for heart failure?
 - Medications will cure heart failure.
 - Most patients with heart failure are managed on one medication.
 - He needs to take the drug therapy for heart failure regularly as prescribed to control his condition.

- I only
- I and II only
- III only
- II and III only
- All of the above

Answer: c. Adherence to medications can decrease morbidity and mortality in patients with heart failure. Most patients must be managed on several classes of medications to improve health and reduces mortality and morbidity, including angiotensin-converting enzyme (ACE) inhibitors, cardioselective beta blockers (e.g., metoprolol or carvedilol), digoxin, and loop diuretics. A patient with heart failure cannot be cured with medications, but the disease can be managed well with proper medication use.

Noncompliance with medication is a significant risk factor and leading contributor to hospitalization in patients with heart failure.

- Several months later, RM is stabilized and back on his usual medications. However, for the last few months he has complained of a nonproductive, annoying cough. Which of the following substitutions could be made in his regimen to resolve this problem?
 - Spironolactone for digoxin
 - Hydrochlorothiazide for furosemide
 - Candesartan for enalapril
 - Spironolactone for furosemide
- Several months later RM has a worsening of heart failure, and carvedilol is added to his current regimen. Which of the following are contraindications to the use of a cardioselective beta blocker?
 - Severe bradycardia
 - Second- or third- degree atrioventricular (AV) block
 - Diabetes mellitus type 2

- I only
- I and II
- II and III
- I, II, and III

Answer: b. Although beta blockers should be used cautiously in patients with diabetes due to their ability to mask symptoms of hypoglycemia, they are not contraindicated.

REVIEW QUESTIONS

(Answers and Rationales on page 344.)

- Which of the following causes increased urine output?
 - Theophylline
 - Furosemide
 - Ethacrynic acid
 - a, b, and c
 - b and c

2. Which of the following is NOT a mechanism of digitalis?
 - a. Decreased sympathetic tone
 - b. Enhances sympathetic responsiveness of Sinoatrial (SA) and AV nodes
 - c. Enhanced vagal tone
 - d. Slowed AV node conduction
 - e. Increased CNS parasympathetic activity
3. Which of the following drugs is correctly matched to its mechanism of action?
 - a. Amrinone: inhibits troponin I
 - b. Dopamine: inhibits troponin I
 - c. Digoxin: inhibits Na^+/K^+ -ATPase
 - d. Digoxin: activates Na^+/K^+ -ATPase
 - e. None of the above
4. Which of the following is the correct explanation for tachycardia that occurs after nitroglycerin ingestion?
 - a. Reflex sympathetic discharge
 - b. Decreased intracranial pressure
 - c. Direct positive chronotropy
 - d. Increased norepinephrine secretion from intracardial nerve endings
 - e. None of the above
5. Which of the following is the mechanism of action of digitalis in the correction of atrial flutter?
 - a. Decreased SA node firing
 - b. Decreased AV node refractory period
 - c. Increased atrial muscle conduction velocity
 - d. Decreased AV node conduction rate
 - e. a and c
6. Which of the following is true of digoxin?
 - a. Only available as oral tablets
 - b. Highly protein bound in circulation
 - c. Increased toxicity in renal failure
 - d. Incomplete gastrointestinal absorption
 - e. Excreted renally without significant metabolism within 24 hours
7. A 45-year-old man receiving digitalis is found to have premature ventricular contractions. What is the most appropriate treatment?
 - a. Quinidine
 - b. Phenytoin
 - c. Digitalis Fab antibody
 - d. Lidocaine
 - e. None of the above
8. Which of the following statements about digitalis is true?
 - a. It increases heart rate.
 - b. It decreases myocardial contractility.
 - c. It increases myocardial oxygen demand.
 - d. It decreases peripheral resistance.
 - e. It increases cardiac output.
9. KP is experiencing a blockage of a cerebral vessel on the right side of her brain in the motor area. This type of cerebral vascular attack (CVA) would be expected to cause:
 - a. Paralysis of both legs.
 - b. Left side paralysis
 - c. Right side paralysis
 - d. None of the above
10. Which of the following is an uncommon effect seen with digitalis toxicity?
 - a. Atrial fibrillation with rapid ventricular response
 - b. Premature ventricular contractions
 - c. Second-degree heart block
 - d. Third-degree heart block
 - e. Atrioventricular junctional escape beats
11. Which of the following may produce thiocyanate toxicity?
 - a. Amrinone
 - b. Nitroprusside
 - c. Nitroglycerine
 - d. Milrinone
 - e. All of the above
12. Which of the following is NOT an effect of digitalis?
 - a. Prolonged function AV node refractory period
 - b. Increased vagal tone
 - c. Decreased Purkinje fiber effective refractory period
 - d. Decreased AV node conduction velocity
 - e. Decreased myocardial contractility
13. Which of the following may cause orthostatic hypotension?
 - a. Metaraminol
 - b. Tetrahydrozoline
 - c. Amyl nitrite
 - d. Reserpine
 - e. Phenylephrine
14. Which of the following is most similar structurally to digitalis?
 - a. Steroids
 - b. Catecholamines
 - c. Salicylates
 - d. Phenothiazines
 - e. Nitrofurantoin
15. Which of the following is NOT an effect of nitrate ingestion?
 - a. Decreased preload
 - b. Decreased systolic blood pressure
 - c. Increased ejection fraction
 - d. Decreased ventricular size
 - e. Increased heart rate
16. Which of the following acts directly on the kidneys to promote diuresis?
 - a. Dobutamine
 - b. Dopamine
 - c. Epinephrine
 - d. Isoproterenol
 - e. Norepinephrine

17. Nitroglycerin decreases myocardial oxygen demand via decreases in:
 - a. intramyocardial tension
 - b. sulfhydryl bonding
 - c. blood pressure
 - d. heart rate
 - e. coronary vascular resistance
18. Which of the following drugs would be contraindicated for someone with a potassium level of 5.2?
 - a. Warfarin
 - b. Hydrochlorothiazide
 - c. Furosemide
 - d. Spironolactone
19. Which of the following is the correct mechanism by which digitalis decreases heart rate?
 - a. Increased AV node conduction
 - b. Atropine-like effects on the AV node
 - c. Blockage of carotid baroreceptors
 - d. Stimulation of medullary vagal center
 - e. All of the above
20. Digoxin:
 - a. is more extensively cleared by the liver than digitoxin.
 - b. is more poorly absorbed orally than digitoxin.
 - c. is more protein bound than digitoxin.
 - d. has a longer half-life than digitoxin.
 - e. All of the above
21. Digitalis:
 - a. decreases ventricular rate in atrial fibrillation.
 - b. decreases atrial rate in sinus tachycardia.
 - c. decreases atrial rate in atrial fibrillation.
 - d. enhances AV node conduction.
 - e. decreases ventricular automaticity.
22. Which of the following statements about digitalis-associated emesis is true?
 - a. It is due to Na^+/K^+ -ATPase inhibition within the stomach.
 - b. It is due to stimulation of chemoreceptor trigger zones.
 - c. It is only seen with oral administration.
 - d. It is only seen with rapid IV administration.
 - e. It is never severe.
23. Digitalis:
 - a. increases heart rate.
 - b. prevents diastolic dysfunction.
 - c. can precipitate arrhythmias.
 - d. increases oxygen consumption in failing hearts.
 - e. None of the above
24. Which of the following statements regarding adenosine is true?
 - a. It increases sinus node rate.
 - b. It increases AV conduction.
 - c. It causes transient postconversion arrhythmias.
 - d. It is extensively metabolized in the liver.
 - e. It causes coronary vasoconstriction.
25. GP's blood pressure is 172/104. This is considered to be:
 - a. Prehypertension
 - b. Stage I hypertension
 - c. Stage II hypertension
 - d. Organ dysfunction
26. Hydrochlorothiazide is used to treat hypertension. The antihypertensive effect of this drug is caused by which of the following?
 - I. Inhibition of the angiotension converting enzyme
 - II. Calcium channel blockade
 - III. Diuresis and vasodilatation
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
27. Which of the following is an incorrect administration of epinephrine for the treatment ventricular fibrillation?
 - a. 2.5 mg diluted with saline to a total of 10 mL via endotracheal tube
 - b. 1 mg IV push, then 3 mg IV push, then 5 mg IV push, with 3-minute intervals
 - c. 0.1 mg/kg IV push every 3–5 minutes
 - d. 0.1 mg IV push every 3–5 minutes
 - e. 1 mg IV push every 3–5 minutes
28. A patient is started on heparin (5000 U bolus followed by 1000 U/h) for the treatment of deep vein thrombosis. When is the earliest time that a blood sample can be drawn to measure aPTT?
 - a. 24 hours
 - b. 12 hours
 - c. 6 hours
 - d. 4 hours
 - e. 2 hours
29. Which of the following is a direct-acting plasminogen?
 - a. Urokinase
 - b. Streptokinase
 - c. Epsilon-aminocaproic acid
 - d. Anistreplase
 - e. Heparin
30. Which of the following statements about warfarin is true?
 - a. It inhibits vitamin K epoxide reductase.
 - b. It prevents carboxylation of factors II, VII, IX, and X.
 - c. It competitively inhibits hepatic liver synthesis of clotting factors.
 - d. a and b
 - e. b and c
31. Which of the following increases the activity of warfarin?
 - a. Aspirin
 - b. Ranitidine
 - c. Trimethoprim-sulfamethoxazole

- d. Rifampin
 - e. a and c
32. Which of the following statement about mini-doses of heparin is true?
- a. It is useful as prophylactic therapy.
 - b. It inhibits factor X activation.
 - c. Factor X is much more sensitive to heparin than other serine proteases.
 - d. All of the above
 - e. None of the above
33. Which of the following statements about fibrinolytic agents is true?
- a. It increases mortality in acute myocardial infarction.
 - b. Urokinase directly activates plasminogen.
 - c. Streptokinase directly activates plasminogen.
 - d. TPA may cause rash.
 - e. TPA may cause the development of antibodies.
34. Which of the following drugs taken for heart failure have been proved to decrease mortality according to clinical study?
- I. Carvedilol
 - II. Lisinopril
 - III. Digoxin
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
35. Which of the following is NOT an adverse effect of amiodarone?
- a. Pulmonary fibrosis
 - b. Hyperthyroidism
 - c. Optic neuropathy
 - d. Thrombocytopenia
 - e. Elevated liver function tests
36. A 35-year-old obese woman presents to the emergency department with complaints of acute shortness of breath, fever, and confusion. Her left lower calf is swollen, and the treating physician suspected pulmonary embolism. Which of the following is the most appropriate laboratory screening test?
- a. D-dimer
 - b. Prothrombin time
 - c. Erythrocyte sedimentation rate
 - d. International normalized ratio (INR)
 - e. Factor VII activity
37. Warfarin acts by:
- a. inhibiting synthesis of calcium-dependent clotting factors.
 - b. decreasing absorption of vitamin K.
 - c. degrading clotting factors in the peripheral circulation.
 - d. binding clotting factors.
 - e. inhibiting hepatic vitamin B₁₂ synthesis and storage.
38. Which of the following is the appropriate goal of INR in a patient with atrial fibrillation and mitral valve disease?
- a. 4.5
 - b. 3.5
 - c. 2.5
 - d. 1.5
 - e. 0.5
39. Which of the following cardiac arrhythmias can be due to a re-entry mechanism?
- a. Atrial fibrillation
 - b. Atrial flutter
 - c. Ventricular fibrillation
 - d. Ventricular tachycardia
 - e. All of the above
40. The most life threatening adverse effect of taking a HMG coenzyme A reductase inhibitor (Statins) is:
- a. Angioedema
 - b. Renal failure
 - c. Myalgia
 - d. Rhabdomyolysis
41. Which of the following factors has NOT been implicated in the pathogenesis of hypertension?
- a. Increased sympathomimetic activity
 - b. Mineralocorticoid excess
 - c. Genetic factors
 - d. Reduced renal function
 - e. All of the above have been implicated in pathogenesis of HTN
42. Which of the following is a risk factor for the development of hypertension during childhood?
- a. African American race
 - b. Anorexia
 - c. Elevated birth weight
 - d. Increased environmental exposure
 - e. Female sex
43. According to the AHA/ACC approach to the classification of chronic heart failure, how is stage A (Class I) defined?
- a. Unable to carry out physical activity without discomfort
 - b. Advanced structural heart disease and marked symptoms
 - c. Symptomatic at rest
 - d. Asymptomatic
 - e. High risk of developing heart failure but with no identified structural or functional abnormalities
44. Which of the following drugs may produce excessive hair growth?
- a. Zyprexa
 - b. Loniten
 - c. Risperidal
 - d. Lasix
 - e. All of the above
45. Which of the following adverse effects occur(s) with ACE inhibitors?
- a. Neutropenia

- b. Hyperkalemia
 - c. Orthostatic hypotension
 - d. a and c
 - e. a, b, and c
46. Congestive heart failure (CHF) is diagnosed in an elderly patient. Which of the following medications should be avoided?
- a. Nitrostat
 - b. Catapres
 - c. Verelan
 - d. Diuril
 - e. All of these drugs are safe for elderly patients with CHF
47. A patient complains of intestinal side effects associated with the recent addition of verapamil (Verelan) to her medication profile. Which of the following would you likely recommend for alleviating of these side effects?
- a. Cessation of Verelan therapy
 - b. Counsel the patient that side effects are untreatable
 - c. Maalox extra strength tablets
 - d. Pericolace
 - e. Alternagel
48. Digitalis toxicity is associated with a
- I. Decrease in serum concentration of K^+
 - II. Decrease in serum concentration of Mg^{+2}
 - III. Increase in serum concentration of Ca^{+2}
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
49. A cardiologist calls a pharmacist to inquire about the use of nesiritide in patients with congestive heart failure. Which of the following is a contraindication for nesiritide use?
- a. Systolic blood pressure less than 90 mm Hg
 - b. Concurrent ACE inhibitor use
 - c. Previous treatment with streptokinase
 - d. Iodine allergy
 - e. None of the above
50. A patient with long-standing congestive heart failure complains of lower leg swelling and nighttime breathing difficulty. Which of the following drugs would be most appropriate?
- a. Digoxin
 - b. Metolazone
 - c. Captopril
 - d. a and b
 - e. a and c
51. Which of the following adverse effects may occur in patients treated concomitantly with propranolol and diltiazem?
- a. Decreased heart rate
 - b. Decreased cardiac output
 - c. Fluid retention
 - d. a and b
 - e. a and c
52. The most accurate measure of cardiac output is:
- a. Systolic blood pressure
 - b. Diastolic blood pressure
 - c. Heart rate
 - d. Urine output
53. What class of antiarrhythmic agent is diltiazem, and what is an appropriate indication for diltiazem treatment?
- a. Class IV, supraventricular tachycardia
 - b. Class IV, atrial fibrillation
 - c. Class I, supraventricular tachycardia
 - d. Class I, atrial fibrillation
 - e. a and b
54. Which of the following antihypertensive medications is most appropriate for use in a patient with asthma with poor compliance?
- a. Acebutolol
 - b. Propranolol
 - c. Esmolol
 - d. a or b
 - e. a or c
55. Chronic hypertension negatively affects what organ(s)?
- a. Lungs
 - b. Brain
 - c. Eyes
 - d. a and b
 - e. b and c
56. Which of the following should be monitored in patients taking thiazide diuretics?
- a. Potassium and glucose
 - b. Potassium, glucose, and uric acid
 - c. Potassium and uric acid
 - d. Glucose and uric acid
 - e. Uric acid
57. Preload is best assessed by:
- a. Peripheral edema
 - b. Jugular veins
 - c. Blood pressure
 - d. Urine output
58. Which of the following is the correct mechanism of action of digitalis in patients with congestive heart failure?
- a. Increased heart rate
 - b. Increased stroke volume
 - c. Decreased blood pressure
 - d. Decreased venous return
 - e. Decreased peripheral resistance
59. Congestive heart failure is diagnosed in a 75-year-old woman. Which of the following medications would improve this patient's symptoms by decreasing preload and afterload?
- a. Nitroprusside

- b. Prazosin
 - c. Felodipine
 - d. Hydralazine
 - e. Isosorbide dinitrate
60. Digitalis toxicity can be managed with which of the following?
- a. Lidocaine
 - b. Phenytoin
 - c. Potassium
 - d. Cholestyramine
 - e. None of the above
61. Right-sided heart failure may result in:
- I. Ascites
 - II. Peripheral edema
 - III. Pulmonary edema
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
62. A 55-year-old woman with breast cancer develops a deep vein thrombosis. She is treated with enoxaparin and warfarin. How long should enoxaparin therapy be continued?
- a. 7 days
 - b. 1 month
 - c. 3–6 months
 - d. 9–12 months
 - e. Indefinitely
63. A 60-year-old man is taken to the emergency department by his wife after taking a full bottle of 0.25 mg digoxin tablets in a suicide attempt. He has a pulse of 45 beats per minute; electrocardiogram shows third-degree heart block. Which of the following is the first therapy that should be initiated?
- a. Potassium
 - b. Lidocaine
 - c. Digoxin immune Fab
 - d. Phenytoin
 - e. Sodium bicarbonate
64. Which of the following patients does NOT require dose adjustment of enoxaparin?
- a. 80-year-old woman with low body weight
 - b. 80-year-old woman with renal insufficiency
 - c. 30-year-old pregnant female with mechanical prosthetic heart valve
 - d. 30-year-old anorexic woman
 - e. 50-year-old man with prostatic hypertrophy and hypertension
65. Digoxin is classified as a(an):
- a. glycoside
 - b. parasympathomimetic
 - c. calcium channel blocker
 - d. potassium channel blocker
 - e. angiotensin receptor blocker
66. Lovenox:
- a. requires monitoring of laboratory coagulation parameters when given presurgically in recommended doses.
 - b. is administered in doses of 300 mg q12h intravenously.
 - c. is administered in doses of 300 mg q12h intramuscularly.
 - d. is administered in doses of 300 mg q12h subcutaneously.
 - e. is used for deep vein thrombosis prophylaxis.
67. Which of the following drugs may result in increased INR in patients on warfarin?
- a. Digoxin
 - b. Cefotetan
 - c. Pantoprazole
 - d. a or b
 - e. b or c
68. JK is a diabetic patient who began atenolol (Tenormin) this morning. What lab value should be monitored?
- a. Glucose
 - b. Calcium
 - c. Magnesium
 - d. Potassium
69. All of the following statements about furosemide are true EXCEPT:
- a. it is useful in the treatment of ascites.
 - b. it may result in hypouricemia.
 - c. it may result in tinnitus.
 - d. it acts at the thick ascending loop of Henle.
 - e. it may result in hypocalcemia.
70. Which of the following statements about spironolactone is FALSE?
- a. It may cause gynecomastia.
 - b. It may cause hypokalemia.
 - c. It may cause urine alkalization.
 - d. It may cause menstrual irregularities.
 - e. It may cause hyponatremia.
71. Diazoxide is most similar in structure to which of the following agents?
- a. Chlorothiazide
 - b. Furosemide
 - c. Spironolactone
 - d. Acetazolamide
 - e. Mannitol
72. Which of the following is NOT a potential side effect of enalapril?
- a. Agranulocytosis
 - b. Acute renal failure
 - c. Reflex hypertension
 - d. Alopecia
 - e. Abnormal taste

73. Cardiac glycosides may cause all of the following EXCEPT:
- anorexia.
 - vomiting.
 - atrioventricular block.
 - confusion.
 - red/blue vision.
74. Beta-adrenergic agents may cause which of the following adverse events?
- Hypotension
 - Congestive heart failure
 - Increased airway resistance
 - Bradycardia
 - All of the above
75. Which of the following statements about warfarin is true?
- Normal daily dosage is 2–10 mcg/d.
 - It is not useful in the management of cardiac valve replacement.
 - It may cause mania.
 - It may cause hematuria.
 - It is safe to use in pregnancy.
76. Which of the following factors are responsible for the longer duration of digoxin compared to digoxin?
- Increased protein binding
 - Decreased polarity
 - Increased tubular reabsorption
 - All of the above
 - None of the above
77. RO is receiving furosemide (Lasix) for fluid retention. Which of the following is a complication of the therapy?
- Hyperkalemia
 - Urinary incontinence
 - Hypercalcemia
 - Ototoxicity
 - Hypermagnesemia
78. A pharmacist is counseling a new patient in the anticoagulant clinic who is beginning warfarin therapy. Which of the following should the patient avoid?
- Red wine
 - Vitamin K
 - Vitamin E
 - High-cholesterol foods
 - All of the above
79. Which of the following should NOT be treated with cardiac glycosides?
- Congestive heart failure
 - Ventricular tachycardia
 - Atrial fibrillation
 - Paroxysmal atrial tachycardia
 - Glycosides can be used in all of the above
80. Which of the following is safe to use in patients with hypokalemia?
- Midamor
 - Lasix
 - Zaroxolyn
 - Hygroton
 - Diuril
81. Which of the following is NOT safe to take in combination with digoxin?
- Tigecycline
 - Etanercept
 - Apreptate
 - Fosaprepate
 - Amiodarone
82. Which of the following statements about clonidine is true?
- It is an alpha-2 antagonist.
 - It may cause drowsiness.
 - It does not require dose adjustment for renal insufficiency.
 - a and b
 - b and c
83. Which of the following is the mechanism of action of clonidine?
- Alpha-2 antagonist
 - Alpha-2 agonist
 - Beta-1 agonist
 - Beta-1 antagonist
 - Mixed alpha-1 and alpha-2 antagonist
84. Which of the following statements about furosemide (Lasix) is FALSE?
- It is available for intramuscular administration.
 - It may cause aortitis.
 - It may cause vertigo.
 - It may be used for the treatment of edema.
 - It is minimally protein bound in circulation.
85. Which of the following statements about heparin is true?
- It may cause rebound hyperlipidemia.
 - It may cause hyperkalemia.
 - It may cause priapism.
 - a and b
 - a, b, and c
86. Which of the following are angiotensin II receptor blockers?
- Cozaar
 - Diovan
 - Avapro
 - a and b
 - a, b, and c
87. Which of the following does NOT carry a risk of myositis?
- Gemfibrozil
 - Colestipol
 - Lovastatin
 - Simvastatin
 - Pravastatin

88. Which of the following has strong anticholinergic effects?
- Disopyramide
 - Procainamide
 - Flecainide
 - Tocainide
 - Quinidine
89. Which of the following has the greatest risk of inducing torsades de pointes?
- Quinidine
 - Flecainide
 - Diltiazem
 - Lidocaine
 - Amiodarone
90. Which drug acts on the atrioventricular node to delay calcium channel depolarization?
- Verapamil
 - Nifedipine
 - Quinidine
 - Bretium
 - Lidocaine
91. Bretium:
- is a class II antiarrhythmic.
 - is useful in the treatment of ventricular tachycardia.
 - is only available for intramuscular injection.
 - may cause hypertension.
 - may cause tachycardia.
92. Which of the following is a potential problem with amiodarone therapy?
- It may cause pulmonary fibrosis.
 - It may cause thyroid disease.
 - It may require multiple daily doses.
 - a and b
 - a, b, and c
93. Which of the following antihypertensive drug may cause headache, postural hypotension, and reflex tachycardia?
- Hydralazine
 - Prazosin
 - Captopril
 - Methyldopa
 - Guanethidine
94. Which of the following is a potential side effect of nitroprusside therapy?
- Thiocyanate intoxication
 - Convulsions
 - Hypotension
 - All of the above
 - None of the above
95. Which of the following is a potential side effect of penbutolol?
- Bronchospasm
 - Cardiac decompensation
 - Bradycardia
 - All of the above
 - None of the above
96. Of the following medications, which may cause rash, cough, and proteinuria?
- Terazosin
 - Penbutolol
 - Nitroprusside
 - Methyldopa
 - Ramipril
97. Methyldopa may cause which of the following?
- Fever
 - Postural hypotension
 - Positive Coombs test
 - All of the above
 - None of the above
98. Which drug has sympathomimetic activity?
- Pindolol
 - Nadolol
 - Labetalol
 - Esmolol
 - Bisoprolol
99. Which drug is an alpha-adrenergic receptor blocker?
- Pindolol
 - Nadolol
 - Labetalol
 - Esmolol
 - Bisoprolol
100. Which drug has the shortest duration of action?
- Pindolol
 - Nadolol
 - Labetalol
 - Esmolol
 - Bisoprolol
101. Which drug is a nonselective blocker with a prolonged duration of action?
- Pindolol
 - Nadolol
 - Labetalol
 - Esmolol
 - Bisoprolol
102. Which drug is the most cardioselective?
- Pindolol
 - Nadolol
 - Labetalol
 - Esmolol
 - Bisoprolol
103. Which of the following statements about clopidogrel is true?
- It has a higher risk of bleeding than aspirin.
 - It is an isomer of ticlopidine.
 - It may cause thrombocytopenia.
 - It is a glycoprotein IIb/IIIa inhibitor.
 - All of the above
104. Which of the following produces prolonged platelet inhibition?
- Aspirin
 - Corticosteroids

- c. Ibuprofen
 - d. Penicillamine
 - e. Auranofin
105. What is normal serum concentration of potassium?
- a. 1 mEq/L
 - b. 1–2 mEq/L
 - c. 3.5–5 mEq/L
 - d. 10 mEq/L
 - e. 35 mEq/L
106. Hypertensive crisis is defined as a diastolic blood pressure greater than 120 mmHg. What is the best medication for initial treatment of hypertensive crisis?
- a. Nitroprusside
 - b. Hydralazine
 - c. Amlodipine
 - d. Esmolol
 - e. Digoxin
107. Chest pain that is NOT relieved by rest and nitroglycerin is referred to as which of the following?
- a. Variant angina
 - b. Stable angina
 - c. Unstable angina
 - d. Prinzmetal's angina
108. Lovastatin works by inhibition of?
- a. Lipolysis of TAGs in adipose tissue
 - b. HMG CoA reductase, the rate-limiting step of cholesterol synthesis
 - c. 7- α hydroxylase, the rate limiting step of bile salt synthesis
 - d. Release of cholesterol in lysosomes
109. Calcium channel blockers have which of the following functions?
- a. Increase cerebral oxygenation
 - b. Increase vascular tone
 - c. Increase velocity of AV conduction
 - d. Decrease cardiac oxygen consumption
110. WP is a 64-year old man with chronic, drug-resistant hypertension that is being treated with furosemide, metoprolol, and a drug that produces a vasodilatory effect on arterial smooth muscles, causing a reduction in blood pressure in peripheral resistance. What is most likely the third drug?
- a. Nitroprusside
 - b. Minoxidil
 - c. Guanethidine
 - d. Clonidine
111. MH is a 42-year old female with type 1 diabetes that is being treated with various drugs including a drug for the prevention of proteinuria associated with diabetic nephropathy. After she began this drug, the patient developed a dry cough. The cough most likely caused by which of the following?
- a. Amlodipine
 - b. Furosemide
 - c. Pioglitazone
 - d. Losartan
 - e. Captopril
112. Which of the following side effects is associated with hydrochlorothiazide?
- a. Photosensitivity
 - b. Hypokalemia
 - c. Hypotension
 - d. Anorexia
 - e. All of the above
113. VH is a 68-year old female with congestive heart failure. She is being treated with enalapril. Which of the following changes in plasma renin and angiotensin II levels would occur?
- a. Decrease; decrease
 - b. Increase; decrease
 - c. Increase, increase
 - d. Increase, no change
114. The antiarrhythmic agent recommended for treating life threatening ventricular fibrillation in a 57-year old man is?
- a. Amiodarone
 - b. Esmolol
 - c. Quinidine
 - d. Adenosine
115. Familial hypercholesterolemia results from defects in?
- a. HMG CoA reductase
 - b. Chylomicron assembly
 - c. Hormone-sensitive lipase
 - d. LDL receptors
116. MS is a 60-year old obese woman with type 2 diabetes, hypertension, and renal disease. She is being treated with a drug that blocks both alpha- and beta-receptors. This drug is likely:
- a. Acebutolol
 - b. Carvedilol
 - c. Doxazosin
 - d. Pindolol
117. LB is a 53-year old female with very high triglycerides and VLDL levels. She is given a drug that decreases hepatic production of apolipoprotein CIII via activation of peroxisome proliferator activator receptors (PPARs) and induces lipoprotein lipase. The drug is likely:
- a. Fenofibrate
 - b. Colestipol
 - c. Ezetimibe
 - d. Lovastatin
118. Which of the following agents are effective in treating congestive heart failure (CHF)?
- I. Digoxin
 - II. Hydralazine
 - III. Hydrochlorothiazide
- a. I only
 - b. III only

- c. I and II only
 - d. II and III only
 - e. I, II and III
119. JW is a 52 year old patient receiving simvastatin for hypercholesterolemia, but is inadequately controlled. The addition of which of the following agents will increase the risk of myopathy?
- a. Psyllium
 - b. Colestipol
 - c. Cholestyramine
 - d. Gemfibrozil
 - e. None of the above
120. Which of the following tests is important when determining the optimal drug therapy for a patient newly diagnosed with heart failure?
- a. Chest x-ray
 - b. Electrocardiogram (ECG)
 - c. Echocardiogram (ECHO)
 - d. Renal arteriography
121. Which of the following drugs has been shown to reduce mortality in patients with heart failure?
- a. Enalapril
 - b. Digoxin
 - c. Furosemide
 - d. Amlodipine
 - e. None of the above
122. NC is a 57-year old female who has diabetes and hypertension. She also takes levothyroxine. NC develops a cold with nasal congestion and asks you which product to use. Which of the following is the safest to recommend to this patient with nasal congestion?
- a. Saline nasal spray
 - b. Phenylephrine nasal spray
 - c. Pseudoephedrine
 - d. Chlorpheniramine
123. How does trimethoprim-sulfamethoxazole affect INR values in patients taking warfarin?
- a. No effect on INR
 - b. Increase in INR
 - c. Decrease in INR
 - d. Increase in INR with high-dose trimethoprim-sulfamethoxazole, and decrease in INR with low-dose trimethoprim-sulfamethoxazole
 - e. Decrease in INR with high-dose trimethoprim-sulfamethoxazole, and increase in INR with low-dose trimethoprim-sulfamethoxazole
124. A 32-year-old woman is taking warfarin for a recent deep vein thrombosis. At her regular check-up, her INR is found to be 9.0. She reports no history of bleeding or bruising. Which of the following is the most appropriate treatment?
- a. Cessation of warfarin
 - b. Oral vitamin K
 - c. Subcutaneous vitamin K
 - d. a and b
 - e. a and c
125. Warfarin:
- a. inhibits vitamin K absorption.
 - b. has a duration of action of 2–5 days.
 - c. is less than 50% protein bound in circulation.
 - d. has an onset of action of 2–5 hours
 - e. is primarily metabolized by CYP2D6.
126. Which of the following statements about class IA antiarrhythmic medications is true?
- a. They prolong PR and QT intervals.
 - b. They reduce Purkinje fiber automaticity.
 - c. They decrease the rate of rise and amplitude of phase 0 depolarization.
 - d. a and b
 - e. a, b, and c
127. All of the following are class IB antiarrhythmic agents EXCEPT:
- a. mexiletine
 - b. lidocaine
 - c. phenytoin
 - d. tocainide
 - e. All of the above are class IB antiarrhythmic agents
128. Which of the following drugs will NOT increase the effective refractory period of the AV node in the treatment of supraventricular tachycardia?
- a. Propranolol
 - b. Tocainide
 - c. Digoxin
 - d. Verapamil
 - e. All of the above will increase the AV refractory period
129. Adverse effects of amiodarone include all of the following EXCEPT:
- a. photosensitivity.
 - b. pseudocyanosis.
 - c. pneumonitis.
 - d. parotitis.
 - e. All of the above may occur with amiodarone
130. Which of the following is an effect of class IC antiarrhythmic agents?
- a. Phase 0 depolarization depression
 - b. Inhibition of calcium transport during action potential plateau
 - c. Inhibition of sodium transport during phase 0 depolarization
 - d. a and b
 - e. a and c
131. Adverse effects of disopyramide include all of the following EXCEPT:
- a. lupus
 - b. urinary retention
 - c. blurry vision
 - d. constipation
 - e. Disopyramide may cause any of the above

132. Which of the following is NOT a type I antiarrhythmic agent?
- Propranolol
 - Lidocaine
 - Procainamide
 - Quinidine
 - Phenytoin
133. Which of the following is an effect of quinidine?
- Increased QRS and PR intervals
 - Increased QRS and QT intervals
 - Increased QRS, PR, and QT intervals
 - Increased PR and QT intervals
 - Increased QT interval
134. Adverse effects of quinidine include all of the following EXCEPT:
- Dry mouth
 - Nausea
 - Tinnitus
 - Torsades de pointes
 - Headache
135. Which of the following has a mechanism of action and electrophysiologic effects most similar to procainamide?
- Lidocaine
 - Bretylium
 - Quinidine
 - Phenytoin
 - Propranolol
136. Which of the following is NOT an effect of quinidine?
- Positive chronotropy
 - Prolongation of effective refractory period
 - Decreased conduction velocity
 - Peripheral vasodilation
137. Which of the following should NOT be used in a patient with complete heart block?
- Atropine
 - Quinidine
 - Isoproterenol
 - Prednisone
 - Hydrochlorothiazide
138. Which of the following is an effect of procainamide?
- Improved myocyte membrane responsiveness
 - Decreased effective refractory period
 - Decreased ectopic myocardial automaticity
 - a and b
 - a and c
139. Decreased numbers of beta-adrenergic receptors may be due to:
- guanethidine.
 - alcohol withdrawal.
 - beta agonists.
 - propranolol.
 - None of the above
140. A 45-year-old man experiences an acute myocardial infarction. The following day he is being treated with an intravenous antiarrhythmic agent to prevent multifocal premature ventricular contractions when he experiences a seizure. What is the most likely cause of the seizure?
- Ventricular asystole
 - Systemic hypotension
 - Lidocaine toxicity
 - Ventricular tachycardia
 - Cardiac embolization
141. Which of the following is NOT a class III antiarrhythmic agent?
- Quinidine
 - Propafenone
 - Flecainide
 - Bretylium
 - a, b, and c
142. Which of the following is first-line treatment for ventricular fibrillation that does not respond to defibrillation or epinephrine?
- Amiodarone
 - Lidocaine
 - Bretylium
 - Adenosine
 - Flecainide
143. Which of the following is the appropriate treatment for supraventricular tachycardia refractory to vagal maneuvers?
- Amiodarone
 - Lidocaine
 - Bretylium
 - Adenosine
 - Flecainide
144. Which of the following causes an initial release of norepinephrine resulting in transient hypertension followed by hypotension?
- Amiodarone
 - Lidocaine
 - Bretylium
 - Adenosine
 - Flecainide
145. Which of the following may cause hyper- or hypothyroidism due to iodine content?
- Amiodarone
 - Lidocaine
 - Bretylium
 - Adenosine
 - Flecainide
146. Which of the following is highly protein bound in circulation, has a large volume of distribution, and has a long half-life (>20 days)?
- Amiodarone
 - Lidocaine
 - Bretylium
 - Adenosine
 - Flecainide

147. Which of the following is a class IB antiarrhythmic agent with rapid association and dissociation with sodium channels?
- Amiodarone
 - Lidocaine
 - Bretylum
 - Adenosine
 - Flecainide
148. Which of the following is a class IC antiarrhythmic agent with a strong affinity and slow dissociation from sodium channels?
- Amiodarone
 - Lidocaine
 - Bretylum
 - Adenosine
 - Flecainide
149. All of the following statements about propafenone are true EXCEPT:
- it is a class III antiarrhythmic agent.
 - it has increased QRS duration.
 - it slows action potential.
 - it has beta-blocking activity.
 - it blocks sodium channels.
150. All of the following statements about sotalol are true EXCEPT:
- it increases effective refractory period.
 - it causes bradycardia.
 - it prolongs action potential duration and effective refractory period via blockage of sodium channels.
 - it blocks potassium channels.
 - it prolongs repolarization.
151. Which of the following is a nonselective beta blocker with quinidine-like effects on cellular membranes?
- Esmolol
 - Propranolol
 - Acebutolol
 - Sotalol
 - Butorphanol
152. Which of the following is a cardioselective beta blocker that is only administered orally and has sympathomimetic activity?
- Esmolol
 - Propranolol
 - Acebutolol
 - Sotalol
 - Butorphanol
153. Which of the following is a nonselective beta blocker that prolongs action potential duration via blockage of potassium transport?
- Esmolol
 - Propranolol
 - Acebutolol
 - Sotalol
 - Butorphanol
154. Which of the following is a cardioselective beta blocker that is only administered intravenously and has a short elimination half-life?
- Esmolol
 - Propranolol
 - Acebutolol
 - Sotalol
 - Butorphanol
155. Which of the following statements concerning calcium channel blockers is FALSE?
- They can be used to slow ventricular rate in atrial fibrillation.
 - Verapamil, diltiazem, and nifedipine have equivalent antiarrhythmic actions.
 - They decrease inward calcium current, causing decreased spontaneous phase 4 depolarization of Purkinje cells.
 - They slow AV node conduction velocity.
 - They increase the functional refractory period of the AV node.
156. Which of the following is most closely related to diazoxide?
- Nitrates
 - Dopamine antagonists
 - Thiazides
 - Nitrofurantoin
 - Sulfonamides
157. Which of the following may cause hyperuricemia and acute gout?
- Chlorothiazide
 - Phenytoin
 - Salicylates
 - Spironolactone
 - a and c
158. Which of the following is a potential side effect of reserpine?
- Diarrhea
 - Bradycardia
 - Postural hypotension
 - a and c
 - a, b, and c
159. Which of the following is NOT a potential side effect of propranolol?
- Angina
 - Hypotension
 - Tachycardia
 - Syncope
 - Raynaud syndrome
160. Which of the following is NOT a side effect of methyl dopa?
- Nephrotic syndrome
 - Fever
 - Hemolytic anemia
 - Positive Coombs test
 - Diarrhea

161. Which of the following is NOT a side effect of hydralazine?
- Depression
 - Disorientation
 - Bradycardia
 - Impotence
 - Muscle cramps
162. Which of the following may cause somnolence?
- Guanethidine
 - Methyldopa
 - Hydralazine
 - a and b
 - b and c
163. Which of the following may cause salt and water retention?
- Guanethidine
 - Methyldopa
 - Clonidine
 - a and b
 - a, b, and c
164. Which of the following is a potential side effect of clonidine?
- Rebound hypertension
 - Lupus
 - Anaphylaxis
 - Ventricular fibrillation
 - Nephrotoxicity
165. Which of the following is NOT an effect of propranolol?
- Negative chronotropy
 - Negative inotropy
 - Decreased plasma renin
 - Hyperglycemia
 - Bronchoconstriction
166. Which of the following will increase cardiac output?
- Hydralazine
 - Guanethidine
 - Methyldopa
 - Reserpine
 - Chlorothiazide
167. Which of the following acts by lowering sympathetic tone of the vasculature?
- Reserpine
 - Methyldopa
 - Trimethaphan
 - Diazoxide
 - Phenoxybenzamine
168. Which of the following are most useful for the long-term management of essential hypertension?
- Osmotic diuretics
 - Xanthine diuretics
 - Mercurial diuretics
 - Thiazide diuretics
 - Carbonic anhydrase inhibitors
169. Which of the following agents acts predominately at the arteriolar level?
- Glazoxide
 - Minoxidil
 - Hydralazine
 - a and b
 - a, b, and c
170. What is the onset of action of IV nitroprusside?
- 24 hours
 - 12 hours
 - 6 hours
 - 2 hours
 - Seconds
171. In which of the following conditions is methyldopa contraindicated?
- Renal insufficiency
 - Hepatic disease
 - Asthma
 - Coronary insufficiency
 - Depression
172. In which of the following conditions is hydralazine contraindicated?
- Renal insufficiency
 - Hepatic disease
 - Asthma
 - Coronary insufficiency
 - Depression
173. In which of the following conditions is reserpine contraindicated?
- Renal insufficiency
 - Hepatic disease
 - Asthma
 - Coronary insufficiency
 - Depression
174. Which of the following may cause decreased tissue concentration of norepinephrine?
- Alpha-methyl-*p*-tyrosine
 - Reserpine
 - Guanethidine
 - a and b
 - b and c
175. In which of the following conditions is propranolol contraindicated?
- Renal insufficiency
 - Hepatic disease
 - Asthma
 - Coronary insufficiency
 - Depression
176. Which of the following is NOT a side effect of guanethidine?
- Constipation
 - Bradycardia
 - Retrograde ejaculation
 - Orthostatic hypotension
 - Dry mouth

177. For which of the following is propranolol safe to use?
- Congestive heart failure
 - Asthma
 - Migraine prophylaxis
 - Third-degree heart block
 - Sinus bradycardia
178. A patient taking hydralazine and hydrochlorothiazide complains of headaches. His blood pressure is 125/75. What is the likely cause of his headaches?
- Hypotension
 - Hypokalemia
 - Hydralazine
 - Stress
 - Agranulocytosis
179. Which of the following statements about clonidine is/are true?
- It can be stopped safely for an outpatient operation.
 - It should not be stopped abruptly.
 - It may cause rebound hypertension.
 - b and c
 - a, b, and c
180. Which of the following medications shows reduced efficacy when combined with tricyclic antidepressants?
- Guanethidine
 - Clonidine
 - Hydralazine
 - a and b
 - b and c
181. Which of the following may cause tachycardia?
- Clonidine
 - Diazoxide
 - Hydralazine
 - a and b
 - b and c
182. Which of the following statements about sodium nitroprusside is INCORRECT?
- It should be given via rapid IV push.
 - Thiocyanate is a metabolite.
 - It is an arterial and venous dilator.
 - a and b
 - a and c
183. Which of the following may occur with chronic ethacrynic acid use?
- Metabolic alkalosis
 - Metabolic acidosis
 - Respiratory alkaloses
 - Potassium retention
 - All of the above
184. Which of the following drugs is most similar to steroids in its chemical composition?
- Triamterene
 - Spironolactone
 - Ethacrynic acid
 - Sucrose
 - Chlorothiazide
185. Which of the following acts via inhibition of aldosterone at the distal tubule?
- Triamterene
 - Spironolactone
 - Ethacrynic acid
 - Sucrose
 - Chlorothiazide
186. Which of the following is potassium sparing and does not act at the renal cortex?
- Triamterene
 - Spironolactone
 - Ethacrynic acid
 - Sucrose
 - Chlorothiazide
187. Which of the following is useful in the management of volume-dependent hypertension but carries a risk of hypokalemic alkalosis?
- Triamterene
 - Spironolactone
 - Ethacrynic acid
 - Sucrose
 - Chlorothiazide
188. Which of the following may occur with hypercalcemia caused by thiazide diuretics?
- Increased serum phosphorus
 - Decreased serum phosphorus
 - Hypercalciuria
 - Hypocalciuria
 - a and c
189. Which of the following is an effect of furosemide?
- Increased glomerular filtration rate
 - Decreased renin production
 - Decreased aldosterone
 - a and b
 - a and c
190. Which of the following is NOT a complication of thiazide diuretics?
- Hyperuricemia
 - Hyperglycemia
 - Hyperkalemia
 - Hyponatremia
 - Alkalosis
191. Which of the following is NOT a complication of thiazide diuretics?
- Thrombocytopenia
 - Jaundice
 - Photosensitivity
 - Hypokalemic nephropathy
 - All of the above are potential complications of thiazides
192. Which of the following may result in hyperkalemia?
- Triamterene

- b. Acetazolamide
 - c. Hydrochlorothiazide
 - d. Ethacrynic acid
 - e. Mercurials
193. Which of the following is an effect of thiazide-induced excretion of sodium, chloride, and water?
- a. Increased glomerular filtration rate
 - b. Acid-base imbalance
 - c. Indirect effects on renal function
 - d. Inhibition of tubular electrolyte transport
 - e. Inhibition of carbonic anhydrase
194. Which of the following is the primary mechanism underlying the chronic antihypertensive effects of oral diuretics?
- a. Decreased plasma volume
 - b. Saluresis
 - c. Decreased potassium
 - d. Decreased adrenergic output
 - e. Decreased cardiac output
195. Which of the following is a potential side effect of spironolactone?
- a. Gynecomastia
 - b. Hyponatremia
 - c. Azotemia
 - d. a and b
 - e. a, b, and c
196. Which of the following is a side effect of ethacrynic acid?
- a. Alkalosis
 - b. Hyperuricemia
 - c. Potassium loss
 - d. a and b
 - e. a, b, and c
197. Which of the following does NOT cause hypokalemia?
- a. Triamterene
 - b. Hydrochlorothiazide
 - c. Flumethiazide
 - d. Chlorthalidone
 - e. Bendroflumethiazide
198. Which of the following may cause hypochloremic alkalosis with prolonged use?
- a. Ethacrynic acid
 - b. Furosemide
 - c. Mannitol
 - d. a and b
 - e. a, b, and c
199. Which of the following statements about traimterene is true?
- a. It is sodium sparing.
 - b. It is not used clinically.
 - c. It can cause hyperkalemia.
 - d. It is an aldosterone antagonist.
 - e. It interacts with spironolactone.
200. Which of the following is a contraindication to spironolactone use?
- a. Hepatic insufficiency
 - b. Renal insufficiency
 - c. Coronary insufficiency
 - d. Asthma
 - e. Depression
201. Captopril may cause all of the following EXCEPT:
- a. angioedema.
 - b. cough.
 - c. rash.
 - d. nasal congestion.
 - e. Captopril may cause all of the above
202. Which of the following is a carbonic anhydrase inhibitor?
- a. Mannitol
 - b. Traimterene
 - c. Acetazolamide
 - d. Furosemide
 - e. Chlormerodrin
203. What is the primary mechanism of action of diuretics for the treatment of edema?
- a. Reduces total body sodium
 - b. Reduces plasma renin
 - c. Reduces vascular smooth muscle activity
 - d. Reduces sympathetic tone
 - e. Depletes potassium
204. Which of the following may cause hyperkalemia, menstrual irregularities, and gynecomastia?
- a. Triamterene
 - b. Spironolactone
 - c. Captopril
 - d. Amiloride
 - e. All of the above
205. Which of the following is/are contraindicated in patients receiving potassium replacement therapy?
- a. Bumetanide
 - b. Traimterene
 - c. Amiloride
 - d. a and b
 - e. b and c
206. Which of the following may cause metabolic alkalosis?
- a. Furosemide
 - b. Hydrochlorothiazide
 - c. Bumetanide
 - d. a and b
 - e. a, b, and c
207. Which of the following should NOT be given concomitantly with spironolactone?
- a. Monoamine oxidase inhibitors
 - b. Epinephrine
 - c. Propranolol
 - d. Potassium
 - e. All of the above

208. Which of the following may occur with spironolactone therapy?
- Hypomagnesemia
 - Hyperkalemia
 - Bronchospasm
 - Acne
 - Male pattern baldness
209. Which of the following is the correct site of action of mannitol?
- Distal tubule
 - Proximal tubule
 - Descending loop of Henle
 - Ascending loop of Henle
 - All of the above
210. Which of the following is contraindicated in hyperkalemic patients?
- Acetazolamide
 - Furosemide
 - Spironolactone
 - Ethacrynic acid
 - Chlorothiazide
211. Which of the following is NOT a mixed or indirect acting molecule?
- Amphetamine
 - Dobutamine
 - Dopamine
 - Ephedrine
 - None of the above
212. Which of the following does NOT occur with ganglion blockade?
- Bradycardia
 - Arteriolar vasodilation
 - Hypotension
 - Decreased cardiac output
 - Constipation
213. Digoxin maintenance dosing is based on:
- pulmonary function.
 - hepatic function.
 - protein level.
 - renal function.
 - serum potassium.
214. Which of the following lowers triglycerides most effectively?
- Colestipol
 - Atorvastatin
 - Gemfibrozil
 - Cholestyramine
 - Lovastatin
215. Which of the following may produce myalgia, abdominal pain, and gallstones?
- Clofibrate
 - Nicotinic acid
 - Colestipol
 - Probucol
 - Lovastatin
216. Which of the following statements is true?
- Atorvastatin increases LDL.
 - Lovastatin decreases HDL.
 - Neomycin increases LDL.
 - Nicotinic acid reduces VLDL and triglycerides only.
 - Clofibrate acts primarily to decreased VLDL and triglycerides.
217. Which of the following is commonly used to enhance the activity of HMG-CoA reductase inhibitors?
- Gemfibrozil
 - Cholestyramine
 - Lovastatin
 - Probucol
 - D-Thyroxine
218. Which of the following is an HMG-CoA reductase inhibitor?
- Gemfibrozil
 - Clofibrate
 - Lovastatin
 - Colestipol
 - Niacin
219. Ingestion of aspirin 30 minutes before niacin may reduce which of the following?
- Flushing
 - Myositis
 - Hepatic injury
 - Diarrhea
 - Acanthosis nigricans
220. Which of the following may occur with niacin?
- Flushing
 - Hyperglycemia
 - Jaundice
 - Hyperuricemia
 - All of the above
221. Which of the following may cause hyperkalemia, gynecomastia, and menstrual irregularities?
- Trimaterene
 - Spironolactone
 - Amiloride
 - a and b
 - b and c
222. Which of the following may cause hyperkalemia in a patient taking concomitant oral potassium?
- Triamterene
 - Amiloride
 - Mannitol
 - a and b
 - a and c
223. Which of the following may cause metabolic acidosis?
- Furosemide
 - Bumetanide
 - Hydrochlorothiazide
 - All of the above
 - None of the above

224. Which of the following is a cardioselective beta blocker?
- Timolol
 - Metoprolol
 - Atenolol
 - a and b
 - b and c
225. Which of the following does NOT cause reflex tachycardia?
- Clonidine
 - Reserpine
 - Minoxidil
 - a and b
 - a and c
226. Which of the following is least likely to produce CNS effects?
- Timolol and metoprolol
 - Timolol and atenolol
 - Nadolol and timolol
 - Nadolol and atenolol
 - Metoprolol and nadolol
227. Which of the following is most similar to guanadrel?
- Guanethidine
 - Methyldopa
 - Clonidine
 - Guanabenz
 - Methyldopa
228. Which of the following adverse effects may occur with guanethidine?
- Diarrhea
 - Sympathomimetic hypersensitivity
 - Orthostatic hypotension
 - All of the above
 - None of the above
229. Which of the following adverse effects may occur with hydralazine?
- Reflex tachycardia
 - Hypertrichosis
 - Orthostatic hypotension
 - a and b
 - b and c
230. Dyazide contains a potassium-sparing diuretic and what other type of drug?
- Nitrate
 - Thiazide
 - Nitrofurantoin
 - Dopamine antagonist
 - Sulfonamide
231. Which of the following is an effect of epinephrine?
- Cardiac stimulation
 - Bronchodilation
 - Peripheral vasodilation
 - All of the above
 - a and c
232. Which of the following is a contraindication to captopril use?
- Bilateral renal artery stenosis
 - Depression
 - Angina
 - COPD
 - Prostatic hypertrophy
233. A 74-year-old man has blood pressure of 135/86 mm Hg. This patient has:
- normal blood pressure.
 - high normal blood pressure.
 - mild (stage 1) hypertension.
 - moderate (stage 2) hypertension.
234. Which of the following parameters should be monitored in a patient receiving heparin?
- Partial thromboplastic time
 - Prothrombin time
 - Bleeding time
 - Platelet count
 - Serum potassium
235. Which medication is the antihypertensive drug of choice during pregnancy?
- Propranolol
 - Methyldopa
 - Nicardipine
 - Enalapril
 - None of the above
236. Bumex is similar to which of the following?
- Plavix
 - Demadex
 - Vytorin
 - Nexium
 - Lescol
237. True or False: Sustained-release nifedipine products may cause what looks to be an intact tablet in the stool.
- True
 - False
238. Which of the following is a side effect of nifedipine?
- Peripheral edema
 - Weakness
 - Nausea
 - Palpitations
 - All of the above
239. All of the following are adverse effects of ACE inhibitors EXCEPT:
- neutropenia.
 - proteinuria.
 - hyperkalemia.
 - dry, hacking cough.
 - sialism.
240. Which of the following drugs is contraindicated in patients with CHF?
- Verelan

- b. Catapres
 - c. Vasotec
 - d. Diuril
 - e. Nitrostat
241. Which of the following drug(s) exhibits antiplatelet action?
- I. Ticlopidine
 - II. Dipyridamole
 - III. Acetylsalicylic acid
- a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III
242. Digitalis toxicity is associated with:
- I. decrease in serum concentration of K.
 - II. decrease in serum concentration of Mg.
 - III. increase in serum concentration of Ca.
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
243. Clonidine does NOT cause which of the following side effects?
- a. Asthma
 - b. Hypertension
 - c. Lethargy
 - d. Dry mouth
 - e. Dizziness
244. Which of the following statements about alpha receptors is FALSE?
- a. Methoxamine and phenylephrine are alpha-2 selective.
 - b. Clonidine is alpha-2 selective.
 - c. Prazosin is alpha-1 selective.
 - d. Epinephrine is nonselective.
 - e. Phetolamine is nonselective.
245. Which of the following agents has a direct effect on the AV node, delaying calcium-channel depolarization?
- a. Lidocaine
 - b. Verapamil
 - c. Bretylium
 - d. Quinidine
 - e. Nifedipine
246. Which of the following drugs is a class III antiarrhythmic agent that is effective in the acute management of ventricular tachycardia, including ventricular fibrillation?
- a. Bretylium
 - b. Lidocaine
 - c. Metoprolol
 - d. Disopyramide
 - e. Diltiazem
247. Reflex tachycardia, headache, and postural hypotension are adverse effects that limit the use of which of the following antihypertensive agents?
- a. Prazosin
 - b. Captopril
 - c. Methyldopa
 - d. Guanethidine
 - e. Hydralazine
248. Which of the following medications commonly causes thiocyanate intoxication, hypotension, and convulsions?
- a. Ramipril
 - b. Methyldopa
 - c. Nitroprusside
 - d. Terazosin
 - e. Penbutolol
249. Which of the following is LEAST effective in the presence of metabolic acidosis?
- a. Triamterene
 - b. Spironolactone
 - c. Acetazolamide
 - d. a and b
 - e. a, b, and c
250. Which of the following is lost in the urine with acetazolamide therapy?
- a. Hydrogen
 - b. Glucose
 - c. Bicarbonate
 - d. Glycine
 - e. All of the above
251. Which of the following statements about mannitol is true?
- a. It acts on the proximal tubules to promote sodium and water retention.
 - b. It is useful for the reduction of intracranial pressure.
 - c. It is safe to use in patients with acute renal failure.
 - d. It may cause hypoglycemia.
 - e. It is a first-line agent for the treatment of hypertension in diabetics.
252. Digitoxin has a half-life of:
- a. 12 hours
 - b. 24 hours
 - c. 48 hours
 - d. 5 days
 - e. 7 days
253. A patient with a medical history significant for major depressive disorder (MDD) has new-onset hypertension. Based on her history of MDD, what medication should be avoided in this patient?
- a. Catapres
 - b. Lasix
 - c. Inderal
 - d. Cordarone
 - e. All of the above medications are safe

I. Acne

Acne is an inflammatory disease of the sebaceous glands (oil-producing glands) and hair follicles of the skin. Acne is marked by the eruption of pimples or pustules, especially on the face, back, and chest. Typically, acne treatments take four to eight weeks for full results.

- A. Conventional acne treatments are based on the concepts of:
 1. Reducing sebum production
 2. Speeding up skin cell turnover
 3. Fighting bacterial infection (i.e., *Propionibacterium acnes*)
- B. Over-the-counter (OTC) topical treatments may dry up the oil, reduce bacteria, and promote exfoliation.
 1. Benzoyl peroxide (e.g., Clean and Clear, Persa-Gel, Oxy 10 Spot Treatment)
 - a) Also available in prescription preparations alone or in combination with sulfur or a topical antibiotic
 2. Salicylic acid (e.g., Biore Blemish Bomb, Clearasil Stay Clear, Zone Control Clearstic).
 3. Sulfur and/or resorcinol (e.g., Clearasil Adult Care)
- C. Prescription topical retinoid products that are derived from vitamin A work by promoting cell turnover and preventing blockage of the hair follicle.
 1. Tretinoin (Avita, Retin-A, Renova)
 2. Adapalene (Differin)
 3. Tazarotene (Tazorac)

D. Antibiotics

For moderate to severe acne (inflammatory or nodulocystic acne), prescription oral or topical antibiotics may be needed to reduce bacteria and fight inflammation. Antibiotics may be used for months or years to control acne and may be used alone or in combination with topical therapy. Antibiotics can also lessen the effectiveness of birth control pills by killing beneficial bacteria in the gastrointestinal tract that are responsible for hormone metabolism.

1. Erythromycin (Erygel, Emcin, Emgel, Aknemycin, others)
 - a) Anti-inflammatory properties that help reduce redness in lesions, in addition to killing bacteria
 - b) Dose
 - (1) Varies with the type used

- (2) Topical application (gel, solution, medicated pledget): Applied twice daily to affected area(s).
- (3) If given systemically, initial dose 500 mg PO twice a day and taken with food; dosage reduced to 250–500 mg/day PO after several weeks once improvement is seen.

c) Side effects

- (1) Stomach upset and nausea, but can be used in pregnant women

2. Clindamycin (Cleocin T, Clindagel, Clindaderm, Evoclin, others)

- a) Widely prescribed as a topical antibiotic for acne, rarely used systemically for acne due to side-effect profile

b) Topical dose

- 1) Gel, solutions, or lotion: Applied twice daily to affected area(s)
- 2) Foam: Applied once daily to affected area(s)

c) Side effects

- (1) Serious intestinal infection, pseudomembranous colitis, caused by the bacteria *Clostridium difficile*. This side effect has been reported rarely with topical clindamycin use.

3. Tetracycline

- a) Most widely prescribed oral antibiotic for acne
- b) Dose

- (1) Initially, 500 mg PO twice a day until a significant decrease in acne lesions is seen; dose may then be decreased to 250–500 mg PO once a day.

- (2) Tetracycline antibiotics must be taken on an empty stomach to be most effective.

c) Caution

- (1) Not recommended for pregnant women or children younger than 9 years because tooth discoloration of the forming teeth is common in children. If all permanent teeth have erupted, tetracycline antibiotics may be a choice in select preteens.
- (2) All tetracyclines may cause sun sensitivity.

- d) Other tetracyclines used for acne include minocycline (Minocin, initially 50–100 mg PO twice daily, especially useful for pustular type acne) and doxycycline (Vibramycin, initially 50–100 mg PO twice daily).

4. Isotretinoin (Accutane, Claravis, Sotret)

- a) Effective for scarring cystic acne or acne that does not respond to other treatments. It is reserved for the most severe forms of acne.

b) Side effects

- (1) Severe mental disorders including depression and suicide
- (2) Heart, brain, bone/muscle, gastrointestinal, cholesterol, hearing, vision, and liver problems
- (3) Severe allergic reactions
- (4) Teratogenic

c) Caution

- (1) Close monitoring is essential to possibility of severe birth defects
- (2) Contraindicated in women trying to become pregnant or during pregnancy
- (3) Pharmacists must also provide a detailed warning brochure called a MedGuide from the United States Food and Drug Administration (FDA) to all patients prescribed isotretinoin. All prescribers, pharmacies, and patients must also register and participate in the iPledge risk-management program in order to prescribe, dispense, or receive the drug.

E. Oral contraceptives (OC)

1. May exacerbate or improve acne depending on the progesterone component's androgenic activity. Those with greater androgenic activity (levonorgestrel) tend to exacerbate acne, and those with less (norgestimate) or no (drospirenone) androgenic activity have been reported to improve acne in women.
2. Oral contraceptives increase the risk of thromboembolic events, especially in women older than 35 years who smoke. Remember ACHES acronym to remember thromboembolic warning signs: Abdominal pain, Chest pain, Headache or pain or changes in the eyes, severe pain or swelling in the legs or the thighs
3. Adverse effects include breast enlargement and tenderness, GI upset, irregular vaginal bleeding, especially during the first 3 months of therapy.
4. Examples of OC brands that are FDA approved for the treatment of acne (acne dosage is the same as for the OC regimen):
 - a) Ethinyl estradiol; Drospirenone (Yaz)
 - b) Ethinyl estradiol; Norethindrone acetate (Estrostep)
 - c) Ethinyl estradiol; Norgestimate (Ortho Tri-Cyclen)

II. Alopecia

- A. Alopecia areata: an autoimmune disorder in which the body's immune system attacks hair follicles, resulting in unpredictable patches of hair loss on the scalp, face, and other parts of the body.

1. Treatment

- a) Corticosteroids: betamethasone (Celestone), monthly injections into the scalp
- b) Corticosteroid pills

- c) Corticosteroid creams and ointments, such as betamethasone (Diprolene), have been applied to affected areas of the skin. However, creams and ointments are generally less effective than injections.

- B. Androgenic alopecia: an inherited form of baldness. Unlike men, women rarely develop complete baldness. Women usually experience hair thinning only.

1. Treatment

a) Minoxidil (Rogaine)

- (1) Available OTC. Applied directly to the area of hair loss at least two times a day for at least 4 months. The medication usually does not take effect until 4 months to 1 year.
- (2) Mechanism of action
 - (a) Enlarges hair follicles
- (3) Caution
 - (a) Patients who discontinue use of minoxidil will likely lose the hair that they have already grown.

b) Finasteride (Propecia)

- (1) Only works in men. This pill must be taken daily to regrow hair.
- (2) Dose
 - (a) 1 mg PO once daily
- (3) Mechanism of action
 - (a) Inhibits high levels of dihydrotestosterone (DHT) around hair follicles. High amounts of DHT cause hair follicles to shrink, and hair falls out as a result.
- (4) Caution
 - (a) Pregnant women and women hoping to become pregnant should avoid contact (including topical contact) with finasteride due to the risk of genital abnormalities to a male fetus.

c) Spironolactone (Aldactone)

- (1) Originally marketed as a diuretic (water pill) for patients suffering from congestive heart failure. Women now take the drug off-label because its antiandrogen properties may stop and sometimes reverse hair loss. It may also be more effective in postmenopausal women and may be taken with a hormone replacement pill.
- (2) It is taken initially at a low dosage (25 mg) once or twice daily. Incremental dosage increases may be used, if needed.
- (3) This medication may take many months to show results in women.

d) Cimetidine (Tagamet)

- (1) Initially used as a prescription drug to treat heartburn and stomach ulcers. Recently, this medication became available OTC.
- (2) Although primarily used as a histamine-blocking agent, it also has some antiandrogen effects and thus only works for women. Cimetidine has been used off-label to treat androgenic alopecia in women.

III. Dry Skin (Xerosis)

- A. Treatment with emollients and/or keratolytic agents; usual application is twice per day, unless otherwise noted on label or directed by prescriber.
1. Lactic acid, glycolic acid, salicylic acid, urea, and sulfur
 2. Ammonium lactate (Lac-Hydrin, others)
 3. Petrolatum (Aquaphor)

IV. Dermatitis

- A. Atopic dermatitis (eczema) is a chronic disease, and symptoms can disappear and recur over time. The skin of an affected individual is flaky, red, and itchy. The skin covering the joints and face is most commonly affected. Symptoms can be managed. Minimizing contact with known allergens can reduce the severity of symptoms.

1. Treatment

- a) Avoidance of any exacerbating allergens, contact irritants, foods, or environmental factors
- b) Antianxiety medications: The condition can cause stress and anxiety; nonpharmacologic methods to reduce stress factors are typically employed before medication
- c) Antibiotics: If co-infection exists
- d) Antihistamines like diphenhydramine (e.g., Benadryl) and hydroxyzine (e.g., Atarax)
- e) Calcineurin inhibitors like pimecrolimus (Elidel) and tacrolimus (Protopic)
- f) Immunosuppressants such as cyclosporine or interferon
- g) Oral corticosteroids such as prednisone and prednisolone
- h) Topical corticosteroids such as hydrocortisone, betamethasone, or fluticasone propionate or OTC hydrocortisone (e.g., Bactine, Cortaid, Dermolate, or Aveeno Anti-Itch cream). Higher-strength (>1%) topical corticosteroids are available by prescriptions only.

- B. Contact dermatitis: a rash that develops after contact with an allergen or skin irritant. Poison ivy, poison oak, and poison sumac produce urushiol, an oil and the allergen responsible for the allergic reaction that usually develops 24–48 hours after contact with the oil. However, it can take several days to 1–2 weeks for the rash to resolve. Patients who are allergic to these plants may experience a rash that consists of swollen, itchy, red bumps and blisters that appear wherever the oil has touched the skin.

- 1) Prevention: Avoidance of contact irritants, wearing of protectant clothing and gloves if irritant exposure is possible or cannot be avoided, skin protectant lotions like Ivy-Block can be tried, but must be applied at least 15 minutes before exposure and reapplied often (after 4 hours) if activity is prolonged.
- 2) Treatment and relief from symptoms
 - (a) General care includes removal of contaminated clothing and washing the affected skin with soap and cool water.

Washing within 10 minutes of exposure may help limit the reaction.

- (b) Systemic antihistamine such as diphenhydramine (Benadryl). Topical application of diphenhydramine is not recommended because it can cause sensitization.
- (c) Calamine lotion (e.g., Calamox) applied three to four times per day; allow to dry before putting on clothing
- (d) Cool showers or compresses
- (e) Colloidal oatmeal such as Aveeno Oatmeal Bath
- (f) Topical corticosteroids (e.g., hydrocortisone cream)
- (g) Oral corticosteroids (e.g., prednisone used for refractory cases or cases with complications)
- (h) Consumers often tout the usefulness of home remedies for relief from itching, including baking soda, vinegar, and aloe vera

V. Pediculosis and Scabies

Lice and scabies are two types of skin conditions that are caused by ectoparasites, parasites that live on the outside of their hosts.

A. Treatment

1. General

- a) Treated with OTC products and/or prescription-strength antiparasitic medications.
- b) To prevent reinfection, it is recommended that individuals wash and vacuum items that may be contaminated.
- c) Individuals who live with or have close personal contact with someone who has lice or scabies should receive treatment as well.

2. OTC

- a) Pyrethrins and piperonyl butoxide (e.g., Pronto) do not kill nits, need to re-treat in 7–10 days
- b) Permethrin (e.g., Nix, RID) kills lice and eggs, may require only one application

3. Prescription

- a) Malathion (Ovide)
- b) Lindane (Kwell) Caution: Neurotoxic. Inappropriate application, inappropriate contact, or too-frequent or excessive application may cause seizures and other serious reactions.

4. Scabicides, such as Lindane, permethrin (Acticin or Elimite), or crotamiton (Eurax Cream or Eurax Lotion)

5. Antihistamines

VI. Warts

- A. Common warts, flat warts, plantar warts (caused by human papillomaviruses [HPV])

1. Treatment

- a) Salicylic acid 17% (Compound W, Occlusal-HP)
- b) Patient-administered cryotherapy OTC products (e.g., Compound W Freeze-Off)
- c) Provider-administered cryotherapy

B. Anogenital warts (caused by select types of HPV)

1. Treatment

a) Administered by physician

- (1) Cryotherapy with liquid nitrogen, cryoprobe weekly, or surgical removal
- (2) Podophyllin resin, 10%–25% weekly for a maximum of 4 weeks
- (3) Trichloroacetic acid or bichloroacetic acid, 80%–90% weekly

b) Administered by patient, but available by prescription only after proper diagnosis

- (1) Podofilox (Condylox), 0.5% solution or gel twice daily for 3 days, followed by 4 days without therapy. This cycle may be repeated four times.
- (2) Imiquimod (Aldara), 5% cream three times per week for a maximum of 16 weeks

VII. Psoriasis

Psoriasis is a chronic skin disease characterized by scaly, reddish patches and itching. The inflammation sometimes manifests as silvery scales that appear on elbows, knees, scalp, and torso. It is not contagious. The cause is generally unknown, although recent studies suggest that it is an autoimmune disorder.

A. Topical treatments for localized exacerbations

1. Corticosteroids
2. Calcipotriene (Dovonex): applied to affected area once or twice daily
3. Tazarotene (Tazorac): applied once daily to affected area
4. Coal tar

B. Systemic treatments

1. Oral

a) Methotrexate

- (1) Antimetabolite
- (2) Dosed weekly
- (3) Adverse effects: hepatotoxicity, pulmonary toxicity, pancytopenia, potential for increased malignancies, ulcerative stomatitis, nausea, diarrhea, teratogenicity

b) Acitretin (Soriatane)

- (1) Retinoid
- (2) Adverse effects: teratogenicity, osteophyte formation, hyperlipidemia, flare of inflammatory bowel disease, hepatotoxicity, depression

c) Cyclosporine (Neoral, Sandimmune)

- (1) Calcineurin inhibitor
- (2) Adverse effects: renal dysfunction, hypertension, hyperkalemia, hyperuricemia, hypomagnesemia, hyperlipidemia, increased risk of malignancies

d) Methoxsalen

- (1) Psoralen photosensitizing agent
- (2) Used in conjunction with UVA light exposure therapy

2. Parenteral

a) Alefacept (Amevive)

- (1) Anti-CD-2
- (2) IM injection once weekly for 12 weeks

- (3) Adverse effects: Lymphopenia, potential for increased malignancies, serious infections

b) Etanercept (Enbrel)

- (1) Anti-Tumor Necrosis Factor Alpha (TNF- α)
- (2) Approved for psoriasis and psoriatic arthritis
- (3) SC injection once or twice weekly
- (4) Adverse effects: serious infections, neurologic events, hematologic events, potential for increased malignancies

c) Efalizumab (Raptiva)

- (1) Anti-CD-11a
- (2) SC injection once weekly
- (3) Adverse effects: serious infections, potential for increased malignancies, thrombocytopenia, hemolytic anemia, worsening psoriasis

d) Adalimumab (Humira)

- (1) Anti-TNF- α
- (2) Approved for psoriatic arthritis
- (3) SC injection every other week
- (4) Adverse effects: serious infections, neurologic events, potential for increased malignancies, hypersensitivity reactions, hematologic events

e) Infliximab (Remicade)

- (1) Anti-TNF- α
- (2) Approved for psoriatic arthritis
- (3) IV infusion at weeks 1, 2, and 6, then every 8 weeks
- (4) Adverse effects: serious infections, hepatotoxicity, hematologic events, hypersensitivity reactions, neurologic events, potential for increased malignancies

VIII. Common Dermatologic Fungal Infections

A. Tinea corporis (ringworm)

B. Tinea cruris (jock itch)

C. Tinea pedis (athletes' foot)

1. Topical treatment with azole antifungals; many agents available without prescription (OTC)
2. Longer duration of therapy required for tinea pedis versus other tinea infections

D. Onychomycosis (toenails or fingernails)

1. Mild infections may be treated with topical antifungal lacquers (e.g., ciclopirox.)
2. Oral antifungal medication (e.g., itraconazole, terbinafine) may be required for several months

IX. Dermatologic Bacterial Infections

A. Impetigo (*S. aureus* or *S. pyogenes*): Highly

contagious skin condition, with small oozing, crusting blisters, it usually begins on hands or face and rapidly spreads.

1. Treatment

- a) Topical antibiotics (mupirocin [Bactroban] 2%, retapamulin [Altabax])
- b) Oral antibiotics (e.g., amoxicillin/clavulanate [Augmentin], cefadroxil [Duricef], levofloxacin [Levaquin])

PATIENT PROFILE

Patient Initials: TH

Sex: Male

Age: 43 years

Height: 5' 11"

Weight: 82 kg

Race: White

Allergies: Penicillin

Chief Complaint:

RM is a 43-year-old man seeking pharmacist assistance for the ongoing topical maintenance management of his psoriasis. His condition is classified as moderate to severe and has affected his joints (symptoms and signs in his hands and knees are consistent with psoriatic arthritis). He has scaling and plaques on more than 20% of his skin.

Recent History: TH underwent biologic aortic valve replacement (BAVR) last month due to newly found congenital valvular disease. He is doing well after open heart surgery to replace the valve.

Social History:

Tobacco use: None

Alcohol use: 1 beer per week, socially

Work: Unemployed; receives disability compensation due to affect of psoriasis on the joints in hands (was formerly a chef)

Exercise: Walks 2 miles daily for heart health and to maintain joint mobility

Medications:

Prednisone 20 mg PO once daily

Tylenol with codeine #3 q6h prn pain (uses roughly once or twice daily)

Metoprolol 25 mg PO twice daily

Warfarin 5 mg PO once daily

Multivitamin with minerals PO once daily

Past medication notes: No longer taking Naprosyn 500 mg PO twice daily after open heart surgery due to warfarin prescription, which is expected to continue for another 2 months; had to discontinue infliximab (Remicade) infusion treatments last year due to cardiac symptoms (slight symptoms of mild heart failure).

PATIENT PROFILE QUESTIONS

- TH asks the pharmacist about skin hygiene tactics that may be useful in limiting scaling and improving skin appearance and that would not interact with his current prescribed medications. Which of the following topical skin care adjuncts are typically recommended for patients with psoriasis?
 - Emollients
 - Keratolytics
 - Topical nonprescription corticosteroids
 - I only
 - II only
 - III only
 - I and II
 - I and III

Answer: d. Given the extensive nature of TH's disease (greater than 20% of body) and information from the course of his treatment history and current medications, topical nonprescription corticosteroids would not be recommended. Nonprescription corticosteroid products would not be of sufficient potency to be helpful. Topical corticosteroids and calcipotriene topically are typically used as first-line therapy in patients with limited psoriatic plaques. TH does not have limited disease and already receives systemic corticosteroid treatment. Current guidelines recommend that all patients with psoriasis maintain good skin hygiene. Nearly all patients with psoriasis generally find emollients and keratolytic agents helpful in improving skin appearance and reducing skin itching.

- Which of the following is an example of a keratolytic agent that TH might employ?
 - AmLactin
 - Eucerin Creme
 - PsoriGel

Answer: a. AmLactin contains lactic acid, a keratinolytic agent. Keratinolytics break down keratin, a fibrous protein in skin cells, and this process helps remove the dead, keratinized cells of the stratum corneum (outer skin layer). Skin may look smoother after the use of these agents, which may help plaque appearance. The original formula of Eucerin creme contains emollients to increase skin hydration. PsoriGel (coal tar) may decrease skin proliferation and have anti-inflammatory properties; however, a precise mechanism in psoriasis is not clear.

REVIEW QUESTIONS

(Answers and Rationales on page 356.)

- The hospital pharmacy in which you work has added mometasone 0.1% cream as the preferred medium potency topical steroid. Which of the following is a medium potency topical steroid and is being replaced by mometasone?
 - Desonide 0.05% cream
 - Mometasone 1% cream
 - Triamcinolone 0.1% cream
 - Clobetasol 0.05% cream
 - Clobetasol 10.0% cream
- Dexamethasone may be used in the treatment of all of the following EXCEPT:
 - Addison's disease
 - dermatitis
 - asthma
 - osteoporosis
- Which of the following is first-line therapy for mild rosacea?
 - Topical metronidazole
 - Adapalene gel
 - Oral doxycycline
 - Oral metronidazole for 7 days
 - a and c

Read the following case study and then answer the questions that follow.

A 25-year-old woman with no medical history presents to a clinic with a rash that has lasted 3 months. The rash is limited to the posterior elbows and knees and is not pruritic. On examination, the rash is scaly and white with an erythematous edge. It is sharply demarcated and raised from the surrounding normal skin. She reports a similar rash in her mother that lasted several years.

4. Which of the following increases the risk of psoriasis?
 - a. Smoking
 - b. Old age
 - c. Low body weight
 - d. Over-cleansing of skin
 - e. Exposure to animals
5. What is an appropriate treatment for mild psoriasis?
 - a. Topical hydrocortisone
 - b. Oral prednisone
 - c. Methotrexate
 - d. Avoidance of sunlight
 - e. Any of the above
6. How does methotrexate alleviate psoriasis?
 - a. Prevention of fungal growth
 - b. Stimulation of epidermal regeneration
 - c. T-cell suppression
 - d. Mast cell stimulation
 - e. Antiangiogenic effects
7. Which of the following is a high potency steroid in appropriate strength for second-line psoriasis treatment?
 - a. Clobetasol 5%
 - b. Clobetasol 0.05%
 - c. Betamethasone 0.01%
 - d. Betamethasone 1%
 - e. Halcinonide 10%
8. Side effects of topical corticosteroids include:
 - a. pruritus
 - b. erythema
 - c. folliculitis
 - d. hypertrichosis
 - e. All of the above
9. Which of the following is NOT an indication for methotrexate?
 - a. Lymphoma
 - b. Rheumatoid arthritis
 - c. Esophageal cancer
 - d. Choriocarcinoma
 - e. All of the above are indications for methotrexate

Common Endocrinologic Disorders

12 CHAPTER

I. Diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disorder characterized by glucose intolerance. People in the United States who are at the highest risk for diabetes are Latino Americans, African Americans, Native Americans, and Asian Americans. It is the leading cause of blindness in adults as well as a major cause of end-stage renal disease and amputations.

A. Classification

1. Type 1 diabetes is a failure of the pancreas to make enough insulin for the body to function. It was previously called insulin-dependent diabetes or juvenile-onset diabetes. It occurs more often in younger patients than older patients. Type 1 diabetes requires insulin therapy.
2. Type 2 diabetes refers to decreased insulin production from the pancreas, decreased sensitivity of cells to insulin, and decreased ability to get glucose into cells. It was previously called non-insulin dependent diabetes and adult-onset diabetes. It occurs more often in older patients than younger patients, although the incidence of type 2 diabetes is increasing in children in the United States. Patients may start with diet and exercise therapy. Most patients start with oral medications but may progress to requiring insulin therapy.
3. Gestational diabetes is diabetes that occurs during pregnancy. It does not mean the patient will have diabetes for the rest of her life, but she will have increased risk of developing type 2 diabetes. Patients typically use insulin therapy due to risk to the fetus when using oral antidiabetic medications. Gestational diabetes is usually detected through administration of an oral glucose tolerance test (OGTT) during pregnancy.
4. Prediabetes is the increased risk of developing DM.
 - a) Impaired fasting glucose (IFG): fasting glucose 100–125 mg/dL
 - b) Impaired glucose tolerance (IGT): Two-hour glucose 140–199 mg/dL during oral glucose tolerance test (OGTT)

B. Signs and symptoms

1. The 3 Ps: **polyuria**, **polydipsia**, **polyphagia**
2. Blurred vision
3. Fatigue
4. Dry, itchy skin

5. Slow wound healing

6. Weight loss (type 1 diabetes)

C. Diagnosis

1. Random plasma glucose > 200 mg/dL plus signs and symptoms of diabetes OR
2. Fasting plasma glucose > 126 mg/dL OR
3. Two-hour postprandial glucose > 200 mg/dL during OGTT
4. Confirm the above.
5. Hemoglobin A1c testing (HbA1c): HbA1c is not used to diagnose DM, but is used for long-term monitoring.

D. Goals of therapy

Goals of Therapy

Target Area	Treatment Goals (for the patient with diabetes)
Preprandial plasma glucose (fasting)	90–130 mg/dL
Postprandial plasma glucose (after meals)	<180 mg/dL
Glycosylated hemoglobin (HbA1c)	<7%
Blood pressure	<130/80 mmHg
Lipid levels	
LDL cholesterol	<100 mg/dL
HDL cholesterol	>40 mg/dL (men); >50 mg/dL (women)
Triglycerides	<150 mg/dL

Based on the American Diabetes Association guidelines. Individual treatment goals may vary slightly from these guidelines based on personal medical history.

E. Treatment

1. Diet
2. Exercise
3. Type 1: insulin therapy, pramlintide (Symlin)
4. Type 2: oral agents and/or insulin, pramlintide (Symlin), exenatide (Byetta)

F. Insulin

1. Background

- a) Insulin is produced in the beta cells of the pancreas. It is released at a basal rate of 0.5 to 1 U/h. Insulin response is increased in response to food.

- b) The mechanism of action is not completely understood.
 - (1) Muscle: increase glucose transport into cell, glycogenesis, protein and triglyceride synthesis
 - (2) Liver: increase glucose transport into cell, glycogenesis, glucose utilization in Krebs cycle, protein synthesis
 - (3) Adipose: increase glucose transport into cell, glycogenesis, triglyceride synthesis
 - (4) Take home point: Insulin is necessary for the body to use glucose.
- 2. Types of insulin
 - a) Short-acting
 - (1) Used for mealtime control
 - (2) Administered 15–30 minutes before meal
 - (3) May also be used for sliding scale
 - (4) Examples
 - (a) Insulin aspart (NovoLog)
 - (b) Insulin lispro (Humalog)
 - (c) Insulin glulisine (Apidra)
 - (d) Regular (Humulin R)
 - b) Intermediate-acting
 - (1) Used for basal control
 - (2) Dosed twice daily for optimal control; may also be dosed once daily at bedtime for patients with type 2 diabetes who also take oral medications to suppress overnight hepatic gluconeogenesis
 - (3) Example
 - (a) Isophane insulin, NPH (Humulin N)
 - c) Long-acting
 - (1) Like intermediate-acting are used for basal control
 - (2) Usually dosed once daily
 - (3) Should not be mixed with any other insulin
 - (4) Examples
 - (a) Insulin glargine (Lantus)
 - (b) Insulin detemir (Levemir)
 - d) Combination products
 - (1) Humulin 70/30 (70% NPH, 30% regular)
 - (2) Humulin 50/50 (50% NPH, 50% regular)
 - (3) Humalog mix 50/50 (50% insulin lispro protamine suspension, 50% lispro)
 - (4) Humalog mix 75/25 (75% insulin lispro protamine suspension, 25% lispro)
 - (5) NovoLog mix 70/30 (70% insulin aspart protamine suspension, 30% aspart)
- 3. Cautions
 - a) Causes hypoglycemia at high doses
 - b) Lispro has more rapid onset than regular and should not be interchanged with it
 - c) Patients with type 1 DM should not use once-daily dosing of insulin initially
 - d) Changes in insulin should only be made under supervision of medical personnel
 - e) Caution is warranted when switching from animal (either pork or bovine) to purified porcine insulin or biosynthetic human insulin due to increased potency or bioavailability and increased risk of hypoglycemia.
 - f) Injection needles should not be reused
 - g) Insulin should not be used during hypoglycemia
 - h) Insulin should still be used when ill (may need more insulin when ill)
 - i) Use of lispro has not been studied in pregnancy, fetal abnormalities occurred in two infants
 - j) Contraindication: hypersensitivity to the medications
 - k) Insulin dosing and use requires constant patient education and monitoring
- 4. Interactions
 - a) Medications affecting glucose: may increase or decrease effect of insulin
 - b) Pork and human insulin should not be mixed or used together
- 5. Toxicity and side effects
 - a) Hypoglycemia
 - b) Lipodystrophy
 - c) Weight gain
 - d) Patients may develop resistance to insulin treatment
 - e) Patients may develop sensitivity to animal insulin
- 6. Remarks regarding insulin
 - a) Should always be dosed in “units” (e.g., 10 units subcutaneous [SC])
 - b) Regular insulin solution should be clear
 - c) Mixing*
 - (1) Semilente/lente/ultralente: can be mixed in any proportion
 - (2) Regular + lente: bind immediately, if mixed, must use immediately after mixing or inject separately
 - (3) Lente + phosphate-buffered insulin (NPH, NovoNordisk, Humulin BR): must never be mixed; lente will become immediate-acting instead of delayed
 - (4) NPH and regular insulin can be combined in the same syringe and refrigerated for a maximum of 21 days
- 7. Injection technique
 - a) Use abdomen, arm, leg, or buttocks
 - b) Clean the injection area first with alcohol
 - c) Examine bottle and roll gently in hands
 - d) Inject air into vial, draw up desired dose
 - e) Pinch the skin with one hand, and insert the needle at an angle of 45°–90°
 - f) Dispose of the syringe properly
 - g) Rotate the injection site
- 8. Adjusting insulin dose
 - a) Adjustments are made based on glucose monitoring and HbA1c as well as pattern of response

*When mixing regular and NPH, regular should be drawn up first or the protamine in NPH will cause the regular insulin in the vial to become cloudy (the same applies to mixing regular with any other insulin).

Insulin Calculations

Starting Insulin: Staged Diabetes Management Guideline (SDM)

Guideline for starting and titrating background insulin: Background insulin + oral agent(s) insulin glargine or insulin detemir

<70 mg/dL	Decrease 1–2 U
140–250 mg/dL	Increase 2–4 U
>250 mg/dL	Increase 4–8 U

0.1 U/kg body weight if A1c levels are <9% (long acting insulin)

0.2 U/kg body weight if A1c levels are ≥9%

Adjustments are made weekly based on fasting blood glucose.

It is common to start insulin therapy by using only insulin glargine (Lantus) at bedtime in combination with oral agents. The use of background insulin with oral antidiabetic agents is a common approach to initiate insulin therapy. The average dose that was effective in the Treat-to-Target study was 0.4 to 0.5 U/kg at bedtime. Continue to escalate dose if goal is not reached. If the dose surpasses 0.7 U/kg, transition return to background insulin. Mealtime regimen is recommended for tighter control.

Guideline for starting and titrating premixed insulin: Premixed insulin Aspart 70/30 or Lispro premix 75/25

Blood Glucose Adjust Insulin*

Prebreakfast

<70 mg/dL	Decrease PM 1–2 U
140–250 mg/dL	Increase PM 1–2 U
>250 mg/dL	Increase PM 2–4 U

Presupper

<70 mg/dL	Decrease AM 1–2 U
140–250 mg/dL	Increase AM 1–2 U
>250 mg/dL	Increase AM 2–4 U

Start

0.1 U/kg in morning **and** evening if A1c <9%

0.2 U/kg in morning **and** evening if A1c ≥9%

Total daily units

0.2–0.4 U/kg

Adjust weekly based on AM or PM blood glucose

Guidelines for starting and titrating background/mealtime insulin: Long-acting insulin (insulin glargine or insulin detemir) + rapid-acting insulin with meals

Blood Glucose	Adjust Insulin [†]
Prebreakfast	Long-acting (detemir or glargine)
Prelunch AM	Rapid acting
Presupper lunch	Rapid acting
Prebedtime supper	Rapid acting
Start	If A1c <9%: • 0.1 U/kg long-acting insulin • 0.1 U/kg rapid-acting insulin divided between meals If A1c ≥9%: • 0.2 U/kg long-acting insulin • 0.2 U/kg rapid-acting insulin divided between meals
Total units	0.2–0.4 U/kg
Adjust	Minimum weekly

*Stop secretagogue; consider continuing insulin sensitizer(s).

[†]Adjust insulin by 1–2 U based on blood glucose pattern. Review insulin-to-carbohydrate ratios and activity. Stop secretagogue; consider continuing insulin sensitizer(s).

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- b) Adjust basic insulin dose 1–2 units at a time; 2–4 units or more for extreme cases
- c) For every unit of rapid-acting insulin, glucose may be reduced by 25–50 mg/dL
- d) Long-acting insulin should be adjusted based on fasting glucose
9. Alternative methods of insulin administration
 - a) Pen
 - (1) Portable and convenient; an alternative to vial and syringe
 - (2) NovoPen 3, Flex Pen (NovoLog, NovoLog 70/30, Levemir)
 - (3) Humalog, Humalog mix 75/25, Humulin N, Humulin 70/30
 - b) Pump
 - (1) Continuous subcutaneous infusion
 - c) Inhaled insulin (Exubera)
 - (1) Withdrawn from the market due to lack of demand
 - (2) High cost
 - (3) Long-term pulmonary safety profile of concern
10. Somogyi effect and dawn phenomenon
 - a) Somogyi effect
 - (1) Rebound hyperglycemia due to insulin-induced hypoglycemia
 - (2) Treatment
 - (a) Adjust evening snack
 - (b) Decrease evening NPH or give at a later time
 - (c) Switch to a basal insulin
 - b) Dawn phenomenon

- (1) Rise in blood glucose level upon waking during the early morning hours (usually between 4 AM and 9 AM)
 - (2) Treatment
 - (a) Limit or regulate evening snacks
 - (b) Possibly increase NPH dose or basal insulin
- G. Synthetic amylin analog, pramlintide acetate (Symlin)
1. Mechanism of action: synthetic analog of human amylin
 - a) Amylin, like insulin, is located in pancreatic beta cells. It is secreted with insulin in response to food intake.
 - b) Reduces postprandial glucose
 - c) Slows gastric emptying
 - d) Decreases food intake
 - e) Increases satiety
 2. Indications
 - a) Type 1 and type 2 diabetes as an adjunct to mealtime insulin
 3. Usual adult dosage
 - a) Type 1 diabetes: initially, 15 mcg SC before meals; may titrate up at 15 mcg increments (without nausea for 3 days); maintenance: 30–60 mcg SC before meals
 - b) Type 2 diabetes: initially, 60 mcg SC before meals; may increase dose to 120 mcg SC before meals (without nausea for three days)
 4. Adverse effects
 - a) Nausea
 - b) Hypoglycemia
 5. Contraindications and considerations
 - a) Avoid in gastroparesis and hypoglycemia unawareness
 - b) Potential for drug interactions due to delayed gastric emptying
 - c) Reduce premeal insulin by 50% when initiating pramlintide
- H. Incretin mimetic agent, exenatide (Byetta)
1. Mechanism of action
 - a) Stimulates the body's ability to produce insulin in response to elevated concentrations of blood glucose
 - b) Inhibits the release of glucagon after meals
 - c) Slows the rate of gastric emptying
 - d) Reduces food intake
 2. Indications
 - a) Treatment of type 2 diabetes (adjunct to metformin, sulfonylurea, or thiazolidinedione)
 3. Usual adult dosage
 - a) Initially, 5 mcg SC bid given within 60 minutes before morning and evening meal
 - b) May increase dose to 10 mcg SC bid after one month
 - c) Available in prefilled pens (must refrigerate)
 4. Adverse effects
 - a) Hypoglycemia (more likely when combined with a sulfonylurea)
 - b) Nausea

5. Contraindications and considerations
 - a) Hypersensitivity to exenatide
 - b) Potential for drug interactions due to delayed gastric emptying
 - c) Has not been studied for use with insulin
 - d) Pancreatitis
- I. Oral agents for diabetes
 1. Sulfonylureas
 - a) Mechanism of action
 - (1) Stimulates insulin release from pancreatic beta cells; increases peripheral sensitivity
 - (2) Inhibits hepatic glucose production; enhances glucose uptake in muscle
 - (3) Insulin secretagogues
 - b) First generation versus second generation-
 - (1) Fewer adverse effects with second generation agents (e.g., glyburide, glipizide), although patient is still at risk for hypoglycemia
 - (2) Second generation (e.g., glyburide, glipizide, glimepiride) more potent
 - (3) Comparable efficacy

Comparable Efficacy

	Generic (Brand)	Adult Daily Dose Range
First generation	Acetohexamide (Dymelor)	250–1500 mg
	Tolbutamide (Orinase)	500–3000 mg
	Tolazamide (Tolinase)	100–1000 mg
	Chlorpropamide (Diabinese)	100–500 mg
Second generation	Glipizide:	
	Glucotrol	2.5–40 mg
	Glucotrol XL	2.5–20 mg
	Glyburide:	
	Micronase, DiaBeta	2.5–20 mg
	Glynase	1.5–12 mg
	Glimepiride (Amaryl)	1–4 mg

- c) Indications: management of type 2 diabetes as monotherapy; also combined with other antidiabetic medications if needed (e.g., metformin, insulin)
- d) Usual adult dosage
- e) Adverse effects
 - (1) Hypoglycemia
 - (2) Nausea/vomiting
 - (3) Weight gain
 - (4) Rash
 - (5) Dyspepsia
 - (6) Hematologic reactions
- f) Contraindications and considerations
 - (1) Hypersensitivity
 - (2) Type 1 diabetes
 - (3) Avoid alcohol

2. Biguanides: Metformin (Glucophage, Glucophage XR, Fortamet, Glumetza, Riomet)
 - a) Mechanism of action
 - (1) Inhibit gluconeogenesis and glycogenolysis
 - (2) Improve insulin sensitivity
 - (3) Does not stimulate insulin secretion; insulin sensitizers
 - b) Indications
 - (1) Management of type 2 diabetes as monotherapy or in combination with sulfonylurea
 - c) Usual adult dosage
 - (1) Initially, 500 mg daily for 7–10 days.
 - (2) Standard dose 500 mg bid with meals
 - (3) May increase at 1- or 2-week intervals by 500 mg if needed
 - (4) Maximum dose: 2550 mg/day for younger adults; pediatric and elderly patients should receive lower maximum daily doses.
 - d) Adverse effects
 - (1) Metallic taste
 - (2) Abdominal discomfort/cramping
 - (3) Diarrhea
 - (4) Nausea/vomiting
 - (5) Decrease vitamin B₁₂ levels
 - (6) Lactic acidosis
 - e) Contraindications
 - (1) Avoid in patients with renal dysfunction (SCr >1.5 mg/dL for men and >1.4 for women)
 - (2) Hypersensitivity
 - (3) History of lactic acidosis
 - (4) Pharmacologically treated heart failure
 - (5) Radiologic contrast procedures (use of contrast increases risk for renal dysfunction and lactic acidosis). Discontinue metformin 48 hours before and after procedure.
 - (6) Alcoholism (especially frequent binge drinking)
3. Thiazolidinediones, pioglitazone (Actos), rosiglitazone (Avandia)
 - a) Mechanism of action
 - (1) Increases peripheral glucose utilization
 - (2) Decreases hepatic glucose production
 - (3) Insulin sensitizer and consequently reduces insulin secretion
 - b) Indications
 - (1) Management of type 2 diabetes as monotherapy or in combination with sulfonylurea, metformin, or insulin
 - c) Usual adult dosage
 - (1) Pioglitazone: initially, 15 or 30 mg daily; may increase at 8- or 12-week intervals; maximum 45 mg daily
 - (2) Rosiglitazone: initially, 4 mg daily or in divided doses; may increase at 8- or 12-week intervals; maximum 8 mg daily
 - d) Adverse effects
 - (1) Edema
 - (2) Weight gain
 - (3) Anemia
 - (4) Cardiovascular event (e.g., heart failure, heart attack risk may be increased with rosiglitazone)
 - (5) Hepatic events (liver damage)
 - (a) Monitor LFT
 - (6) Potential increased fracture risk (hands, feet) in women with long-term use
 - e) Contraindications and considerations
 - (1) Avoid in patients with congestive heart failure (CHF) or liver disease
4. Meglitinides, repaglinide (Prandin), nateglinide (Starlix)
 - a) Mechanism of action
 - (1) Similar to sulfonylureas
 - (2) Stimulates insulin release from beta cells in a glucose-dependent manner
 - (3) Insulin secretagogues
 - b) Indications
 - (1) Management of type 2 diabetes as monotherapy or in combination with metformin or thiazolidinedione
 - c) Usual adult dosage
 - (1) Repaglinide: If patients have HbA_{1c} <8% or are naïve: 0.5 mg before meals. If they have been previously treated with HbA_{1c} >8%, 1–2 mg before meals may be used. Maximum dose 16 mg daily
 - (2) Nateglinide: Initially, 120 mg tid before meals; maintenance 120 mg tid before meals; patients near goal HbA_{1c} may use 60 mg tid
 - (3) For both: Doses should be skipped if a meal is skipped
 - d) Adverse effects
 - (1) Hypoglycemia
 - (2) GI upset
 - (3) Headache
 - (4) Weight gain
 - (5) Flu-like symptoms
 - e) Contraindications and considerations
 - (1) Type 1 diabetes or for the treatment of diabetic ketoacidosis (DKA)
5. Alpha glucosidase inhibitors, acarbose (Precose), miglitol (Glyset)
 - a) Mechanism of action
 - (1) Competitive inhibition of disaccharidases and pancreatic enzymes
 - (2) Delays intestinal absorption of carbohydrates (starch blockers)
 - b) Indications
 - (1) Management of type 2 diabetes as monotherapy or in combination with sulfonylurea, metformin, or insulin
 - c) Usual adult dosage
 - (1) Initially, 25 mg daily with the first bite of main meal
 - (2) May titrate up at 2-week intervals
 - (3) Maximum 100 mg TID with main meals
 - (4) For both: Dose should be skipped if meal is skipped
 - d) Adverse effects
 - (1) Flatulence

- (2) Abdominal cramps
- (3) Diarrhea
- (4) Borborygmus (stomach rumbling sounds)
- e) Contraindications
 - (1) Inflammatory bowel disease (IBD)
 - (2) Intestinal obstruction
- 6. Dipeptidyl peptidase-4 (DPP-4) inhibitors: sitagliptin phosphate (Januvia)
 - a) Mechanism of action
 - (1) Blocks dipeptidyl peptidase IV (DPP-4), results in increased insulin release after meals and when glucose levels are high
 - b) Indications
 - (1) Monotherapy or in combination with other hypoglycemic agents for type 2 diabetes
 - c) Usual adult dosage
 - (1) 100 mg once daily with or without food
 - d) Adverse effects
 - (1) Nasopharyngitis
 - (2) Upper respiratory tract infection
 - (3) Headache
 - e) Contraindications and considerations
 - (1) Type 1 diabetes or for the treatment of diabetic ketoacidosis (DKA)
- J. Complications of diabetes
 - 1. Acute
 - a) Hyperglycemia
 - b) Hypoglycemia
 - c) Diabetic ketoacidosis (DKA)
 - (1) Characterized by high levels of ketones in the blood
 - (2) Signs and symptoms
 - (a) Loss of appetite
 - (b) Nausea
 - (c) Vomiting
 - (d) Fever
 - (e) Stomach pain
 - (f) A sweet, fruity smell on the breath, especially if the blood sugar level has been consistently greater than 250 mg/dL
 - (3) More common in type 1 diabetes than type 2
 - (4) Treated with insulin therapy (typically therapy is begun as an insulin infusion in intensive care setting) and intravenous fluids
 - 2. Microvascular complications
 - a) Diabetic neuropathy (nerve damage caused by prolonged hyperglycemia, often occurring in feet and legs)
 - (1) Peripheral neuropathy
 - (2) Autonomic neuropathy
 - b) Diabetic retinopathy (a leading cause of blindness in the United States)
 - c) Diabetic nephropathy (kidney damage, nephrons lose filtering capacity, may lead to kidney failure and need for dialysis or transplant)
 - 3. Macrovascular complications
 - a) Hyperlipidemia

- b) Hypertension
- c) Cardiovascular disease, atherosclerosis
- d) Stroke
- 4. Other complications
 - a) Increased risk for skin and skin structure infection (e.g., diabetic foot ulcer)
 - b) Gum disease; oral health complications

K. Patient education

- 1. Diet
- 2. Exercise
- 3. Home blood glucose monitoring
- 4. Action plan for hypo- and hyperglycemia
- 5. Insulin administration; administration and timing of other antidiabetic medications
- 6. Complications and prevention of diabetes
- 7. Eye care
- 8. Dental care
- 9. Foot care

II. Thyroid Disorders

Thyroid disorders are among the most common medical endocrine conditions but, because their symptoms often appear gradually over time, they are commonly misdiagnosed. There are two main types of thyroid disease: hyperthyroidism, or too much thyroid hormone, and hypothyroidism, or too little thyroid hormone.

The thyroid produces hormones, called thyroxine (T_4) and triiodothyronine (T_3), which affect the body's metabolism and energy level. T_3 is the short-acting and more potent of the two hormones. Thyroid hormone is also produced in response to thyroid stimulating hormone (TSH, also known as thyrotropin) secreted by the pituitary gland.

A. Hypothyroidism occurs when the thyroid gland does not produce enough thyroid hormone.

1. Hashimoto thyroiditis

- a) Most common type
- b) Inflammation of thyroid gland (not caused by infection)
- c) Occurs when the individual's immune system attacks the thyroid gland, causing low levels of thyroid hormone
- d) Exhibits low plasma free T_4 and elevated TSH levels

2. Signs and symptoms

- a) Cold intolerance
- b) Fatigue
- c) Somnolence
- d) Constipation
- e) Menorrhagia
- f) Myalgia
- g) Hoarseness
- h) Gland enlargement
- i) Bradycardia
- j) Edema
- k) Dry skin
- l) Weight gain

3. Treatment

- a) Thyroid replacement hormones
 - (1) Levothyroxine (T_4) (Synthroid, Levothroid, Levoxyl, others)
 - (a) Typical adult maintenance dose after titration: 100–120 mcg PO daily as a

single dose 30 minutes before breakfast, given with plenty of plain water

- (i) Adjust dose in the elderly and in patients with coronary artery disease
 - (ii) Initial dose in elderly 25 mcg per day versus the initial dose for younger adults, which is typically 50 mcg per day
 - (iii) Those with cardiac disease also start at 25 mcg daily
 - (b) Highly protein bound
 - (c) Precautions
 - (i) Long-term use has been associated with increased bone reabsorption and decreased bone density
 - (d) Drug interactions
 - (i) Antacids, calcium, or iron supplements should not be taken within four hours of levothyroxine dose; may decrease T_4 absorption
 - (ii) Warfarin effects are enhanced by levothyroxine
 - (iii) Digoxin levels may be reduced by levothyroxine
 - (2) Liothyronine (T_3) (Cytomel, Triostat)
 - (a) Adult dose: 25 mcg PO qd
 - (3) Liotrix (T_4 and T_3 , 4:1 ratio) (Thyrolar)
 - (a) Adult dose: 60–120 mg PO qd
 - (4) Desiccated thyroid, variable T_4 and T_3 content due to animal gland sourcing (Armour Thyroid, Naturethroid, Westthyroid)
 - (a) Adult dose: 60–120 mg PO qd
- B. Hyperthyroidism (thyrotoxicosis): occurs when the thyroid gland produces too much thyroxine. As a result, the individual's metabolism increases dramatically, leading to weight loss and irregular heartbeat.
1. Graves disease
 - a) Most common cause
 - b) Malfunction in the body's immune system releases abnormal antibodies that mimic thyroid-stimulating hormone (TSH)
 - c) Thyroid hormone factories work overtime and produce an excess of thyroid hormone
 - d) Exhibits elevated T_4 and subnormal TSH levels
 - e) Can lead to thyroid storm: a life-threatening and sudden exacerbation of symptoms of thyrotoxicosis
 - (1) Characterized by fever, tachycardia, frank diarrhea, delirium, and coma
 - (2) Treatment: antipyretic (not aspirin); antithyroid drug plus Lugol solution 1 hour later; beta blockers
 2. Signs and symptoms
 - a) Sudden and unexplained weight loss
 - b) Increased or irregular heartbeat
 - c) Nervousness

- d) Irritability
- e) Tremors (especially in the hands)
- f) Increased sweating
- g) Abnormal menstruation
- h) Increased sensitivity to warmth
- i) More frequent bowel movements
- j) Enlarged thyroid gland (goiter)
- k) Fatigue
- l) Difficulty sleeping
- m) Muscle weakness
- n) Inability to close the eyelid (eyelid retraction)

3. Treatment

a) Antithyroid drugs

(1) Methimazole (Tapazole)

- (a) Adult dose: 5–40 mg QD
- (b) Favored over propylthiouracil (PTU) due to longer half-life, which allows for once a day dosing
- (c) More potent than PTU

(2) Propylthiouracil (PTU)

- (a) Adult dose: Initially, 300 mg QD, then usually 100–150 mg daily
- (b) Although both drugs cross the placenta, the drug of choice in pregnant patient is PTU because it crosses less

(3) Strong iodine solution (Lugol's solution)

- (a) Adult dose: 0.1–0.3 mL (3–5 gtts) PO TID

(4) Saturated solution of potassium iodide (SSKI)

- (a) Usual adult dose: 1–5 gtts PO TID in water or juice

b) Surgery

c) Radioactive iodine

- (1) Sodium iodide-131 (^{131}I), the agent of choice for Graves disease
- (2) Most will require thyroid hormone supplementation after radioactive iodine treatment

PATIENT PROFILE

Patient Initials: CC

Sex: Female

Age: 22 years

Height: 5' 4"

Weight: 68 kg

Race: Latin American

Allergies: No known drug allergies (NKDA)

Chief Complaint:

CC is a 22-year-old woman with a history of gestational diabetes; she has one child, now 2 years old. She presents to the pharmacist clinic service for the first time because her family doctor has just told her that she now has type 2 diabetes. "My blood sugars were high on two tests," she explains, "but I feel great, and I am young. Why do I have to take medications? Can't I just exercise and lose some weight?"

Social History:

Tobacco use: None

Alcohol use: A few glasses of wine per week, usually with dinner

Exercise: Began walking program last week with her mother, who also has type 2 diabetes and is overweight

Medications:

Multivitamin once daily

New prescription: Metformin 500 mg PO twice daily

Other: Wears eyeglasses for reading

Laboratory:

Blood glucose: 220 mg/dL, nonfasting

Blood glucose: 140 mg/dL, fasting

Hemoglobin A1c (HbA1c): 8.6%

PATIENT PROFILE QUESTIONS

- After discussion with the patient, it is clear that CC has little understanding of her new diagnosis and will need extensive diabetic education. When discussing blood sugar and HbA1c tests, which of the following would a pharmacist state as CC's HbA1c treatment goal?
 - <6.5%
 - <8%
 - <7.5%
 - <7%

Answer: d. Based on well-known studies such as the Diabetes Control and Complications Trial (DCCT), a goal HbA1c of less than 7% reduces the risk of microvascular complications, such as diabetes-related nephropathy and retinopathy. Higher HbA1c levels increase the risk of chronic complications of diabetes. Some organizations recommend more aggressive goals (e.g., HbA1c <6.5%), but aggressive goals expose a patient to a greater risk of severe hypoglycemia.

- The pharmacist encourages CC's new exercise routine and weight loss goals. These plans are endorsed by her family doctor. Exercise may improve insulin sensitivity, promote weight reduction, and improve overall health. Weight reduction can lower the need for medications in some patients. In addition to exercise, what other preventative options should be recommended for CC at this time?
 - Checking with her doctor regarding her cholesterol levels
 - Taking a "baby aspirin" (aspirin 81 mg) daily to prevent heart disease
 - Performing daily foot self-examinations
 - Keeping regularly scheduled ophthalmic exams
 - I and II
 - III and IV
 - I, III, and IV
 - All of the above

Answer: c. All patients with diabetes should be screened for lipid disorders because early management can help prevent macrovascular complications, such as myocardial infarction (MI). Current evidence suggests that aspirin is ONLY

recommended for patients with diabetes with known heart disease and as primary prevention ONLY in patients with diabetes older than 30 years old with heart disease risk factors. CC is 22 years of age and is in an age bracket where insufficient benefit and risk information is available regarding preventative aspirin therapy. Daily self-examinations of the feet for cracks, callus formation, ulcers, and other issues will help avoid serious foot problems. Routine eye exams are recommended for any patient with diabetes with known visual difficulty; how often they are performed depends on age and known visual problems. Annual eye exams are recommended for those older than 30 years of age without any current visual difficulties. Younger patients should have routine exams at least every 5 years or more frequently if they already have visual impairment or changes.

- CC will begin the metformin prescription as prescribed. During discussion with CC, the pharmacist should include which of the following in the counseling about the new prescription?
 - Metformin is often a drug of choice when type 2 diabetes is first diagnosed. It is effective at lowering blood sugar, does not cause weight gain, and does not cause low blood sugar when used alone.
 - Common side effects that usually decrease in a few weeks include nausea or reduced appetite.
 - CC should avoid binge drinking of alcohol to avoid lactic acidosis, a serious but rare side effect that can harm the kidneys.
 - If CC follows her recommended diet and exercise plan, maintains a recommended body weight, and takes the metformin as prescribed, she can expect her HbA1c to drop about 1.5% with the medication.
 - I only
 - II only
 - I, II, and III
 - All of the above

Answer: d. Diabetes treatment guidelines place metformin monotherapy as first-line treatment for healthy, adults newly diagnosed with type 2 diabetes who have no other contraindications to metformin use. Common side effects are nausea, diarrhea, reduced appetite, and sometimes a metallic-like taste. These usually go away in a few weeks. Binge drinking of alcohol can be a risk factor for lactic acidosis and is often an important counseling point in a young patient with an active social life. Metformin will reduce HbA1c, will not cause weight gain, and can help CC reach her optimal health goals. If she is educated and adherent, she may avoid the need for additional medications.

REVIEW QUESTIONS

(Answers and Rationales on page 356.)

- Lipohypertrophy in patients with diabetes is due to which of the following?
 - Repeated injections into the same site
 - Injections into fat-rich tissue

- c. Too-rapid insulin injection
 - d. Hypersensitivity to insulin
 - e. Hypersensitivity to insulin vehicle
2. Which of the following is true of insulin?
- a. It is secreted by pancreatic alpha cells
 - b. It promotes peripheral glucose uptake and utilization
 - c. It inhibits hepatic gluconeogenesis
 - d. a and b
 - e. b and c
3. Which of the following insulin preparations is available as a recombinant human analog?
- a. Insulin lispro
 - b. Lente insulin
 - c. Regular insulin
 - d. None of the above
 - e. All of the above
4. Which of the following steroids have the longest duration of action?
- I. Betamethasone
 - II. Dexamethasone
 - III. Hydrocortisone
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
5. Which of the following conditions increases the risk of amputations in diabetics?
- a. Peripheral Neuropathy
 - b. Peripheral Vascular Disease
 - c. Erythema
 - d. All of the above
 - e. None of the above
6. Which of the following is used for treatment of thyroid storm:
- I. levothyroxine
 - II. hydrocortisone
 - III. propylthiouracil
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
7. Which of the following classes of drugs requires periodic monitoring of liver function?
- a. Thiazolidinedione
 - b. Biguanide
 - c. Meglitinide
 - d. Sulfonylurea
 - e. None of these drugs requires monitoring of liver function
8. Which of the following should be monitored in patients with diabetes treated with ACE inhibitors?
- a. Serum creatinine, blood urea nitrogen, potassium, and sodium
 - b. Serum creatinine and blood urea nitrogen
 - c. Urine protein and sodium
 - d. Urine protein, sodium, and glucose
 - e. Urine protein, sodium, glucose, and potassium
9. Of the following patients, which is most likely to experience an adverse drug reaction?
- a. 30-year-old man taking chlorpropamide and atenolol
 - b. 40-year-old woman taking pioglitazone with a serum BUN of 17 mg/dL
 - c. 30-year-old woman taking acarbose with an ALT of 80 IU/L and AST of 90 IU/L
 - d. 40-year-old man taking lisinopril and pioglitazone
 - e. 40-year-old woman taking lisinopril with an ALT of 30 IU/L and AST of 30 IU/L
10. Androgens are associated with which of the following adverse effects?
- a. Priapism
 - d. Jaundice
 - c. Gynecomastia
 - d. Urinary retention
 - e. All of the above
11. Sulfonylureas are associated with which of the following adverse effects?
- a. Jaundice
 - b. Photosensitivity
 - c. Nausea
 - d. a and b
 - e. a, b, and c
12. Which of the following statements about insulin is true?
- a. It is secreted by pancreatic alpha cells,
 - b. It promotes peripheral glucose uptake and utilization,
 - c. It inhibits hepatic gluconeogenesis,
 - d. a and b
 - e. b and c
13. Which of the following is a useful feature to differentiate cholinesterase inhibitor overdose with myasthenia gravis exacerbation?
- a. Sweating
 - b. Weakness
 - c. Fasciculations
 - d. Salivation
 - e. All of the above
14. Which of the following agents can cause the syndrome of inappropriate secretion of antidiuretic hormone (SIADH)?
- a. Fluoxetine
 - b. Vincristine
 - d. MDMA
 - d. Risperidone
 - e. All of the above
15. Which of the following is TRUE about sulfonylureas?
- a. Tolazamide is a second generation agent

- b. Chlorpropamide is a first generation agent
 - c. Safe to use during pregnancy
 - d. a and b
 - e. b and c
16. What is the standard daily dose of glyburide?
- a. 1.25–20 mg/day
 - b. 20–80 mg/day
 - c. 100–400 mg/day
 - d. 200–800 mg/day
 - e. 500–2000 mg/day
17. Patients taking chlorpropamide should be counseled to avoid which of the following?
- a. Cheese
 - b. Vitamin K
 - c. Milk
 - d. Alcohol
 - e. Acetaminophen
18. Which of the following are responsible for inhibiting insulin release?
- a. Secretin
 - b. Gastrin
 - c. Somatostatin
 - d. Cholecystokinin
 - e. All of the above
19. Which of the following drugs increase pancreatic insulin secretion?
- a. Glipizide
 - b. Metformin
 - c. Acarbose
 - d. All of the above
 - e. None of the above
20. Oral medications to treat type 2 diabetes do which of the following?
- I. Reduce insulin resistance
 - II. Stimulate endogenous insulin
 - III. Delay carbohydrate absorption
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
21. Which of the following is/are the active ingredient(s) of Avandamet?
- a. Rosiglitazone
 - b. Glipizide
 - c. Metformin
 - d. a and b
 - e. a and c
22. CO is a taking Precose (acarbose) 100 mg PO tid. Which of the following should be monitored?
- a. AST
 - b. CK
 - c. PT
 - d. INR
 - e. CK
23. Glyset is a drug that inhibits:
- a. alpha glucosidase
 - b. angiotensin-converting enzyme (ACE)
 - c. protease
 - d. acetylcholinesterase
 - e. topoisomerase
24. Which of the following is NOT an appropriate treatment for hyperthyroidism?
- a. Propranolol
 - b. Corticosteroids
 - c. Bromocriptine
 - d. Propylthiouracil
 - e. Lugol solution
25. Which of the following is a side effect of biosynthetic growth hormone?
- a. Hepatitis B
 - b. Antibody formation
 - c. Creutzfeldt-Jakob disease
 - d. HIV transmission
 - e. Hypoglycemia
26. Which of the following statements about insulin is true?
- a. It is reabsorbed in the renal tubules.
 - b. It is metabolized in the liver.
 - c. It has a half-life of less than 10 minutes.
 - d. a and b
 - e. a, b, and c
27. Which of the following causes increased insulin activity after glucose consumption?
- a. Gastrin
 - b. Secretin
 - c. Gastric inhibitory polypeptide (GIP)
 - d. a and b
 - e. a, b, and c
28. Which of the following is an effect of insulin?
- a. Inhibition of hormone sensitive lipase
 - b. Increased glycogenolysis
 - c. Increased CNS glucose uptake
 - d. a and b
 - e. a and c
29. Insulin ultralente:
- a. has an onset of action in 1–2 hours.
 - b. has peak activity at 4–6 hours.
 - c. has a duration of action of 18–24 hours.
 - d. All of the above
 - e. None of the above
30. Which of the following is NOT a side effect of chlorpropamide?
- a. Hypoglycemia
 - b. Rash
 - c. Lactic acidosis
 - d. Syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH)
 - e. Disulfiram-type reaction
31. Which of the following is an effect of sulfonylureas?
- a. Decreased hepatic gluconeogenesis

- b. Increased peripheral tissue insulin sensitivity
 - c. Increased insulin-receptor binding
 - d. a and b
 - e. a, b, and c
32. Which of the following may cause SIADH?
- a. Acetohexamide
 - b. Chlorpropamide
 - c. Glipizide
 - d. Tolazamide
33. Which of the following statements about oral hypoglycemic agents is true?
- a. Second-generation agents have less affinity for albumin.
 - b. First-generation agents are more potent due to larger R substituents.
 - c. First- and second-generation hypoglycemic agents are sulfonylureas.
 - d. a and b
 - e. a and c
34. Which of the following is NOT a mechanism of oral sulfonylureas?
- a. Regeneration of pancreatic beta cells
 - b. Correction of post receptor defects
 - c. Increased tissue insulin sensitivity
 - d. Decreased hepatic gluconeogenesis
 - e. All of the above are mechanisms of sulfonylureas
35. Which of the following is the correct insulin: onset of action pair?
- a. Insulin Lispro: 1–3 hrs
 - b. Regular: 10–15 min
 - c. Insulin glargine: 0.5–1 hr
 - d. All of the above.
 - e. None of the above.
36. Effects of insulin include:
- a. increased glycogenolysis.
 - b. increased glycosuria.
 - c. increased conversion of protein to glucose.
 - d. increased transport of glucose into the central nervous system.
 - e. inhibition of hormone sensitive lipase.
37. Which of the following statements is correct?
- a. Lente insulin has an initial onset of 1–2 hours, a peak at 6–14 hours, and a duration of 24 or more hours.
 - b. Regular insulin has an initial onset of 30 minutes to 1 hour, a peak at 2–4 hours, and a duration of 5–7 hours.
 - c. NPH insulin has an initial onset at 10–15 minutes, a peak at 2–4 hours, and a duration of 3–5 hours.
 - d. a and b
 - e. a and c
38. Which of the following may occur with methimazole?
- a. Pruritus
 - b. Neutropenia
 - c. Decreases peroxidase activity
 - d. a and c
 - e. a, b, and c
39. What is the standard recommended dose range of glyburide?
- a. 0.5–2 mg/day
 - b. 1.25–20 mg/day
 - c. 50–100 mg/day
 - d. 200 mg/day
 - e. 200–1000 mg/day
40. Patients taking chlorpropamide should avoid products containing:
- a. acetaminophen.
 - b. ethanol.
 - c. vitamin A.
 - d. penicillins.
 - e. milk products.
41. Which of the following pregnant patients does NOT need to undergo a 50 g glucose screening test during weeks 24–28 of pregnancy?
- a. 30-year-old Latin woman with a negative screen at 15 weeks
 - b. 30-year-old Pacific Island woman who has a body mass index of 30 and no family history of diabetes
 - c. 20-year-old African American woman with a body mass index of 22 and no family history of diabetes
 - d. 20-year-old Caucasian woman with normal body weight
 - e. 20-year-old Latin woman with a body mass index of 30 and no family history of diabetes
42. A 22-year-old patient is admitted to the hospital with diabetic ketoacidosis (DKA). What is the most appropriate treatment to decrease cerebral edema in this patient?
- a. Sodium bicarbonate
 - b. Insulin
 - c. Methylprednisolone
 - d. Mannitol
 - e. None of the above
43. Normal blood glucose for a fasting patient is between:
- a. 20–40 mg/dl
 - b. 60–80 mg/dl
 - c. 80–120 mg/dl
 - d. 180–200 mg/dl
 - e. 220–240 mg/dl
- Read the following case study and answer the questions that follow.
- A 55-year-old man goes to the physician for his annual check-up. He has a medical history significant for obesity, hypertension, gout, and hypercholesterolemia. He reports that 1 week earlier, he attended a free health clinic at his place of work where his random blood glucose was found to be 220 mg/dL. On examination, he has decreased hair growth over the lower legs, decreased sensation over the feet and ankles, and flame hemorrhages on

ophthalmoscopic examination. Laboratory diagnosis on a fasting blood sample shows a blood glucose of 175 mg/dL. His physician diagnoses DM.

44. Which of the following is NOT a risk factor for DM type 2?
- Poor diet
 - Obesity
 - High fiber intake
 - Family history
 - Sedentary lifestyle
45. Which of the following is the most appropriate dosage and medication for the initial treatment of DM type 2?
- Pioglitazone, 500 mg once per day
 - Metformin, 500 mg twice per day
 - Insulin glargine, 15 units once per day
 - Glipizide, 5 mg once per day
 - Repaglinide, 5 mg before each meal
46. Metformin:
- may cause diarrhea.
 - is safe to use in diabetic ketoacidosis.
 - decreases gluconeogenesis.
 - a and b
 - a and c
47. Glipizide:
- enhances insulin release.
 - enhances peripheral insulin sensitivity.
 - inhibits hepatic glucose production.
 - a and b
 - a, b, and c
48. True or False: Pioglitazone does not require dose adjustments for renal impairment.
- True
 - False
49. Pioglitazone:
- may cause myalgia.
 - should be taken on an empty stomach.
 - is poorly protein bound in circulation.
 - is excreted predominately (>90%) in the urine.
 - All of the above
50. Hemoglobin A1c (HbA1c):
- Represents the average blood glucose for 3 months
 - Helps determine glycemic control
 - Should be more than 6%
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
51. Diabinese (chlorpropamide):
- Is a sulfonylurea
 - Has a prolonged duration of action
 - May cause disulfiram-like reactions
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
52. Avandia:
- Improves insulin secretion
 - Improves insulin sensitivity
 - Inhibits hepatic glucose production
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
53. Humalog:
- Has a rapid onset of action
 - Should be administered subcutaneously
 - Should be given within 15 minutes of a meal
 - Is insulin Lispro
 - All of the above
54. Which of the following is a rare but serious side effect of Glucophage?
- Pulmonary fibrosis
 - Neurotoxicity
 - Lactic acidosis
 - Pulmonary embolism
 - Infertility
55. Which of the following insulin preparations has a prolonged duration of action?
- Lantus
 - Humalog
 - Humulin R
 - NovoLog
 - All of the above

Gastrointestinal Disorders

13 CHAPTER

I. Gastrointestinal System Anatomy

- A. Mouth
- B. Esophagus
- C. Stomach
- D. Gallbladder
- E. Pancreas
- F. Small bowel
- G. Large bowel
- H. Rectum

II. Peptic Ulcer Disease

A peptic ulcer is a sore in the lining of the stomach, esophagus, or the first portion of the small intestine. Peptic ulcers may also be referred to as an ulcer.

A. Pathology

1. Peptic ulcers occur when the digestive juices that help food digest damage the walls of the stomach or duodenum. The most common cause is infection with a bacterium called *Helicobacter pylori*, or *H. pylori*. Another cause is the long-term use of nonsteroidal anti-inflammatory drugs (NSAID) such as aspirin and ibuprofen (e.g., Motrin, Advil) (Table 13-1). Spicy foods do not cause ulcers, but can aggravate them and make them worse.

B. Risk factors

1. *H. pylori*
 - a) Sex (men more than women)
 - b) Age (risk increases with age)
 - c) Smoking
 - d) Caffeine consumption
 - e) Stress
 - f) Excessive alcohol consumption
 - g) Other conditions
 - (1) Achalasia (failure of pyloric sphincter to relax)
2. NSAID-induced
 - a) Presence of *H. pylori*
 - b) Corticosteroid use
 - c) Age (older than 70 years old)
 - d) Anticoagulant use (the use of anticoagulants increases risk for NSAID-induced ulcer bleed)
 - e) Dose of NSAID
 - f) Use of multiple NSAIDs
 - g) Previous uncomplicated ulcer or ulcer-related complication

C. Signs and symptoms

1. Burning pain is the most common peptic ulcer symptom. The pain is caused by the ulcer and is aggravated by stomach acid contacting the ulcerated area. The pain may last from a few

minutes to many hours and may flare up at night. Peptic ulcers also tend to be worse when the stomach is empty.

D. Prevention

1. Smoking cessation
2. Decreasing alcohol consumption
3. Controlling acid reflux
4. Dietary modifications (more whole grains, vegetables, fresh fruit; less red meat and fatty foods)

E. Treatment

1. Because many ulcers are caused by *H. pylori* bacteria, an approach to peptic ulcer treatment that eradicates the bacteria and reduces the level of acid in the digestive system is used. The result of the treatment is pain relief and ulcer healing.
2. Histamine H₂ antagonists or H₂ blockers
 - a) Mechanism of action: reversible H₂ antagonism in gastric parietal cells
 - (1) Inhibits secretions caused by histamine, gastrin, and muscarinic agonists
 - (2) Reduces the amount of hydrochloric acid released into the digestive tract
 - (3) Examples
 - (a) Cimetidine (Tagamet)
 - (i) Usual adult dose (oral): prophylaxis, 400 mg qhs; active ulcers (short term), 300 mg qid or 800 mg qhs or 400 mg bid for 4 to 8 weeks
 - (ii) Adverse effects: antiandrogenic effects (gynecomastia, impotence), anticholinergic effects
 - (iii) Drug interactions: inhibits cytochrome P-450 (CYP) 1A2, 2C9, 3A4; interacts with many prescription and nonprescription drugs; classic drug interactions include narrow-therapeutic index drugs (e.g., theophylline, warfarin, phenytoin)
 - (b) Ranitidine (Zantac)
 - (i) Usual adult dose (oral): 150 mg bid or 300 mg qhs
 - (ii) Adverse effects: well tolerated
 - (iii) Drug interactions: drugs that require acid for absorption (e.g., ketoconazole)

Table 13-1 Characteristics of *H. pylori* versus NSAID-induced ulcers

<i>H. pylori</i>	Nonsteroidal anti-inflammatory drugs (NSAIDs)
Direct mucosal damage caused by hypergastrinemia	Direct mucosal damage associated with prostaglandin inhibition
Ulcers are superficial; chronically inflamed	Ulcers are deep; no inflammation
Symptoms: epigastric pain (may be nocturnal), nausea, indigestion, fatigue	Patients are usually asymptomatic; complications cause bleeding perforation

- (c) Famotidine (Pepcid)
 - (i) Usual adult dose (oral): 20 mg qhs
 - (ii) Adverse effects: well tolerated
 - (iii) Drug interactions: drugs that require acid for absorption (e.g., ketoconazole)
 - (d) Nizatidine (Axid)
 - (i) Usual adult dose (oral): 150 mg bid or 300 mg qhs
 - (ii) Adverse effects: well tolerated
 - (iii) Drug interactions: Drugs that require acid for absorption (e.g., ketoconazole)
- 3. Antibiotics
 - a) A combination of antibiotics is usually used to treat *H. pylori* infections because one antibiotic alone is not usually sufficient to eradicate the organism. (See Box 13-1)
 - b) Commonly prescribed antibiotics for treatment of *H. pylori* include amoxicillin (Amoxil), clarithromycin (Biaxin), and metronidazole (Flagyl).
- 4. Antacids
 - a) Mechanism of action
 - (1) Neutralize gastric acid
 - (2) Inhibit proteolytic activity of pepsin
 - (3) Raise pH
 - (4) Do not absorb acid or coat the mucosal lining
 - b) Adverse effects
 - (1) Diarrhea (magnesium)
 - (2) Constipation (aluminum)
 - (3) Edema (sodium)
 - (4) Milk alkali syndrome
 - c) Drug interactions
 - (1) Quinolones, tetracyclines, iron salts, itraconazole, ketoconazole
 - d) Examples
 - (1) Calcium carbonate (Tums, Titralac)
 - (2) Aluminum hydroxide and magnesium hydroxide combinations (Mylanta, Maalox)
 - (3) Aluminum hydroxide alone (Alternagel)
- e) Antacids should be taken 1 hour before or 2 hours after taking other prescribed medications.
- 5. Proton pump inhibitors (PPI)
 - a) Superior to H_2 blockers in the healing, recurrence, and prevention of ulcers. Used preferentially with antibiotics in *H. pylori* eradication and ulcer treatment regimens.
 - b) Mechanism of action
 - (1) Inhibits H^+/K^+ -ATPase enzyme system at the gastric parietal cell thereby blocking the last step of acid production
 - c) Adverse effects and precautions
 - (1) All PPI are generally well tolerated. Occasionally, they may cause nausea, diarrhea, headache or serious allergic-type reactions.
 - (2) All PPI should be taken 30 minutes before eating (i.e., on an empty stomach).
 - d) Drug interactions
 - (1) Omeprazole, lansoprazole, esomeprazole: substrates and inhibitors of CYP450 3A4 phenytoin, warfarin
 - (2) Rabeprazole, esomeprazole: substrates and inhibitors of CYP450 2C19
 - (3) All PPI may decrease the absorption of azole antifungals, protease inhibitors, iron salts.
 - e) Usual adult dose (oral)
 - (1) Omeprazole (Prilosec): 20 mg qd
 - (2) Lansoprazole (Prevacid): 15 mg qd
 - (3) Rabeprazole (Aciphex): 20 mg qd
 - (4) Esomeprazole (Nexium): 40 mg qd
 - (5) Pantoprazole (Protonix): 20 mg qd
- 6. Cytoprotective agents
 - a) Sucralfate (Carafate)
 - (1) Mechanism of action
 - (a) As an aluminum salt of sulfated sucrose, the aluminum ion splits away in the acid of gastric juice, which leaves a polar ion that is not absorbed. A viscous, adhesive substance is formed and acts locally to protect the site against acid, pepsin, and bile salts.
 - (2) Adverse effects: well tolerated; constipation
 - (a) Caution in patients with renal failure
 - (3) Drug interactions
 - (a) Sucralfate may decrease the absorption of azole antifungal agents, quinolones, phenytoin, and phosphate supplements
 - (b) Doses to be separated by 2 hours from sucralfate to avoid binding interactions
 - (4) Usual adult dose (oral)
 - (a) 1 g bid (maintenance/prophylaxis)
 - (b) 1 g qid or 2 g bid (treatment)
 - b) Misoprostol (Cytotec)
 - (1) Mechanism of action
 - (a) Synthetic prostaglandin E analog

Box 13-1 Treatment Regimens for *H. Pylori*

- Combination therapy of a proton pump inhibitor (PPI) plus two antibiotics is generally recommended for treating *H. pylori*.
- Strategies will vary from one practitioner to another, but generally are as follows:

First-Line Treatment

- Used for 7–14 days

Regimen 1	PPI bid	Clarithromycin 500 mg bid	Amoxicillin 1 g bid
Regimen 2	PPI bid	Clarithromycin 500 mg bid	Metronidazole 500 mg bid

First-Line Treatment in Patients with Macrolide Allergy or as Retreatment

- Used for 14 days
- Can also be used for retreatment

Regimen 1	PPI bid	Amoxicillin 1 g bid	Metronidazole 1 g bid

Second-Line Treatment (or can use biopsy to culture for sensitivities)

- Used for 7–14 days
- Can be used as an alternative to first-line therapy but typically is reserved for retreatment (14 days)

Regimen 1	PPI bid	Bismuth subsalicylate 525 mg qid	Tetracycline 500 mg qid	Metronidazole 500 mg qid

- (b) Antisecretory and mucosal-protecting properties
- (2) Adverse effects
 - (a) Diarrhea (self-limiting; resolves after 8 days)
 - (b) Abdominal pain
 - (c) **Contraindicated** in pregnancy or women of child-bearing age because the drug causes strong uterine contractions and may induce miscarriage.
- (3) Drug interactions: not clinically significant
- (4) Usual adult dose: 100–200 mcg PO qid with food

III. Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD), also called acid reflux disease, occurs when liquid from the stomach regurgitates into the esophagus. This liquid may contain stomach acids and bile. In some cases, the regurgitated stomach liquid can cause inflammation (esophagitis), irritation, and damage to the esophagus.

A. Pathology

1. Develops when normal protective mechanisms of the esophagus begin to fail
2. Gastric acid enters into the distal esophagus, causing a burning sensation behind the breastbone, and sometimes leads to regurgitation of ingested food.

B. Risk factors

1. Tea, coffee, chocolate consumption
2. Tobacco
3. Obesity
4. Over-eating
5. Spicy foods
6. Hiatal hernias (the stomach pushes up through a hole in the diaphragm muscle)

7. Abnormally weak contractions of the lower esophageal sphincter
 8. Abnormal emptying of the stomach after a meal
- C. Signs and symptoms
1. Heartburn: a burning sensation in the chest that may spread to the throat
 2. Regurgitation
 3. Water brash (hypersalivation)
 4. Belching
 5. Several factors may worsen symptoms of the condition including spicy foods, fatty foods, chocolate, caffeine, tomato sauce, carbonated beverages, mint, alcoholic beverages, large meals, lying down after eating, some medications (e.g., sedatives, tranquilizers, or blood pressure drugs), and cigarette smoking.

D. Complications

1. If GERD persists for a long time it causes esophagitis, ulceration, bleeding, scar, stricture formation, and Barrett's esophagus

E. Treatment

1. Lifestyle modifications
 - a) Eating slowly
 - b) Eating three small meals
 - c) Weight loss
 - d) Smoking cessation
 - e) Sleeping in an upright position
 - f) Avoiding lying down after eating
2. Mild symptoms
 - a) Over-the-counter (OTC) antacids
 - b) OTC H₂ blockers
 - c) OTC PPI
3. Mild refractory
 - a) Prescription H₂ blockers
4. Moderate to severe
 - a) Prescription PPI
 - b) Metoclopramide

- (1) Mechanism of action
 - (a) Enhances motility of GI contents through the upper GI tract (prokinetic agent)
- (2) Adverse effects
 - (a) Neurologic alterations (e.g., confusion)
 - (b) Dystonic reactions
- (3) Drug interactions
 - (a) Concurrent use with antipsychotic agents may increase risk of extrapyramidal symptoms (EPS)
- (4) Usual adult dose
 - (a) 10–15 mg/dose PO, maximum of four times per day, each dose given 30 minutes before meals or food and at bedtime

IV. Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) refers to two chronic diseases that cause inflammation of the intestines: ulcerative colitis and Crohn's disease.

A. Etiology

1. The cause of IBD remains unknown. However, current research indicates that IBD most likely involves a complex interaction of factors, including heredity, the immune system, and antigens in the environment.

B. Pathophysiology (Table 13-2)

C. Complications

1. Toxic megacolon
2. Colon cancer

D. Signs and symptoms

1. The symptoms of these two illnesses are similar, which often makes it difficult to distinguish between the two. In fact, about 10% of colitis (inflamed colon) cases cannot be diagnosed as either ulcerative colitis or Crohn's disease. When physicians cannot diagnose the specific IBD, the condition is called indeterminate colitis.
2. IBD causes chronic inflammation in the gastrointestinal tract and may lead to complications, such as colon cancer. The most common symptoms of both ulcerative colitis

and Crohn's disease are diarrhea (ranging from mild to severe), abdominal pain, decreased appetite, and weight loss. If the diarrhea is extreme, it may lead to dehydration, increased heartbeat, and decreased blood pressure. As food moves through inflamed areas of the gastrointestinal tract, it may cause bleeding.

E. Treatment

1. Nonpharmacologic treatment: nutritional support
2. Surgery: for complications (abscess, fistula, perforation)
3. Pharmacologic therapy

a) Corticosteroids

- (1) Reduce inflammation of the gastrointestinal tract
- (2) Oral and rectal therapy used for acute management only; IV therapy reserved for severe disease
- (3) Adverse effects
 - (a) Hypertension
 - (b) Sodium and water retention
 - (c) Glucose intolerance
- (4) Examples and typical adult doses
 - (a) Rectal
 - (i) Cortifoam 90 mg qd or bid
 - (ii) Cortenema 100 mg in 60 mL applied qhs
 - (b) Oral
 - (i) Prednisone 20–60 mg qd
 - (ii) Budesonide (Entocort EC) 9 mg qAM for maximum 8 weeks for active episodes (used for Crohn's disease involving the ileum or ascending colon); a dose of 6 mg PO qAM may be used for maintenance therapy for up to 3 months.

b) Immunosuppressants

- (1) Used for severe colitis, steroid dependent
- (2) Adverse effects
 - (a) Bone marrow suppression
 - (b) Hepatitis
 - (c) Pancreatitis
- (3) Examples and typical adult dose
 - (a) Azathioprine (Imuran) 75–150 mg PO qd
 - (b) 6-mercaptopurine (Purinethol) 50–100 mg PO qd
 - (c) Cyclosporine (Neoral or Sandimmune)
 - (i) Dose: 4 mg/kg PO per day
 - (ii) Monitor levels
 - (iii) Adverse effects: hypertension, nephrotoxicity, electrolyte abnormalities
 - (iv) Drug interactions: major CYP 450 3A4 substrate and inhibitor

c) 5-aminosalicylates

- (1) Used for acute management and maintaining remission
- (2) Oral and rectal therapies available
- (3) Adverse effects
 - (a) Nausea/vomiting

Table 13-2 Characteristics of Inflammatory Bowel Disease

	Ulcerative colitis	Crohn disease
Anatomic sites	Colon and rectum	Any part of the GI tract
Lesions	Continuous and superficial	Discontinuous
Depth of involvement	Mucosa and submucosa inflammation	Transmural inflammation
Pathologic findings	Polyps	Obstruction due to inflammation Perforation Perianal fistulas

- (b) Diarrhea
- (c) Malaise
- (d) Fever
- (e) Headache
- (f) Rash
- (g) Impairs absorption of folic acid
- (h) Contraindicated in patients with sulfa allergy (sulfasalazine only)
- (4) Examples and typical adult dose
 - (a) Mesalamine suppository: 500 mg rectally qd or bid
 - (b) Mesalamine enema: 4 g in 60 mL rectally qhs
 - (c) Sulfasalazine (Azulfidine): 4–6 g PO qd (acute); 2–4 g qd (chronic)
 - (d) Olsalazine (Dipentum): 1.5–3 g PO qd (acute); 2 g qd (chronic)
 - (e) Mesalamine (Asacol): 2.4–4.8 g PO qd (acute); 1.6–2.4 g qd (chronic)
 - (f) Mesalamine (Pentasa): 2–4 g PO qd (acute); 1–2 g (chronic)
- d) Antibiotics and typical adult dose
 - (1) Metronidazole 10–20 mg/kg per day PO; ciprofloxacin 1 g PO qd
 - (2) Used for perianal fistula
- e) Tumor necrosis factor (TNF) blocking agents, examples
 - (1) Infliximab (Remicade)
 - (2) Used for moderate to severe disease and for perianal fistula
 - (3) Typical adult dose
 - (a) 5 mg/kg IV at 0, 2, 6 weeks then every 8 weeks as maintenance
 - (4) Adverse effects
 - (a) Infusion-related reactions (premedicate with antihistamines and/or corticosteroids)
 - (b) Abdominal pain
 - (c) Infection
 - (d) Development of antinuclear antibodies
 - (e) Development of new abscess
 - (f) Contraindicated in heart failure (New York Heart Association class III/IV)
 - (5) Drug interactions
 - (a) May enhance the toxic effects of live vaccines
 - (b) May reduce the effect of inactivated vaccines

V. Irritable Bowel Syndrome

Irritable bowel syndrome (IBS), also called spastic colon, mucous colitis, spastic colitis, nervous stomach, or irritable colon, is a long-term condition that is characterized by abdominal pain, cramping, diarrhea, and constipation. IBS is a functional bowel disorder because the bowel appears normal but does not function properly.

A. Pathophysiology

1. Motility disorders of the GI tract
2. Intestinal secretion
3. Visceral hypersensitivity

B. Etiology

1. Although the exact cause of IBS is unknown, it may be due, at least in part, to poor diet, neurotransmitter imbalances, and infections.

C. Clinical presentation

1. Constipation predominant
2. Diarrhea predominant
3. Alternating constipation and diarrhea

D. Signs and symptoms

1. In patients with IBS, the muscles of the colon, sphincters, and pelvis do not contract properly. As a result, patients experience constipation or diarrhea. This causes symptoms of abdominal pain, cramping, bloating, and a sense of incomplete stool movement. Symptoms may improve after the patient has a bowel movement.

E. Treatment

1. Nonpharmacologic
 - a) Dietary modification
 - b) Stress management
2. Pharmacologic
 - a) Constipation predominant IBS
 - (1) Bulking agents
 - (a) Psyllium (e.g., Metamucil, Konsyl)
 - (2) Tegaserod (Zelnorm)
 - (a) Selective serotonin 5-HT₄ agonist
 - (b) Withdrawn from the market due to increased risk of heart attack and stroke
 - (3) Lubiprostone (Amitiza)
 - (a) Prostaglandin E₁ derivative, chloride channel activator
 - (b) Usual adult dose: 8 mcg PO twice daily with food
 - (4) Osmotic, stimulant, and emollient laxatives may be used, but not routinely
 - b) Diarrhea-predominant IBS
 - (1) Antidiarrheals and typical adult dose
 - (a) Loperamide (Imodium)
 - (i) Dose: 4 mg followed by 2-mg PO after each loose stool. Maximum of 16 mg daily
 - (b) Diphenoxylate/atropine (Lomotil)
 - (i) Dose: 5 mg PO four times daily as needed
 - (2) Alosetron (Lotronex)
 - (a) Selective serotonin 5-HT₃ antagonist
 - (b) Used for women who fail conventional therapy
 - (c) Withdrawn from the market in 2000 due to reported serious GI adverse effects (obstruction, perforation, impaction, toxic megacolon), but in 2002 became available again under a risk-management program
 - (d) Typical adult dose: 0.5 mg–1 mg PO twice daily
 - c) Antispasmodics
 - (1) Used in patients with abdominal pain
 - (2) Examples: hyoscyamine (Levsin or Levsinex), dicyclomine (Bentyl), and methscopolamine (Pamine)
 - d) Antidepressants-Selective Serotonin Reuptake Inhibitors (SSRIs)
 - (1) Used to improve abdominal pain
 - (2) Examples: citalopram (Celexa)

VI. Nausea and Vomiting

A. Pathophysiology

1. Three stages
 - a) Nausea is the subjective feeling of needing to vomit.
 - b) Retching is a strong, belching-like, rhythmic movement that may or may not be followed by vomiting.
 - c) Vomiting (emesis) is the forcible expulsion of stomach contents through the mouth.
2. The brain and the GI tract are involved in the processes of nausea and vomiting, which include chemoreceptor trigger zone (CTZ) in the brain, the vestibular system, visceral afferents from the GI tract, and the cerebral cortex. The stimulation of the CTZ sends impulse to the vomiting center. The CTZ contains dopamine, histamine, acetylcholine, serotonin receptors, and neurokinin-1.

B. Potential causes and risk factors

1. Chemotherapy
2. Diabetes (e.g., poorly controlled blood sugar)
3. Pregnancy
4. After surgery
5. Peptic ulcer
6. Stress
7. Gallstones
8. Gastroenteritis
9. GERD
10. Headache
11. Kidney failure
12. Liver disease
13. Motion sickness and vestibular disorders
14. Pancreatitis
15. Radiation
16. Toxins (alcohol)
17. Other
 - a) Female sex
 - b) Use of opioids during postoperative period
 - c) Negative smoking history
 - d) Obesity

C. Signs and symptoms

1. Nausea is a subjective sensation that is difficult to define. It is an unpleasant feeling in the abdomen often associated with the sense of being ill and the urge to vomit. Other related symptoms include increased salivation, loss of color, sweating, tachycardia (increased heart rate), and the urge to defecate.

D. Treatment

1. Home treatment
 - a) Drinking clear liquids only
 - b) Eating no solid food until the vomiting episode has passed
 - c) Getting plenty of rest because more movement and exertion may worsen the symptoms
2. Medications
 - a) 5-HT₃ antagonists
 - (1) Mechanism of action
 - (a) Blocks serotonin receptors peripherally and centrally; when the receptors are blocked, emesis is suppressed

- (2) Adverse effects
 - (a) Headache and diarrhea
- (3) Examples
 - (a) Dolasetron (Anzemet)
 - (i) Adults: 100 mg within 1 hour of chemotherapy on days chemotherapy is given
 - (ii) Children: 1.8 mg/kg (not to exceed maximum dose of 100 mg) within 1 hour of chemotherapy on days chemotherapy is given
 - (b) Granisetron (Kytril): Adults: 2 mg PO daily in single or divided doses (q12h) within 1 hour of chemotherapy on days chemotherapy is given
 - (c) Ondansetron (Zofran)
 - (i) Adults, children 12 years and older: 8 mg or 10 mL PO bid (q12h) on days chemotherapy is given and continued for 1–2 days after chemotherapy ends
 - (ii) Children 4–11 years: 4 mg or 5 mL PO tid (q8h) on days chemotherapy is given and continued for 1–2 days after chemotherapy ends
 - (d) Palonosetron (Aloxi): Adults, 0.25 mg PO, 30 minutes before the start of chemotherapy administration, day 1 of each cycle

b) Anticholinergics

- (1) Mechanism of action
 - (a) Block acetylcholine at parasympathetic sites in smooth muscle, secretory glands, CNS
- (2) Adverse effects
 - (a) Drowsiness
 - (b) Dry mouth
- (3) Example
 - (a) Scopolamine: 0.3–0.65 mg IM, IV, or SQ before surgery; 1 patch applied q72h for motion sickness

c) Antihistamines

- (1) Mechanism of action
 - (a) Block acetylcholine in vestibular apparatus and H₁ receptors in vomiting center
- (2) Drugs of choice for motion sickness
- (3) Examples and typical adult doses
 - (a) Diphenhydramine (Benadryl): 10–50 mg q4–6h given PO, IM, or IV
 - (b) Meclizine (Antivert): 12.5–100 mg qd in divided doses PO
 - (c) Promethazine (Phenergan): 12.5–25 mg q4–6h given PO, IV, or IM as needed

d) Benzamides

- (1) Metoclopramide (Reglan)
 - (a) Mechanism of action
 - (i) Activate 5-HT₄ receptors and block D₂ receptors
 - (ii) Central and peripheral effects
 - (b) Common adult doses

- (i) 1–2 mg/kg IV or PO for two doses for acute chemotherapy-induced N/V, given 2h apart
 - (ii) 0.5–1 mg/kg IV or PO q4–6h for 3–5 days for delayed chemotherapy-induced N/V
 - (iii) 10 mg IV before the end of surgery to prevent postoperative N/V
- e) Butyrophenones
 - (1) Mechanism of action
 - (a) Blocks D₂ receptors at CTZ
 - (2) Example and typical adult dose
 - (a) Haloperidol (Haldol): 1–4 mg PO, IV, or IM q6h as needed
- f) Cannabinoids
 - (1) Mechanism of action
 - (a) The exact mechanism of action is not well understood. It may be due to its effects on cannabinoid receptors in the central CNS
 - (2) Example and typical adult dose
 - (a) Dronabinol (Marinol): 5–20 mg PO q3–6h, or 5 mg/m² q2–4h upto 4–6 doses per day
- g) Corticosteroids
 - (1) Mechanism of action
 - (a) May work by reducing inflammation and/or enhancing efficacy of dopamine and 5-HT₃ antagonists for chemotherapy-induced N/V
 - (2) Example and typical adult dose
 - (a) Dexamethasone
 - (i) 20 mg IV or PO, 30 minutes before chemotherapy
 - (ii) 8 mg IV or PO bid for 2 days, 4 mg bid for 2 days for delayed chemotherapy-induced N/V
 - (b) Methylprednisolone
 - (i) 40–125 mg IV, 30 minutes before chemotherapy
- h) Phenothiazines
 - (1) Mechanism of action
 - (a) Inhibits D₂ receptors at CTZ
 - (2) Examples and typical adult dose
 - (a) Prochlorperazine (Compazine): 10–20 mg PO, IV, or IM q4–6h
 - (b) Perphenazine (Trilafon): 2–8 mg PO, IV, or IM q6h
- i) Neurokinin-1 receptor antagonist
 - (1) Aprepitant (Emend)
 - (a) Mechanism of action
 - (i) Inhibits the substance P/neurokinin 1 (NK₁) receptor
 - (b) Adverse effects
 - (i) Fatigue
 - (ii) Weakness
 - (iii) Dizziness
 - (c) Drug interactions
 - (i) Substrate and inhibitor of CYP450 3A4
 - (ii) Increases bioavailability of corticosteroids

- (a) Dexamethasone doses should be decreased by 50% (oral)
- (b) Methylprednisolone doses should be decreased by 25% (IV) or by 50% (oral)
- (d) Aprepitant adult dose: 125 mg PO on day 1, 80 mg PO on days 2 and 3
 - (i) Given with dexamethasone 12 mg PO or IV on day 1, 8 mg PO or IV on days 2–4
 - (ii) Given with ondansetron 16–24 mg PO or 8 mg IV on day 1, plus 8 mg PO or IV on days 2–4

PATIENT PROFILE

Patient Initials: NB

Sex: Female

Age: 36 years

Height: 5' 6"

Weight: 55 kg

Race: White

Allergies: No known drug allergies (NKDA)

Chief Complaint: NB goes to the pharmacy to ask questions regarding selection of products to treat heartburn. She states troublesome symptoms of heartburn roughly 2 or 3 days a week) within several hours of ingesting a meal. The symptoms began 2 weeks ago. She sometimes experiences the symptoms at night after retiring. She cannot pinpoint any specific dietary items that cause the heartburn to appear. She needs assistance in selecting an over-the-counter (OTC) product. She has been ingesting Tums for symptoms, and these help "a bit," but the effect does not last long and her heartburn returns.

Social History:

Tobacco use: None

Alcohol use: Minimal, socially only

Exercise: Walking several days per week, some weight training

Medications:

Levothyroxine 75 mcg PO once daily (hypothyroidism diagnosed 2 years ago, stable)

Laboratory: Not available

PATIENT PROFILE QUESTIONS

1. Certain patients with symptoms consistent with heartburn or gastroesophageal reflux (GERD) are not initial candidates for self-treatment. Which of the following are considered reasons for physician referral?
 - I. Difficulty swallowing (dysphagia)
 - II. Persistent symptoms (e.g., >3 months)
 - III. Symptoms occur >2 times per week
 - IV. Symptoms occur at night
 - a. I only
 - b. II only
 - c. I and II
 - d. I, II, and III
 - e. All of the above

Answer: c. If a patient has experienced symptoms intermittently 1–2 or more times per week for just a short period, self-treatment can be pursued for a limited time. The patient should not have had chronic or persistent symptoms for months. To be amenable to self-treatment, a patient should not have any alarm symptoms (e.g., pain or difficulty on swallowing, choking, nausea with vomiting, bleeding, weight loss, chest pain), or symptoms that might indicate other problems (e.g., chest pain, jaw pain, dental erosion, hoarseness of the voice, coughing, or wheezing). The presence of any unusual or alarm symptoms should prompt physician referral.

2. Which of the following would represent the BEST choice for an initial nonprescription (OTC) regimen for NB?

- I. AcipHex 20 mg PO once daily
- II. Prilosec OTC 20 mg PO once daily
- III. Kapidex 30 mg PO once daily
- IV. Pepcid AC 20 mg before meals known to cause heartburn

- a. I only
- b. II only
- c. III only
- d. II or IV
- e. III or IV

Answer: b. NB can choose an OTC regimen. Either II or IV are potential regimens; the other two (AcipHex, Kapidex) are prescription-only. Pepcid AC is not the best choice for this patient because she cannot identify triggering meals, and symptoms sometimes occur at night hours. However, for many patients, a H_2 antagonist like famotidine is a reasonable choice for heartburn prevention if heartburn symptoms can be tied to a trigger meal (e.g., pasta with tomato sauce) or for treatment of heartburn if symptoms only occur intermittently. A proton-pump inhibitor (PPI) is used OTC when symptoms occur several times (>2 times) per week and would help control symptoms in this patient; this is probably the best choice at this time given her history.

3. NB should also inform her physician of her use of a proton-pump inhibitor (PPI) at her next doctor visit, which is scheduled in 3 weeks. Why might she need to tell her doctor about her heartburn and treatment?
- I. Both her choice of antacid (Tums) and a PPI could interfere with her levothyroxine prescription and the maintenance of euthyroid status.
 - II. If her symptoms are not controlled in 2 weeks, she will need to tell the physician and see if longer term treatment or further evaluation is needed.
 - III. The PPI could interfere with other prescribed medications, resulting in drug interactions.
- a. I only
 - b. II only
 - c. II and III
 - d. I, II, and III

Answer: d. All of the above would be reasons for NB to inform her doctor of her use of a PPI. The PPI may cause

a change in levothyroxine absorption, and the patient may need to have thyroid function tests monitored more frequently and be aware of symptoms that could indicate hypothyroidism if PPI treatment is continued. If symptoms do not resolve in 2 weeks, the patient should see a doctor for further evaluation, and the need for other tests and or treatments. Because PPIs block stomach acid and also may affect cytochrome P450 (CYP450) isoenzymes, they do have the ability to interfere with other prescription medications. A PPI should not be given with atazanavir, for example, because the PPI substantially decreases the bioavailability of atazanavir; atazanavir requires an acidic environment for oral absorption.

REVIEW QUESTIONS

(Answers and Rationales on page 359.)

1. Lansoprazole is used to treat which of the following?
 - a. Hypertension
 - b. Congestive heart failure
 - c. Gastric reflux (GERD)
 - d. Peptic ulcer disease
 - e. c and d
2. Fiber-Con is:
 - a. used in the treatment of constipation.
 - b. used in the treatment of diarrhea.
 - c. to be avoided when taking tetracycline.
 - d. All of the above
 - e. None of the above
3. What class of drug is famotidine?
 - a. H_1 receptor blocker
 - b. H_2 receptor blocker
 - c. H_3 receptor blocker
 - d. Gastrin inhibitor
 - e. COX-1 inhibitor
4. Which of the following is true of cimetidine?
 - a. It may cause confusion and dizziness.
 - b. It may cause hepatic dysfunction.
 - c. It is useful for the treatment of duodenal ulcers.
 - d. a and b
 - e. a, b, and c
5. Histamine can cause all of the following except:
 - a. Elevated blood pressure
 - b. Capillary dilation
 - c. Gastric hypersecretion
 - d. Vascular permeability
 - e. Decreased airway mucus production
6. Which one of the following statements about Dulcolax is true?
 - a. Normal oral dosing is 50–100 mg.
 - b. It produces colonic mucosal irritation and fluid secretion.
 - c. Oral onset of action is 2–4 hours.
 - d. It is 90% absorbed and secreted in the bile.
 - e. It should be ingested with a glass of milk for maximum effect.

7. Which of the following may cause breakdown of the protective gastric mucosal barrier?
 - a. Aspirin
 - b. Ethanol
 - c. Caffeine
 - d. a and b
 - e. a, b, and c
8. Which of the following statements is/are correct?
 - a. Atropine, when administered in full doses, causes prolonged inhibition of stomach, duodenum, jejunum, ileum, and colon function.
 - b. Atropine reduces pancreatic secretions.
 - c. Belladonna alkaloids significantly alter gastric secretions.
 - d. All of the above
 - e. None of the above
9. True or False: Increases in blood urea nitrogen (BUN) and serum creatinine (SCr) generally indicate liver damage.
 - a. True
 - b. False
10. Which of the following medications is indicated for treatment of chronic idiopathic constipation in adults?
 - a. Loperamide
 - b. Octreotide
 - c. Lubiprostone
 - d. Opium tincture
 - e. None of the above
11. Select the correct statement(s) about sulfasalazine is true?
 - I. It is a prodrug.
 - II. The active moiety is mesalamine.
 - III. It has its effect in the colon.
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
12. Which of the following best describes the mechanism of action of Anzemet?
 - a. 5-HT₃ antagonist
 - b. Histamine antagonist
 - c. Beta-2 antagonist
 - d. Alpha-2 antagonist
 - e. None of the above
13. Which one of the following antiemetic medications also decreases gastric emptying time?
 - a. Codeine
 - b. Metoclopramide
 - c. Dronabinol
 - d. Meclizine
 - e. Aprepitant
14. Which one of the following drugs is most similar in action to cimetidine?
 - a. Gaviscon
 - b. Imodium
 - c. Donnatal
 - d. Nexium
 - e. Axid
15. Ranitidine may best be described as a(n):
 - a. antacid.
 - b. histamine receptor antagonist.
 - c. proton pump inhibitor.
 - d. cytoprotective agent.
 - e. anticholinergic agent.
16. Select the over-the-counter (OTC) anti-nausea medicine that is more effective than cyclizine?
 - a. Scopolamine
 - b. Promethazine
 - c. Diphenhydramine
 - d. All of the above
 - e. None of the above
17. Which of the following is an effect of antacids?
 - a. Inactivation of pepsin at alkaline pH
 - b. Decreased lower esophageal pressure
 - c. Increased gastric pH
 - d. Increased gastric motor activity
 - e. a and c
18. What is the effect of calcium or magnesium antacids on tetracycline?
 - a. Increased toxicity
 - b. Enhanced activity
 - c. Decreased action
 - d. Suppression of adverse effects
 - e. No significant change
19. Which of the following conditions requires consideration of the sodium, magnesium, or phosphate content of a laxative before administration?
 - a. Ascites
 - b. Congestive heart failure
 - c. Renal insufficiency
 - d. a and c
 - e. a, b, and c
20. Which of the following acts via inhibition of the H⁺/K⁺ ATPase pump?
 - a. Omeprazole
 - b. Serotonin
 - c. Isoniazid
 - d. Misoprostol
 - e. Pirenzepine
21. Which of the following is a stimulant cathartic?
 - a. Mineral oil
 - b. Castor oil
 - c. Sodium citrate
 - d. Sodium bicarbonate
 - e. Methylcellulose

22. Which of the following is minimally absorbed systemically?
- Calcium carbonate
 - Aluminum hydroxide
 - Sodium bicarbonate
 - a and b
 - a, b, and c
23. Which of the following is a correct mechanism of action of lactulose?
- Induces osmotic diarrhea
 - Reduces fecal pH
 - Increases bacterial assimilation of ammonia
 - a and b
 - All of the above
24. Clearance of which of the following is NOT affected by cimetidine?
- Theophylline
 - Warfarin
 - Digoxin
 - Quinidine
 - Phenytoin
25. Which of the following is an adverse effect of prostaglandin E_2 ?
- Gynecomastia
 - Thrombocytopenia
 - Diarrhea
 - Headache
 - Seizure
26. Which of the following will be poorly absorbed in the presence of aluminum hydroxide?
- Penicillin G
 - Tetracycline
 - Cephalexin
 - Erythromycin
 - Chloramphenicol
27. Which of the following is no longer the most appropriate agent to use in the treatment of peptic ulcer disease?
- Muscarinic antagonists
 - Prostaglandins
 - Antacids
 - Proton pump inhibitors
 - All of the above are appropriate
28. Which of the following is the principal component of emollient laxatives?
- Magnesium hydroxide
 - Docusate
 - Bran
 - Methylcellulose
 - Phenolphthalein
29. Which of the following is a histamine-2 receptor blocker?
- Sucralfate
 - Misoprostol
 - Ranitidine
 - Metoclopramide
 - Omeprazole
30. Which of the following is NOT an appropriate medication to treat esophagitis?
- Amitriptyline
 - Metoclopramide
 - Omeprazole
 - Dexlansoprazole
 - Cimetidine
31. Which of the following is NOT an adverse effect associated with laxative use?
- Spastic colitis
 - Dehydration
 - Intestinal obstruction
 - Hypokalemia
 - All of the above are potential side effects
32. Which of the following statements about saline cathartics is true?
- They decrease surface tension of fecal matter.
 - They increase intestinal volume.
 - They are readily absorbed in the stomach.
 - They act more slowly than bulk-forming laxatives.
 - They are safe to use in patients with renal failure.
33. Which of the following is an indication for laxative use?
- Drug overdose
 - Prevent straining in patients with cardiovascular disease
 - Diverticulosis
 - All of the above
 - None of the above
34. Which of the following is a possible mechanism of laxatives?
- Increases peristaltic activity
 - Increases stool bulk
 - Lubrication of stool
 - All of the above
 - None of the above
35. Select the statement regarding metoclopramide.
- It causes extrapyramidal.
 - It blocks peripheral muscarinic synapses.
 - It decreases lower esophageal sphincter pressure.
 - a and b
 - a, b, and c
36. Which of the following statements about sucralfate is true?
- It increases gastric motility.
 - It enhances Na^+/K^+ -ATPase activity.
 - It antagonize gastrin.
 - It causes constipation.
 - It antagonizes acetylcholine.
37. Which of the following acts as a saline cathartic?
- Sodium phosphate
 - Sodium bicarbonate
 - Methylcellulose
 - a and b
 - a, b, and c

The following is a case study. Read the case study and answer the questions after.

A 30-year-old woman presents to her physician with complaints of chest pain for 3 months. She describes the pain as substernal and epigastric, burning, and worse after eating. She also complains of occasional regurgitation of stomach contents. She reports some relief with over-the-counter antacids.

38. What is the mechanism of gastroesophageal reflux?
 - a. Lower esophageal sphincter relaxation
 - b. Depressed esophageal mucus production
 - c. Increased acidity of gastric fluid
 - d. All of the above
 - e. None of the above
39. Which of the following is a potential complication of gastroesophageal reflux?
 - a. Asthma
 - b. Laryngitis
 - c. Subglottic stenosis
 - d. Peptic stricture
 - e. All of the above
40. Which of the following is an appropriate initial treatment for this patient?
 - a. Bethanechol
 - b. Cimetidine
 - c. Dextromethorphan
 - d. a or b
 - e. b or c
41. Which of the following is a potential side effect of cimetidine?
 - a. Constipation
 - b. Headache
 - c. Urinary frequency
 - d. Hypotension
 - e. Hypothermia
42. This patient should be counseled to:
 - a. Elevate the head of her bed.
 - b. Wait at least 30 minutes after eating before lying down.
 - c. Avoid aggravating foods.
 - d. Avoid smoking.
 - e. All of the above
43. What is the correct dosage of cimetidine for GERD?
 - a. 300 mg PO bid
 - b. 400 mg PO qid
 - c. 400 mg PO qd
 - d. 400 mg PO tid
 - e. 1000 mg PO qd
44. Cimetidine may interact with all of the following EXCEPT:
 - a. warfarin
 - b. lidocaine
 - c. cyclosporine
 - d. dofetilide
 - e. All of the above
45. Peptic ulcers are caused by:
 - a. Infection
 - b. Long-term NSAID use
 - c. Spicy foods
 - d. a and b
 - e. b and c
46. The most common GERD symptoms are:
 - a. Laryngitis and hoarseness
 - b. Heartburn and regurgitation
 - c. Cough and wheezing
 - d. Stomach pains and diarrhea
 - e. Constipation and anal fissures

- I. Definitions
 - A. Geriatrics is the branch of medicine concerned with the health care of the elderly. It aims to promote health and to prevent and treat disease and disabilities in older adults.
 - B. A geriatrician is a medical doctor who is specially trained to prevent and manage the unique and, oftentimes, multiple health concerns of older adults. Geriatricians are able to treat older patients, manage multiple disease symptoms, and develop care plans that address the special health care needs of older adults.
- II. Conditions Commonly Seen in Geriatric Patients
 - A. Parkinson disease
 1. Pathophysiology and epidemiology
 - a. Progressive, neurologic disorder due to degeneration of presynaptic dopaminergic neurons in the substantia nigra equals the loss of postsynaptic dopamine activity in the striatum (dopamine involved in inhibition of cholinergic and glutamatergic loops and increased activity in these systems)
 - b. Mean age of diagnosis: 55–60 years; incidence approximately 20/100,000; mortality not greatly increased
 - c. Etiology of idiopathic Parkinson disease unknown: possibly a combination of genetic predisposition and environmental factors. Hereditary accounts for less than 2% of all diagnosed cases. Oxidative stress and free radical damage may contribute to neuronal degeneration.
 - d. Drug-induced: Caused by antidopaminergic agents (metoclopramide, prochlorperazine, neuroleptics, reserpine, methyldopa, etc.); rarely amiodarone, selective serotonin reuptake inhibitors (SSRIs), valproic acid, diltiazem, verapamil
 - e. Treatment for drug-induced Parkinson disease: discontinue drug, administer anticholinergic agents (e.g., diphenhydramine or benztropine)
 - f. Other secondary causes: neurovascular lesions, brain neoplasms, normal pressure hydrocephalus, parathyroid abnormalities, hypothyroidism, hepatocerebral degeneration, CNS infection, toxins, head trauma
 2. Signs and symptoms (Figure 14-1)
 - a. Onset: tremor, rigidity, akinesia, postural instability
 - b. Minor: difficulty with fine coordinated movements; postural disturbance (later in disease state); flattened facial expression (masked facies); voice may become hypophonic, monotonal; shuffling gait; micrographia; drooling, difficulty swallowing liquids; pain in affected limb; depression or dementia; constipation; orthostatic hypotension; urinary frequency; sweating; dermatitis; sexual dysfunction
 - c. Essential tremor characterized by an action tremor (as opposed to resting tremor) is commonly misdiagnosed as Parkinson disease
 3. Treatment
 - a. The goal is to improve motor symptoms (tremor, bradykinesia, rigidity), inhibit cholinergic action, ease dopaminergic action
 - b. Guidelines differ regarding initial therapy: dopamine first line versus last. Treatment should not be initiated in most patients until motor symptoms significantly impair quality of life (QOL) and/or daily function.
 - 1) Mild disease: amantadine (Symmetrel), selegiline (selegiline monotherapy provides mild-to-modest relief of motor symptoms and delays need for levodopa)
 - 2) Dystonias and muscle cramps: baclofen (Lioresal)
 - 3) Tremor: anticholinergic agent like benztropine (Cogentin)
 - 4) Motor symptoms: anticholinergic drugs such as benztropine in combination with levodopa
 - c. All treatments are patient specific: doses must be tailored and changed according to patient's disease state, progression, and side effects.
 - d. Drug holidays: no longer widely recommended due to risk of severe immobility, aspiration pneumonia, venous thromboembolism, depression
 - e. Adjunctive therapy to treat comorbidity: depression, hallucinations, anxiety, constipation, orthostatic hypotension, pain, etc.
 4. Nondrug therapy
 - a. Exercise, physical and occupational therapy, speech therapy, nutrition (difficulty swallowing may impair intake of foods; constipation also a problem), psychological support, and surgery

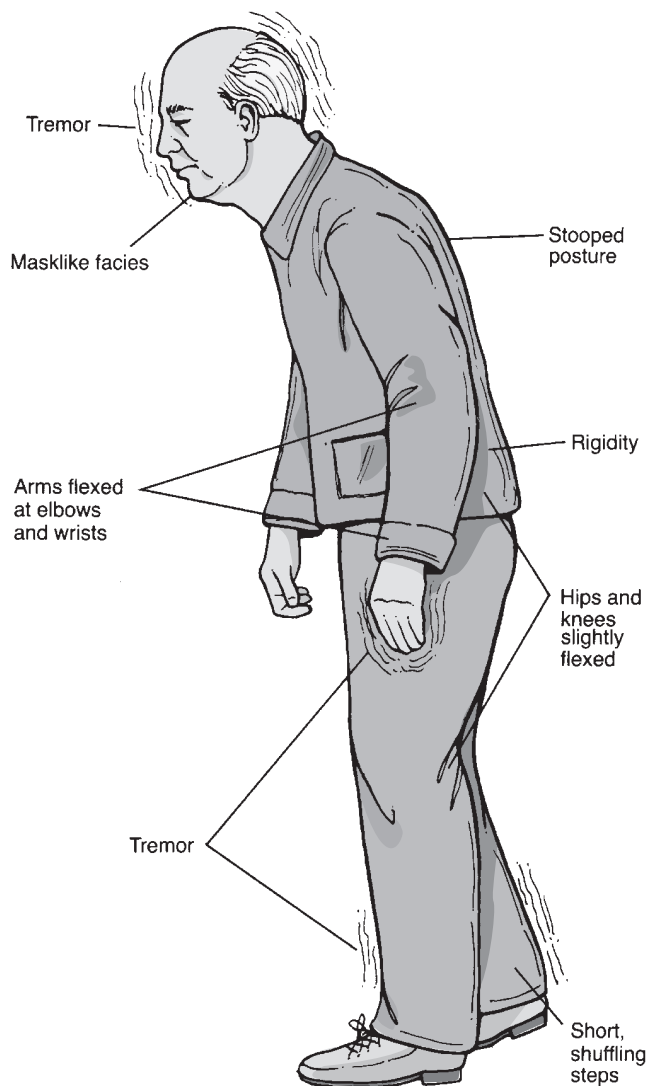


Figure 14-1 — **Signs and symptoms of Parkinson's disease.** (From Monahan FD, Drake T, Neighbors M: Nursing care of adults. Philadelphia, 1994, Saunders)

5. Medications

a. Levodopa/carbidopa (Sinemet, Sinemet CR)

- 1) Mechanism of action: Levodopa is a dopamine precursor that can cross the blood-brain barrier and replace dopamine in the brain (metabolized by dopa-decarboxylase to dopamine). Carbidopa inhibits peripheral dopa-decarboxylase and allows more dopamine to enter brain, which allows lower levodopa dose, more-rapid dosage titration, and reduced peripheral side effects (nausea/vomiting, arrhythmias, orthostatic hypotension).
- 2) Usual dose: minimum 75–100 mg/day carbidopa required. Initial dose is one carbidopa 25 mg/levodopa 100 mg tablet PO three times per day. Levodopa absorption is impaired by high-protein meals.

- 3) Side effects (levodopa): nausea/vomiting, insomnia or sedation, confusion, hallucinations, dyskinesias, muscle cramping (dystonias), wearing off phenomenon (end-of-dose failure), hypersexuality

- 4) Levodopa/carbidopa (Sinemet): Approximately 5 years after initiation, many patients experience motor complications (wearing off phenomenon, dyskinesia). Recent guidelines recommend initiating a dopamine agonist early in therapy, which delays need for levodopa and complications of therapy. As disease progresses, dopamine will be needed.

b. Amantadine (Symmetrel): mildly effective against tremor and rigidity

- 1) Mechanism of action: unclear, may be an NMDA (*N*-methyl *D*-aspartate) antagonist; blocks uptake and enhances the release of dopamine
- 2) Has antiviral properties
- 3) Side effects: dry mouth, peripheral edema, livedo reticularis, sedation, confusion, hallucinations; may cause insomnia if taken in late evening (stimulating effect in some patients), may be useful for young patients with fatigue
- 4) Usual dose: 100 mg PO twice daily when used as monotherapy; adjust for renal impairment. For elderly: initially 100 mg PO once daily; titrate the dosage carefully upward if needed.

c. Selegiline (Eldepryl): mild to moderate symptom relief as monotherapy in early disease; also used for adjunctive therapy late in disease to prevent wearing-off phenomenon. Some studies show increased morbidity when used with levodopa. Multiple other studies do not show increased morbidity; however, may want to avoid if patients have history of dementia, frequent falls, or postural hypotension

- 1) Mechanism of action: selective, irreversible MAO-B inhibitor. Selectivity is lost if the dose is >20 mg/day; metabolized to amphetamine/methamphetamine
- 2) Side effects: insomnia, sedation, confusion, agitation, hallucinations, vivid dreams; may enhance levodopa-induced dyskinesias
- 3) Contraindicated with meperidine (Demerol)
- 4) Usual dose: 5 mg PO twice daily with breakfast and lunch, may cause insomnia if taken in late evening; consider lowering levodopa dosage by 20% when starting selegiline
- 5) Also available in orally disintegrating tablet; maximum dose 2.5 mg/day

- d. Dopamine receptor agonists: bromocriptine (Parlodel), pergolide (Permax), pramipexole (Mirapex), ropinirole (Requip)
 - 1) Dopamine agonists may be used as monotherapy early in the disease; adjunctive therapy in late disease to manage motor complications
 - 2) Usual dose: start doses low and titrate slowly. It may take months to achieve therapeutic dosage; taper up and taper down. Reduce the dose in patients with renal disease.
 - a) Bromocriptine: 1.25 mg PO twice daily, increasing the total daily dose by 2.5 mg every 14–28 days until the desired therapeutic response occurs
 - b) Pergolide: this drug is discontinued in the United States.
 - c) Pramipexole: initially, 0.125 mg PO three times per day. Gradually increase by 0.125–0.25 mg/dose (0.375–0.75 mg/day) every 5–7 days to a maximum dosage of 1.5 mg PO three times per day (4.5 mg/day).
 - d) Ropinirole: initially, 0.25 mg PO three times per day for the first week. Gradually titrate at weekly intervals to a maximum of 24 mg/day.
 - 3) Side effects: nausea/vomiting, constipation, orthostatic hypotension, nightmares, hallucinations, confusion, psychosis, sedation, hypersexuality, yawning, neuroleptic malignant syndrome (NMS)
 - e. Catechol-*O*-methyltransferase (COMT) inhibitors: tolcapone (Tasmar), entacapone (Comtan)
 - 1) These drugs are useful for wearing-off phenomenon.
 - 2) Mechanism of action: inhibits the action of COMT
 - 3) COMT inhibitors work with levodopa and prolong its action. Because they affect levodopa metabolism, they are only effective in patients receiving levodopa therapy.
 - 4) Entacapone is a reversible peripheral COMT inhibitor. It is the preferred COMT inhibitor because it does not require liver function test (LFT) monitoring. Tolcapone is a peripheral and central COMT inhibitor. It achieves greater COMT inhibition than entacapone. However, its use is restricted due to occurrence of fatal hepatotoxicity; discontinue tolcapone use after 3 weeks if patient fails to show expected benefit from the drug. Patients must give consent, and LFTs should be performed every 2 weeks for the first 12 months, then every 4 weeks for the next 6 months, and then every 8 weeks for the duration of therapy.
 - 5) Usual dose
 - a) Tolcapone: initially 100 mg PO three times per day. The maximum recommended dose is 600 mg/day PO given in three divided doses.
 - b) Entacapone: 200 mg PO administered with each levodopa/carbidopa dose to a maximum of 8 times per day (1600 mg/day)
 - 6) Side effects: exacerbation of levodopa side effects, such as nausea, urine discoloration (dark yellow to orange-brown), diarrhea (after several weeks). Be alert to signs of liver problems, such as worsening abdominal pain, yellowing of the skin or whites of the eyes (especially with tolcapone). Retroperitoneal fibrosis and other lung problems are rare.
 - 7) Drug interactions: Do not use with nonselective MAO inhibitors. Iron decreases absorption of both COMT inhibitors; separate administration times.
 - d. Drug side effects
 - 1) Nausea/vomiting: Patients should take levodopa and dopamine agonists with nonprotein snack. If antiemetics are needed, do not use dopamine receptor blockers (see section on drug-induced Parkinson disease).
 - 2) Hallucinations/psychosis: taper off suspected agents until determination of which agent caused the effect; if taper causes significant worsening of Parkinson disease, atypical antipsychotics should be considered (avoid phenothiazine and other traditional antipsychotics).
 - a) Quetiapine and clozapine are preferred over olanzapine and risperidone (latter two drugs may increase motor symptoms)
 - 3) Anticholinergics for tremor control: trihexyphenidyl (Artane), benztropine (Cogentin), diphenhydramine (Benadryl), procyclidine (Kemadrin), biperiden (Akineton)
 - a) Elderly are more sensitive to anticholinergic side effects.
- B. Alzheimer disease and dementia
1. Pathophysiology/epidemiology
 - a. Genetic factors: known to play a role in some cases of Alzheimer disease (AD). Some families with a history of early-onset AD have a mutation on the amyloid beta precursor protein (APP) gene. Another gene, the apolipoprotein (Apo) E gene, also has been implicated in the disease. Apo E is a protein found with beta amyloid (a protein found in the brains of patients with AD) in neuritic (inflamed nerve) plaques. Together, these genetic mutations account for less than 10% of all patients with AD.
 - b. Plaques and tangles: The causes of AD are poorly understood, but its effect on brain tissue has been demonstrated clearly. AD damages

and kills brain cells. Neurons generate electrical and chemical signals that are relayed from neuron to neuron to help an individual think, remember, and feel (physically and emotionally). Brain chemicals called neurotransmitters help these signals flow seamlessly between neurons. Initially in people with AD, neurons in certain locations of the brain begin to die. When they die, lower levels of neurotransmitters are produced, creating signaling problems in the brain. One neurotransmitter, acetylcholine, has been found to be deficient in the brains of those with AD. Medication treatment is based around increasing the amount of acetylcholine in the brain.

- 1) Plaques and tangles in brain tissue are considered hallmarks of AD. Plaques are made up of beta-amyloid, a normally harmless protein. Although the ultimate cause of neuron death in AD is not known, mounting evidence suggests that a form of beta-amyloid protein may be the cause. The plaque is responsible for memory deterioration in individuals with AD.
- c. Inflammation: Researchers have observed inflammation in the brains of some people with AD. As beta-amyloid plaques develop in the spaces between neurons, immune cells are getting rid of dead cells and other waste products in the brain. Although research has found that the inflammation occurs before plaques have fully formed, it is not known how this development relates to the disease process. There is also debate about whether inflammation has a damaging effect on neurons or whether it is beneficial in clearing away plaques.
- d. Age is the most important risk factor for AD. The number of people with the disease doubles every 5 years beyond age 65 years.
- e. It is estimated that about five million Americans have AD, and about 360,000 people are newly diagnosed every year. AD affects about 10% of people ages 65 years and older, and the number doubles roughly every 10 years after age 65 years. Half of the population ages 85 years and older may have AD.
- f. Signs and symptoms
 - 1) Mild symptoms: mental deterioration, such as memory impairment and confusion, difficulty learning and remembering new information, difficulty with daily tasks, and depression (sadness, decreased interest in usual activities, loss of energy)
 - 2) Moderate symptoms: forgetting old facts, continually repeating stories, and/or asking the same questions over and over, deficiencies in intellect and reasoning, a lack of concern for appearance, hygiene, and sleep
 - 3) Severe symptoms: groaning, screaming, mumbling, or speaking gibberish, failing to recognize the faces of family members or caregivers, great difficulty with all essential activities of daily life
- 4) Apraxia: inability to perform physical tasks such as dressing, eating
- 5) Aphasia: loss of ability in comprehension of spoken or written language
- 6) The primary symptoms of AD include memory loss, disorientation, confusion, and problems with reasoning and thinking. These symptoms worsen as brain cells die and the connections between cells are lost.
- g. Medications
 - 1) Cholinesterase inhibitors: donepezil (Aricept), rivastigmine (Exelon), galantamine (Razadyne), and tacrine (Cognex)
 - a) Mechanism of action: inhibits the degradation of acetylcholine by inhibiting the enzyme acetylcholinesterase
 - b) Usual doses
 - (1) Donepezil (Aricept): initial 5 mg/day at bedtime; may increase to 10 mg/day at bedtime after 4–6 weeks
 - (2) Rivastigmine (Exelon): initial 1.5 mg twice daily; may increase by 3 mg/day (1.5 mg/dose) every 2 weeks based on tolerability (maximum recommended dose 6 mg twice daily)
 - (3) Galantamine (Razadyne): initial 4 mg twice a day for 4 weeks; if tolerated, increase to 8 mg twice daily for 4 weeks; if tolerated, increase to 12 mg twice daily; ranges 16–24 mg/day in two divided doses
 - c) Side effects: gastrointestinal effects (diarrhea, nausea, vomiting, anorexia) are most common and may require dose reductions for some agents (e.g., galantamine). Increased salivation, increased respiratory secretions, bradycardia, headache, fatigue, and vertigo are other side effects. Hepatotoxicity has been attributed to the use of tacrine and has limited the drug's clinical use.
 - d) Cautions: Individuals with liver disease, peptic ulcer disease, chronic obstructive pulmonary disease (COPD), and slow heart rate should not take these drugs.
 - 2) Memantine (Namenda)
 - a) Mechanism of action: NMDA antagonist, blocks glutamate activity and prevents excessive influx of calcium and, thereby, neuronal death
 - b) Usual dose: Initial 5 mg/day; increase dose by 5 mg/day to a target dose of 20 mg/day; wait at least 1 week between dosage changes; doses >5 mg/day should be given in two divided doses.
 - c) Side effects include headache, constipation, confusion, and dizziness.
 - 3) Other medications
 - a) Vitamin E
 - b) Selegiline (Eldepryl)

4) Adjunct therapies

- a) Depression that occurs during the early stages is commonly treated with antidepressant medications, such as selective serotonin reuptake inhibitors (SSRI) including fluoxetine (Prozac) and sertraline (Zoloft), and the tricyclic antidepressants (TCA), including amitriptyline (Elavil). Side effects include drowsiness, fatigue, and sedation. TCA may increase mental confusion.
- b) Agitation may be treated with an antipsychotic medication, such as haloperidol (Haldol), risperidone (Risperdal), olanzapine (Zyprexa), and quetiapine (Seroquel). NOTE: Antipsychotics are not FDA approved to treat behavioral symptoms of AD and may increase the risk for death in elderly patients with dementia. Side effects include sedation, confusion, and tardive dyskinesia (an irreversible movement disorder characterized by lip smacking, facial grimacing, and unsteady walking).

C. Glaucoma

1. Pathophysiology and epidemiology

- a. Glaucoma is the name given to a group of conditions caused by increased intraocular (inside the eye) pressure (IOP), resulting either from a malformation or malfunction of the eye's drainage system. Left untreated, an elevated IOP may cause irreversible damage to the optic nerve and retinal fibers, resulting in a progressive, permanent loss of vision. However, early detection and treatment can slow or even halt the progression of the disease.
- b. It is estimated that more than three million Americans have glaucoma but only half of those know they have it. Most individuals with glaucoma are not aware of problems with their vision. This is because the central vision (for reading and recognizing people) is only affected when glaucoma has advanced to a late stage. Even when central vision is still good, glaucoma may affect the vision needed for driving and other daily functions, including seeing stair steps or reading.
- c. Approximately 120,000 are blind from glaucoma, accounting for 9%–12% of all cases of blindness in the United States. About 2% of the population 40–50 years old and 8% older than 70 years of age have elevated IOP.
- d. Glaucoma is the second leading cause of blindness in the world, according to the World Health Organization (WHO). Glaucoma is the leading cause of blindness among African Americans.
- e. Estimates put the total number of suspected cases of glaucoma at approximately 65 million worldwide.

2. Most common forms of glaucoma

- a. Open-angle glaucoma (chronic): Open angle (also called chronic open angle or primary

open angle) is the most common type of glaucoma and usually causes no symptoms at first. Even though the anterior structures of the eye appear normal, aqueous fluid builds within the anterior chamber, causing the IOP to become elevated. Left untreated, this may result in permanent damage of the optic nerve and retina.

- b. Angle-closure glaucoma (acute): Acute angle closure glaucoma, or closed-angle glaucoma, occurs because of an abnormality of the trabecular mesh work and the canal of Schlemm in the eye that keeps aqueous humor fluid from draining. In most of these cases, the space between the iris and cornea is narrower than normal, putting pressure on the canal of Schlemm and leaving a smaller channel for the aqueous humor to drain. If the flow of aqueous becomes completely blocked, the IOP rises sharply, causing a sudden angle closure attack. Only about 10% of the population with glaucoma has acute angle closure glaucoma.
 - c. Secondary glaucoma: Secondary glaucoma can develop as complications of other medical conditions, such as inflammation, trauma, previous surgery, diabetes, or a tumor. These types of glaucoma are sometimes associated with eye surgery or advanced cataracts, eye injuries, certain eye tumors, uveitis (eye inflammation), and certain medications (including topical steroid creams, cocaine, chlorpromazine or Thorazine, and phenelzine or Nardil).
- #### 3. Signs and symptoms
- a. Symptoms may vary depending on the type
 - 1) Acute angle-closure glaucoma: Serious signs and symptoms include eye soreness, blurred vision, colored halos around lights, swollen eyelids, severe eye pain, headache, and nausea and vomiting.
 - b. Blind spots
 - c. Halos
 - d. Reddening around the eye
 - e. Blurred vision
 - f. Tunnel vision
 - g. Rise in eye pressure
 - h. Eye pain
 - i. Difficulty focusing
 - j. Loss of vision
- #### 4. Treatment
- a. The treatment of glaucoma is aimed at reducing IOP by improving aqueous humor outflow from the eye, reducing the production of aqueous humor, or both. These treatment goals are accomplished with eye drops, systemic medications, laser treatment, surgery, or a combination of treatments.
- #### 5. Medications
- a. Prostaglandin analogs
 - 1) Mechanism of action: increases outflow of aqueous humor
 - 2) Adverse effects: may change the pigment of the iris (may be permanent); may change

- direction of eyelashes (may be permanent) and increase growth of eyelashes
- 3) Examples
 - a) Latanoprost (Xalatan): 1 drop (1.5 mcg) in the affected eye(s) once daily at bedtime
 - b) Bimatoprost (Lumigan): 1 drop in the affected eye(s) once daily at bedtime
 - c) Travoprost (Travatan): 1 drop in the affected eye(s) once daily at bedtime
 - d) Unoprostone (Rescula): 1 drop in the affected eye(s) twice daily
 - b. Sympathomimetics
 - 1) Mechanism of action: increase outflow of aqueous humor
 - 2) Examples
 - a) Apraclonidine (Iopidine): used with other drugs before surgery
 - b) Brimonidine (Alphagan): 1 drop in the affected eye(s) three times daily (q12h)
 - c) Dipivefrin (Propine): 1 drop in the affected eye(s) q12h
 - d) Epinephrine (Epifrin, Glaucon): 1 drop in affected eye(s) daily or twice daily
 - 3) Drug interactions: Some sympathomimetic eye drops (e.g., brimonidine) should not be used with MAO inhibitor therapy.
 - c. Beta blockers (nonselective)
 - 1) Mechanism of action: suppresses production of aqueous humor
 - 2) Caution: Beta blockers are absorbed systemically and should be used cautiously in patients with heart, lung, or endocrine disorders. The use of lacrimal occlusion technique upon administration reduces potential for systemic absorption of the eye drops.
 - 3) Examples
 - a) Timolol (Timoptic): 1 drop in the affected eye(s) twice daily
 - b) Timolol gel (Timoptic XE): 1 drop once daily
 - c) Carteolol (Ocupress): 1 drop in the affected eye(s) twice daily
 - d) Levobunolol (Betagen): 1–2 drop(s) in the affected eye(s) twice daily
 - e) Metipranolol (OptiPranolol): 1 drop in the affected eye(s) twice daily
 - f) Combination product: Timolol/dorzolamide (Cosopt): check for sulfa allergy
 - d. Beta blockers (beta-1 selective)
 - 1) Mechanism of action: suppresses production of aqueous humor
 - 2) Less effect on blood pressure and heart rate compared with nonselective beta blockers. The use of lacrimal occlusion technique upon administration reduces potential for systemic absorption of the eye drops.
 - 3) Examples
 - a) Betaxolol (Betoptic): 1 to 2 drop(s) in the affected eye(s) twice daily
 - b) Levobetaxolol (Betaxon): 1 drop in the affected eye(s) twice daily
 - e. Carbonic anhydrase inhibitors
 - 1) Mechanism of action: suppresses production of aqueous humor
 - 2) Do not use in patients with sulfa allergy
 - 3) Systemic preparations: not to be used as monotherapy
 - 4) Examples
 - a) Acetazolamide (Diamox): has been associated with tachyphylaxis
 - b) Dichlorphenamide (Daranide)
 - c) Methazolamide (Neptazane)
 - f. Miotics (cholinergic)
 - 1) Mechanism of action: increases outflow of aqueous humor
 - 2) Examples
 - a) Pilocarpine (Isopto Carpine, Pilocar): 1 or 2 drop(s) in the affected eye(s) three or four times daily
 - b) Pilocarpine insert (Ocuser Pilo-20): releases 20 mcg/h for 1 week; replace once weekly
 - c) Carbachol (Isopto carbachol): two drops in the affected eye(s) a maximum of three times daily
- D. Osteoporosis
1. Pathophysiology and epidemiology
 - a. Osteoporosis is more common in older individuals and non-Hispanic white women, but it can occur at any age, in men as well as in women, and in all ethnic groups.
 - b. In the United States, about eight million women and two million men have osteoporosis. Those older than 50 years are at greatest risk of developing osteoporosis and suffering related fractures. In this age group, one in two women and one in six men will have an osteoporosis-related fracture at some point in their lives.
 2. Signs and symptoms
 - a. In the early stages of bone loss, there usually is no pain or symptoms. After bones have been weakened by osteoporosis, signs and symptoms may include back pain, which can be severe with a fractured or collapsed vertebra; loss of height over time, with an accompanying stooped posture; and fracture of the vertebrae, wrists, hips, or other bones.
 3. Treatment
 - a. Nutrition and lifestyle
 - 1) Dietary factors: calcium intake of 1200 mg daily is recommended for adults older than 50 years. Adequate vitamin D intake is also important for calcium absorption and to maintain muscle strength; adults older than 60 years of age should take 600–800 IU per day. Milk and milk products are calcium-dense foods providing about 300 mg of calcium per serving. These foods also contain other nutrients important to bone health such as vitamin D (if fortified), phosphorus, and magnesium.
 - 2) Weight-bearing exercises: Weight-bearing aerobic activities, involving the bones supporting body weight, have a positive

effect in maintaining and increasing bone mass and preventing osteoporosis. These activities include weight-lifting, jogging, hiking, stair-climbing, step aerobics, dancing, racquet sports, and other activities that require muscles to work against gravity.

b. Medications

1. Bisphosphonates

- a) Mechanism of action: inhibits osteoclast-mediated bone resorption.
- b) Dose: Alendronate (Fosamax) or risedronate (Actonel) can be taken daily or are available in a once-weekly dosage form; ibandronate (Boniva) can be taken once a month. An IV form of ibandronate is infused every 3 months. Another IV bisphosphonate is zoledronic acid (Reclast); it is infused once yearly.

- c) Side effects: nausea, abdominal pain, and the risk of an inflamed esophagus or esophageal ulcers, especially if the individual has had acid reflux or ulcers in the past.

Osteonecrosis of the jaw is a rare but serious side effect.

- 1) A baseline and pre-dose determination of serum creatinine is necessary in individuals receiving IV bisphosphonates to determine kidney function.

- 2) When taking an oral bisphosphonate, proper administration is necessary to reduce the risk of esophageal side effects. Proper directions include: On the day of dosing, take dose first thing in the morning. Do not eat or drink anything before taking medicine. Swallow with a full glass (6 to 8 fluid ounces) of plain water only. Do not chew or crush. After taking, do not eat breakfast, drink, or take any other medicines or vitamins for at least 30 minutes. Stand or sit up for at least 30 minutes after taking; do not lie down.

d) Examples

- 1) Alendronate (Fosamax)
 - (a) Currently approved for management of osteoporosis in both men and women; also approved for the prevention and treatment of steroid-induced osteoporosis in men and women.
- 2) Risedronate (Actonel): like alendronate, approved for the prevention and treatment of steroid-induced osteoporosis in men and women
- 3) Ibandronate (Boniva)
- 4) Zoledronate (Reclast)

- e) Adequate calcium and vitamin D intake are needed to achieve results.

2. Calcitonin salmon (Miacalcin):

- a) A naturally occurring hormone produced by the thyroid gland that can be given as an injection or is more commonly used in ambulatory settings as a nasal spray.

- b) Mechanism of action: inhibits the function of the cells that breakdown bone, the osteoclasts

c) Dose

- 1) Miacalcin: IM or SC, 100 units every other day
- 2) Fortical, Miacalcin: Intranasal 200 units (1 spray) in one nostril daily

- d) Side effects: rhinitis, flushing, injection site reactions, back pain, dizziness, fatigue, nausea.

3. Teriparatide (Forteo)

- a) Synthetic parathyroid hormone (PTH) analog

- b) Increases the number and action of osteoblasts

- c) Daily SC injections

- d) Given to men and women with osteoporosis at risk for bone fracture

4. Hormone replacement therapy (HRT)

- a) Estrogen therapy alone or in combination with another hormone—progestin—has been reported to decrease the risk of osteoporosis and osteoporotic fractures in women.

- 1) May increase risk of breast cancer with long-term use

- 2) Example: conjugated estrogen (Premarin)

5. Selective estrogen receptor modulators (SERM)

- a) Mimic the positive effects of estrogen on bones without some of the undesirable and serious adverse effects

- b) Raloxifene (Evista)

- 1) Decreases spine fractures in women and is approved for use only in women at this time

- 2) Dose: 60 mg/day

- 3) Side effect: hot flashes; individuals with a history of blood clots should not use this drug.

6. Tamoxifen (Nolvadex)

- a) Used to treat breast cancer; has some beneficial effects on the bones and does not stimulate the endometrium

E. Benign prostatic hyperplasia (BPH)

1. Pathophysiology/epidemiology

- a. Benign prostatic hyperplasia (BPH) is a normal, gradual enlargement of the prostate caused by hormonal fluctuations, such as decreases in testosterone and increases in dihydrotestosterone (DHT) and estrogen in prostate tissue. BPH usually begins in middle age. BPH does not lead to cancer. BPH does not generally cause pain, but there is often a general discomfort (a feeling of pressure) in the groin area.

- b. As the prostate enlarges, it presses against the urethra and interferes with urination. At the same time, the bladder wall becomes thicker and irritated and begins to contract, even when it contains small amounts of urine, which causes more frequent urination. Additionally, as the bladder weakens, it may not empty

- completely, leaving some urine. Blocking or narrowing of the urethra by the prostate and partial emptying of the bladder cause many of the problems associated with BPH.
- c. BPH affects about half of men older than 60 years, and 80% of men aged 80 years or older; it is considered to be a condition related to aging. Almost every man older than 45 years experiences some prostate enlargement, but symptoms are rarely felt before the age of 60 years. BPH affects all men differently and therefore treatment varies.
2. Diagnosis
 - a. Digital rectal exam (DRE)
 - b. Prostate-specific antigen (PSA) test
 - c. Prostate biopsy
 3. Signs and symptoms
 - a. Delay in start of urine stream
 - b. Poor urinary flow and a variable flow rate
 - c. Frequent urination
 - d. Difficulty postponing urination (urgency)
 - e. Dribbling of urine at the end of urination
 - f. Nocturia (waking at night to urinate)
 4. Treatment
 - a. Treatment options for BPH include lifestyle changes, “watchful waiting,” drug therapy, nonsurgical procedures, and major surgery. The goals of treatment are to improve urinary flow and decrease the symptoms an individual may be experiencing. Treatment should also delay or prevent the progression of BPH.
 5. Medications
 - a. 5-Alpha reductase inhibitors: dutasteride (Avodart), finasteride (Proscar)
 - 1) Mechanism of action: inhibits the production of the hormone DHT
 - 2) Usual dose
 - a) Dutasteride (Avodart): 0.5 mg once daily alone or in combination with tamsulosin
 - b) Finasteride (Proscar): 5 mg/day as a single dose
 - 3) Side effects: weakness, postural hypotension, allergic reactions (skin rash, itching or hives, swelling of the face, lips, or tongue), change in sex drive or performance, changes in breast-like lumps, pain or fluids leaking from the nipple, pain in the testicles
 - 4) Contraindications: pregnancy category X; not indicated for use in women or children; pregnant women or women trying to conceive should not handle the products.
 - b. Alpha-1 blockers: alfuzosin (UroXatral), doxazosin (Cardura), tamsulosin (Flomax), terazosin (Hytrin)
 - 1) Mechanism of action: blocks adrenergic receptors on smooth muscle of the prostate and bladder neck to improve urine flow and to reduce bladder outlet obstruction
 - 2) Usual dose
 - a) Alfuzosin (UroXatral): 10 mg once daily
 - b) Doxazosin (Cardura): immediate release: 1 mg once daily in morning or evening may titrate to response; goal of 4–8 mg/day; maximum dose 8 mg/day. Extended release: 4 mg once daily with breakfast; titrate based on response and tolerability every 3–4 weeks to maximum recommended dose of 8 mg/day
 - c) Tamsulosin (Flomax): 0.4 mg once daily ~30 minutes after the same meal each day; dose may be increased after 2–4 weeks to 0.8 mg once daily to achieve desired result
 - d) Terazosin (Hytrin): initial 1 mg at bedtime, increasing as needed; most patients require 10 mg day; if no response after 4–6 weeks of 10 mg/day, may increase to 20 mg/day
- 3) Side effects: dizziness, fatigue, headache, orthostatic hypotension, muscle weakness
- 4) **Contraindication** and interaction: concurrent use with phosphodiesterase-5 (PDE-5) inhibitors (commonly used for erectile dysfunction) including sildenafil (>25 mg), tadalafil, or vardenafil. Substrate of CYP 3A4, avoid St. John’s wort, strong inhibitors (ketoconazole, itraconazole, ritonavir); beta blockers may enhance the orthostatic effect of alpha-1 blockers
- F. Erectile Dysfunction (ED)
 1. Pathophysiology and epidemiology
 - a. Erectile dysfunction (ED), sometimes called impotence, is the repeated inability to obtain or retain an erection firm enough for sexual intercourse. Impotence may also be used to describe other problems that interfere with sexual intercourse and reproduction, such as lack of sexual desire and problems with ejaculation or orgasm.
 - b. Estimates suggest that between 15 and 30 million (20%–40%) Americans have ED. In men 40 to 69 years of age in the United States, the incidence of new cases of ED is approximately 26 per 1,000 annually. More than 150 million men worldwide have ED.
 - c. Risk factors: smoking, being overweight, eating unhealthy foods (such as a high-fat diet), avoiding exercise, the presence of diabetes or vascular disease (atherosclerosis, hypertension), and taking certain medications (antidepressants, stimulants, anticholinergics, antihypertensive agents)
 2. Signs and symptoms
 - a. Occasional inability to obtain a full erection
 - b. Inability to maintain an erection throughout intercourse
 - c. Complete inability to achieve an erection
 - d. Lack of morning erections are also seen along with a decrease in sex drive (libido)
 3. Treatment
 - a. Treatments include psychological counseling, medications, mechanical devices, and surgery. The cause and severity of ED are important factors in determining the best treatment or combination of treatments for the individual.

b. Medications

1. Phosphodiesterase-5 (PDE-5) inhibitors:

sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra): first-line medication

- a) Mechanism of action: inhibition of PDE-5 by sildenafil causes increased levels of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood to the corpus cavernosum

b) Usual dose

- 1) Sildenafil: usual dose 50 mg once daily 1 hour (range 30 minutes to 4 hours) before sexual activity; dosing range 25–100 mg once daily
- 2) Tadalafil: 10 mg at least 30 minutes before anticipated sexual activity (dosing range 5–20 mg); to be taken as one single dose and not taken more than once daily
- 3) Vardenafil: 10 mg 60 minutes before sexual activity; dosing range 5–20 mg; to be taken as one single dose and not taken more than once daily

- c) Side effects: headache, reddening of the face and neck (flushing), indigestion, insomnia, pyrexia, and nasal congestion

- d) Contraindications/drug interactions: Do not use with organic nitrates in any form (e.g., nitroglycerin, isosorbide dinitrate), alpha-1 blockers, azole antifungals, protease inhibitors.

2. Prostaglandin E₁ analogs: alprostadil (Muse, Caverject, Edex)

- a) Mechanism of action: causes vasodilation by means of direct effect on vascular and ductus arteriosus smooth muscle; relaxes trabecular smooth muscle by dilation of cavernosal arteries when injected along the penile shaft, allowing blood flow to and entrapment in the lacunar spaces of the penis

b) Usual dose

- 1) Intracavernous (Caverject, Edex): no more than three times per week with at least 24 hours between doses
- 2) Intraurethral (Muse Pellet): Initial 125–250 mcg; maintenance doses administered as needed to achieve an erection; duration of action is about 30–60 minutes; use only two systems per 24-hour period

- c) Side effects: penile pain, urethral burning, headache, dizziness, pain

- d) **Contraindication** and interaction: no significant interactions

3. Yohimbine (Erex, Yocon)

- a) Mechanism of action: has selective alpha-2 adrenergic blocking properties, may increase libido (sexual desire)

- b) Side effects: elevated heart rate and blood pressure, mild dizziness, nervousness, and irritability

- c) Contraindications: individuals taking MAOI or antihypertensives; do not use in hypertensive patients; avoid in individuals with BPH

PATIENT PROFILE

Patient Initials: SR

Sex: Female

Age: 76 years

Height: 5' 2"

Weight: 40 kg

Race: White

Allergies: No known drug allergies (NKDA)

Chief Complaint/History: SR was recently found to have Alzheimer disease. Before the diagnosis, her family noted that she was constantly misplacing familiar items, such as her keys and eyeglasses, and seemed to be having difficulty remembering regular appointments and medications. She also often speaks of certain long-deceased relatives as being still alive and sometimes calls her son by her brother's name. Around the house, she often leaves the stove on after cooking and regularly seems to get disoriented. She seems more irritable and anxious, even around familiar friends. Her family is concerned about her ability to remain living at home independently and recently started looking at group homes focusing on care of patients with early stage Alzheimer disease. This has been difficult because SR gets angry during any conversations regarding leaving her home.

Medical History:

Osteoarthritis

Hypertension

History of iron-deficiency anemia, no longer treated

Frequent urinary tract infections (UTIs)

Laboratories at last medical appointment:

Sodium: 137 mEq/L

Potassium: 3.9 mEq/L

Chloride: 110 mEq/L

CO₂: 25 mEq/L

BUN: 22 mg/dL

Serum creatinine: 0.9 mg/dL

Glucose: 105 mg/dL

Cholesterol: normal

Liver function tests: within normal limits

CBC and differential: within normal limits

Urine: clear, no bacteria or protein

Social History:

Tobacco use: None

Alcohol use: None in recent years

Medications:

Lodine XL 400 mg PO once daily

Univasc 3.75 mg PO once daily

Hydrochlorothiazide 12.5 mg PO once daily

PATIENT PROFILE QUESTIONS

1. What is the estimated creatinine clearance (CrCl) for this patient?
 - a. 110 mL/min
 - b. 40 mL/min
 - c. 34 mL/min
 - d. 70 mL/min

Answer: c. 34 mL/min. In geriatrics, it is often important to calculate an estimated creatinine clearance because the serum creatinine level may not reflect renal function due to declining muscle mass and organ function. The Cockcroft-Gault equation is used clinically when other means are not available. An estimate of CrCl is important in the dosing of many medications because many medications require adjustment for renal impairment. The CrCl calculation for this female patient is:

$$\begin{aligned}\text{CrCl} &= 0.85 \times \frac{(140 - \text{Patient age in years}) \times \text{Body weight(Kg)}}{72 \times \text{Serum Creatinine(mg/dL)}} \\ &= 0.85 \times \frac{(140 - 76) \times 40}{72 \times 0.9} \\ &= 0.85 \times \frac{2560}{64.8}\end{aligned}$$

Answer = 33.5 mL/min
= 34 mL/min

2. The physician would like to prescribe donepezil (Aricept) for this patient. Which of the following represents the correct starting dose?
 - a. 5 mg PO once daily
 - b. 10 mg PO once daily
 - c. 5 mg PO twice daily
 - d. 2.5 mg PO once daily

Answer: a. The initial starting dose for Aricept is 5 mg PO once daily. No initial dosage adjustment is necessary for renal impairment. The dose may be titrated up to 10 mg PO once daily after 1 month to 6 weeks of treatment, if needed.
3. Which of the following regarding donepezil are true?
 - I. Common side effects are cholinergic in nature and include nausea, diarrhea, GI disturbances, and dizziness.
 - II. Treatment effect should be noticeable in a few days.
 - III. In early stage disease, the drug may help improve concentration and focus on tasks of daily living and help with orientation
 - IV. Progression of the dementia will be halted.
 - a. I only
 - b. II only
 - c. II and III only
 - d. I and III only
 - e. I, II, III, and IV are all true

Answer: d. Common side effects of donepezil are cholinergic in nature, and the patient will usually notice that these lessen after several weeks of treatment. If the symptoms do not resolve, dose reduction may be necessary to help tolerance. Treatment effect is usually only noted after 4–6 weeks of use, and it is important for the family to have an understanding of what results are likely to be noticed, and when. Donepezil may help slow the progression of the disease, but progression will continue; the medication is not a cure.
4. After several months of treatment, SR is having difficulty swallowing her medications. The patient's family would like her to remain on a cholinesterase inhibitor because

they feel she has done well on the medications. However, they would like something that is not swallowed, if available. They are concerned about choking. Which medication comes in a nonoral dose form?

- a. Rivastigmine
- b. Galantamine
- c. Tacrine
- d. Donepezil

Answer: a. Rivastigmine is available as a transdermal patch (Exelon) that can be removed and replaced every 24 hours. Donepezil is available in an orally-disintegrating tablet (Aricept ODT) that can be easy to swallow but is not available in a nonoral dosage form. Rivastigmine (Exelon) and galantamine (Razadyne) are available in oral solutions.

REVIEW QUESTIONS

(Answers and Rationales on page 361.)

1. What is akathisia?
 - a. Prolonged unilateral muscular spasms
 - b. Feeling of inner restlessness
 - c. Rigidity of the upper extremities
 - d. Inability to enjoy normal daily activities
 - e. Insomnia due to frequent muscular contractions
2. Which of the following statements regarding Alzheimer disease is/are true?
 - I. Diagnosis is based on the exclusion of other causes of dementia plus a review of history of memory loss and other cognitive impairments.
 - II. Agitation associated with Alzheimer disease can be treated with low doses of antipsychotics.
 - III. Cholinesterase inhibitors may improve memory.
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
3. Which of the following medications exhibit age-related hepatic clearance changes?
 - I. Warfarin
 - II. Theophylline
 - III. Alprazolam
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
4. Levodopa is associated with which of the following adverse effects?
 - I. Gastrointestinal upset
 - II. Orthostatic hypotension
 - III. Involuntary movements
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III

5. Which of the following drugs improves parkinsonian symptoms via anticholinergic activity?
 - a. Benztropine
 - b. Trihexyphenidyl
 - c. Tolcapone
 - d. a and b
 - e. a and c
6. What is NOT true regarding levodopa therapy?
 - a. Levodopa monotherapy requires low doses
 - b. A dopa decarboxylase inhibitor is often administered with levodopa
 - c. Tachycardia and ventricular extrasystoles are adverse effects
 - d. All are false statements
 - e. All are true statements
7. Which of the following drugs improves symptoms of Parkinson disease by increasing levels of dopamine in the brain?
 - a. Selegiline
 - b. Bromocriptine
 - c. Levodopa
 - d. a and b
 - e. a and c
8. Which of the following symptoms is NOT associated with hypothyroidism?
 - a. Decreased appetite
 - b. Drooping eyelids
 - c. Nervousness
 - d. All of the above
 - e. None of the above
9. Which of the following statements regarding cholinesterase inhibitors is true?
 - a. They can be used to treat glaucoma.
 - b. They are ineffective in the treatment of myasthenia gravis.
 - c. They decrease the smooth muscle tone of the bladder.
 - d. a and b
 - e. a and c
10. Which of the following should NOT be used in the treatment of glaucoma?
 - a. Pilocarpine
 - b. Timolol
 - c. Epinephrine
 - d. Atropine
 - e. Physostigmine
11. Alfuzosin relieves symptoms of prostatic hypertrophy via:
 - a. alpha-1 blockage.
 - b. alpha-2 blockage.
 - c. beta-1 blockage.
 - d. beta-2 blockage.
 - e. a and b
12. Total daily doses of levodopa should not exceed _____ per day.
 - a. 0.8 mg
 - b. 8 mg
 - c. 18 mg
 - d. 80 mg
 - e. 800 mg
13. What effect does the addition of carbidopa have on levodopa dosage?
 - a. Levodopa dosage is decreased by 50%.
 - b. Levodopa dosage is increased by 50%.
 - c. Levodopa dosage is decreased by 25%.
 - d. Levodopa dosage is increased by 25%.
 - e. Levodopa dosage is increased by 75%.
14. Which of the following should be avoided in patients on levodopa?
 - a. Monoamine oxidase inhibitors
 - b. Carbidopa
 - c. Diphenhydramine
 - d. Amantadine
 - e. Benztropine
15. Which of the following side effects may occur with levodopa?
 - a. Gastric upset
 - b. Reduced efficacy with prolonged use
 - c. Involuntary movements
 - d. a and b
 - e. a, b, and c
16. What is NOT true regarding amantidine therapy?
 - a. Is an antibiotic with dopaminergic function
 - b. Drug of choice in patients with Parkinson's disease and seizures
 - c. Safer side-effect profile when compared to other Parkinson's drugs
 - d. All of the above
 - e. None of the above
17. What body changes in the elderly can affect pharmacokinetics of drugs?
 - a. Serum albumin
 - b. Body water
 - c. Blood glucose
 - d. a and b
 - e. b and c
18. Which of the following drugs is/are dopamine receptor agonists?
 - I. Tranylcypromine
 - II. Pergolide
 - III. Bromocriptine
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
19. Which of the following drug classes is most often associated with acute cognitive decline?
 - a. Diuretics
 - b. Benzodiazepines

- c. Antidepressants
 - d. Antiarrhythmics
 - e. Antilipemics
20. Which of the following neurochemical changes is most likely the cause of Parkinson's disease?
- a. Increased dopamine
 - b. Decreased dopamine
 - c. Increased acetylcholine
 - d. Decreased acetylcholine
 - e. Increased serotonin
21. The most common community-acquired infection that results in hospitalization for the elderly patient is:
- a. Influenza
 - b. Tuberculosis
 - c. Urosepsis
 - d. Pneumonia
 - e. Infected pressure ulcers
22. Which of the following statements about carbonic anhydrase inhibitors is FALSE?
- a. They can be used preoperatively in acute angle closure glaucoma.
 - b. They inhibit hydrogen ion excretion in the renal tubules.
 - c. They are excreted in the urine predominately as inactive metabolites.
 - d. They may cause ataxia.
 - e. All of the above are true
23. Pilocarpine:
- a. may be used to treat chronic simple glaucoma.
 - b. may cause ciliary spasms.
 - c. is safe in patients with acute inflammation of the anterior chamber.
 - d. a and b
 - e. a, b, and c
24. Phenylephrine:
- a. is an alpha-adrenergic antagonist.
 - b. can be used to treat narrow-angle glaucoma.
 - c. activates the pupillary dilator muscle to cause contraction.
 - d. has a slow onset of action.
 - e. All of the above
25. Physostigmine:
- a. may cause urinary retention.
 - b. inhibits acetylcholine degradation.
 - c. has a duration of action of 5–20 minutes.
 - d. is safe to use in patients with cardiovascular disease.
 - e. All of the above
26. In which of the following patients is physostigmine safe to use?
- a. Patient with type 2 diabetes
 - b. Patient with GI obstruction
 - c. Patient with asthma
 - d. Patient with urinary obstruction
 - e. None of the above
27. Urinary incontinence:
- I. Increases with age
 - II. Can lead to physical and social problems
 - III. Is more common in men than women
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
28. Alzheimer's disease is defined as a:
- a. Psychological condition
 - b. Disease of the arteries
 - c. Physical, degenerative disease of the brain
 - d. Temporary, reversible disease
29. Which of the following diseases or conditions may cause dementia?
- a. Head trauma
 - b. Vitamin b12 deficiency
 - c. Hypothyroidism
 - d. All of the above
 - e. None of the above
30. Which of these conditions may cause dementia?
- a. Excessive exercise
 - b. Fatigue
 - c. Chronic alcoholism
 - d. Overeating
31. Geriatric patients are more sensitive to what drug classes?
- I. Antimicrobials
 - II. Opioids
 - III. Sedative-hypnotics
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
32. Which of the following is NOT a direct-acting alpha agonist?
- a. Metaproterenol
 - b. Amphetamine
 - c. Phenylephrine
 - d. a and b
 - e. a and c
33. Which following agents are selective for beta-1 adrenoceptors?
- a. Brimonidine
 - b. Apraclonidine
 - c. Adrenaline
 - d. Betaxolol
 - e. Timolol
34. Parkinson's disease:
- I. Impairs motor skills and speech
 - II. Is characterized by muscle rigidity and tremor
 - III. Is chronic and progressive

- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
35. Which of the following statements is true?
- a. Alpha agonists stimulate pre- and postsynaptic receptors.
 - b. Cholinergic agonists antagonize acetylcholine at muscarinic and nicotinic sites.
 - c. Atropine antagonizes acetylcholine at muscarinic and nicotinic sites.
 - d. Ganglion blockers enter the CNS and have severe CNS toxicities.
 - e. All of the above
36. Which of the following statements is correct?
- a. Physostigmine and neostigmine are reversible cholinesterase inhibitors.
 - b. Neostigmine is a tertiary amine and physostigmine is a quaternary salt.
 - c. Neostigmine is the drug of choice for reversal of central anticholinergic toxicity.
 - d. Neostigmine has severe adverse effects.
 - e. All are correct
37. Risk factors for glaucoma include the following:
- a. Advanced age
 - b. Elevated intraocular pressure
 - c. African American heritage
 - d. Family history
 - e. All of the above
38. Where are cholinergic synapses NOT located?
- a. Sympathetic ganglion cells
 - b. Motor end plates
 - c. Autonomic effector sites
 - d. Adrenal medulla
 - e. They are located at all of the above
39. Which of the following is most likely to cause the following symptom constellation?
Iris radial muscle contraction
Hyperglycemia
Arteriolar constriction
- a. Alpha agonist
 - b. Alpha antagonist
 - c. Beta agonist
 - d. Muscarinic agent
 - e. Antimuscarinic agent
40. Which of the following is true regarding diphenhydramine?
- I. Possesses local anesthetic activity
 - II. May be used to treat tremor of early Parkinson's disease
 - III. Originally marketed as Bendectin
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
41. Which best describes the mechanism of action of donepezil?
- a. Histamine antagonist
 - b. NMDA receptor antagonist
 - c. Acetylcholinesterase inhibitor
 - d. Beta-2 antagonist
 - e. None of the above
42. Primary open-angle glaucoma:
- a. is more likely to result in blindness in blacks than in whites.
 - b. usually has an onset in the second decade of life.
 - c. can be treated with topical medications that decrease aqueous outflow.
 - d. a and b
 - e. b and c
43. On ophthalmologic examination of an eye with glaucoma, which of the following findings is expected?
- a. Optic nerve cupping
 - b. Retinal hemorrhage
 - c. Retinal exudates
 - d. Optic nerve edema
 - e. Vascular blebbing
44. Which of the following is the appropriate dosage for immediate treatment of acute angle-closure glaucoma?
- a. 10% timolol
 - b. 10% apraclonidine
 - c. 20% apraclonidine
 - d. 2% pilocarpine
 - e. 20% pilocarpine
45. Risk factors for angle-closure glaucoma include:
- a. male sex.
 - b. Asian race.
 - c. age older than 40 years.
 - d. a and b
 - e. b and c
46. Side effects of glaucoma treatments include:
- I. Sweating for pilocarpine
 - II. Eyelid swelling for apraclonidine
 - III. Hypertension for timolol
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
47. Which best describes the mechanism of action of entacapone?
- a. Catechol-O-methyltransferase (COMT) inhibitor
 - b. Alpha agonist
 - c. Acetylcholinesterase inhibitor
 - d. NMDA receptor antagonist
 - e. None of the above

48. Which of the following is/are a direct-acting cholinergic agonist?
- Pilocarpine and propantheline
 - Pilocarpine and bethanechol
 - Propantheline and physostigmine
 - Physostigmine and muscarine
 - Physostigmine
49. Which of the following is NOT correct regarding anticholinesterases?
- They cause bronchoconstriction
 - They augment bronchiolar and lacrimal secretory activity
 - They cause urinary retention
 - They increase peristaltic activity
 - They cause miosis when applied topically
50. Which of the following is the most common joint disorder in the elderly?
- Neuropathic osteoarthropathy
 - Rheumatoid arthritis
 - Osteoarthritis
 - Osteoporosis
 - Gout

Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome (HIV/AIDS)

15 CHAPTER

I. Introduction and Definitions

- A. The human immunodeficiency viruses (HIV-1 or HIV-2) are the viruses that cause HIV infection and the acquired immune deficiency syndrome (AIDS). HIV primarily attacks the immune system, making the patient extremely vulnerable to opportunistic infections (infections caused by pathogens that generally do not affect those with healthy immune systems). HIV primarily infects and destroys immune T-cells that have the CD4 receptor protein on their cell surfaces (also called CD4-positive or CD4+ T-cells). Healthy individuals have a CD4+ cell count between 600 and 1200 cells per microliter of blood. HIV patients have less than 600 CD4+ cells per microliter of blood; the lower the CD4+ count, the weaker the immune system.
- B. When a patient is determined to be HIV-positive, CD4+ cell counts and the measurement of the HIV-RNA level (a determinant of viral load) are assessed to determine when treatment should be initiated and with what medications. These tests are also monitored on a regular basis after treatment is initiated to determine clinical response. A lack of clinical response to treatment may indicate viral resistance or patient noncompliance, and a regimen change may be needed.
- C. HIV infection progresses to AIDS if the CD4+ cell counts drop to less than 200 cells per microliter. This may happen if the infected individual receives inadequate treatment or develops a major infection. Individuals with a CD4+ cell count less than 200 have the greatest risk of developing opportunistic infections, such as *Pneumocystis pneumonia* (PCP), *Mycobacterium avium* complex (MAC) infections, or Kaposi sarcoma.
- D. According to the United States Centers for Disease Control and Prevention (CDC), approximately 56,300 patients were newly infected with HIV in 2006, which is a 40% increase from the 40,000 annual estimate used for past years. The increased number may be due to more accurate lab testing and new statistical methods, not a worsening of the epidemic. The number of AIDS-related deaths continues to decline, with an 8% decrease from 2000 through 2004. Advanced treatments can attribute to increased survival, thus resulting in an increased number of people in the United States who are living with HIV infection and AIDS.

II. Signs and Symptoms

- A. Many patients are asymptomatic when they first become infected with HIV. One to 2 months after infection, some HIV patients develop flu-like or mononucleosis-like symptoms that last about 1 to 3 weeks. For the next several months or years, patients usually do not experience any symptoms of the disease. Once this asymptomatic period ends, symptoms may include enlarged lymph nodes (persistent lymphadenopathy), fatigue, weight loss, frequent fevers and sweats, persistent or frequent yeast infections of the mouth or vagina, persistent skin rashes, flaky skin, pelvic inflammatory disease (PID) in women, and short-term memory loss. As the immune system continues to weaken, patients may eventually progress to AIDS. During this stage, patients have the greatest risk of developing life-threatening opportunistic infections. HIV-related cachexia, HIV-associated dementia, and certain cancers may also occur in late-stage disease.

III. Treatment

- A. Antiretroviral agents should be used in combination with at least three agents, a strategy known as highly active antiretroviral therapy (HAART). In the United States, updated treatment guidelines, drug information, and other resources formulated for consumers and healthcare professionals can be found at the following website: (www.aidsinfo.nih.gov)
- B. Initial combination regimen (antiretroviral naïve patients): use either a nonnucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI) or integrase strand transfer inhibitor (INSTI) in combination with at least two nucleoside/nucleotide reverse transcriptase inhibitors (NRTI):
 1. one NNRTI + two NRTI
 2. single PI or ritonavir-boosted PI + two NRTI
 3. INSTI + two NRTI

The selection of specific agents to use for a particular individual is determined by efficacy and safety of the agents in combination in controlled clinical trials, and the regimens are individualized by considering side effects, drug interactions, compliance factors (pill burden), concurrent disease states, and other factors. Combination dosage forms are available that may help patients with compliance goals.

1. Individual antiretroviral agents used in treatment of HIV-positive patients
 - (a) NRTI

Table 15-1 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI) Combination Products

Brand Name	Active Ingredients	Normal Adult Dosage
Atripla	Efavirenz 600 mg, Emtricitabine 200 mg, Tenofovir 300 mg	1 PO qd
Combivir	Zidovudine 300 mg, Lamivudine 150 mg	1 PO bid
Epzicom	Abacavir 600 mg, Lamivudine 300 mg	1 PO qd
Trizivir	Zidovudine 300 mg, Lamivudine 150 mg, Abacavir 300 mg	1 PO bid
Truvada	Tenofovir 300 mg, Emtricitabine 200 mg	1 PO qd

- (i) Mechanism of action: cause chain termination thereby inhibiting HIV viral replication
- (ii) Examples
 - a. Zidovudine (AZT; Retrovir)
 - b. Didanosine (ddI, Videx, Videx EC)
 - c. Lamivudine (3TC, Epivir)
 - d. Zalcitabine (ddC, Hivid)
 - e. Stavudine (d4T, Zerit)
 - f. Abacavir (ABC, Ziagen)
 - g. Emtricitabine (Emtriva)
- (iii) Adverse effects (primary drug examples noted in parenthesis where relevant):
 - a. All have boxed warning: lactic acidosis with hepatic steatosis. Gastrointestinal disturbances (diarrhea, nausea/vomiting), and headache are common side effects of all.
 - b. Myelosuppression (including neutropenia and anemia) (primary example: zidovudine)
 - c. Pancreatitis (primary examples: didanosine [boxed warning], stavudine)
 - d. Peripheral neuropathy (primary examples: zalcitabine and stavudine)
 - e. Fatal hypersensitivity reactions (primary example: abacavir [boxed warning], genetic screening required before drug use with HLA-B*5701 test)
- (iv) Avoid using these NRTI together due to poor efficacy in combination:
 - a. Thymidine analogs: zidovudine + stavudine
 - b. Cytidine analogs: lamivudine + emtricitabine
- (v) Use caution with these NRTI together (regimens not recommended per expert guidelines):
 - a. Didanosine + stavudine due to increased toxicities

- b. Didanosine + tenofovir due to drug interaction; dose reduction of didanosine required

(b) NNRTI

- (i) Mechanism of action: bind to site on viral reverse transcriptase, different from NRTI; results in blockade of RNA and DNA dependent DNA polymerase activity
 - a. Does not compete with nucleoside triphosphates
 - b. Does not require phosphorylation
- (ii) Examples
 - a. Nevirapine (Viramune)
 - b. Delavirdine (Rescriptor)
 - c. Efavirenz (Sustiva)
 - d. Etravirine (Intelence)
- (iii) Adverse effects (primary examples in parenthesis)
 - a. Rash; Stevens-Johnson syndrome (nevirapine)
 - b. Elevated liver function tests (LFT); severe hepatotoxicity (nevirapine)
 - c. Central nervous system (CNS) symptoms (efavirenz)
 - d. Teratogenic (delavirdine and efavirenz)
- (iv) Drug interactions
 - a. Inhibitor of CYP3A4 (delavirdine)
 - b. Inducer of CYP3A4 (nevirapine)
 - c. Mixed induction/inhibition of CYP3A4 (efavirenz)
 - d. St. John's wort reduces activity of all NNRTI and should be avoided.
- (c) Protease inhibitors (PI)
 - (i) Mechanism of action: protease enzyme cleaves precursor molecules to produce mature, infectious virions
 - a. Inhibit protease and prevent the spread of infection
 - b. Metabolized through the liver through CYP3A4 pathway
 - (ii) Examples:
 - a. Atazanavir (Reyataz)
 - b. Darunavir (Prezista)
 - c. Fosamprenavir (Lexiva)
 - d. Indinavir (Crixivan)
 - e. Lopinavir/Ritonavir (Kaletra)
 - f. Nelfinavir (Viracept)
 - g. Saquinavir (Invirase)
 - h. Tipranavir (Aptivus)
 - i. Ritonavir (Norvir)
 - (iii) Adverse effects (common to many PI, primary examples noted in parenthesis where relevant)
 - a. Fat redistribution
 - b. Insulin resistance
 - c. Lipid abnormalities
 - d. GI intolerance
 - e. Headache
 - f. Hyperbilirubinemia (indinavir and ritonavir)
 - g. Rash, including Stevens-Johnson syndrome (amprenavir)

- h. Hepatitis, intracranial hemorrhage (tipranavir, boxed warning)
 - i. Nephrolithiasis (indinavir)
 - (iv) Drug interactions
 - a. St. John's wort reduces activity of all PI and should be avoided.
 - b. PI agents exhibit complicated drug interaction profiles and drug interactions should be reviewed for each specific agent with proper drug information resources. Ritonavir is an especially potent inhibitor of CYP isoenzymes.
 - (d) Nucleotide inhibitors
 - (i) Tenofovir (Viread)
 - a. Mechanism of action: competitively inhibits HIV reverse transcriptase and causes chain termination after incorporation into DNA
 - b. Used in combination with other antiretrovirals for HIV-1 suppression
 - (ii) Adefovir (Hepsera)
 - a. Mechanism of action: Competitively inhibits HBV DNA polymerase and results in chain termination after incorporation into viral DNA
 - b. Used for hepatitis B, not for HIV
 - c. Adverse effects: nephrotoxicity
 - (e) Fusion inhibitors: Enfuvirtide (Fuzeon)
 - (i) Mechanism of action: binds to gp41 subunit and prevents conformational changes for fusion
 - (ii) Dosage: 90 mg SC bid
 - (iii) Adverse effects: injection site reactions, fever, flu like symptoms. May cause allergic reactions.
 - (f) Entry inhibitor: Maraviroc (Selzentry)
 - (i) Mechanism of action: Blocks CCR5 receptor, one of the receptors HIV uses to enter its target cell; prevents infection of the cell
 - (ii) Used in treatment-experienced patients
 - (iii) Adverse effects: Cough, rash, dizziness. May cause liver toxicity (boxed warning), allergic reaction
 - (g) Integrase inhibitor: Raltegravir (Isentress)
 - (i) Mechanism of action: Interferes with integrase, a viral enzyme responsible for replication
 - (ii) Used in treatment-experienced patients with documented resistant strains and per guidelines can be used first line treatment in naive patients
 - (iii) Adverse effects: Nausea, diarrhea, headache. May cause myopathy and rhabdomyolysis.
2. Treatment of specialized circumstances resulting in HIV exposure
- a. Vertical transmission, also known as mother-to-child transmission
 - (1) Two drugs effective as monotherapy to prevent perinatal transmission
 - (a) Zidovudine
 - (b) Nevirapine
 - b. Postexposure prophylaxis (HIV-PEP)
 - (1) Basic regimens
 - (a) Zidovudine + lamivudine (available as Combivir)
 - (b) Zidovudine + emtricitabine
 - (c) Tenofovir DF + lamivudine
 - (d) Tenofovir DF + emtricitabine (available as Truvada)
 - (i) Alternative regimens
 - a. Lamivudine + stavudine
 - b. Emtricitabine + stavudine
 - c. Lamivudine + didanosine
 - (2) Expanded regimens consist of one of the following
 - (a) Lopinavir/ritonavir (Kaletra)
 - (b) Atazanavir + ritonavir
 - (c) Fosamprenavir + ritonavir
 - (d) Indinavir + ritonavir
 - (e) Saquinavir + ritonavir
 - (f) Nelfinavir
 - (g) Efavirenz
 - (3) Antiretrovirals NOT generally recommended for prophylaxis
 - (a) Nevirapine
 - (b) Delavirdine
 - (c) Abacavir
 - (d) Zalcitabine

References

1. Depiro J: *Pharmacotherapy: A pathophysiological approach*, ed 7, McGraw-Hill Medical, 2008.
2. AIDS info, Clinical Guidelines Portal. US Department of Health and Human Services. Available at: <http://www.aidsinfo.nih.gov/guidelines>. (Accessed Feb 2, 2010)

PATIENT PROFILE

Patient Initials: KT

Sex: Male

Age: 33 years

Height: 5' 10"

Weight: 64 kg

Race: Latin American

Allergies: Penicillin (rash)

Chief Complaint/History: None. Patient goes to clinic pharmacy today for new highly active antiretroviral therapy prescriptions; recently HIV regimen changed due to HIV viral load studies and decreasing CD4 counts. Reyataz and Truvada are new prescriptions.

Medical History:

Diagnosed with HIV in 2001

Episode of *Pneumocystis pneumonia* (PCP) in 2006

Significant laboratories at last medical appointment:

CD4+ cell count: 150 per mm³ (was >200 cells/mm³ 6 months ago)

Social History:

Tobacco use: 1 pack-per-day until 2002; none currently

Alcohol use: 1 glass of wine or a beer with dinner several times per week

Medications:

Truvada 1 tablet PO q day (new)

Reyataz 150 mg, 2 capsules PO q day (new)

Norvir 100 mg, 1 capsule PO q day

Therapeutic multivitamin with minerals PO once per day

PATIENT PROFILE QUESTIONS

- When dispensing Norvir capsules to KT, which of the following apply?

- If stored at room temperature, the patient should discard the capsules after 60 days.
- The capsules are best stored refrigerated.
- The capsules should be dispensed in the original container.

- I only
- II only
- III only
- I and III
- II and III

Answer: b. If Norvir is stored at room temperature, the capsules should be discarded after 30 days, not 60 days. There is no requirement to dispense the capsules in the original container. Preferably, the capsules are stored under refrigeration.

- Based on current CD4 counts, the practitioner decides that a PCP prophylaxis regimen should be initiated. Which of the following is considered the first-line regimen for prophylaxis of PCP?

- Dapsone 100 mg PO every day
- Bactrim DS 1 tablet PO every day
- Atovaquone 750 mg PO twice daily

Answer: b. The combination of sulfamethoxazole (SMZ) with trimethoprim (TMP) is considered first line for PCP prophylaxis. Numerous trials have indicated its effectiveness; patients taking SMZ-TMP regimens have approximately a 5% chance of developing PCP. SMZ-TMP treatment may also prevent other infections, such as toxoplasmosis. PCP prophylaxis is usually started when CD4 counts are lower than 200, as is the case with KT's most recent laboratories. The other regimens are acceptable alternatives; however, atovaquone is expensive, and is not always recommended by organizations that govern guidelines for patients with HIV.

- Appropriate counseling regarding how KT should take the Reyataz in the antiviral regimen include which of the following?

- Take at the same time as Norvir.
- Take on an empty stomach, 2 hours before a meal.
- Take with food.
- Take at the same time as Truvada.

- I only
- II only
- III only
- II and IV
- I and III

Answer: e. To reach appropriate serum concentrations for efficacy in this triple drug antiretroviral regimen, Reyataz (atazanavir) is "boosted" with Norvir (ritonavir), and the two drugs are best taken at the same time to accomplish this. Also, Reyataz is taken with food for best absorption. The patient should be counseled with regard to optimal drug administration and compliance.

- Which of the following are the most common side effects for Truvada?

- Diarrhea, nausea, headache, strange dreams, sleeping problems
- Lipodystrophy
- Lactic acidosis
- Liver problems

- I and II
- II and III
- III and IV

Answer: a. Lipodystrophy (change in distribution of body fat) is a common side effect with longer use of antiretroviral medications such as Truvada (emtricitabine, tenofovir). The side effects listed in I are the most common patients notice. Lactic acidosis, liver problems (steatosis and hepatomegaly), kidney problems, or pancreatitis are potential serious side effects of this drug combination that are less common.

REVIEW QUESTIONS

(Answers and Rationales on page 363.)

- A 21-year-old, HIV-positive man presents to the HIV clinic for examination. A PPD is placed, and when he returns to clinic 3 days later, is found to be positive. His LFTs are normal, and he is begun on anti-TB therapy. In addition to clinical evaluation for adverse events, what is the most appropriate monitoring regimen?
 - Only clinical examination and interview is needed
 - Measure LFT monthly
 - Measure LFT every 8 weeks
 - Measure LFT at 2, 4, and 6 weeks
 - None of the above
- Which of the following are non-nucleoside reverse transcriptase inhibitors?
 - Ganciclovir
 - Nevirapine
 - Efavirenz
 - I only
 - III only
 - I and II
 - II and III
 - I, II, and III

3. A 35-year-old HIV-positive woman goes to the urgent care clinic with complaints of genital herpes. She reports parasthesias for 4 days and developed vesicular lesions on her labia this morning. The patient explains that this is her third outbreak in 6 months. What is the most appropriate therapy?
 - a. Valacyclovir, 1 g PO bid for 5 days
 - b. Valacyclovir, 500 mg PO bid for 3 days
 - c. Famciclovir, 500 mg PO qd for 5 days
 - d. Acyclovir, 400 mg PO tid as continuous suppressive therapy
 - e. Acyclovir, 400 mg PO tid for 3 days
4. A 30-year-old woman presents to the HIV clinic after diagnosis at another hospital. Laboratory evaluation reveals the following:

RPR: positive
FTA-ABS: positive
Lumbar puncture: 70 WBC, normal protein, negative VDRL

The patient reports anaphylactoid reaction to penicillin several years ago. What is the most appropriate course of therapy?
 - a. Perform penicillin skin test followed by desensitization
 - b. Benzathine penicillin G 2.4 mU IM q week for 3 weeks
 - c. Benzathine penicillin G 2.4 mU IM for one dose
 - d. a and b
 - e. a and c
5. What statements are TRUE about protease inhibitors?
 - a. Ritonavir (Norvir), saquinavir (Invirase, Fortovase) and indinavir (Crixivan) are examples of protease inhibitors
 - b. Protease inhibitors inhibit cytochrome P450 oxidations
 - c. Select antihistamines and benzodiazepines are contraindicated with protease inhibitors
 - d. All of the above
 - e. None of the above
6. CO is a 35 year-old HIV-positive patient who is receiving HAART regimen. About a month after initiating therapy, he comes to the emergency department complaining of severe flank pain, frequent urination, and nausea. Which of the following drugs is the most likely cause of his symptoms?
 - a. Nevirapine
 - b. Indinavir
 - c. Didanosine
 - d. Efavirenz
 - e. Zidovudine

Kidney Disorders

16 CHAPTER

I. Background

- A. The kidneys are responsible for removing toxins, chemicals, and waste products from the blood; regulating acid concentration; and maintaining water and electrolyte balance in the body by excreting urine.

Table 16-1 National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI™) Staging System for Chronic Kidney Disease

Stage	Description	Glomerular Filtration Rate (GFR) (mL/min/1.73 m ²)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with a mild decrease in GFR	60–89
3	Moderate decrease in GFR	30–59
4	Severe decrease in GFR	15–29
5	Kidney failure	<15 (or dialysis)

Reprinted from American Journal of Kidney Diseases, 39(2):35, 2002, with permission from Elsevier.

II. Common Types and Causes of Kidney Disorders

A. Fanconi syndrome

1. Definition: The tubes in the kidneys do not work properly.
 - a) Unable to reabsorb glucose, amino acids, small proteins, water, calcium, potassium, magnesium, bicarbonate, and phosphate, making the blood overly acidic
 - b) May be caused by inherited disorders such as cystinosis, galactosemia, glycogen storage disease, hereditary fructose intolerance, Lowe syndrome, Wilson's disease, tyrosinemia, medullary cystic disease, and vitamin D dependency; exposure to heavy metals, certain drugs, chemicals (e.g., toluene), or dietary supplements (e.g., lysine); and may even result from kidney transplantation
2. Signs and symptoms
 - a) Increased urination, excessive thirst, dehydration, constipation, anorexia nervosa, vomiting, high levels of sugar, phosphate,

calcium, uric acid, amino acids, and protein in the urine, high levels of chloride and low levels of phosphate and calcium in the blood

3. Treatment

- a) Replacement of fluids and nutrients lost in urine
- b) Addition of sodium bicarbonate, a diuretic such as hydrochlorothiazide, and supplementation with vitamin D and phosphate

B. Glomerulonephritis

1. Definition: an acute or chronic kidney disease that occurs when the kidneys are unable to properly remove waste and excess fluids from the body. This occurs when there is glomerular damage from immune or inflammatory reactions and lesions.
2. It can occur by itself or in conjunction with other diseases such as lupus, Goodpasture syndrome, diabetes, immunoglobulin A (IgA) nephropathy, polyarteritis, Wegener granulomatosis, or infection with streptococcus, HIV, hepatitis B or C
3. Signs and symptoms: dark-colored urine, foamy urine, high blood pressure, fluid retention that causes swelling, fatigue, and less-frequent urination
4. Treatment
 - a) The goal of treatment is to reduce the decline of kidney function and control blood pressure. Corticosteroids are often used to reduce kidney inflammation. Diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor agonists (ARB), calcium channel blockers, or beta blockers may be used.

C. Focal segmental glomerulosclerosis (FSGS)

1. Definition: A type of glomerular disease that can cause permanent kidney disease in children and adults by attacking the glomeruli, the tiny structures inside the kidneys where blood is filtered. The most common sign of FSGS is the nephrotic syndrome, which is characterized by fluid in the body tissues that causes swelling, excess protein in the urine, hypoalbuminemia, and high cholesterol.
2. Signs and symptoms
 - a) Fatigue, nausea, headache, foamy urine, weight gain, poor appetite, proteinuria

- b) Patients develop nephrotic syndrome, which is characterized by fluid retention that causes swelling and weight gain of 15 to 20 pounds or more, foamy urine, abnormally low levels of albumin in the blood, hypertension, and high cholesterol. Fluid in the lung cavity, abdomen, and in the sac that surrounds the heart may build-up and fill the cavities.
- c) Treatment
 - (1) Nonpharmacologic
 - (a) Reducing daily intake of salt to 2 grams
 - (b) Reduce fat intake
 - (c) Protein restriction
 - (2) Pharmacologic
 - (a) Immunosuppressants such as prednisone, cyclophosphamide, cyclosporine, or mycophenolate mofetil may be used.
 - (b) Diuretics, ACE inhibitors, ARB, calcium channel blockers, or beta blockers may also be used for treatment.
- D. Kidney stones: Kidney stones (also called renal calculi, urinary calculi, urolithiasis, or nephrolithiasis) usually develop when the urine becomes too concentrated. As a result, minerals and other substances in the urine form hard crystals on the inner surfaces of the kidneys. Over time, these crystals may combine to form a small, hard mass, or stone.
 - 1. Calcium stones are the most common type of kidney stones, accounting for 80% of cases. Calcium stones develop when there are high levels of calcium (hypercalcemia) and oxalate in the blood.
 - 2. Struvite stones are usually caused by chronic urinary tract infections. The bacteria that cause these infections release enzymes that increase the amount of ammonia in the urine. This excess ammonia may form large, sharp stones that can potentially damage the kidneys.
 - 3. Cystine stones develop in patients who have an inherited disorder called cystinuria. This disorder causes the kidneys to release too many amino acids, which then form stones.
 - 4. Signs and symptoms
 - a) Patients may experience intense pain that comes and goes, lasting 5 to 15 minutes at a time. Pain usually begins in the lower back and moves to the abdomen, groin, or genital areas as the stone moves from the kidney toward the bladder. Other symptoms include blood in the urine, cloudy or foul-smelling urine, nausea, vomiting, and constant urge to urinate
 - 5. Treatment
 - a) Calcium stones: Thiazide diuretics lower urine calcium in idiopathic hypercalciuria and are effective in preventing the formation of stones.
 - b) Uric acid stones: The two goals of treatment are to raise urine pH and to lower excessive urine uric acid excretion to less than 1 g per day. Supplemental alkali, 1–3 mmol/kg of body weight per day, should be given in three or four evenly spaced, divided doses, one of which should be given at bedtime.
 - c) Cystine stones: high fluid intake, even at night. Daily urine volume should exceed 3 L. Raising urine pH with alkali is helpful, provided the urine pH exceeds 7.5.
 - d) Struvite stones: Complete removal of the stone and subsequent sterilization of the urinary tract is the treatment of choice for patients who can tolerate the procedures. Irrigation of the renal pelvis and calyces with hemiacidrin, a solution that dissolves struvite. For patients who are not candidates for surgery, acetohydroxamic acid, and inhibitor of urease, can be used.
- E. Nephrotoxicity
 - 1. Definition: A term used to describe toxic damage in the kidneys; electrolytes in the blood, including potassium and magnesium, build up to toxic levels.
 - a) Certain medications, such as cyclosporine (Neoral or Sandimmune), tenofovir (Viread), intravenous vancomycin (Vancocin), and systemic gentamicin (Garamycin) and other aminoglycosides, may have toxic effects on the kidneys.
 - 2. Signs and symptoms
 - a) Increased urination, dark urine, blood in the urine, and frequent urge to urinate
- F. Diabetic nephropathy
 - 1. Kidney disease that develops as a result of diabetes mellitus (DM); most common cause of kidney failure in the United States, accounts for more than one third of all patients who are on dialysis
 - 2. Approximately 25% to 40% of patients with DM type 1 ultimately develop diabetic nephropathy (DN), which progresses through five predictable stages.
 - a) Stage 1 (very early diabetes): above-normal glomerular filtration rate (GFR)
 - b) Stage 2 (developing diabetes): GFR remains elevated or has returned to normal, but glomerular damage has progressed to significant microalbuminuria (small but above-normal level of the protein albumin in the urine).
 - c) Stage 3 (overt, or dipstick-positive diabetes): Glomerular damage has progressed to clinical albuminuria.
 - d) Stage 4 (late-stage diabetes): Glomerular damage continues, with increasing amounts of protein albumin in the urine. The kidneys' filtering ability has begun to decline steadily, and blood urea nitrogen (BUN) and serum creatinine (SCr) has begun to increase. The GFR decreases approximately 10% annually. Almost all patients have hypertension at stage 4.
 - e) Stage 5 (end-stage renal disease [ESRD]): GFR has fallen to approximately 10 mL/min, and renal replacement therapy (i.e., hemodialysis,

peritoneal dialysis, kidney transplantation) is needed.

G. Nephrotic syndrome

1. Nephrotic syndrome is a disorder of the glomeruli (clusters of microscopic blood vessels in the kidneys that have small pores through which blood is filtered) in which excessive amounts of protein are excreted in the urine (proteinuria). This typically leads to accumulation of fluid in the body (edema), low levels of the protein albumin (hypoalbuminemia), and high levels of fats (hyperlipidemia) in the blood.
2. Causes: DM, systemic lupus erythematosus, amyloidosis certain viral infections, glomerulonephritis, nonsteroidal anti-inflammatory drugs (NSAID), allergies to insect bites and to poison ivy or poison oak, hereditary
3. Signs and symptoms: loss of appetite, a general feeling of illness (malaise), puffy eyelids and tissue swelling, abdominal pain, wasting of muscles (atrophy), frothy urine, swollen abdomen, shortness of breath, swelling of the knees and, in men, the scrotum, shock. Blood pressure is generally low in children and may fall when the child stands up. Adults may have low, normal, or high blood pressure, urine production may decrease, and kidney failure may develop if the leakage of fluid from blood vessels into tissues depletes the liquid component of blood and the blood supply to the kidney is diminished. Other signs and symptoms are in nutritional deficiencies, growth may be stunted, calcium loss from bones, brittle nails and hair, hair loss

H. Drug-induced glomerular disease: Various drugs damage the glomerular filtration barrier and induce proteinuria and nephritic syndrome. Drugs that may cause glomerular disease include NSAID, recombinant interferon A, rifampin, penicillin, ampicillin, amoxicillin, gold, penicillamine, trimethadione, captopril, chlormethiazole, ciprofloxacin, hydralazine, allopurinol, sulfonamides, thiazides, warfarin, carbimazole, heroin, and amphetamines

1. Acute renal failure (ARF): a syndrome characterized by rapid decline in glomerular filtration rate (hours to days), retention of nitrogenous waste products, and perturbation of extracellular fluid volume and electrolyte and acid-base homeostasis. Discontinuation of the offending agents such as NSAID and hydration can be used to treat ARF.
- I. End-stage renal disease (ESRD): End-stage kidney disease is a complete or near complete failure of the kidneys to function to excrete wastes, concentrate urine, and regulate electrolytes. End-stage kidney disease occurs when the kidneys are no longer able to function at a level that is necessary for day-to-day life. It usually occurs as chronic renal failure worsens to the

point where kidney function is less than 10% of normal. At this point, the kidney function is so low that without dialysis or kidney transplantation, complications are multiple and severe, and death occurs from accumulation of fluids and waste products in the body.

1. Treatment of renal disease

The following treatments are intended for treatment or prevention of the worsening or progression of renal disease

a) Diuretics

- (1) Loop diuretics (furosemide, torsemide, and bumetanide) inhibit the body's ability to reabsorb sodium at the ascending loop of Henle, which leads to a retention of water in the urine because water normally follows sodium back into the extracellular fluid (ECF).
- (2) Thiazides such as hydrochlorothiazide act on the distal tubule and inhibit the sodium-chloride symporter leading to retention of water in the urine as water normally follows penetrating solutes. Metolazone is not a true thiazide, but it is a sulfonamide derivative such as thiazides, and its site of action is similar. Metolazone is an oral quinazoline diuretic for the management of edema and hypertension.
- (3) Potassium-sparing diuretics such as spironolactone, amiloride, and triamterene do not promote the secretion of potassium into the urine; thus, potassium is spared and not lost as much as in other diuretics.
- (4) Osmotic diuretics (e.g. mannitol, glucose) are filtered in the glomerulus, but cannot be reabsorbed. Their presence leads to an increase in the osmolarity of the filtrate. To maintain osmotic balance, water is retained in the urine.

b) Albumin: Exogenous administration of albumin increases the oncotic pressure of the intravascular system, pulling fluids from the interstitial space, thereby decreasing edema and increasing the circulating blood volume.

c) Antihypertensives (ACE inhibitors, ARB): reduces the amount of protein in the urine by reducing the amount of pressure and resistance on blood as it circulates through the body. Patients who cannot tolerate ACE inhibitors may use an ARB (e.g., losartan, valsartan). Both ACE inhibitors and ARB can cause hyperkalemia (abnormally high level of potassium in the blood) in patients with chronic renal failure.

2. Dosing Adjustments: Dosages of renally excreted drugs may need to be adjusted according to kidney function. Dose adjustment can be based on serum creatinine level, subsequent creatinine clearance estimation,

and dosage calculation. Cockcroft-Gault equation or the Modification of Diet in Renal Disease (MDRD) study equations may be used for routine estimation of GFR.

- a) Drugs that may require dosage adjustments include ACE inhibitors, beta blockers, diuretics, antimicrobial agents, some hypoglycemic agents (metformin is not recommended for use in patients with kidney failure), some antimicrobial agents (e.g., azole antifungals, acyclovir, carbapenems, cephalosporins, penicillins, quinolones), analgesics, statins, and others.
 - b) Dosing recommendations for individual drugs can be found in *Drug Prescribing in Renal Failure: Dosing Guidelines for Adults* (Aronoff GR: *Drug prescribing in renal failure: dosing guidelines for adults*, ed 4, Philadelphia, 1999, American College of Physicians)
3. Dialysis
- a) Dialysis works on the principles of the diffusion of solutes and convection of fluid across a semipermeable membrane. Blood flows by one side of a semipermeable membrane, and a dialysate or fluid flows by the opposite side. Smaller solutes and fluid pass through the membrane. The blood flows in one direction and the dialysate flows in the opposite direction. The concentrations of undesired solutes (e.g., potassium, calcium, and urea) are high in the blood, but low or absent in the dialysis solution, and constant replacement of the dialysate ensures that the concentration of undesired solutes is kept low on this side of the membrane. The dialysis solution has levels of minerals such as potassium and calcium that are similar to their natural concentration in healthy blood. For another solute, bicarbonate, dialysis solution level is set at a slightly higher level than in normal blood, to encourage diffusion of bicarbonate into the blood, to neutralize the metabolic acidosis that is often present in these patients.
 - b) There are two primary types of dialysis: hemodialysis and peritoneal dialysis.
 - (1) In hemodialysis, the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a semipermeable membrane. The cleansed blood is then returned via the circuit back to the body.
 - (2) In peritoneal dialysis, a sterile solution containing minerals and glucose is run through a tube into the peritoneal cavity, the abdominal body cavity around the intestine, where the peritoneal membrane acts as a semipermeable membrane. The dialysate is left there for a period of time to absorb waste products, and then it is drained out through the tube and

discarded. This cycle or "exchange" is normally repeated 4 to 5 times during the day or sometimes more often overnight with an automated system.

- c) Continuous veno-venous hemofiltration (CVVH): a short-term treatment, used in patients with kidney failure. The kidney failure may be new or already present. Hemodialysis (kidney dialysis) is usually done for kidney failure. However, if a patient has low blood pressure, CVVH may be needed. As in dialysis, in hemofiltration one achieves movement of solutes across a semipermeable membrane. However, solute movement with hemofiltration is governed by convection rather than by diffusion. With hemofiltration, dialysate is not used. Instead, a positive hydrostatic pressure drives water and solutes across the filter membrane from the blood compartment to the filtrate compartment, from which it is drained. Solute, both small and large, get dragged through the membrane at a similar rate by the flow of water that has been engineered by the hydrostatic pressure. Convection overcomes the reduced removal rate of larger solutes (due to their slow speed of diffusion) seen in hemodialysis.
- J. IgA nephropathy is a common kidney disease that progresses very slowly. It often leads to decreased kidney function and ultimately to kidney failure. The cause of this disease is not known, although most people with the disease have abnormalities in their immune system. Patients with IgA nephropathy treated with immunosuppressive drugs, such as steroids, may be less likely to develop kidney failure.

PATIENT PROFILE

Patient Initials: AM

Sex: Male

Age: 43

Height: 5'11"

Weight: 180 lb

Race: White

Allergies: No known drug allergies (NKDA)

Chief Complaint/History: AM is admitted to the hospital after progression of renal disease secondary to diabetes (diabetic nephropathy). He will receive an arteriovenous (AV) fistula and will begin dialysis sessions this week; a central line is inserted for dialysis until the fistula is deemed ready for use.

Medical History:

Diabetes type 2 for 10 years, has been insulin dependent for 3 years

Hypertension

Family History: Significant for obesity, hypertension, and cardiovascular disease. Father had myocardial infarction (MI) last year at age 67.

Admission Laboratories:

Sodium: 136 mEq/L

Potassium: 5.0 mEq/L
 Chloride: 102 mEq/L
 CO₂ content: 20 mEq/L
 BUN: 60 mg/dL
 Serum creatinine: 6 mg/dL
 Glucose: 202 mg/dL
 Calcium: 10.1 mg/dL
 Phosphorous: 6.6 mg/dL
 Albumin: 2.5 g/dL

Social History:

Tobacco use: None

Alcohol use: Occasional beer on weekends

Employment: Postal carrier, job requires several miles of walking daily for deliveries

Medications before this admission:

Diovan 80 mg PO once daily

Furosemide 40 mg PO once daily

Humulin N insulin 20 units SQ in morning and 10 units in evening

Insulin aspart, SQ sliding scale with meals; amount adjusted based on carbohydrate intake

Calcium acetate 667 mg, 2 tablets PO three times daily at meals

Nephro-Vite 1 tablet PO daily

PATIENT PROFILE QUESTIONS

1. All of the following are some of the potential complications of chronic renal failure and end-stage renal disease (ESRD) EXCEPT:

- a. hyperphosphatemia.
- b. hypokalemia.
- c. anemia.
- d. bone disease (renal osteodystrophy).

Answer: b. Renal insufficiency causes accumulation of potassium, resulting in hyperkalemia (increased serum potassium).

2. AM has edema on admission. What would be an appropriate diuretic to add to AM's existing regimen to reduce edema?

- a. Bumex
- b. Diuril
- c. Zaroxolyn
- d. Edecrin

Answer: c. Bumex and Edecrin are loop diuretics like furosemide, and duplication of therapy is not recommended. Diuril (chlorothiazide) is a thiazide diuretic; thiazides are ineffective in patients with end-stage renal disease and often lose effectiveness when creatinine clearance is less than 30 mL/min. Zaroxolyn (metolazone), unlike thiazide diuretics, remains effective even when the glomerular filtration rate drops to less than 30 mL/min. Metolazone could be added to help with the acute edema in this patient.

3. Which of the following brand names contains calcium acetate?

- a. Tums EX
- b. Renagel
- c. Phos-Lo

- d. Caltrate

Answer: c. Tums EX and Caltrate are products containing calcium carbonate. Renagel contains sevelamer, a noncalcium-containing phosphate binder. Phos-Lo contains calcium acetate. Sevelamer can be added to a calcium-containing phosphate binder if calcium dosing is maximized, but further phosphate binding is needed to bring phosphate levels down. It can also be used in place of calcium-containing phosphate binders when a patient's calcium-phosphate product or calcium levels are too high.

4. Later in the week, AM develops symptoms consistent with a *Staphylococcus* infection at the catheter site. The decision is made to begin vancomycin until blood culture results are known. Which of the following represents an appropriate initial dose of vancomycin at this time?

- a. Vancomycin 1 g IV q12h
- b. Vancomycin 1 g IV q24h
- c. Vancomycin 1 g, given after dialysis, and dose repeated after dialysis when needed according to trough levels on dialysis days
- d. Vancomycin 500-mg IV q12h

Answer: c. The first two answers would not be appropriate for initial dosing in someone dependent on renal dialysis. Initial doses are usually 12 to 15 mg/kg, so the 500-mg dose is too small, and the interval of dosing too frequent to provide therapeutic peak and appropriate trough concentrations. Maintenance dosing is adjusted according to trough levels following a dialysis session until a preferred maintenance regimen is identified and dialysis is stable; the frequency of dosing is dependent on whether high-flux dialysis or low-flux dialysis membranes and techniques are used. Typically, low-flux dialysis methods remove little vancomycin and dosing is generally every 72 hours to once per week. High-flux dialysis methods remove more vancomycin and typically dosing is more frequent, such as every 24-72 hours, following dialysis sessions.

REVIEW QUESTIONS

(Answers and Rationales on page 364.)

1. A 60-year-old patient is admitted for surgical correction of a femoral fracture. Postoperative laboratory evaluation revealed severe metabolic acidosis (ph 7.0). What is the most appropriate therapy for the metabolic acidosis?
 - a. Normal saline bolus
 - b. Sodium bicarbonate
 - c. Oxygen
 - d. Calcium gluconate
 - e. None of the above
2. Which of the following is a primary strategy used in management of patients with acute glomerulonephritis?
 - a. High-protein diet
 - b. Maintenance of fluid balance
 - c. Correct high cholesterol
 - d. a and b
 - e. b and c

3. Which of the following drugs acts on the renal convoluted tubule to induce water resorption?
 - a. Vasopressin
 - b. Corticotropin
 - c. Testosterone
 - d. Estradiol
 - e. Insulin
4. A 58-year-old patient with renal failure secondary to diabetes mellitus has anemia secondary to renal disease. After an initial epoetin alfa dose of 75 U/kg, three times per week, the patient's hematocrit increases from 22% to 30%. What is the next appropriate step in management of this patient?
 - a. Cease erythropoietin therapy
 - b. Add ferrous sulfate
 - c. Increase the dose of erythropoietin
 - d. Continue the same dose of erythropoietin
 - e. Perform bone marrow biopsy
5. What is the normal range for blood sodium levels?
 - a. 4–20 mEq/L
 - b. 16–56 mEq/L
 - c. 78–122 mEq/L
 - d. 135–146 mEq/L
 - e. 225–275 mEq/L
6. JP is 57-year-old male that presents with fatigue and the lab work shows advanced renal failure. Which finding would help you determine if his renal failure is chronic?
 - a. Low-serum bicarbonate
 - b. Low-serum calcium
 - c. Elevated-serum phosphorus
 - d. Waxy casts in urinalysis
 - e. Protein in urinalysis
7. Which of the following drugs is correctly paired with its main site of action in the kidney?
 - a. Hydrochlorothiazide: descending limb of the loop of Henle
 - b. Acetazolamide: proximal tubule
 - c. Triamterene: ascending limb of loop of Henle
 - d. Furosemide: collecting duct
 - e. Spironolactone: distal tubule
8. KL is a 58-year-old female with a history of cirrhosis and small-cell lung cancer. Her routine bloodwork reveals a sodium level of 120 mEq/L. Which laboratory test is most useful in determining which of these diseases as the cause of hyponatremia?
 - a. Serum creatinine
 - b. Serum osmolarity
 - c. Urine osmolarity
 - d. Urine sodium
 - e. Serum vasopressin
9. WW is a 60-year-old male with chronic renal failure. The patient develops abdominal cramping, nausea, and vomiting from food poisoning. Laboratory examination reveals: sodium 143, potassium 4.1, chloride 94, and bicarbonate 24. What is your conclusion?
 - a. Metabolic acidosis
 - b. Respiratory alkalosis
 - c. Metabolic alkalosis
 - d. Normal acid-base balance
 - e. Metabolic alkalosis and metabolic acidosis
10. A patient with chronic renal failure was started on erythropoietin for anemia. The hospital protocol follows the manufacturer's guidelines. The starting dose was 75 U/kg three times a week and the patient's hematocrit was 25%. One month later, the patient's hematocrit is reported at 30%, and the patient is asymptomatic. The hemoglobin is 10 g/dL. Which of the following should the pharmacist do?
 - A. Increase the dose.
 - B. Continue the same dose.
 - C. Decrease the dose.
 - D. Stop the erythropoietin
11. Systemic alkalosis is most likely to be caused by:
 - a. mineral oil.
 - b. sodium bicarbonate.
 - c. methylcellulose.
 - d. castor oil.
 - e. sodium phosphate.

- I. Definitions
 - A. Cancer: Typically defined as a group of diseases characterized by uncontrolled and abnormal local cellular growth, local tissue invasion, and distant spread to other locations (metastases).
 - B. Second to cardiovascular disease for all-cause mortality
 - C. Etiology
 1. Carcinogenesis: process by which normal mechanisms for control or growth and proliferation of cells are altered
 - a. Initiation: exposure of normal cells to a carcinogenic substance
 - b. Promotion: alteration of environment to favor growth of mutated cell over normal cells
 - c. Progression: genetic changes leading to cell proliferation, invasion, and development of metastasis
- II. Risk factors
 - A. Environmental
 1. Radiation
 2. Virus
 - B. Occupational
 1. Asbestos
 2. Benzene, chromium, nickel
 - C. Lifestyle
 1. Tobacco
 2. Alcohol
 3. Diet
- III. Principles of tumor growth
 - A. Tumor growth is exponential.
 - B. Chemotherapy kills a certain percentage of cells, not a particular number.
 - C. Metastasis
 1. Spread of cancer cells from tumor site to distant sites
 - a. Spread by blood and lymphatic pathways
- IV. Cancer sites and types include, but are not limited to:
 - A. Acute myeloid leukemia (AML)
 - B. Bladder cancer
 - C. Bone cancer
 - D. Breast cancer
 - E. Chronic myelogenous leukemia (CML)
 - F. Central nervous system cancers
 - G. Kidney cancer
 - H. Colon and rectal cancer
 - I. Ovarian cancer
 - J. Cervical cancer
 - K. Prostate cancer
 - L. Gastric cancer
 - M. Head and neck cancers
 - N. Hepatobiliary cancers
 - O. Melanoma
 - P. Multiple myeloma
 - Q. Myelodysplastic syndromes
 - R. Neuroendocrine tumors
 - S. Hodgkin and non-Hodgkin lymphomas
 - T. Nonmelanoma skin cancers
 - U. Occult primary
 - V. Pancreatic adenocarcinoma
 - W. Soft-tissue sarcoma
 - X. Thymic malignancies
 - Y. Thyroid carcinoma
 - Z. Uterine neoplasms
 - AA. Testicular cancer
- V. Prevention and screening
 - A. Breast
 1. Women 40 years and older should have an annual mammogram and clinical breast exam by a health-care professional; individuals should perform monthly self-examinations.
 - B. Colon/rectum
 1. Persons 50 years and older should have at least one of the following: colonoscopy, fecal occult blood test, flexible sigmoidoscopy, or double contrast barium enema; combination testing is preferred. Earlier screening examination is recommended in those with familial risk factors.
 - C. Prostate
 1. Men 50 years and older should have a prostate-specific antigen (PSA) test and digital rectal exam annually.
 - D. Cervix
 1. Women 18 years and older or who are sexually active should have Pap test and pelvic exam annually.
- VI. Diagnosis and staging
 - A. Diagnosis: pathologic evaluation and biopsy
 - B. Staging: determines prognosis, metastasis, and treatment
 - C. TNM classification (T = tumor, N = node, M = metastasis)
- VII. Types of cancer
 - A. Carcinoma: cancer that begins in the skin or in tissues that line or cover internal organs
 - B. Sarcoma: cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue

- C. Leukemia: cancer that starts in blood-forming tissue such as bone marrow and causes production of large numbers of blood cells to be produced and enter the bloodstream
 - D. Lymphoma: cancer that begins in cells of the immune system. There are two basic categories of lymphomas. One kind is Hodgkin lymphoma, which is marked by the presence of a type of cell called the Reed-Sternberg cell. The other category is non-Hodgkin lymphomas, which includes a large, diverse group of cancers of immune system cells. Non-Hodgkin lymphomas can be further divided into cancers that have an indolent (slow-growing) course and those that have an aggressive (fast-growing) course.
 - E. Adenoma: a noncancerous tumor that starts in gland-like cells of the epithelial tissue (thin layer of tissue that covers organs, glands, and other structures within the body)
- VIII. Cancer treatment
- A. Surgery
 - B. Radiation
 - C. Chemotherapy
 - D. Immunotherapy
 - E. Hormone therapy
- IX. Chemotherapy
- A. Purpose: destroy cells that may have spread from primary site
 - 1. Curative: entirely free of disease
 - 2. Adjuvant: keep it from spreading
 - 3. Neoadjuvant: reduce tumor burden or spare organ
 - 4. Palliative: relieve symptoms (i.e., pain) and allow individual to live comfortably
 - B. Cell cycle actions of chemotherapy
 - 1. Many drugs are cell cycle specific.
 - 2. Phases
 - a. G₁ phase
 - (1) Manufacture necessary enzymes for DNA synthesis
 - b. S phase
 - (1) DNA replication
 - c. G₂ phase
 - (1) Cell prepares for mitosis after DNA synthesis.
 - d. M phase
 - (1) Mitosis (cell division)
 - e. G₀ phase
 - (1) Resting phase
 - C. Common routes of chemotherapy administration
 - 1. Oral
 - 2. Intravenous (IV)
 - 3. Intrathecal
 - 4. Intracavitary
 - 5. Intra-arterial
 - D. Classification of chemotherapeutic agents
 - 1. Alkylating agents
 - a. Nitrogen mustards
 - (1) Examples: cyclophosphamide, ifosfamide, mechlorethamine, thiotepa, melphalan, chlorambucil
 - b. Nitrosoureas
 - (1) Examples: carmustine (BCNU), lomustine (CCNU)
 - c. Platinum compounds
 - (1) Examples: cisplatin, carboplatin, oxaliplatin
 - d. Miscellaneous
 - (1) Examples: busulfan, dacarbazine, temozolomide, procarbazine
2. Antimetabolites
- a. Folic acid analogs
 - (1) Example: methotrexate
 - b. Pyrimidine analogs
 - (1) Examples: fluorouracil (5-FU), capecitabine, cytarabine, gemcitabine, floxuridine, tegafur/uracil
 - c. Purine analogs
 - (1) Examples: mercaptopurine, cladribine, fludarabine, thioguanine, pentostatin
3. Plant alkaloids
- a. Vinca alkaloids
 - (1) Examples: vincristine, vinblastine, vinorelbine, vindesine
 - b. Podophyllotoxins
 - (1) Examples: etoposide, teniposide
 - c. Taxanes
 - (1) Examples: paclitaxel, docetaxel
 - d. Camptothecins (topoisomerase inhibitors)
 - (1) Examples: irinotecan, topotecan
4. Antibiotics
- a. Anthracycline antibiotics
 - (1) Examples: daunorubicin, liposomal daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin
 - b. Miscellaneous
 - (1) Examples: bleomycin, mitomycin, plicamycin, dactinomycin
5. Biologic Response Modifiers
- a. Monoclonal antibodies
 - (1) Examples: rituximab, trastuzumab, gemtuzumab, ozogamicin, alemtuzumab, cetuximab, bevacizumab
 - b. Monoclonal antibody/radiopharmaceuticals
 - (1) Examples: tositumomab ¹³¹I, ibritumomab tiuxetan ⁹⁰Y
 - c. Miscellaneous
 - (1) Examples: interferon, interleukin-2, bacillus Calmette-Guérin (BCG)
6. Tyrosine kinase inhibitors
- (a) Examples: imatinib, gefitinib
7. Miscellaneous
- (1) Examples: L-asparaginase, hydroxyurea, estramustine, bexarotene, arsenic trioxide, denileukin diftitox, bortezomib
8. Hormone agents
- a. Adrenocorticosteroids
 - (1) Examples: dexamethasone, prednisone, methylprednisolone
 - b. Progestins
 - (1) Examples: megestrol, medroxyprogesterone

- c. Estrogens
 - (1) Examples: diethylstilbestrol, ethinyl estradiol
 - d. Antiestrogens
 - (1) Examples: tamoxifen, raloxifene, anastrozole, letrozole, exemestane, fulvestrant
 - e. Androgens
 - (1) Examples: testosterone, fluoxymesterone
 - f. Antiandrogens
 - (1) Examples: flutamide, bicalutamide, nilutamide
 - g. Gonadotropin-releasing hormone analog
 - (1) Examples: leuprolide, goserelin, triptorelin
 - E. Adverse effects of chemotherapy
 - 1. Nonspecific
 - a. Fatigue
 - 2. Extravasation
 - a. Leakage of drug into surrounding tissues
 - b. For doxorubicin, daunorubicin, may apply cold pack
 - c. For vincristine, vinblastine, vinorelbine, taxanes, mechlorethamine, apply warm pack (avoid cold application)
 - 3. Bone marrow suppression: Common dose-related toxicity
 - a. Neutropenia: calculate absolute neutrophil count (ANC)

$$\text{ANC} = \frac{(\text{segs} + \text{bands}) \times \text{WBC}}{100}$$

ANC = 3000 – 7000 = normal
 ANC > 1000 = minimal risk of infection
 ANC = 500 – 1000 = moderate risk of infection
 ANC < 500 = severe risk of infection
 - (1) Busulfan, carmustine, lomustine, cyclophosphamide, semustine, chlorambucil, dacarbazine, ifosfamide, carboplatin, cytarabine, fluorouracil, methotrexate, daunorubicin, doxorubicin, paclitaxel, docetaxel, topotecan, mitomycin, and others
 - (2) Treatment of neutropenia
 - (i) Filgrastim (Neupogen)
 - (a) Stimulates neutrophil production
 - (b) Dose: 5 mcg/kg per day SQ or IV; give at least 24 hours after last dose of chemotherapy
 - (ii) Pegfilgrastim (Neulasta)
 - (a) Same mechanism as filgrastim but has prolonged renal elimination and half-life
 - (b) Dose: 6 mg AQ once per cycle (adults only)
 - (iii) Sargramostim (Leukine)
 - (a) Used for cancer chemotherapy and bone marrow transplant
 - (b) Dose: 250 mcg/m² per day SQ or IV (dose based on body surface area [BSA])
- b. Thrombocytopenia
 - (1) Platelets <100,000
 - (2) Carboplatin, gemcitabine, mitomycin, BCNU, vinorelbine
 - (3) Treatment
 - (i) Transfusions
 - (ii) Oprelvekin (Neumega)
 - (a) Dose: 50 mcg/kg SQ daily; give 24–36 hours after chemotherapy
- c. Anemia
 - (1) Cisplatin and carboplatin
 - (2) Treatment
 - (i) Recombinant human erythropoietin (EPO) (Epogen, Procrit)
 - (a) Used in patients with Hct <33% or Hb <11%
 - (b) Dose: 40,000 units SQ or IV weekly or 150 units/kg three times weekly SQ or IV; dose adjustment may be needed
 - (ii) Darbepoetin (Aranesp)
 - (a) Same mechanism as EPO and similar side effects but three times longer half-life and duration of action
 - (b) Dose: 200 mcg SQ every 2 weeks
4. Cardiotoxicity
 - a. Doxorubicin, daunorubicin, cyclophosphamide
 - b. Patients should be monitored; early detection is key.
 - c. Dexrazoxane, a cardioprotectant (Totect, Zinecard); also used for treatment of extravasation
5. Nephrotoxicity
 - a. Cisplatin, carboplatin, carmustine
 - 1. Prevention
 - 2. Diuresis with mannitol and/or furosemide
 - 3. Amifostine (Ethyol) may be given before cisplatin but may cause hypotension
6. Hemorrhagic cystitis
 - a. Cyclophosphamide, ifosfamide
 - b. Treatment: mesna reduces the incidence of hemorrhagic cystitis
7. Hepatotoxicity
 - a. L-asparaginase, nitriturias, methotrexate, 6-mercaptopurine, and others
8. Neurotoxicity
 - a. CNS (headache, somnolence, confusion): cytarabine (cerebellar toxicity), asparaginase, ifosfamide, fluorouracil, vincristine, vinblastine
 - b. Peripheral neuropathy: vincristine, cisplatin, paclitaxel, fludarabine, docetaxel
9. Pulmonary toxicity
 - a. Bleomycin (pulmonary fibrosis, infiltrates, cough), busulfan
 - (1) Interstitial pneumonitis: carmustine, chlorambucil, cyclophosphamide, mitomycin, methotrexate, fludarabine, melphalan, cytarabine

10. Gastrointestinal toxicity
 - a. Nausea/vomiting
 - (1) Methotrexate, fluorouracil, cisplatin, cyclophosphamide, doxorubicin, hydroxyurea, dacarbazine, nitrosoureas, cytarabine
 - (2) Treatment: 5-HT₃ antagonists
 - b. Diarrhea
 - (1) Irinotecan, methotrexate, fluorouracil, cytarabine, dactinomycin, 5-azacytadine, hydroxyurea, nitrosoureas, cyclophosphamide
 - (2) Treatment
 - (a) Hydration, IV fluids
 - (b) Loperamide
 - (c) Octreotide
 - (d) Codeine
 - c. Constipation
 - (1) Vinca alkaloids
 - (a) Treatment: laxative or stool softener
 - d. Stomatitis/mucositis
 - (1) Bleomycin, methotrexate, fluorouracil, doxorubicin, cytarabine
 - (2) Treatment and prevention
 - (i) Antifungal agents: nystatin, fluconazole
 - (ii) Chlorhexidine
 - (iii) Magic mouthwash (various combinations including nystatin, Mylanta, viscous lidocaine, dexamethasone)
11. Hypersensitivity reactions
 - a. Fever
 - (1) Bleomycin, 5-azacytadine
 - b. Anaphylactic reactions
 - (1) Paclitaxel, docetaxel, bleomycin, etoposide, cisplatin, procarbazine, anthracyclines
 - c. Photosensitivity
 - (1) Methotrexate, fluorouracil, vinblastine, dacarbazine
 - d. Pigment changes
 - (1) Busulfan, bleomycin, doxorubicin, fluorouracil
12. Alopecia
 - a. Cyclophosphamide, ifosfamide, fluorouracil, dactinomycin, doxorubicin, daunorubicin, bleomycin, paclitaxel, docetaxel
13. Sterility/infertility
 - a. Alkylating agents, procarbazine, methotrexate, fluorouracil, busulfan, cyclophosphamide
14. Ocular toxicity
 - a. Cytarabine (conjunctivitis), busulfan (cataracts), vinca alkaloids (optic neuritis), cisplatin (optic neuritis)
- F. Radiation therapy
 1. Uses high-energy rays to kill cancer cells
 2. Local therapy
 3. Used alone or in conjunction with chemotherapy

G. Surgery

- 1) Depends on the stage of the disease and the overall health of the patient
- 2) Used in conjunction with chemotherapy and radiation therapy

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PATIENT PROFILE

Patient Initials: DB

Sex: Male

Age: 72

Height: 5' 9"

Weight: 77 kg

Race: White

Allergies: No known drug allergies (NKDA)

Current: Three months ago, the patient reported significant urinary flow symptoms to physician. At that time, the patient had an elevated PSA and a noted mass with digital rectal exam. The mass was confirmed with an ultrasound procedure, and a biopsy revealed that DB had prostate cancer. There is no metastatic disease at this time.

Medical History:

None significant to current issues. No chronic health problems except mild osteoarthritis of the knees and hands.

Social History:

Tobacco use: None in the past 40 years; smoked in young adulthood but less than 1 pack per day

Alcohol use: Rare

Current Medications:

None, occasional use of nonprescription Aleve for osteoarthritis

PATIENT PROFILE QUESTIONS

1. Part of DB's treatment regimen will include the use of a luteinizing hormone-releasing hormone (LHRH) agonist to significantly reduce androgen levels. Which of the following is an LHRH agonist?

- a. Finasteride
- b. Goserelin
- c. Tamsulosin
- d. Saw palmetto

Answer: b. Goserelin is the LHRH agonist. Finasteride is an antiandrogen (5-alpha reductase inhibitor) that reduces conversion of testosterone

Chemotherapeutic Agent (generic name)	Brand	Indications
ALKYLATING AGENTS		
Nitrogen mustards		
Chlorambucil	Leukeran	Chronic lymphocytic leukemia
Cyclophosphamide	Cytoxan, Neosar	Hodgkin and non-Hodgkin lymphoma
Ifosfamide	IFEX	Waldenström macroglobulinemia
Mechlorethamine	Mustargen	Lymphomas
Melphalan	Alkeran	Ovary
		Breast (palliative)
		Bladder
		Chronic lymphocytic leukemia
		Recurrent testicular cancer and germ cell tumors
		Sarcomas
		Hodgkin and non-Hodgkin lymphoma
		Non-small cell lung cancer (NSCLC)
		Head and neck
		Cervix
		Lung (palliative)
		Cutaneous T-cell lymphoma
Thiotepa	Thioplex	Chronic myelogenous leukemia (CML)
Busulfan	Busulfex (IV) Myleran (oral)	CML
		CML (palliative)
Nitrosoureas		
Carmustine	BCNU, BiCNU	Brain neoplasms (malignant glioma)
Lomustine	Gliadel CCNU, CeeNU	Multiple myeloma
		Hodgkin's and non-Hodgkin's lymphoma
		Colon
		Lung
Dacarbazine	DTIC-Dome	Melanoma
		Hodgkin lymphoma
		Soft tissue sarcomas
Procarbazine	Matulane	Hodgkin lymphoma
		Brain
Platinum compounds		
Cisplatin	Platinol	Lung
Carboplatin		Testicular
		Bladder
		Breast
		Ovarian
		Colorectal
		Head and neck
ANTIMETABOLITES		
Fluorouracil, 5-FU	Adrucil	Prolong survival (combination with leucovorin)
Floxuridine	FUDR	Colon
		Kidney
		Stomach
Methotrexate	Methotrexate	Osteosarcoma
Leucovorin	Wellcovorin, Leucovorin	Colorectal (palliative; combination with 5-FU)
Hydroxyurea		
	Hydrea	CML
	Droxia	Head and neck
	Mylocel	Melanoma
		Ovarian (refractory)
		Essential thrombocytosis and polycythemia vera
Thioguanine, 6-TG	Thioguanine	Acute lymphocytic leukemia (ALL)
	Tabloid	CML
Mercaptopurine, 6-MP	Purinethol	ALL
Cytarabine	DepoCyt	Lymphomatous meningitis (intrathecal)
Pentostatin	Nipent	Hairy cell leukemia

Continued

Chemotherapeutic Agent (generic name)	Brand	Indications
Fludarabine	Fludara	B-cell lymphocytic leukemia (CLL)
Cladribine	Leustatin, 2-CdA	Active hairy cell leukemia
Asparaginase	Elspar	ALL (combination)
Gemcitabine (Gemzar)		NSCLC (advanced (Stage IIIA or IIIB) or metastatic (Stage IV))
ANTIBIOTIC AGENTS		
Doxorubicin	Adriamycin PFS	Breast (adjunct)
Doxorubicin liposomal	Adriamycin, Rubex	Ovarian
	Doxil	AIDS-related Kaposi sarcoma
Epirubicin	Ellence	Ovary
Daunorubicin	DaunoXome	Breast
daunorubicin liposomal	Cerubidine	Advanced, HIV-related Kaposi sarcoma
daunorubicin, daunomycin		ALL
Idarubicin	Idamycin	Acute myeloid leukemia (AML)
		Acute nonlymphocytic leukemia (ANLL)
Mitoxantrone	Novantrone	ANLL
		Prostate (advance refractory, combination therapy)
Dactinomycin	Cosmegen	Testicular
		Melanoma
		Uterine
		Soft tissue sarcoma
		Wilms tumor
		Rhabdomyosarcoma
		Germ cell tumors
		Gestational trophoblastic disease
		Ewing sarcoma
		Choriocarcinoma
		Neuroblastoma
		Retinoblastoma
		Kaposi sarcoma
		Sarcoma botryoides
Bleomycin	Blenoxane	Malignant pleural effusion (MPE), prevention of recurrent pleural effusions
BIOLOGIC AGENTS		
Interleukin		
interleukin-2	Proleukin	Renal cell
Interleukin-11, oprelvekin	Neumega	Melanoma
		Supportive treatment (stimulate bone marrow to produce platelets; decrease the need for platelet transfusions)
Interferon		
interferon alpha 2a	Roferon	Hairy cell leukemia
interferon alpha 2b	Intron A	CML
		AIDS-related Kaposi sarcoma (interferon alpha 2b)
		Malignant melanoma (interferon alpha 2b)
		Non-Hodgkin lymphoma (interferon alpha 2b)
BCG	TICE BCG	Bladder
	TheraCys	Immunization against tuberculosis (TB)
Levamisole	Ergamisol	Colon cancer (combination with 5-FU)
Sargramostim, GM-CSF	Leukine	Accelerate WBC recovery (used in AML, non-Hodgkin lymphoma, acute lymphocytic leukemia, or Hodgkin disease)
Octreotide	Sandostatin	Control certain symptoms (e.g., diarrhea, flushing)
Retinoids		
Alitretinoin	Panretin	AIDS-related Kaposi sarcoma

Continued

Chemotherapeutic Agent (generic name)	Brand	Indications
Tretinoin, ATRA	Vesanoid	Acute promyelocytic leukemia (APL)
HORMONAL AGENTS		
Tamoxifen	Nolvadex	Breast
Megestrol acetate	Megace	Breast Endometrial Supportive treatment for severe loss of appetite
Anastrozole	Arimidex	Breast (adjunct)
Letrozole	Femara	Breast
Goserelin	Zoladex Zoladex Implant	Breast
Leuprolide	Eligard	Prostate
Bicalutamide	Casodex	Prostate
Flutamide	Eulexin	Prostate
PLANT-DERIVED AGENTS		
Vincristine	Oncovin	Brain Thyroid Acute leukemia Hodgkin and non-Hodgkin lymphoma Neuroblastoma Rhabdomyosarcoma Ewing sarcoma Wilms tumor Multiple myeloma Chronic leukemias
Vinblastine	Velban	Breast Lung Head and neck Bladder Testicular Hodgkin and non-Hodgkin lymphoma Kaposi sarcoma Mycosis fungoides (T-cell lymphoma) Choriocarcinoma
Vinorelbine	Navelbine	NSCLC
Etoposide	Etopophos VePesid	Testicular NSCLC Small cell lung cancer (SCLC)
Teniposide	Vumon	ALL
Paclitaxel	Abraxane Paxane Taxol	Breast AIDS-related Kaposi sarcoma Ovarian NSCLC
Docetaxel	Taxotere	Breast NSCLC Prostate Head and neck
Topotecan	Hycamtin	Ovarian NSCLC
Irinotecan	Camptosar	Cervical Colon

Continued

Chemotherapeutic Agent (generic name)	Brand	Indications
		Rectum
MISCELLANEOUS		
Monoclonal antibodies		
Trastuzumab	Herceptin	Breast
Rituximab	Rituxan	Non-Hodgkin lymphoma
Cetuximab	Erbix	Colorectal
Tyrosine Kinase Inhibitor		
Imatinib	Gleevec	Gastrointestinal CML
EGFR Inhibitors		
Erlotinib	Tarceva	NSCLC
Gefitinib	Iressa	Pancreatic NSCLC
VEGF inhibitors		
Bevacizumab	Avastin	Reversible posterior leukoencephalopathy syndrome (NSCLC)

to dihydrotestosterone (DHT). Tamsulosin is a selective alpha receptor antagonist. Saw palmetto is a natural dietary supplement used for prostate health.

2. Counseling DB on potential side effects of LHRH agonist treatment would include all of the following EXCEPT:
- hot flashes.
 - decreased libido and potential sexual dysfunction.
 - myelosuppression.
 - cold flashes.
 - decreased bone density.

- I only
- III only
- I and III
- III and IV
- III and V

Answer: d. Common side effects of the use of LHRH agonists include hot flashes, changes in sexual desire and function, confusion or memory changes, and, with chronic use, decreased bone density. Cold flashes do not occur. Myelosuppression is not a side effect.

- Vincristine
- Methotrexate
- Hydrocortisone

3. Which of the following is NOT an alkylating agent?
- Etoposide
 - Mechlorethamine
 - Ifosfamide
 - Melphalan
 - Carmustine

4. Which of the following is NOT a side effect of tamoxifen?
- Leukopenia
 - Mania
 - Rash
 - Flushing
 - Peripheral edema

5. Which of the following is a proposed mechanism of doxorubicin?
- Intercalation
 - Inhibit protein synthesis
 - Iron chelation
 - All of the above
 - None of the above

REVIEW QUESTIONS

(Answers and Rationales on page 364.)

- Which of the following drugs is NOT a part of the chemotherapy regimen-MOPP?
 - Mechlorethamine
 - Prednisone
 - Procarbazine
 - Vincristine
 - Dacarbazine
- Which of the following agents CANNOT be injected intrathecally?
 - Thiotepa
 - Cytarabine

6. A healthy 30-year-old female is diagnosed with anemia. Her laboratory values are as follows:
- Hgb 10g/dL (normal:12-15 g/dL)
 Hct 31% (normal: 30%-45%)
 MCV 74 uL3 (normal: 80-100 uL3)
 MCH 25 pg/RBC (normal: 26-34 pg/RBC)

Which of the following is the most appropriate next step?

- Treatment with ferrous sulfate
- Treatment with cyanocobalamin
- Treatment with erythropoietin
- Bone marrow biopsy
- Hemoglobin electrophoresis

7. Depolymerization of microtubules is the mechanism of action of:
 - a. Vinblastine
 - b. Cladribine
 - c. Methotrexate
 - d. Azatadine
 - e. Rituximab
8. Which of the following is true of irinotecan?
 - a. It may cause diarrhea
 - b. It may cause hypovolemia
 - c. It may be used to treat colon cancer
 - d. It is a topoisomerase II inhibitor
 - e. a, b, and c
9. All of the following are true about nilutamide (Nilandron) EXCEPT:
 - a. It is an antiandrogen
 - b. It is used for prostate cancer
 - c. It is not available for oral use
 - d. May elevate liver enzymes
 - e. Patients using nilutamide should wear tinted glasses
10. 5-Fluorouracil:
 - a. Is used to treat colorectal carcinoma
 - b. Can be administered orally
 - c. May cause constipation
 - d. Activates thymidylate synthetase
 - e. Has a duration of action of 2-3 days
11. What is a correct drug:acute toxicity pair?
 - I. Carmustine: nausea and vomiting
 - II. Cisplatin: nausea and vomiting
 - III. Cyclophosphamide: hemorrhagic cystitis
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
12. Doxorubicin may cause all of the following EXCEPT:
 - a. Nephrotoxicity
 - b. Myelosuppression
 - c. Cardiac disease
 - d. Gastrointestinal toxicity
 - e. It may cause any of the above
13. Allopurinol and mercaptopurine, when combined, produce severe side effects. This is caused by:
 - a. Quanylate kinase inhibition
 - b. Xanthine oxidase inhibition
 - c. Accumulation of allopurinol
 - d. Accumulation of chemotherapeutic agent
 - e. b and d
14. Which of the following is an alkylating agent:
 - a. Busulfan
 - b. Carmustine
 - c. Cyclophosphamide
 - d. a and c
 - e. a, b, and c
15. Which of the following may cause hemorrhagic cystitis?
 - a. Cyclophosphamide
 - b. Cisplatin
 - c. Methotrexate
 - d. Dacarbazine
 - e. None of the above
16. What is the correct cancer:chemotherapy acronym pair ?
 - I. Hodgkin's disease:ABVD
 - II. Hodgkin's disease:MOPP
 - III. Prostate Cancer:MOPP
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
17. Cyclosporine:
 - a. Causes severe myelosuppression
 - b. Causes hepatotoxicity
 - c. Does not elevate serum creatinine
 - d. Is useful in the treatment of many solid tumors
 - e. a and c
18. What is the most common use of cyclosporine?
 - a. CNS tumors
 - b. Leukemia
 - c. Immunosuppression
 - d. a and b
 - e. b and c
19. What side effect is associated with cisplatin?
 - a. Nephrotoxicity
 - b. Ototoxicity
 - c. Electrolyte imbalance
 - d. a and c
 - e. a, b, and c
20. Why are most cancers treated with a combination of chemotherapeutic agents?
 - a. Different mechanisms of action
 - b. Different toxicity profiles
 - c. Different mechanisms of tumor resistance
 - d. a and b
 - e. a, b, and c
21. Which of the following may cause congestive heart failure?
 - a. Doxorubicin
 - b. L-Asparaginase
 - c. Vincristine
 - d. Cyclophosphamide
 - e. Cisplatin
22. Which of the following is a side effect of 17-alpha alkylated androgens?
 - a. Hepatic adenocarcinoma
 - b. Peliosis hepatitis
 - c. Elevated hepatic transaminases
 - d. Cholestatic hepatitis
 - e. All of the above

23. Which of the following is an appropriate use of androgens?
- Breast carcinoma
 - Hereditary angioneurotic edema
 - Hypogonadism
 - Erythropoiesis
 - All of the above
24. What is a correct drug:delayed toxicity pair?
- Carmustine:Alopecia
 - Cisplatin:Renal Dysfunction
 - Cyclophosphamide:Hemorrhagic cystitis
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
25. Which of the following is an appropriate indication for anti-androgens?
- Prostate cancer
 - Male pattern baldness
 - BPH
 - Acne
 - All of the above
26. Which of the following is INCORRECT?
- Aminoglutethimide inhibits the rate-limiting step in cortisol synthesis
 - Trilostane decreased aldosterone synthesis
 - Metyrapone inhibits 11-hydroxylase
 - Ketoconazole inhibits cortisol synthesis
 - Aminoglutethimide inhibits androstenedione conversion to testosterone
27. Interferons:
- Enhance MHC class I and II expression
 - Have antioncogenic effects
 - Are produced in response to viral infections
 - a and c
 - a, b, and c
28. Interleukin 1:
- Enhances endothelial adhesion factor expression
 - Are analgesic
 - Act to reset the hypothalamic thermoregulatory center
 - a and b
 - a and c
29. Which of the following is true regarding interleukins (IL)?
- IL-2 is produced by B-lymphocytes
 - IL-4 causes IgG and IgE synthesis and B cell proliferation
 - IL-6 is immunosuppressive
 - IL-7 is produced by Th2 cells
 - IL-10 activates Th1 cytokine production
30. What is a correct drug:delayed toxicity pair ?
- Carmustine:Leukopenia
 - Cisplatin:Renal Dysfunction
 - Cyclophosphamide:Alopecia
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
31. Which of the following is true regarding lymphocytes?
- NK cells causes lysis of tumor cells
 - Helper T cells cause lysis of virally infected cells
 - B cells cause lysis of virally infected cells
 - Cytotoxic T cells release cytokines that promote B cell activation
 - B cells account for 80% of all lymphocytes
32. Which of the following is FALSE concerning the complement pathway?
- The classical pathway is initiated by the C1 complex
 - Decay accelerating factor can inhibit C3 convertase
 - C3a and C5b are opsonins
 - The membrane attack complex is made up of C5b, C6, C7, C8 and C9
 - CD59 activates the membrane attack complex
33. IgG:
- Is the primary antibody found in mucosal secretions
 - Can cross the placenta
 - Can be one of eight subclasses
 - Is secreted by T cells
 - All of the above
34. Antigen presenting cells:
- Activate cytotoxic T cells
 - Internalize antigens from the extracellular space
 - Include dendritic cells, macrophages, and B-cells
 - All of the above
 - a and b
35. Leukoran is a member of which drug class?
- Hormones
 - Alkylating agents
 - Antimetabolites
 - Anthracyclines
 - Topoisomerase inhibitors
36. LE is a 77-year-old woman with node positive breast cancer. The treatment of choice is:
- Tamoxifen alone
 - Chemotherapy
 - Mastectomy
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III

37. Which of the following drugs is fatal when given intrathecally
- Doxorubicin
 - Oxaliplatin
 - Vincristine
 - Methotrexate
 - None of the above
38. Which of the following drugs is cardiotoxic:
- Rituximab
 - Doxorubicin
 - Methotrexate
 - Vincristine
 - Lomustine
39. Which of the following drugs may cause peripheral neuropathy?
- Paclitaxel
 - Cetuximab
 - Daunorubicin
 - Mitomycin C
 - Dacarbazine
40. Which of the following drugs is NOT a part of the chemotherapy regimen–ABVD?
- Dacarbazine
 - Adriamycin
 - Bleomycin
 - Vinblastine
 - Cyclophosphamide
41. Which drug(s) may cause respiratory distress?
- Bleomycin
 - Cyclophosphamide
 - Daunorubicin
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
42. Which of the following best describes the mechanism of action of Anzemet?
- 5-HT₃ antagonist
 - Histamine antagonist
 - Beta-2 antagonist
 - Alpha-2 antagonist
 - None of the above
43. Which of the following are considered mitotic inhibitors?
- Oncovin
 - Taxotere
 - Taxol
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
44. Although it may be useful in control of metastatic ovarian cancer, this topoisomerase I inhibitor's dose-limiting adverse effects include: neutropenia, thrombocytopenia, and anemia.
- Vincristine (Oncovin)
 - Topotecan (Hycamtin)
 - Doxorubicin (Adriamycin)
 - Mitomycin (Mutamycin)

I. Definition

Pain is a common condition that manifests as many different forms and severities. Pain is defined as an unpleasant sensory and emotional experience associated with damage to body tissues, including organs, bones, and muscles. Acute pain occurs after tissue injury and often resolves soon after the body has healed. Chronic pain occurs either from continual damage or constant stimulation of nerve fibers lasting at least 6 months. The cause of some chronic pain may not be known. The treatment of pain depends upon the causes of the pain and the individual's tolerance of pain.

II. Types of Pain

The different types of pain include acute pain, chronic pain, nerve pain, nociceptive pain, and psychogenic pain.

- A. Acute pain: results from injury to tissues and/or inflammation. Acute pain generally has a sudden onset. For example, after trauma or surgery, acute pain may be accompanied by anxiety or emotional distress.
- B. Chronic pain: Pain signals keep firing in the nervous system for weeks, months, even years. Initial injuries, such as an infection, sprained back, or sprained muscle, may cause acute pain that may lead to chronic pain. There may be an ongoing cause of pain, such as in back pain, arthritis, diabetes (diabetic neuropathy), or cancer.
- C. Nerve pain (neuropathic pain): pressure or damage to nerves or the spinal cord. Nerve pain can be caused by tumors; injury, such as during surgery or falls; chemical damage, such as with mercury, lead, chemotherapy, and radiation; or viruses, such as herpes zoster (shingles or chicken pox).
- D. Nociceptive pain: aching, sharp, or throbbing pain that includes somatic pain (body surface, deep tissues) and visceral pain (not well localized, pressure-like, deep squeezing)
- E. Psychogenic pain: mostly related to psychological disorders. Goals of treatment are to improve comfort and physical and psychological function. Treatment includes antidepressants, psychological counseling.

III. Acute Pain Control

- A. Pain management required for a short duration (e.g., following surgery, accident)
- B. Known end period for required pain management
- C. Monitor for addiction

IV. Chronic Pain Control

- A. Disease state management (e.g., cancer, rheumatoid arthritis, osteoarthritis)
- B. Pain management required for a long period, possibly until end of life
- C. Acute control (e.g., breakthrough pain) may be required for short duration events during chronic control
- D. Monitor for addiction

V. Pyramid Control

- A. Start with mild agents, increase to narcotics
- B. Ceiling effect (i.e., a limited dose requirement) with most analgesics
 1. Narcotics (opioids) like morphine do not have a ceiling effect.
- C. Controlled substances potentially addictive
- D. Start with lowest doses possible

VI. Patient Assessment

- A. Use the mnemonic: PQRST
 1. P = Palliative factors: What makes the pain better?
 - a) Provocative factors: What makes the pain worse?
 2. Q = Quality: Describe the pain.
 3. R = Radiation: Where is the pain?
 4. S = Severity: How does this pain compare with other pain you have experienced?
 5. T = Temporal factors: Does the intensity of the pain change with time?

VII. Patient Management

- A. Identify the source of pain.
- B. Eliminate the underlying cause.
- C. Select the most effective analgesic with the fewest side effects.
- D. Properly titrate the dose for each patient and administer for an appropriate duration.
- E. Always consider around-the-clock regimens for acute and chronic pain.
- F. Use as-needed regimens for breakthrough pain.
- G. Assess for side effects of analgesics (i.e., constipation with opioids).
- H. Avoid excessive sedation by titrating the opioids tentatively.
- I. Adjust the route of administration to the needs of each patient, using oral administration whenever possible.
- J. Use equianalgesic doses when converting from one agent to another and titrate accordingly.
- K. Consider antidepressants, anticonvulsants, or opioids for neuropathic pain.

- L. Consider a multidisciplinary approach:
pharmacologic + nonpharmacologic therapies.

VIII. Pharmacologic Therapies

A. Acetaminophen (paracetamol; tylenol)

1. Mechanism of action: not fully understood at this time; possibly centrally acting; derivative of p-aminophenol; analgesic
2. Maximum dose 4 g/day for adults (lower maximum dosages currently under consideration by Food and Drug Administration [FDA]); less with hepatic dysfunction and/or alcohol use
3. Caution: anemia or cardiac, pulmonary, renal or hepatic disease, alcoholism
4. Interactions: alcohol, liver enzyme inducers
5. Toxicity and side effects: Narrow therapeutic index; do not exceed maximum dose limits. Liver toxicity (acetaminophen is the primary agent associated with liver failure and need for transplantation in the United States), nephrotoxicity
 - a) Overdose: nausea, vomiting, diarrhea, methemoglobinemia

- (1) Treatment with supportive measures and acetylcysteine

B. Nonsteroidal anti-inflammatory drugs (NSAIDs) (Table 18-1)

1. Mechanism of action: nonspecific inhibition of cyclooxygenase (COX)-2 and COX-1 receptors, decreasing prostaglandins produced by the arachidonic acid cascade in response to

noxious stimuli, thereby decreasing the number of pain impulses received by the central nervous system (CNS)

2. Use lowest effective dose for shortest possible duration; OTC NSAID not to exceed 10 days unless a physician directs otherwise
3. Caution: Avoid in patients with recent coronary artery bypass graft surgery (CABG). Caution in bleeding disorders, hepatic or renal disease, GI disorders; women who are pregnant or lactating or who are trying to conceive
4. Interactions: Methotrexate, medications which increase the risk of bleeding (anticoagulants, e.g., warfarin), medications causing liver or renal damage, medications causing GI disturbance, diuretics, lithium, aspirin, antihypertensive agents
5. Toxicity and side effects: bleeding, upset stomach, ulcers, nausea, vomiting, diarrhea, constipation, fluid retention, edema, tinnitus, increased risk of bleeding, increased risk of Reye syndrome in children

C. Aspirin

1. Prototype of the salicylates; also a nonsteroidal anti-inflammatory drug (NSAID)
2. Mechanism of action: irreversibly inhibits COX-1 and COX-2, decreasing prostaglandins produced by the arachidonic acid cascade in response to noxious stimuli, thereby decreasing the number of pain impulses received by the CNS

Table 18-1 Nonsteroidal Anti-inflammatory Drugs (NSAID)

NSAID	Usual Oral Adult Doses	Comments
Ibuprofen (Motrin)	200–400 mg PO q4–6h prn	Maximum 1200 mg/day (OTC); 3200 mg/day (R _x)
Naproxen (Aleve, Naprosyn, Anaprox)	200–400 mg PO (initial dose), followed by 200 mg PO q8–12h	Maximum 600 mg/day (OTC); 1000 mg/day (R _x)
Diclofenac (Cataflam, Voltaren)	May initiate with 100 mg PO followed by 50 mg tid Delayed-release, 75–150 mg/day PO in divided doses	
Etodolac (Lodine)	Immediate release 200–400 mg PO 6–8h prn	Maximum 1200 mg/day
Fenoprofen (Nalfon)	200 mg PO every 4–6h prn	
Flurbiprofen (Ansaid)	Postoperative/dental pain 50 mg PO 4–6h prn	
Ketoprofen (Orudis, Orudis KT, Oruvail)	12.5 mg PO 4–6h prn, may initiate with 25 mg	Maximum 75 mg/day (OTC); 300 mg/day (R _x)
Indomethacin	75–150 mg/day PO in 3 or 4 divided doses for 7–14 days	
Nabumetone (Relafen)	1000–2000 mg/day PO divided 1 or 2 times	
Ketorolac (Toradol)	Only used acutely following IV or IM dosing; give 20 mg × 1 dose, then 10 mg PO 4–6h prn	Maximum 40 mg/day PO; maximum combined duration of parenteral and oral routes is 5 days; if ≥65 years of age OR weight <50 kg do not exceed 10 mg PO 4–6h prn
Piroxicam (Feldene)	20 mg/day PO	
Sulindac (Clinoril)	150–200 mg PO twice a day	Maximum 400 mg/day

3. Maximum dose 5400 mg per day; less in some situations
 4. Caution: bleeding disorders, hepatic and/or renal disease, GI disorders, use in children, pregnancy, fertility, lactation
 5. Interactions: other medications that increase the risk of bleeding, medications containing salicylates, medications causing GI disturbance
 6. Toxicity and side effects: increased risk of Reye syndrome in children, GI disturbance, GI bleeding and/or mucosal lesions, otic effects (tinnitus and hearing loss at high doses), hepatotoxicity, nephrotoxicity is rare, and increased risk of bleeding
- D. COX-2 inhibitors (a subset of NSAID class) (Table 18-2)
1. Mechanism of action: selectively inhibits the activity of the enzyme COX-2, resulting in a decreased prostaglandin production, thereby decreasing the number of pain impulses received by the CNS
 2. May have fewer GI effects than COX-1 inhibitors
 3. Common side effects: peripheral edema, abdominal pain, diarrhea, dyspepsia, flatulence, nausea, back pain, dizziness, headache, insomnia, pharyngitis, rhinitis, sinusitis
 4. Caution: same risks as traditional NSAIDs
 5. Avoid in patients with recent coronary artery bypass graft surgery (CABG), creatinine clearance <30 mL/min
 6. Interactions: medications that increase the risk of bleeding, hepatotoxic or nephrotoxic medications, medications that cause GI disturbance
 7. Toxicity: GI disturbance, hepatotoxicity, nephrotoxicity, increased risk of bleeding GI ulceration, cardiovascular events, including stroke

Table 18-2 COX-2 Inhibitors—Adult Recommended Dose

COX-2 Inhibitors	Dose
Celecoxib (Celebrex)	For acute pain: initial dose 400 mg PO once plus one additional dose of 200 mg PO if needed on the first day; maintenance 200 mg PO twice a day as needed Arthritis, RA: 100–200 mg PO twice a day

- E. Narcotic analgesics (Table 18-3)
1. Overview
 - a. Mechanism of action: binds to opiate receptors in the CNS causing inhibition on ascending pain pathways thereby altering the perception of and response to pain

- b. Caution: physically addictive, controlled substances
- c. Interactions: additive CNS depression with alcohol
- d. Toxicity and side effects: constipation, drowsiness, nausea/vomiting, sedation, itching, difficulty urinating, miosis, toxicity may result in respiratory depression
- e. Antidote for opioid overdose: naloxone (Narcan)

Table 18-3 Actions of Opiate Receptors

Opiate Receptor	Action
Mu-1	Analgesia
Mu-2	Respiratory depression Euphoria Physical dependence Constipation
Delta	Analgesia
Sigma	Autonomic stimulation Dysphoria Hallucinations
Kappa	Analgesia Sedation Miosis
Epsilon	Analgesia

2. Morphine
 - a. The prototype opioid narcotic
 - b. Schedule II
 - c. Mechanism of action: Acts on mu, kappa, and sigma receptors
 - 1) Decreases pain by depressing opioid receptors in the limbic system
 - 2) Activates certain midbrain neurons that relay inhibitory impulses from periphery to brain
 - 3) Alter brain's perception of pain, decrease substance P, decrease nerve conduction of pain
 - d. Used for relief of severe acute and chronic pain when other drugs have failed
 - e. No maximum dose: must titrate up slowly to lessen side effects, especially respiratory depression
 - f. Can suppress cough reflex
 - g. Adverse effects: euphoria, feelings of relaxation, reduced anxiety, respiratory depression, sedation, constipation, papillary constriction, and cough suppression, itching, sweating, and hypotension (caused by histamine release)
3. Hydromorphone (Dilaudid)
 - a. Mechanism of action: Similar to morphine
 - 1) Faster onset of action and shorter duration of action
 - 2) 8–10 times stronger than morphine
 - b. Used for moderate to severe pain
 - c. Schedule II

4. Codeine (methyl morphine)
 - a. Mechanism of action: similar to morphine but not as potent and shorter duration of action
 - b. Combination therapy with other agents in same formulation
 - c. Also used for suppressive therapy of cough
 - d. Used for moderate pain
 - e. Must monitor contents when using multiple agents
 - f. Schedule II or III
 - g. Adverse effects: constipation, nausea, and vomiting
5. Synthetic and semisynthetic narcotics
 - a. Oxycodone (OxyContin)
 - 1) Mechanism of action: similar to morphine; alters perception and response to pain
 - a) As potent as morphine
 - b) 10–12 times less potent than codeine
 - 2) Used for moderate to moderately severe pain
 - 3) Schedule II
 - 4) Combination products containing oxycodone
 - (a) Percocet = acetaminophen + oxycodone
 - (b) Percodan = aspirin + oxycodone
 - 5) Dose
 - (a) Percocet: Doses should be given every 4–6 hours as needed and titrated to appropriate analgesic effects. Maximum daily dose based on acetaminophen content: oral 4 g/day for adults
 - (b) Percodan: 1 tablet every 6 hours as needed for pain; maximum aspirin dose should not exceed 4 g/day for adults
 - 6) Metabolized in liver by cytochrome P-450 (CYP) 2D6
 - b. Meperidine (Demerol)
 - 1) No maximum dose: must titrate up slowly to lessen side effects, especially respiratory depression
 - 2) Can suppress cough reflex
 - 3) Useful in treatment of rigors
 - 4) Schedule II
 - 5) Contraindicated for use with monoamine oxidase inhibitors (MAOIs)
 - 6) Adverse effects: itching, sweating, and hypotension (caused by histamine release)
 - 7) Toxic metabolite = normeperidine; patient must have good renal function to use medication
 - c. Propoxyphene (Darvon)
 - 1) Combination therapy with other agents in same formulation
 - 2) Must monitor contents when using multiple agents
 - 3) Less addictive than opioids
 - 4) Used for moderate pain
 - 5) Schedule IV
 - 6) Adverse effects: constipation, GI upset, CNS disturbance
 - d. Fentanyl (Actiq, Duragesic, Fentora)
 - 1) Mechanism of action: mu agonist
 - 2) Highly lipophilic (rapid onset and short duration of action)
 - 3) No active metabolites
 - 4) Used for breakthrough cancer pain, chronic pain, analgesia and anesthesia
 - 5) No maximum dose: must titrate up slowly to lessen side effects, especially respiratory depression
 - 6) Schedule II
 - 7) Available as oral transmucosal lozenges (“lollipops” [Actiq]), effervescent buccal tablets (Fentora), buccal film (Onsolis) transdermal patches (Duragesic), and injectable formulations
 - 8) Adverse effects: itching, sweating, and hypotension (caused by histamine release)
3. Drugs used in treatment of narcotic dependency
 - a. Methadone (Dolophine)
 - 1) Mechanism of action: mu-opioid receptor agonist activity; synthetic drug
 - 2) Used for detoxification and maintenance treatment of opioid addiction
 - 3) Also used for pain relief
 - 4) Patients must be in authorized methadone program; prescribers who prescribe for narcotic dependency must have special DEA registration; such registration is not needed for those using methadone for pain
 - 5) High abuse potential
 - 6) Schedule II
 - b. Buprenorphine (Suboxone and Subutex)
 - 1) Both products are available as 2-mg and 8-mg sublingual (under the tongue) tablets; buprenorphine injection is also available.
 - a) Subutex contains only buprenorphine.
 - b) Suboxone is a combination product with buprenorphine and naloxone in a 4:1 ratio, respectively.
 - 2) Mechanism of action: produces effects typical of both pure mu agonists and partial agonists depending on dose and pattern of use
 - 3) Patients must be in authorized opioid maintenance program; prescribers who prescribe for narcotic dependency must have special DEA registration; such registration not needed for those using drug management for pain
 - 4) Schedule III
 - 5) Adverse effects: respiratory depression especially when used with benzodiazepines
- F. Narcotic antagonists
 1. Naloxone (Narcan)

- a. Mechanism of action: opioid antagonists; displaces opiates from receptor site without activating receptor site
- b. Used for reversal of opioid depression
 - 1) Diagnosis of suspected opioid tolerance
 - 2) Increase blood pressure (adjunct)
- c. May precipitate acute withdrawal symptoms
- 2. Naltrexone (ReVia)
 - a. Used as opioid antagonist
 - b. Also used for alcohol dependence
 - c. Adverse effect: dose-related hepatocellular injury; will cause narcotic withdrawal symptoms
- G. Antidepressants used for pain management
 - 1. Tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have been found to provide some relief depending on the type of pain to be treated.
 - 2. Used for chronic pain (e.g., neuropathic pain). Some SSRIs used for fibromyalgia.
 - 3. TCA examples: amitriptyline (Elavil), nortriptyline (Pamelor), desipramine (Norpramin)
 - 4. Narrow therapeutic window for TCA
 - 5. TCAs associated with side effects: sedation, orthostatic hypotension, urinary retention
- H. Anticonvulsants used for pain management
 - 1. Used for chronic pain (e.g., neuropathic pain)
 - 2. Liver function tests (LFT) should be obtained at baseline and throughout use with many of these drugs (e.g., phenytoin, valproic acid, carbamazepine).
 - 3. Examples: gabapentin (Neurontin); carbamazepine (Tegretol); phenytoin (Dilantin), valproic acid (Depakote), lamotrigine (Lamictal)
 - a. Gabapentin is the most promising with the fewest side effects.
 - 1. Initial adult dose: 100 mg twice daily, may titrate up to 1200–2400 mg daily divided in three doses
- I. Local anesthetics
 - 1. Topical local anesthetics (e.g., Lidoderm, EMLA) are used for neuropathic pain and postherpetic neuralgia.
 - 2. Use only on intact skin.
- J. Capsaicin
 - 1. Over-the-counter (OTC) topical products: Zostrix, Axsain
 - 2. Composed of an extract of chili peppers
 - 3. Also used for rheumatoid arthritis and osteoarthritis
 - 4. Rarely recommended due to overall poor efficacy
 - 5. Adverse effect: burning at site of administration
- K. Corticosteroids
 - 1. May be used for neuropathic symptoms when associated with inflammation and edema
 - a. Also used for bone pain, spinal metastasis, rheumatoid arthritis, other acute inflammatory disorders
 - 2. Example: dexamethasone commonly used
 - 3. Many potential adverse effects: hyperglycemia, insomnia, GI irritation, psychosis, osteoporosis
- L. Other neuropathic pain medications

- 1. Clonidine
- 2. Baclofen
- 3. Mexiletine

PATIENT PROFILE

Patient Initials: PB

Sex: Male

Age: 33

Height: 5' 11"

Weight: 70 kg

Race: White

Allergies: Codeine (rash, itching)

Current: PB was admitted to the hospital via the trauma team with multiple large bone fractures due to a motorcycle accident. He broke his left leg, his left collarbone, some rib bones, and his left radius and ulna in the accident. He also has serious contusions over his body. He had orthopedic surgery for his fractures. One of the main immediate issues for postoperative care is providing adequate pain control as he heals and gets ready for extensive rehabilitation.

Medical History:

No chronic health problems; family practice clinic chart states occasional treatment for seasonal rhinitis (takes nonprescription Claritin during allergy season)

Social History:

Tobacco use: None.

Alcohol use: Frequent, drinks several beers per day

Current Medications: No regular medications at present time at home.

Postoperative medications include:

D5%/1/2NS with 20 mEq KCl per liter at 125 mL/h: each day 1L of these fluids with a vial of multivitamins and thiamine 100 mg

Cefazolin 1 gm IV q8h

Lorazepam 1 mg IV q4–6h as needed (PRN) for anxiety

Pain management consult for ordering of pain medications; morphine 10 mg IV given 10 minutes ago in the post anesthesia care unit (PACU).

PATIENT PROFILE QUESTIONS

1. The pain management team decides that initial pain management will be in the form of patient-controlled analgesia (PCA) because this will likely provide the best pain control in the immediate postoperative period. Which medications would be appropriate to use for DB in a hospital setting using a PCA device?
 - I. Morphine
 - II. Codeine
 - III. Hydromorphone
 - IV. Oxycodone
 - a. I only
 - b. II only
 - c. III only
 - d. IV only
 - e. I and II
 - f. I and III
 - g. I and IV

Answer: g. Morphine and hydromorphone are potential choices for DB, and both are commonly used in PCA devices. Codeine has been used for PCA, but is not a choice for DB given his stated allergy status. Oxycodone is not available in dosage forms amenable for PCA.

2. The pain team decides that morphine will be used for the initial PCA regimen. Which of the following represents a practical initial PCA order for DB?
 - a. After the initial loading dose for acute pain control, begin morphine PCA at 1 mg bolus with a 10-minute lockout interval.
 - b. After the initial loading dose for acute pain control, begin morphine PCA at 10 mg bolus with an 8-minute lockout interval.
 - c. After the initial loading dose for acute pain control, begin morphine PCA at 0.05 mg/kg bolus with a 15-minute lockout interval.

Answer: a. A typical postoperative PCA morphine regimen begins with 0.5–2 mg boluses and 8–10 minute lockout intervals. Answer b would provide too-high and too-frequent dosing for PCA delivery, potentially resulting in overdosage. There is no weight-based analgesia dosage for morphine, and the lockout period is too long for a postoperative patient for option c to be practical.

3. After several weeks, DB is taking food well and recovering nicely despite his injuries. He still needs a significant amount of medication to manage his pain, especially during rehabilitation sessions. He will be released to home with a prescription for Percocet 5/325, 1 tablet PO q6h as needed for pain and a prescription for ibuprofen 400 mg PO q6h for inflammation and pain. What should patient counseling for DB regarding the Percocet prescription include?
 - I. The risk of medication dependence is overall very low for DB.
 - II. DB should avoid the use of alcohol because this can increase the side effects of Percocet such as dizziness, drowsiness, and difficulty breathing, or the risk for liver problems.
 - III. DB should not exceed the recommended dosage for Percocet and not take additional acetaminophen (e.g., Tylenol) because this could result in acetaminophen overdosage.
 - IV. Percocet may cause constipation; the use of stool softeners and the occasional use of a laxative may be needed to maintain bowel regularity.
 - a. II and III only
 - b. I, II, and III
 - c. All of the above

Answer: c. Appropriate counseling regarding the use of Percocet (oxycodone-acetaminophen combination) would include all of the above points. Patients have a very low risk of dependency when opioids are prescribed for the acute management of pain. Alcohol should be avoided while receiving regular acetaminophen and opioid treatment; this is of concern for DB, who had daily alcohol intake before admission. Acetaminophen overdose can

be unintentional because patients may not realize that many products contain acetaminophen; appropriate counseling can help avoid liver problems. Constipation due to opioids is common and may require the occasional use of laxatives.

REVIEW QUESTIONS

(Answers and Rationales on page 369.)

1. Dexamethasone can be used in the treatment of all of the following except?
 - a. Addison's disease
 - b. Dermatitis
 - c. Asthma
 - d. Cushing's disease
2. Codeine is metabolized by which of the following enzymes?
 - a. Sulfotransferase
 - b. Glutathione transferase
 - c. Cyclooxygenase
 - d. Catechol-O-methyltransferase
 - e. Acetylcholinesterase
3. Which of the following anesthetic/partition coefficient/minimum alveolar concentration would have the fastest onset of action?
 - a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0.16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
4. Which of the following anesthetic/partition coefficient/minimum alveolar concentration would have the least effect on uterine smooth muscle?
 - a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0.16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
5. Which of the following anesthetic/partition coefficient/minimum alveolar concentration would have the highest potency?
 - a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0.16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
6. Which of the following anesthetic/partition coefficient/minimum alveolar concentration would have the lowest potency?
 - a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0.16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
7. Which of the following statements about acetaminophen is true?
 - a. It may cause blood dyscrasias.

- b. It is safe to use in patients with glucose-6-phosphate dehydrogenase (G6PD).
 - c. It does not cross the placenta.
 - d. It inhibits peripheral COX-1 enzymes.
 - e. Its duration of action is 18–24 hours.
8. Which of the following statements about aspirin is true?
 - a. Its analgesic duration of action is 18–24 hours.
 - b. It is primarily excreted in bile.
 - c. It is hydrolyzed in the bloodstream.
 - d. Has an onset of action of 120 minutes
 - e. It may cause hypertension.
9. Which of the following statements regarding acetaminophen is FALSE?
 - a. It may cause a skin rash.
 - b. It causes hepatotoxicity in overdose.
 - c. It is an antipyretic agent.
 - d. It is safe to use in children with influenza infection.
 - e. It is an anti-inflammatory agent.
10. Salicylates may be used to treat all of the following EXCEPT a:
 - a. 6-year-old girl with fever, dry cough, fatigue and muscle aches.
 - b. 65-year-old woman with stiffening of the wrists and interphalangeal joints.
 - c. 65-year-old woman with knee pain after a minor fall.
 - d. 30-year-old man with family history of early-onset myocardial infarction.
 - e. 25-year-old woman with spasmodic dysmenorrhea.
11. Injection of a local anesthetic into a circulatory vessel may result in which of the following?
 - a. Circulatory collapse
 - b. Myocardial depression
 - c. Respiratory depression
 - d. Seizures
 - e. All of the above
12. Which of the following is NOT an indication for opioid use?
 - a. Pain
 - b. Diarrhea
 - c. Cough
 - d. Inflammation
 - e. Preanesthesia
13. Which of the following statements about meperidine is true?
 - a. It produces CNS excitation.
 - b. It crosses the placenta.
 - c. It is excreted predominately in bile.
 - d. It may cause hypertension.
 - e. It may cause dysuria.
14. Which of the following is a neuromuscular blocking agent that may cause muscarinic side effects?
 - a. Succinylcholine
 - b. Gallamine
 - c. Pancuronium
 - d. Decamethonium
 - e. Tubocurarine
15. What is the active ingredient in Toradol?
 - a. Ketorolac
 - b. Oxaprozin
 - c. Acetaminophen
 - d. Cortisol
 - e. Amitriptyline
16. Which of the following is NOT a method of administering ketorolac tromethamine (Toradol)?
 - a. IV
 - b. IM
 - c. Oral
 - d. Topical
 - e. Rectal
17. Adverse effects of ketorolac tromethamine (Toradol) include all of the following EXCEPT:
 - a. headache.
 - b. pruritus.
 - c. abdominal pain.
 - d. hypotension.
 - e. edema.
18. Which of the following is safe to take with ketorolac tromethamine (Toradol)?
 - a. Warafin
 - b. Alcohol
 - c. NSAID
 - d. Aspirin
 - e. None of the above is safe.
19. Naproxen:
 - a. can be used to treat gout.
 - b. can be prescribed as a tablet or suspension.
 - c. may cause edema.
 - d. is more than 90% absorbed after oral administration.
 - e. All of the above
20. Among glucocorticoids, which drug has the shortest duration of acting?
 - a. Dexamethasone
 - b. Betamethasone
 - c. Prednisolone
 - d. Methylprednisolone
 - e. Hydrocortisone
21. Ketamine:
 - a. can be administered IM or IV.
 - b. has minimal effect on the cardiovascular system.
 - c. has a duration of action of 30–60 minutes.
 - d. a and b
 - e. a, b, and c
22. Which of the following can be administered intra-articularly?
 - a. Aspirin
 - b. Corticosteroids
 - c. Ibuprofen

- d. Penicillamine
 - e. Auranofin
23. Which of the following drugs may produce drowsiness?
 - a. Aspirin
 - b. Corticosteroids
 - c. Ibuprofen
 - d. Penicillamine
 - e. Auranofin
 24. Which of the following is notable for more severe CNS effects than most NSAIDs?
 - a. Aspirin
 - b. Hydroxychloroquine
 - c. Indomethacin
 - d. Cyclophosphamide
 - e. Methotrexate
 25. Which of the following is available in enteric-coated tablets?
 - a. Aspirin
 - b. Hydroxychloroquine
 - c. Indomethacin
 - d. Cyclophosphamide
 - e. Methotrexate
 26. Aspirin slows secretion of which drug?
 - a. Aspirin
 - b. Hydroxychloroquine
 - c. Indomethacin
 - d. Cyclophosphamide
 - e. Methotrexate
 27. Ibuprofen is:
 - a. A derivative of phenylpropionic acid
 - b. An anti-inflammatory and analgesic
 - c. Unsafe in rheumatoid arthritis
 - d. Only available orally
 - e. All of the above
 28. Which of the following anesthetic/partition coefficient/minimum alveolar concentration should be avoided in epileptic patients?
 - a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0/16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
 29. A 36-year-old man is taken to the emergency department with respiratory depression. Which of the following drugs is a likely culprit?
 - a. Atropine
 - b. Amphetamine
 - c. Oxycodone
 - d. Kerosene
 - e. Mushrooms
 30. Which of the following statements is correct?
 - a. Propoxyphene may be used to suppress withdrawal symptoms of heroin.
 - b. Propoxyphene is not addictive.
 - c. Methadone is not addictive.
 - d. Propoxyphene may be discontinued abruptly 1 month after successful heroin cessation.
 - e. Methadone withdrawal is of shorter duration than heroin withdrawal.
 31. Which of the following statements is FALSE?
 - a. Phenacetin may cause renal damage.
 - b. Meperidine may cause renal damage.
 - c. Salicylates may cause renal damage.
 - d. Combinations of analgesics may be more nephrotoxic than single drugs.
 - e. Phenacetin is metabolized to acetaminophen.
 32. Which of the following anesthetic/partition coefficient/minimum alveolar concentration is not used due to nephrotoxicity?
 - a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0/16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
 33. Which of the following causes increased hydrogen ion permeability of the gastric mucosa?
 - a. Aspirin
 - b. Indomethacin
 - c. Erythromycin
 - d. a and b
 - e. a, b, and c
 34. What is the antidote for pentazocine overdose?
 - a. Naloxone
 - b. Nalorphine
 - c. Levallorphan
 - d. Any of the above
 - e. None of the above
 35. What is the mechanism underlying hemorrhagic gastritis secondary to aspirin therapy?
 - a. Back diffusion of hydrogen ions across gastric mucosa
 - b. Inhibition of prostaglandin synthesis
 - c. Decreased renal salicylate excretion
 - d. a and b
 - e. a, b, and c
 36. Which of the following may cause increased biliary duct pressure?
 - a. Warfarin
 - b. Morphine
 - c. Phenytoin
 - d. Carbon tetrachloride
 - e. Acetazolamide
 37. Which of the following may cause analgesic nephropathy?
 - a. Prolonged use of an NSAID
 - b. Prolonged use of aspirin combinations
 - c. Chronic overuse of an NSAID
 - d. All of the above
 - e. None of the above

38. Which of the following is NOT true of acetaminophen toxicity?
- 10 g or more may produce hepatic necrosis in adults.
 - Diuresis may be effective therapy.
 - Liver necrosis is centrilobular and midzonal.
 - Phenacetin was metabolized principally to acetaminophen.
 - Transient azotemia may occur.
39. Which of the following is the most common pulmonary complication associated with opioid ingestion?
- Interstitial fibrosis
 - Pulmonary calcification
 - Bronchoconstriction
 - Respiratory depression
 - Pleural effusion
40. Which of the following is seen in acute opioid overdose?
- Coma
 - Pinpoint pupils
 - Respiratory depression
 - All of the above
 - None of the above
41. Which of the following is an effect of opioids?
- Stimulation of antidiuretic hormone (ADH) secretion
 - Suppression of luteinizing hormone (LH) secretion
 - Suppression of prolactin secretion
 - a and b
 - a, b, and c
42. Which opioid has the shortest duration of action?
- Meperidine
 - Methadone
 - Morphine
 - Hydromorphone
 - Codeine
43. Which of the following is an opioid receptor antagonist?
- Buprenorphine
 - Butorphanol
 - Pentazocine
 - Naloxone
 - All of the above
44. Which of the following is true?
- Aspirin is metabolized by both first- and zero-order kinetics.
 - High-dose aspirin can lower serum urate.
 - Aspirin acts via inhibition of cyclooxygenase.
 - All of the above
 - None of the above
45. Which of the following has the shortest duration of action when administered subcutaneously?
- Meperidine
 - Methadone
 - Morphine
 - Hydromorphone
 - Codeine
46. Which of the following can be used to prevent abstinence withdrawal syndrome in heroin-addicted patients in the inpatient setting?
- Meperidine
 - Methadone
 - Butorphanol
 - a and b
 - All of the above
47. Which of the following statements is FALSE?
- High-dose salicylates may increase serum uric acid.
 - Salicylate effect on platelet aggregation is irreversible.
 - Salicylates inhibit prostaglandin synthetase.
 - Salicylates only act on central cyclooxygenase enzymes.
 - All of the above are true.
48. Which of the following is most likely to produce dysphoria?
- Codeine
 - Pentazocine
 - Methadone
 - Meperidine
 - Morphine
49. Which of the following statements about morphine is true?
- It decreases pupillary light responsiveness.
 - It acts directly on extrinsic muscles of the eye.
 - It acts directly on the smooth muscle of the iris.
 - It produces mydriasis via sympathetic activation.
 - It produces miosis via effects on the oculomotor nerve.
50. Which of the following is inhibited by aspirin?
- Prostaglandin synthetase and prostaglandin reductase
 - Prostaglandin synthetase and thromboxane synthetase
 - Prostaglandin synthetase and cyclooxygenase
 - Prostaglandin reductase and cyclooxygenase
 - Thromboxane synthetase and cyclooxygenase
51. Which of the following is seen with salicylate overdose?
- Acid-base disturbances
 - Hypothermia
 - Electrolyte imbalances
 - Fever
 - a, c, and d
52. What is the primary mechanism of death with acetaminophen overdose?
- Hepatic necrosis
 - Myocarditis
 - Neutropenia

- d. Hemolysis
 - e. Renal necrosis
53. Which of the following is NOT an effect of morphine?
- a. Diarrhea
 - b. Miosis
 - c. Respiratory depression
 - d. Postural hypotension
 - e. Behavioral changes
54. Which of the following is NOT true of indomethacin?
- a. It can be used to treat bursitis
 - b. Dosage for rheumatoid arthritis is 25–50 mg, 2 to 3 times per day
 - c. It may cause indigestion
 - d. It is not metabolized by the liver
 - e. It is excreted in both urine and feces
55. Zanaflex (tizanidine) is?
- I. A centrally acting alpha-2 antagonist
 - II. A muscle relaxer
 - III. Primarily metabolized by the CYP1A2
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
56. A patient undergoing a dental procedure should stop aspirin therapy for how many days before his appointment?
- a. 7 days
 - b. 5 days
 - c. 3 days
 - d. 1 day
 - e. It is not necessary to stop aspirin therapy
57. Which of the following has a rapid onset of action and causes involuntary muscle movements?
- a. Etomidate
 - b. Ketamine
 - c. Thiopental
 - d. Fentanyl
 - e. Propofol
58. Which of the following is true regarding Fentanyl?
- I. Used as an adjunct in anesthesia
 - II. Requires patient receive mechanical ventilation when used during surgery
 - III. Available as a transdermal patch, transmucosal lozenge, and parenteral formulation
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
59. Which of the following is true about ketamine?
- I. Classified as an NMDA antagonist
 - II. May cause hallucinations during recovery
 - III. Used for the induction and maintenance of general anesthesia
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
60. Which opioid has the longest duration of analgesic action?
- a. Meperidine
 - b. Methadone
 - c. Morphine
 - d. Hydromorphone
 - e. All have similar durations of analgesic actions
61. Which of the following inhibits cyclooxygenase?
- a. Ticlopidine
 - b. Dipyridamole
 - c. Tranexamic acid
 - d. Aspirin
 - e. c and d
62. The Pain Ladder, a widely accepted three-step approach to implementing the three categories of pain medication, was developed by the?
- a. WHO
 - b. CDC
 - c. AMA
 - d. FDA
 - e. JCAHO
63. Which of the following anesthetic/partition coefficient/minimum alveolar concentration is most likely to produce hepatitis?
- a. Isoflurane/1.40/1.15
 - b. Nitrous oxide/0.47/105
 - c. Methoxyflurane/12/0/16
 - d. Enflurane/1.8/1.68
 - e. Halothane/2.3/0.75
64. Which of the following has minimal effects on the cardiovascular system and has depressant CNS effects?
- a. Etomidate
 - b. Ketamine
 - c. Thiopental
 - d. Fentanyl
 - e. Propofol
65. Which of the following results in cardiac stimulation?
- a. Etomidate
 - b. Ketamine
 - c. Thiopental
 - d. Fentanyl
 - e. Propofol
66. All of the following are true of propofol EXCEPT:
- a. it is highly lipophilic.
 - b. the half-life does not correlate with duration of CNS depression.
 - c. it is useful as a skeletal muscle relaxant.
 - d. it may result in hypotension.
 - e. it provides a rapid recovery from anesthesia.

67. All of the following are true of ketamine EXCEPT:
- it is a strong analgesic.
 - it may cause bronchoconstriction.
 - it may cause hallucinations during recovery.
 - it causes dissociative anesthesia.
 - All of the above are true.
68. All of the following are true of etomidate EXCEPT it:
- is a potent analgesic and hypnotic.
 - inhibits adrenal function.
 - has no adverse adrenal effects with short-term use.
 - has minimal effects on cardiac function.
 - All of the above are true.
69. Midazolam:
- is contraindicated in COPD.
 - produces skeletal muscle relaxation.
 - produces analgesia.
 - is useful in treating seizures.
 - is cardiostimulative.
70. All of the following are true of bupivacaine EXCEPT it:
- is rapidly hydrolyzed by plasma esterase.
 - has a high risk of side effects when used in epidural anesthesia.
 - should not be used in lidocaine-allergic patients.
 - should be used in higher doses for epidural than spinal anesthesia.
 - is metabolized primarily in the liver.
71. The visual analog scale is used to measure pain?
- Location
 - Severity
 - Signs and symptoms
 - Quality
 - All of the above
72. Neuropathic pain is classified as?
- Pain mediated through c-fibers in the sensory nervous system.
 - Pain that is mediated by a normal pain system.
 - Pain that is due to a damaged sensory nervous system.
 - Pain that is imagined or otherwise psychologically mediated.
73. Which of the following is not treated with dexamethasone?
- Inflammation
 - Asthma
 - Addison disease
 - Wilson disease
 - None of the above
74. Which of the following is/are complication(s) of prednisone?
- Osteonecrosis
 - Hyperglycemia
 - Cataracts
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
75. Methadone has which of the following property?
- NMDA antagonistic properties
 - Free of active metabolites
 - A short half-life
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
76. Which of the following NSAID is a prodrug?
- Nabumetone
 - Piroxicam
 - Sulindac
 - Meloxicam
 - a and c
77. A ceiling dose is?
- The individual starting dosage for each patient receiving a narcotic
 - Determined by the individual patient's pain threshold
 - The highest dose at which analgesia that can be achieved without significant side effects or toxicity
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
78. Which of the following is a side effect of corticosteroids?
- Telangiectasias
 - Acne
 - Ecchymosis
 - Striae
 - All of the above
79. Which of the following statements about hydrocortisone is true?
- It has a half-life of elimination of 8–12 hours.
 - It is metabolized in the liver.
 - It is predominately excreted in the feces.
 - a and b
 - a, b, and c
80. Which of the following drugs is/are used to reduce opiate-induced nausea and vomiting?
- Promethazine
 - Granisetron
 - Droperidol
- I only
 - III only
 - I and II only

- d. II and III only
 - e. I, II, and III
81. Which of the following is a common opioid side effect?
- a. Constipation
 - b. Pruritus
 - c. Sedation
 - d. Mental confusion
 - e. All of the above
82. Which of the following opioids is/are used for spinal drug delivery?
- a. Morphine
 - b. Fentanyl
 - c. Meperidine
 - d. Hydromorphone
 - e. All of the above

I. Introduction

A. Psychiatric disorders

1. Patients who have one psychiatric disorder will usually have multiple psychiatric disorders.
2. Patients must be carefully assessed to develop an individualized treatment plan.
3. Must determine if new symptoms are due to treatment or new psychiatric disorder.

B. Therapeutic options

1. Psychotherapy

- a. Combination of psychotherapy and pharmacotherapy is the optimal approach for most patients
- b. Psychotherapy is often difficult to obtain or is not covered by insurance.
- c. Helps with psychosocial or coping skills that may contribute to the specific illness

2. Pharmacotherapy

- a. Improves mood and somatic symptoms

3. Other modalities

a. Electroconvulsive therapy (ECT)

- (1) Very effective form of treatment, unknown mechanism of action, generally reserved for treatment-resistant or delusional depression.
- (2) Controversial form of treatment
- (3) Patients who have responded to it in the past and have relapsed may benefit.
- (4) Most common side effects include short-term memory problems, which tend to improve with time after treatment.

II. Anxiety disorders

A. Types

1. Generalized anxiety disorder (GAD): 6 months or more of excessive worry or anxiety generally with an unidentified cause
2. Panic disorder: discrete periods of sudden intense fear or terror and feelings of impending doom. Usually the precipitating cause is not known; the patient can become conditioned to believe it is caused by some environmental cause. Disorder can lead to agoraphobia: fear or avoidance of certain situations (e.g., going to the store) because they think they will have an attack.
3. Obsessive-compulsive disorder (OCD): characterized by obsessive or intrusive thoughts that one cannot control and that are repetitive in nature: ritualistic behaviors (e.g., repetitive hand washing, combing the hair, cleaning the house)

4. Posttraumatic stress disorder (PTSD): follows a traumatic event and is characterized by increased arousal and avoidance of stimuli that approximate the original traumatic event
5. Phobic disorders: characterized by anxiety out of proportion to the stimulus that is the object of fear

B. Treatments

1. Benzodiazepines (Table 19-1)

- a. Anxiolytic treatment and prophylaxis of panic attacks
 - b. A reduction in anxiety may be seen with first dose.
 - c. Five properties common to all
 - (1) Anxiolytic
 - (2) Hypnotic
 - (3) Muscle relaxant
 - (4) Anticonvulsant
 - (5) Amnesic
 - d. Tolerance to the anxiolytic action is uncommon, but tolerance may occur to the hypnotic action (which is why benzodiazepines should only be used for insomnia for a few days at a time).
 - e. Anxiolytics are differentiated by half-life, metabolites (active/inactive), potency.
 - f. Abrupt cessation can lead to withdrawal, depending on length of therapy.
- #### 2. Antidepressants (discussed in more detail under Depression)
- a. Tricyclic antidepressants (TCA)
 - (1) Anxiety treatment and prophylaxis of panic disorders
 - b. Selective serotonin reuptake inhibitors (SSRI)

Table 19-1 Benzodiazepines used for Anxiety

Agent	Half-life (hours)	Equivalent Dose (mg, approximate only)
Alprazolam (Xanax)	6–12	1
Chlordiazepoxide (Librium)	5–30	25
Diazepam (Valium)	20–100	10
Lorazepam (Ativan)	10–18	1
Oxazepam (Serax)	4–15	10

- (1) Anxiety treatment and prophylaxis of panic disorders
- c. Serotonin-norepinephrine reuptake inhibitors
 - (1) Venlafaxine (Effexor) has FDA approval for treatment of generalized anxiety disorder.
- d. Buspirone
 - (1) May be effective for anxiety
 - (2) Little value for panic disorder
 - (3) Long onset of action: 4–6 weeks, must use another anxiolytic until onset occurs
- e. Beta blockers
 - (1) May block peripheral symptoms of panic disorders
- f. Monoamine oxidase inhibitors (MAOIs)
 - (1) May be effective for panic disorders in patients with atypical depression

III. Schizophrenia

Psychotic disorder that has multiple symptoms involving perception (e.g., hallucinations), ideation, reality (e.g., delusions), cognition (e.g., loose associations), emotions (e.g., flat affect), behavior (e.g., disorganization), attention, concentration, motivation (e.g., avolition or lack of motivation), concentration, judgment.

Schizophrenia usually occurs between adolescence and early adulthood, earlier in men (early 20s) than women (late 20s to early 30s). The incidence is almost equal between sexes.

A. Signs and symptoms

- 1. Positive
 - a. Delusions
 - (1) Erroneous beliefs that involve misinterpretations of reality and are relatively resistant to evidence that refutes them
 - (2) A “fixed” delusion that will not change no matter how much evidence is offered to the contrary
 - b. Hallucinations
 - (1) Perceptual abnormalities that can involve any sensory system
 - (2) Schizophrenia often involves auditory hallucinations that can be persecutory (e.g., someone’s going to get me), paranoid (e.g., someone is watching me), commanding (e.g., someone told me to do it), etc.
- 2. Negative
 - a. Lack of facial expression
 - b. Blank stares
 - c. Monotone and monosyllabic speech
 - d. Seeming lack of interest in the world and other people
 - e. Inability to feel pleasure or act spontaneously
 - f. Disorganization (speech, behavior, poor attention)
- 3. Cognitive
 - a. Difficulty paying attention
 - b. Memory problems
 - c. Difficulty planning or structuring activities
 - d. Lack of insight and understanding

B. Four phases

- 1. Prodromal
 - a. Characterized by gradual development of symptoms that may go unnoticed until major symptom occurs
 - b. May include isolation, deterioration of hygiene, loss of interest in work, or school, dysphoria
- 2. Acute phase
 - a. Full-blown episode of psychotic behavior
 - b. Patient may be unable to care for self at times
- 3. Stabilization phase
 - a. Acute symptoms begin to decrease
 - b. Phase may last for several months
- 4. Stable phase
 - a. Acute symptoms have markedly declined and may not be present
 - b. Nonpsychotic symptoms such as anxiety and depression may be present (complete remission without symptoms is uncommon)

C. Risk factors for schizophrenia

- 1. Family history of schizophrenia
- 2. Lower socioeconomic status
- 3. Poor birth history
- 4. Intrauterine trauma
- 5. Living in an urban area
- 6. Stress
- 7. Being born during the winter

D. Treatment

- 1. Antipsychotic agents
 - a. Two classes: atypical (or second generation) and conventional antipsychotics
 - b. Atypical antipsychotics (Table 19-2)
 - (1) Block dopamine, serotonin, and other neurotransmitters
 - (a) Block dopamine more selectively than conventional antipsychotics, thereby reducing the probability of extrapyramidal symptoms (EPS)
 - (2) First-line therapy
 - (3) Maintain indefinitely
 - (4) Complications of treatment
 - (a) Metabolic syndrome (excess abdominal fat, insulin resistance, hyperlipidemia, hypertension)
 - (b) Tardive dyskinesia is possible with all atypical antipsychotic agents.
 - c. Conventional antipsychotic agents
 - (1) Primarily block dopamine
 - (2) Classified as high, mild, or low potency depending on affinity for dopamine
 - (3) High potency
 - (a) Haloperidol (Haldol)
 - (i) Prototypical high-potency drug
 - (ii) Haloperidol decanoate available as IM depot
 - (b) Fluphenazine (Prolixin)
 - (i) IM depot form also available
 - (c) Thiothixene (Navane)
 - (i) Notably high incidence of akathisia (“inner restlessness”)

Table 19-2 Atypical Antipsychotics Comparison Table

Generic/Brand Name	Typical Adult Oral Dose	Comments
Risperidone (Risperdal)	Initial 1–2 mg daily Maintenance 2–6 mg daily (average dose 4 mg daily)	Most widely prescribed antipsychotic Rapid absorption and 20-hour elimination half-life Dose-related EPS Serum levels are modestly decreased by cytochrome P-450 (CYP) inducers
Olanzapine (Zyprexa)	Initial 5–10 mg daily Maintenance 30 mg daily	Effective for schizophrenia as well as for Tourette syndrome and borderline personality disorder Gradual absorption and 30-hour elimination half-life Highest risk of weight gain; risk of diabetes Drug levels may be increased by CYP inducers; drug levels may be decreased by cigarette smoking
Quetiapine (Seroquel)	Initial 25 mg twice daily Titrate at rate of 25–50 mg daily to a total daily dose of 300–600 mg daily Maximum daily dose 800 mg daily (although doses up to 1200 mg daily have been used)	Sedation noted early in treatment Low incidence of EPS even at high doses
Ziprasidone (Geodon)	20–40 mg twice daily May titrate to maximum of 80 mg daily	Bioavailability increases when taken with food Risk of QTc prolongation; avoid with drugs that cause QT prolongation Drug levels may be altered by CYP inhibitors and inducers
Paliperidone (Invega)	3–12 mg at bedtime	Less chance of weight gain and diabetes Active metabolite of risperidone Bioavailability is increased by 50% when taken with a high-calorie meal 23-hour elimination half-life Does not require intact hepatic function for metabolism or excretion
Aripiprazole (Abilify)	10–30 mg at bedtime	Dopamine agonist/antagonist Long elimination half-life Causes little weight gain but little EPS, and has fewer cardiovascular adverse effects
Clozapine (Clozaril)	400 mg at bedtime	First atypical antipsychotic agent, with low risk of EPS but high risk of agranulocytosis; frequent WBC monitoring is required

- (d) Trifluoperazine (Stelazine)
- (e) Pimozide (Orap)
 - (i) Approved only for Tourette syndrome
- (4) Mild potency
 - (a) Perphenazine (Trilafon)
 - (b) Molindone (Moban)
 - (i) May cause weight reduction
 - (c) Loxapine (Loxitane)
 - (i) High affinity for dopamine and serotonin receptors
 - (d) Prochlorperazine (Compazine)
- (5) Low-potency
 - (a) Chlorpromazine (Thorazine)
 - (i) Prototypical low-potency drug
 - (b) Thioridazine (Mellaril)
 - (i) May cause QT prolongation

- (c) Mesoridazine (Serentil)
- (6) Complications of treatment: associated with EPS and increased prolactin (hyperprolactinemia)
- IV. Mood disorders
 - A. Depression
 - 1. Major depressive disorder
 - a. Unipolar depression, may experience one (first episode is a “major depressive disorder single episode”) or more episodes (“major depressive disorder recurrent”)
 - b. Number of episodes and periods between them is variable from patient to patient.
 - c. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)
 - (1) Depressive syndromes are defined in the DSM-IV.

- (2) Health professionals use the DSM-IV criteria to diagnose depressive disorders and other mental disorders.
2. Dysthymia
 - a. Chronic condition of depressed mood for at least 2 years
 - b. Symptoms not severe enough to meet DSM-IV criteria for major depressive disorder
 - c. Periods of normal mood last only for short periods
 - d. Patients may also experience major depressive disorder ("double depression").
 - e. May be difficult to treat, often not as responsive to therapy as major depressive disorder
3. Treatment
 - a. FDA warning: Patients taking antidepressants should be monitored closely for signs of suicide, worsening depression, anxiety, and panic attacks.
4. Tricyclic antidepressants (TCA)
 - a. Mechanism of action
 - (1) Block reuptake of norepinephrine
 - (2) Less effect on serotonin
 - (3) Increases concentration of norepinephrine in synapse
 - b. Dose
 - (1) Start with low dose and titrate up
 - c. Adverse effects
 - (1) Anticholinergic side effects
 - (2) Drowsiness
 - (3) Insomnia/agitation
 - (4) Gastrointestinal (GI) distress
 - (5) Weight gain
 - (6) Orthostatic hypertension
 - (7) Cardiac arrhythmia
 - d. Drug interactions
 - (1) TCA are metabolized by CYP enzymes, and drugs that inhibit/induce CYP may alter the concentrations of TCA.
 - e. Cautions
 - (1) Avoid during pregnancy
 - (2) Drugs that prolong the QT interval should be avoided with TCA.
 - f. Examples
 - (1) Imipramine, amitriptyline, amoxapine, desipramine, doxepin, nortriptyline, protriptyline, trimipramine
5. Serotonin reuptake inhibitors (SSRI)
 - a. Considered first-line therapy
 - b. May also be useful for OCD, bulimia nervosa, panic disorder, and premenstrual syndrome (PMS)
 - c. Mechanism of action
 - (1) Downregulates postsynaptic serotonin receptor in response to the increased amount of synaptic serotonin
 - d. Adverse effects
 - (1) Generally mild
 - (2) May be associated with sexual dysfunction
 - (3) Serotonin syndrome caused by overstimulation of serotonin receptors
- e. Examples
 - (1) Fluoxetine (Prozac)
 - (a) Elimination half-life of 4–6 days
 - (b) Potent inhibitor of CYP 2D6; mild inhibitor of CYP 3A4
 - (c) Usual adult initial dose: 20 mg daily; may be increased to 80 mg/day if needed (immediate-release)
 - (2) Paroxetine (Paxil)
 - (a) Potent inhibitor of CYP2D6
 - (b) Possibility of birth defects if taken during first trimester of pregnancy
 - (c) Usual adult initial dose: 20 mg daily; may be increased to 40 mg daily (immediate-release)
 - (3) Sertraline (Zoloft)
 - (a) Has the most dopaminergic reuptake blockage than any other SSRI
 - (b) Mild inhibitor of CYP 2D6
 - (c) Usual adult initial dose: initial 50 mg daily; maintenance 50–100 mg daily. Doses of a maximum of 200 mg daily may be used.
 - (d) Side effects: gastrointestinal complaints (nausea, diarrhea)
 - (4) Citalopram (Celexa)
 - (a) Major CYP 2C19 and 3A4 substrate
 - (b) Usual Adult initial dose: Dose 20–40 mg daily
 - (5) Escitalopram (Lexapro)
 - (a) Because escitalopram is the enantiomer of citalopram, it is considered to be more potent than citalopram.
 - (b) Major substrate of CYP C19, 3A4, and weak inhibitor of 2D6
 - (c) Usual adult initial dose: 10 mg daily (immediate-release)
 - (6) Fluvoxamine (Luvox)
 - (a) Approved for obsessive compulsive disorder
 - (b) Potent inhibitor of CYP450, 1A2, 3A4, and 2C19
 - (c) Usual Adult initial dose: Dose 50 mg daily; may increase to 150–250 mg daily
6. Monoamine oxidase inhibitors (MAOI)
 - a. Monoamine oxidase breaks down norepinephrine, epinephrine, dopamine, and serotonin; interference causes neurotransmitters to accumulate in the synapse
 - b. May increase tyramine and cause hypertensive crisis (headache, stiff neck, palpitations, chest pain, increased or decreased heart rate, nausea/vomiting, pyrexia, chills, flushing), cerebrovascular accident, death
 - c. Tyramine is broken down by MAO-A, and inhibiting its action may result in excessive build-up of tyramine. Patients taking MAOI should limit intake of foods that contain tyramine, including aged cheese, wines like Chianti, broad bean (fava bean) pods, chocolate, soy sauce, and others.

- d. Drug interactions
 - (1) Avoid sympathomimetics (e.g., pseudoephedrine), reserpine, TCA, levodopa, and anticholinergic agents
- e. Examples of MAOI
 - (1) Tranylcypromine, phenelzine, isocarboxazid, moclobemide, selegiline
- 7. Atypical antidepressants
 - a. Bupropion (Wellbutrin)
 - (1) Useful if patient did not respond to TCA or SSRI
 - (2) Also used for smoking cessation (Zyban)
 - (3) Mechanism of action: blocks reuptake of norepinephrine
 - (4) Usual adult dose: 150 mg twice daily
 - (5) Adverse effects: increased risk of seizures
 - (6) Drug interactions: Use cautiously in patients using other agents that may lower the seizure threshold (e.g., antipsychotics, antidepressants, fluoroquinolones)
 - b. Nefazodone (Serzone)
 - (1) Mechanism of action
 - (a) Inhibits reuptake of serotonin and norepinephrine
 - (b) Also blocks alpha-1 receptors
 - (2) Usual adult dose: 300–600 mg/day in two divided doses
 - (3) Adverse effects: associated with hepatic injury
 - (4) Drug interactions
 - (a) Major CYP 2D6 substrate
 - (b) Major CYP 3A4 inhibitor
 - c. Trazodone (Desyrel)
 - (1) Mechanism of action
 - (a) Serotonin antagonist
 - (b) Also blocks histamine and alpha-1 receptors
 - (2) Dose
 - (a) Usual adult dose: 150 mg daily in three divided doses
 - (b) Maximum 600 mg daily
 - (3) Adverse effects
 - (a) Dizziness
 - (b) Headache
 - (c) Sedation
 - (d) Also associated with priapism
 - (4) Drug interactions: major CYP 3A4 substrate
 - d. Venlafaxine (Effexor)
 - (1) Mechanism of action (serotonin-norepinephrine reuptake inhibitor (SNRI))
 - (a) Potent inhibitor of serotonin reuptake
 - (b) Inhibits norepinephrine at higher doses
 - (2) Usual adult dose: maximum 225–375 mg daily (immediate release), given in 2-3 divided doses
 - (3) Adverse effects
 - (a) May cause increased sweating
 - (b) Increased blood pressure
 - (4) Drug interactions: major CYP 2D6 substrate
 - e) Mirtazapine (Remeron)
 - (1) Mechanism of action: central presynaptic alpha-2 adrenergic antagonist effects, which thereby increases release of serotonin and norepinephrine
 - (2) Dose
 - (a) Usual adult dose: Starting dose is 15 mg, with a dosage range of 15–30 mg per day
 - (b) Taken at bedtime
 - (3) Adverse effects: may cause drowsiness and weight gain
 - (4) Drug interactions
 - (a) Major CYP 1A2, 2D6, 3A4 substrate
 - (b) Avoid with MAOI
- B. Bipolar disorder
 - 1. Bipolar: elevated mood with or without periods of major depressive disorder
 - a. Bipolar I: classic mania, majority also have major depressive disorder
 - b. Bipolar II: do not meet criteria for manic episode; have a milder form called hypomania, interspersed with major depressive disorder
 - 2. Etiology
 - a. Exact cause is unknown
 - 3. Signs and symptoms
 - a. Usually begins with an acute phase of symptoms followed by a course of relapse and remission
 - b. Episodes are manic, depressive, hypomanic, or a combination
 - 4. Diagnosis is based on signs and symptoms
 - 5. Treatment
 - a. Mood stabilizers
 - b. Lithium
 - (1) Mechanism of action: alters cation transport across cell membrane in nerve and muscle cells
 - (2) Onset of action: 4- to 10-day latency period
 - (3) Usual adult dose
 - (a) Initial dose of lithium is 300 mg two or three times daily
 - (b) May increase dose every 4 to 5 days based on levels
 - (c) Maintenance dose 900–1200 mg daily
 - (4) Target blood level for acute phase management: between 0.8 and 1.2 meq/L; maintenance levels: 0.6–1.2 meq/L
 - (5) Monitor blood urea nitrogen (BUN), serum creatinine (SCr), thyroid function
 - (6) Adverse effects
 - (a) Polyuria
 - (b) Tremor
 - (c) Loose stools
 - (d) Cognitive side effects
 - (e) Weight gain
 - (7) Longer term complications
 - (a) Renal impairment
 - (b) Cardiac rhythm disturbances
 - (c) Hypothyroidism

- (8) Drug interactions
 - (a) Drugs that may increase lithium levels: thiazide diuretics, NSAID, Angiotensin converting enzyme (ACE) inhibitors
 - (b) Drugs that may decrease lithium levels: potassium-sparing diuretics
 - (c) Drugs that may increase or decrease lithium levels: loop diuretics, calcium channel blockers
- c. Valproate (Depakote)
 - (1) Mechanism of action: causes increased availability of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter, to brain neurons or may enhance the action of GABA
 - (2) Usual adult dose (immediate release)
 - (a) Initial 750 mg daily in divided doses
 - (b) Maximum dose 60 mg/kg per day
 - (3) Depakote ER (once-daily) adult dose
 - (a) Initial 25 mg/kg per day given once daily
 - (b) Maximum dose 60 mg/kg per day
 - (4) Target blood level between 50 and 125 g/mL
 - (5) Adverse effects
 - (a) Weight gain
 - (b) Nausea
 - (c) Vomiting
 - (d) Hair loss
 - (e) Easy bruising
 - (f) Tremor
 - (6) Cautions
 - (a) Hepatic failure may occur; monitor liver function
 - (b) Increased risk of suicidal behavior
 - (7) Drug interactions: valproic acid may increase the levels of some TCA
- d. Carbamazepine (Tegretol)
 - (1) Usual adult dose
 - (a) Initially 400 mg daily in two divided doses (tablets, extended-release tablets, or extended release capsules) or four divided doses (oral suspension)
 - (b) Maximum dose 1600 mg daily
 - (2) Target blood level between 8 and 12 mcg/mL
 - (3) Adverse effects
 - (a) Nausea
 - (b) Vomiting
 - (c) Diarrhea
 - (d) Hyponatremia
 - (e) Rash
 - (f) Pruritus
 - (g) Leukopenia
 - (h) Fluid retention
 - (4) Cautions
 - (a) Neurotoxic side effects include drowsiness, dizziness, blurred vision, lethargy, and headache
 - (b) Potential for serious, and potentially fatal, skin reactions (Stevens-Johnson

syndrome and toxic epidermal necrolysis, particularly during the first 8 weeks of therapy)

- (c) Increased risk of suicidal behavior
- (5) Drug interactions: may induce CYP enzymes, including 1A2, 2B6, 2C9, 2C19, and 3A4 (high potential)

PATIENT PROFILE

Patient Initials: AC

Sex: Female

Age: 39

Height: 5'11"

Weight: 50 kg

Race: Caucasian

Allergies: No known drug allergies (NKDA)

Current Medical Problem: AC is a married female with one child (6 years old) who lost her mother to cancer about 7 months ago. She reports that she just "has not been the same" since that time, and has continual difficulty coping with the loss of her "best friend". She is tearful when talking about her family. She feels overwhelmed by her daily tasks as a mom, has a hard time getting motivated to do daily activities, and has recently even stopped her running program. It is difficult to concentrate on needed work, and she "feels like sleeping all the time". She does not interact with friends the way she used to. She states she has a supportive husband and loves her family, but it is just hard to get through the day and "feel worthwhile".

Health Conditions:

Occasional migraine headaches, several times per year, usually hormonally triggered.

Social History:

Tobacco use: None.

Alcohol use: Infrequent, occasional wine when out to dinner

Exercise: Avid runner; frequently runs in local 5K races

Current Medications/Devices:

Treximet 1 tablet PO as directed for migraine

Paraguard (non-medicated) IUD implanted 2 years ago

Laboratories: No out of range results reported, all within normal limits

Diagnosis: AC finally went to her family practitioner, who recommended she begin meeting with a family therapist and psychologist, and has prescribed a new prescription for Paxil.

PATIENT PROFILE QUESTIONS

1. The patient's current diagnosis is most likely:

- I. Seasonal affective disorder (SAD)
- II. Major depression
- III. Bipolar depression

Answer: II. AC's symptoms are most consistent with a major depression episode. Her symptoms do not appear to coincide with a particular season (e.g., winter), and she does not describe the typical

“ups and downs” in mood (mood swings) seen in patients with bipolar disorder.

2. What should be the usual initial starting and maximum dose of Paxil (immediate release) for depression in a younger healthy adult?
 - I. Initial dose 30 mg once daily PO, maximum dose 60 mg/day PO.
 - II. Initial dose 20 mg once daily PO, maximum dose 50 mg/day PO.
 - III. Initial dose 10 mg once daily PO, maximum 40 mg/day PO.

Answer: II. Paxil has many dosing regimens, depending on the condition to be treated. Answer II gives the usual dosage range for a healthy young adult for depression. If the patient had hepatic disease, then the initial dose would be 10 mg/day. The dosage for Paxil CR would be 25 mg/day initially, up to 62.5 mg/day PO.

3. After 8 weeks, AC is beginning to feel like herself again. How long should her Paxil prescription be continued?
 - I. After 1 year of treatment.
 - II. Since AC is feeling better, she should be able to stop her prescription now.
 - III. There is not an exact answer; stopping medication too soon may cause depression to return. Usually patients are evaluated every 6 months after becoming euthymic.

Answer: III. It takes several weeks to see the full effect of antidepressant treatment; AC is just beginning to respond fully to the medication, so answer II is not correct. Many patients do not understand depression treatment and stop their medication too soon in the process, risking relapse. Answer I is a wrong answer, because it does not state that the patient's symptoms have responded and resolved in the 1-year period; the 1-year period would be an arbitrary endpoint. Answer III is the best answer since there is no exact length of time and therapy is individualized to patient response. In patients with recurrent episodes, treatment may be indefinite. In patients who have had only one episode, most experts continue antidepressants for several months after all symptoms have resolved.

4. Which of the following would be an important counseling point for AC?
 - I. Use caution when taking Treximet for migraines, since serotonin syndrome is a possible risk.
 - II. Avoid alcohol.
 - III. Report any worsening depression to her doctor right away.
 - IV. Inform her doctor if she discontinues use of her IUD and wishes to become pregnant.
 - V. Do not suddenly discontinue the medication.
 - a. I and III
 - b. II and III
 - c. I, III, and IV.
 - d. I, II, III, IV, and V

Answer: d. Patients taking a “triptan” containing medication like Treximet need to be informed about the possibility of serotonin syndrome, and the signs and symptoms of serotonin syndrome. The risk of

serotonin syndrome seems to be highest from the serotonergic medications when Paxil is started or a Paxil dose is increased. Alcohol can worsen depression, and alcohol is generally best avoided in any patient taking antidepressant medications. Because patients with depression taking antidepressants are at increased risk of suicide, any worsening of symptoms should be promptly reported. Paxil and other selective serotonergic reuptake inhibitors (SSRIs) have been associated with adverse fetal effects, and AC should inform her doctor of any wish to become pregnant while on Paxil so treatment may be re-evaluated prior to pregnancy. SSRIs have been associated with a discontinuation syndrome when suddenly halted. A patient should not halt treatment suddenly, and, even when the doctor decides discontinuation is advisable, the dose should be gradually tapered down before completely ending therapy. A MedGuide is available that helps explain some of these important counseling points to patients and should be dispensed with each new prescription and refill for Paxil.

REVIEW QUESTIONS

(Answers and Rationales on page 371.)

1. The mechanism of action of benzodiazepines is thought to be:
 - a. blockage of dopamine receptors.
 - b. blockage of the reuptake of serotonin.
 - c. alpha-2 blockage.
 - d. beta-2 blockage.
 - e. potentiation of GABA.
2. Which of the following is NOT a symptom of schizophrenia?
 - a. Delusions
 - b. Flat affect
 - c. Alogia
 - d. Dysphoria
 - e. All of the above are symptoms of schizophrenia.
3. How is delusion defined?
 - a. An incorrect belief that continues despite adequate evidence to the contrary
 - b. Assignment of inappropriate social roles
 - c. Sensation of inner restlessness without outward signs
 - d. Hearing voices
 - e. Disorganized thought pattern
4. The majority of antipsychotic medications work by reducing the levels or activity of which substance?
 - a. Norepinephrine
 - b. Epinephrine
 - c. Dopamine
 - d. Serotonin
 - e. Acetylcholine
5. Which of the following statements regarding tardive dyskinesia is true?
 - a. It occurs after prolonged use of antipsychotic medication.

- b. It is recognized by choreoathetotic movements.
 - c. It can be treated with clonazepam.
 - d. a and b
 - e. a and c
6. Extrapyramidal side effects due to chlorpromazine should be treated with:
 - a. diphenhydramine
 - b. propranolol
 - c. physostigmine
 - d. bethanechol
 - e. metoclopramide
7. A patient presents to a clinic with complaints of right face and neck stiffness. The patient is taking fluphenazine. What reaction is this patient having, and what is the treatment?
 - a. Acute dystonia; treat with benztropine
 - b. acute dystonia; treat with diphenhydramine
 - c. Tardive dyskinesia; treat with benztropine
 - d. Tardive dyskinesia; treat with diphenhydramine
 - e. Tardive dyskinesia treat with levodopa
8. A 25-year-old man was diagnosed with bipolar disorder several months ago but has experienced no improvement in symptoms with lithium therapy. What is an appropriate alternative?
 - a. Amantidine
 - b. Chlorpromazine
 - c. Fluoxetine
 - d. Carbamazepine
 - e. Sertraline
9. Which of the following therapeutic interventions is recommended for the treatment of schizophrenia in addition to antipsychotic medication?
 - a. Antidepressant
 - b. Mood stabilizer
 - c. Psychosocial rehabilitation
 - d. Cognitive behavioral therapy
 - e. Psychoanalysis
10. Which of the following is/are characteristics of neuroleptic malignant syndrome?
 - I. Hyperpyrexia
 - II. Encephalopathy
 - III. Increase in serum creatine phosphokinase
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
11. Which of the following compounds is not produced naturally in the human body?
 - a. Norepinephrine
 - b. Epinephrine
 - c. Dopamine
 - d. Serotonin
 - e. Imipramine
12. Which of the following drug(s) may cause neuroleptic malignant syndrome?
 - I. Haloperidol
 - II. Fluphenazine
 - III. Prochlorperazine
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
13. Which of the following may increase lithium concentrations?
 - a. NSAIDs
 - b. Increased fluid intake
 - c. Osmotic diuretics
 - d. Caffeine
 - e. None of the above
14. Which of the following foods and/or beverages should not be ingested by patients taking isocarboxazid?
 - a. Tuna
 - b. Aged cheese
 - c. Red wine
 - d. a and b
 - e. b and c
15. Patients who take which of the following should avoid ingestion of aged cheese and wine?
 - a. Trazodone
 - b. Sertraline
 - c. Phenelzine
 - d. Maprotiline
 - e. Doxepin
16. An otherwise healthy 28-year-old man is diagnosed with major depressive disorder. Which of the following is the most appropriate initial therapy?
 - a. Sertraline
 - b. Nortripline
 - c. Gabapentin
 - d. Mirtazapine
 - e. Phenylzine
17. A 20-year-old woman is taken to the emergency department by her family for "psychotic behavior." She is admitted and later diagnosed with schizophrenia. Which of the following is the most appropriate therapy at this time?
 - a. Thiothixene
 - b. Lithium
 - c. Risperidone
 - d. Clozapine
 - e. Chlorpromazine
18. Which of the following serotonin reuptake inhibitors may cause memory impairment, menstrual irregularities, and akathisia?
 - a. Trazodone
 - b. Imipramine
 - c. Phenelzine
 - d. Buspirone
 - e. Tranylcypromine

19. Which of the following statements about imipramine is true?
- It is a serotonin-norepinephrine reuptake inhibitor.
 - It does not cross the placenta.
 - It can be used to treat enuresis.
 - a and b
 - a, b, and c
20. What drug is an anxiolytic that does not produce anticonvulsant or hypnotic effects?
- Buspirone
 - Trazodone
 - Imipramine
 - Phenelzine
 - Tranlycypromine
21. Which of the following is NOT an indication for benzodiazepine treatment?
- Convulsions
 - Anesthesia (a preanesthetic)
 - Anxiety
 - During acute alcohol withdrawal
 - Dementia
22. Which of the following is an appropriate indication for aripiprazole (Abilify)?
- Hypertension
 - Congestive heart failure
 - Rheumatoid arthritis
 - Osteoarthritis
 - Schizophrenia
23. Ziprasidone may cause all of the following adverse effects EXCEPT:
- gait disturbances.
 - insomnia.
 - constipation.
 - weight gain.
 - postural hypotension.
24. Which of the following statements about aripiprazole (Abilify) is true?
- IM dosing for acute agitation is 1–3 mg.
 - It can be used as adjunctive treatment for major depression.
 - It may cause somnolence.
 - It acts on cholinergic receptors.
 - It is poorly absorbed orally.
25. Which of the following atypical antipsychotic is most likely to cause weight gain?
- Aripiprazole
 - Olanzapine
 - Risperidone
 - Quetiapine
 - None of the above
26. Which of the following statements about haloperidol is FALSE?
- It should not be taken with ziprasidone.
 - It may cause QT prolongation.
 - It may cause akathisia.
 - It is safe in patients with hepatic failure.
 - It may cause bronchospasm.
27. Which of the following statements about selective serotonin-reuptake inhibitors is true?
- They are renally metabolized.
 - They have a narrow therapeutic window.
 - They produce changes in sleep architecture.
 - They do not produce sexual dysfunction.
 - They are safe to administer with monoamine oxidase inhibitors.
28. Patients with a history of hypersensitivity to tricyclic antidepressants should not be given which of the following?
- Phenobarbital
 - Carbamazepine
 - Phenytoin
 - Ethosuximide
 - Acetazolamide
29. Lithium:
- should not be administered with sibutramine.
 - may cause weight loss.
 - may cause leukopenia.
 - does not affect serotonin reuptake.
 - is 99% protein bound in circulation.
30. Which of the following statements about tricyclic antidepressants is true?
- All have strong anticholinergic effects.
 - All produce similar side-effect profiles.
 - All inhibit the synthesis of neurotransmitters.
 - All have similar therapeutic efficacy.
 - None have histamine-blocking effects.
31. Which of the following is associated with lithium treatment?
- Dystonia
 - Hand tremor
 - Parkinsonism
 - Blurred vision
 - Tinnitus
32. A patient with a medical history significant for major depressive disorder (MDD) is diagnosed with new-onset hypertension. Based on her history of MDD, what medication should be avoided in this patient?
- Catapres
 - Lasix
 - Vasotec
 - Cordarone
 - All of the above medications are safe.
33. What medication needs an extensive amount of patient counseling regarding dietary changes?
- Nortriptyline
 - Sertraline
 - Isocarboxazid
- I only
 - III only
 - I and II

- d. II and III
 - e. I, II, and III
34. Which of the following lithium levels is within the therapeutic range during initiation of therapy?
- a. 0.4 mEq/L
 - b. 0.6 mEq/L
 - c. 1.2 mEq/L
 - d. 2.0 mEq/L
 - e. 2.4 mEq/L
35. A patient is referred to a psychiatric clinic for a major affective disorder. Which of the following medications will provide immediate onset of action?
- a. Chlorpromazine
 - b. Lithium
 - c. Isocarboxazid
 - d. Protriptyline
 - e. None of the above
36. Which of the following benzodiazepines has an active metabolite?
- a. Lorazepam
 - b. Triazolam
 - c. Alprazolam
 - d. Clonazepam
 - e. All of the above
37. Which of the following is considered a negative symptom of schizophrenia?
- a. Hallucinations
 - b. Racing thoughts
 - c. Apathy
 - d. Delusions
 - e. None of the above
38. Which of the following is not a potential side effect of risperidone?
- a. Weight gain
 - b. Sedation
 - c. Urinary retention
 - d. Sexual dysfunction
 - e. Tremor
39. What is the appropriate therapeutic range for lithium?
- a. 0.4–0.6 mEq/L
 - b. 0.8–1.0 mEq/L
 - c. 1.0–1.6 mEq/L
 - d. 1.2–1.6 mEq/L
 - e. 1.5–2.0 mEq/L
40. Use(s) for antipsychotics include:
- I. Tourette syndrome
 - II. Asperger's syndrome
 - III. Hiccups
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
41. Which of the following is a neurotransmitter within the CNS?
- a. Norepinephrine
 - b. 5-Hydroxytryptamine
 - c. Gamma-aminobutyric acid
 - d. Dopamine
 - e. All of the above
42. Which of the following statements about nerve action potential is correct?
- a. Inhibitory neurotransmitters cause Hyperpolarization.
 - b. Excitatory neurotransmitters cause an excitatory postsynaptic potential.
 - c. Inhibitory neurotransmitters decrease potassium and chloride permeability.
 - d. a and b
 - e. a, b, and c
43. Which antidepressant has anticholinergic activity?
- I. Sertraline
 - II. Bupropion
 - III. Amitriptyline
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
44. Which of the following causes anticholinergic side effects?
- a. Beta blockers
 - b. Tricyclic antidepressants
 - c. Thyroid replacement therapy
 - d. All of the above
 - e. None of the above
45. Which of the following antipsychotic agents will most likely cause agranulocytosis?
- a. Risperidone
 - b. Prochlorperazine
 - c. Clozapine
 - d. Quetiapine
 - e. Olanzapine
46. Seizures are most likely to occur with the use of which of the following antidepressants?
- a. Escitalopram
 - b. Bupropion
 - c. Sertraline
 - d. Duloxetine
47. Which of the following medications may provoke serotonin syndrome in a person who recently received a selective serotonin reuptake inhibitor?
- a. Ketoconazole
 - b. Donepezil
 - c. Linezolid
 - d. Ibandronate
 - e. None of the above

48. Which of the following adverse effects of phenothiazines is thought to be irreversible?
- Tardive dyskinesia
 - Weight gain
 - Orthostatic hypotension
 - Urinary retention
 - Edema
49. Which of the following should be monitored in a patient taking lithium carbonate?
- Serum potassium
 - Serum magnesium
 - Serum calcium
 - Serum sodium
 - Serum creatinine
50. Which of the following statements about lithium overdose is true?
- It may cause edema and tremor.
 - It may cause polyuria.
 - Activated charcoal can prevent absorption.
 - Hemodialysis can remove circulating lithium.
 - All of the above
51. Which of the following is most likely to cause cholestatic jaundice?
- Chlorpromazine
 - Amitriptyline
 - Lithium
 - Alprazolam
 - Chlordiazepoxide
52. Which of the following is most likely to cause extrapyramidal effects?
- Mesoridazine
 - Thioridazine
 - Trifluoperazine
 - Haloperidol
 - a and c
53. Which of the following is NOT an adverse effect of lithium?
- Hypothyroidism
 - Tardive dyskinesia
 - Sedation
 - Tremor
 - Polyuria
54. Which of the following does NOT occur with chronic lithium use?
- Tremor
 - Hypothyroidism
 - Vomiting
 - Polyuria
 - Leucopenia
55. Which antidepressant has inhibits both serotonin and norepinephrine uptake?
- Amitriptyline
 - Clomipramine
 - Paroxetine
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
56. A patient is taken to the hospital after taking an overdose of chlorpromazine. He is hypotensive and is given IV epinephrine. Immediately following the injection, blood pressure becomes undetectable. What is the likely cause?
- Bradycardia induced by epinephrine
 - Positive inotropic effects of epinephrine
 - Hypertensive effects of chlorpromazine
 - Depression of respiratory center by chlorpromazine
 - Alpha adrenergic blockade by chlorpromazine
57. Which antidepressant has both anticholinergic and sedative properties?
- Amitriptyline
 - Doxepin
 - Trazodone
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
58. Which antidepressant would you choose for a patient with sleep disturbances and is least likely to cause anticholinergic effects?
- Nortriptyline
 - Doxepin
 - Trazodone
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
59. Which antidepressant inhibits reuptake of norepinephrine?
- Nortriptyline
 - Doxepin
 - Sertraline
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
60. Which of the following can cause extrapyramidal effects?
- Dopamine deficiency in the basal ganglia
 - Dopamine excess in the basal ganglia
 - Dopamine hypersensitivity in the basal ganglia
 - Serotonin deficiency in peripheral nerve endings
 - Serotonin excess in autonomic ganglia

61. Which of the following is NOT an indication for cyclic antidepressant therapy?
- Major depression
 - Chronic pain
 - Epilepsy
 - Obsessive compulsive disorder
 - Anorexia
62. Which of the following is the dopamine hypothesis of schizophrenia?
- Dopamine deficiency causes schizophrenia.
 - Dopamine excess causes schizophrenia.
 - Dopamine hypersensitivity causes schizophrenia.
 - Dopamine receptor deficiency causes schizophrenia.
 - b and c
63. A patient on several medications eats a meal of wine and cheese and develops hypertension. What is the most likely cause?
- Interaction between phenelzine and tyramine
 - Interaction between phenelzine and dopamine
 - Interaction between phenelzine and acetylcholine
 - Interaction between phentolamine and dopamine
 - Missed dose of antihypertensive
64. Which of the following is NOT an adverse effect of antipsychotics?
- Mydriasis
 - Orthostatic hypotension
 - Jaundice
 - Gynecomastia
 - Hypothyroidism
65. Which of the following is NOT an effect of monoamine oxidase inhibitors (MAOI)?
- Orthostatic hypotension
 - Hypertension when combined with tyramine
 - Increased seizure threshold
 - Dry mouth
 - Urinary retention
66. Which of the following selectively blocks serotonin reuptake?
- Fluoxetine
 - Maprotiline
 - Amoxapine
 - Doxepin
 - Imipramine
67. Which of the following is NOT metabolized to an active compound?
- Diazepam
 - Lorazepam
 - Midazolam
 - Chlordiazepoxide
 - Alprazolam
68. A 35-year-old woman is diagnosed with neurotic depression. During the course of her treatment a clinician prescribes amitriptyline. She calls 5 days later and says she has not received any relief of her depressive symptoms. What is the most appropriate next step?
- Increasing the amitriptyline dose by 50%
 - Increasing the morning dose of amitriptyline
 - Changing to an atypical antipsychotic
 - Adding an atypical antipsychotic
 - Continuing the current treatment and advising the patient that it may take a few weeks to see improvements
69. Antipsychotic drugs block what receptors to produce akathisia and dystonia adverse effects?
- Dopamine receptors
 - Cholinergic receptors
 - Alpha receptors
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
70. Which of the following statements about the extrapyramidal effects of antipsychotics is true?
- Tardive dyskinesia is thought to be due to excess dopamine activity.
 - Tardive dyskinesia occurs with initiation of therapy and is rapidly reversible.
 - Oral facial dyskinesia is a feature of akathisia.
 - a and b
 - a, b, and c
71. Which of the following is an effect of haloperidol?
- Dopamine blockade
 - Cholinesterase inhibition
 - Dopamine reuptake
 - Monoamine oxidase inhibition
 - Serotonin blockade
72. Antipsychotic drugs block what receptors to produce constipation, dry mouth, and urinary retention adverse effects?
- Cholinergic receptors
 - Dopamine receptors
 - Alpha receptors
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
73. Which of the following is available as a depot injection?
- Chlorpromazine hydrochloride
 - Molindone hydrochloride
 - Fluphenazine enanthate
 - Loxapine hydrochloride
 - None of the above

74. Which of the following is an FDA-approved use of fluoxetine?
- Anxiety
 - Depression
 - Obesity
 - Mania
 - Schizophrenia
75. Which of the following may produce excitement when given concomitantly with reserpine?
- Antihistamines
 - Monoamine oxidase inhibitors
 - Anticholinesterases
 - Alpha adrenergic blockers
 - All of the above
76. Which of the following is the first strategy employed to treat tardive dyskinesia?
- Decreasing the neuroleptic dose
 - Bromocriptine
 - Diphenhydramine
 - Amantadine
 - All of the above
77. Phenothiazines may cause all of the following EXCEPT:
- antiemesis.
 - anesthesia.
 - autonomic effects.
 - antipsychotic effects.
 - extrapyramidal effects.
78. Which of the following is not a component of neuroleptic malignant syndrome?
- Catatonia
 - Hyperpyrexia
 - Akathisia
 - a and b
 - a, b, and c
79. Which of the following may cause pigment deposition on the anterior lens and posterior cornea?
- Thioridazine
 - Chlorpromazine
 - Promazine
 - a and b
 - b and c
80. Which of the following is NOT an effect of thioridazine?
- Antiemesis
 - Hypoprolactinemia
 - Orthostatic hypotension
 - Antipsychotic effects
 - All of the above are effects of thioridazine.
81. Which of the following inhibits the metabolism of benzodiazepines to their active metabolites?
- Cimetidine
 - Rifampin
 - Carbamazepine
 - Phenytoin
 - Ranitidine
82. Which of the following body systems is NOT affected by antipsychotic medications?
- Endocrine
 - Cardiovascular
 - Autonomic nervous system
 - Pulmonary
 - Central nervous system
83. Which of the following is NOT an effect of cyclic antidepressants?
- Inverted T waves on electrocardiogram
 - Mood elevation
 - Increased seizure threshold
 - Sedation
 - Urinary retention
84. Which of the following is NOT an appropriate use of antipsychotics?
- Tourette syndrome
 - Parkinson disease
 - Hiccups
 - Schizophrenia
 - Mania
85. Which of the following is useful in the treatment of vomiting?
- Epinephrine
 - Caffeine
 - Chlorpromazine
 - Tetracycline
 - Naloxone
86. Which of the following is NOT a monoamine oxidase inhibitor (MAOI)?
- Tranlycypromine
 - Maprotiline
 - Phenelzine
 - a and b
 - b and c
87. Which of the following is a mechanism of action of monoamine oxidase inhibitors (MAOI)?
- Inhibition of monoamine metabolism
 - Decreased serotonin amines
 - Blocking monoamine reuptake
 - Increasing REM sleep
 - All of the above
88. Which of the following is NOT an effect of benzodiazepines?
- Paradoxical stimulation
 - Dependence
 - Respiratory depression
 - Decreased seizure threshold
 - Withdrawal
89. Which of the following is an effect of lorazepam?
- Anterograde amnesia
 - Increased seizure threshold
 - Sedation
 - Hypnosis
 - All of the above

90. Which of the following is the correct tricyclic antidepressant-metabolite pair?
- Imipramine-nortriptyline
 - Imipramine-desipramine
 - Amitriptyline-desipramine
 - Fluoxetine-protriptyline
 - Imipramine-trimipramine
91. Which of the following is a side effect of lithium?
- Hypermagnesemia
 - Decreased creatinine
 - Polyuria
 - Proximal tubular degeneration
 - Hypochloremia
92. Which of the following is NOT an effect of chlorpromazine?
- Decreased thyroid hormone production
 - Increased prolactin
 - Decreased adrenocorticotropin
 - Decreased gonadotropin
 - Decreased growth hormone
93. Which of the following causes cholestasis?
- Monoamine oxidase inhibitors
 - Carbon tetrachloride
 - Para-aminosalicylic acid
 - Phenothiazine
 - All of the above
94. Which of the following may cause hypertensive crisis if administered with phenelzine?
- Ephedrine
 - Phenylpropanolamine
 - Diazepam
 - a and b
 - a and c
95. Which of the following is available as an ester salt for IM injection?
- Prochlorperazine
 - Haloperidol
 - Thioridazine
 - Perphenazine
 - All of the above

Respiratory Disorders

20 CHAPTER

Respiratory disorders, or lung diseases, are disorders such as asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis. Lung disease can affect people of all ages and both sexes. Lung disease is the fourth leading cause of death in the United States.

I. Asthma

A. Background

1. Asthma is a chronic, inflammatory lung disease.
2. In people with asthma, the air passages within the lungs are constantly swollen, which restricts the amount of air that can pass through the trachea.
3. Those with asthma have recurrent breathing problems and a tendency to cough and wheeze.
4. According to the American Lung Association, approximately 20 million Americans have asthma, which causes about 5000 deaths each year.
5. There is no cure for asthma, but many medications and lifestyle changes help manage the condition.
6. According to a 2002 National Health Interview Survey, asthma has been diagnosed in nine million children, from newborns to 18-year-olds, in the United States.
 - a. Asthma rates in children younger than 5 years of age have increased more than 160% between 1980 and 1994.
 - b. One study found a strong correlation between obesity and asthma but no similar relationship between obesity and allergies. Some researchers believe this is the result of increased physical exertion of the lungs in obese individuals.

B. Classifications

1. There are various classifications of asthma. These conditions cause airway obstruction and inflammation that is partly reversible by medication. The symptoms are usually similar; however, the main difference is their cause.
 - a. Allergic (extrinsic) asthma
 - (1) An allergic reaction triggers allergic asthma, which is an immune system response that causes the airway to become inflamed.
 - (2) Inhaled allergens, such as dust mites, mold spores, pollen, and pet dander, may trigger allergic asthma.
 - (3) It is the most common form of asthma, affecting more than 50% of asthma sufferers.

b. Nonallergic (intrinsic) asthma

- (1) Nonallergic asthma is not related to allergies and does not involve the immune system.
- (2) Instead, the disease is triggered by factors like anxiety, stress, exercise, cold air, dry air, smoke, hyperventilation, viruses, and other irritants.

c. Exercise-induced asthma

- (1) When the airway becomes constricted during vigorous physical activity, the condition is known as exercise-induced asthma.

d. Cough-variant asthma

- (1) Cough-variant asthma is a chronic, persistent cough without shortness of breath.

e. Occupational asthma

- (1) Occupational asthma occurs as a result of a particular environment.

C. Pathophysiology

1. Because asthma is an inflammatory process, several cells (mostly immune system-mediated cells) have been identified as playing a role in the disease process (Figure 20-1).
2. There are three major parts of the immune system response
 - a. Antibodies
 - (1) The antibody or immunoglobulin (IgE) is responsible for carrying out the body's allergic reaction (shortness of breath, inflammation, closing of airways).
 - b. Inflammatory cells
 - (1) The major inflammatory cells involved in asthma are mast cells and eosinophils.
 - (2) Mast cells, which can be found in the lungs, mediate the inflammatory response that is triggered by IgE.
 - (3) The inflammatory eosinophil cells are closely associated with all types of asthma and can be found in various parts of the lungs and respiratory system.
 - (4) Activation of these inflammatory cells causes a release of inflammatory mediators.
 - c. Inflammatory mediators
 - (1) The mediators that are often involved in asthma are histamine, leukotrienes, prostaglandins, and cytokines.

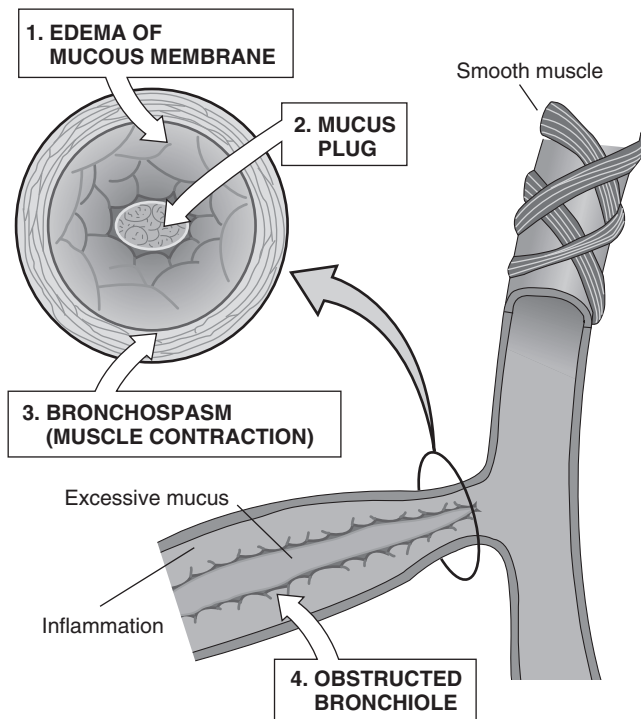


Figure 20-1 — Airway changes during asthma. (From Gould BE: Pathophysiology for the health professions, ed. 3, St. Louis, 2007, Saunders)

3. The whole inflammatory process contributes to airway restriction and bronchospasms.
 - a. Airway restriction and bronchospasms are produced by the tightening of the muscles that surround the respiratory system. This tightening is achieved by the binding of catecholamines, such as epinephrine or norepinephrine, to beta-2 receptors in the lungs and airway.

D. Signs and symptoms

1. Asthma symptoms may appear at any time in life. Individuals who develop asthma as adults have adult-onset asthma. This condition may develop as late as age 50 or older. Unlike children, who usually experience intermittent symptoms, individuals with adult-onset asthma are more likely to experience persistent symptoms. The cause of adult-onset asthma is unknown. However, some evidence suggests that allergy and asthma may be genetically determined. In addition, obesity, which has both genetic and environmental influences, appears to significantly increase the risk of developing asthma in adulthood. The following symptoms may occur in any age group, unless otherwise noted.
 - a. Bronchospasm (abnormal contraction of the bronchi, which obstructs the airway), coughing (constant or intermittent)
 - b. Wheezing or whistling sounds when exhaling
 - c. Shortness of breath or rapid breathing
 - d. Chest tightness or pain and fatigue
 - e. Infants may have trouble feeding and may grunt during suckling.

E. Diagnosis

1. Spirometry

- a. Spirometry is a noninvasive way to evaluate the air capacity of the lungs.
- b. In a spirometry test, a person breathes into a mouthpiece that is connected to an instrument called a spirometer.
- c. The spirometer records the amount and the rate of air that is breathed in and out over a specified time.

F. Treatment

1. Short-term relief: bronchodilation

a. Beta-2 adrenoceptor agonists

(1) Mechanism of action

- (a) Relaxes bronchial smooth muscle by activating beta-2 receptors
- (b) Increases cyclic adenosine monophosphate (cAMP) levels and subsequent relaxation of smooth muscle and bronchodilation

(2) Indications

- (a) Relieve bronchospasm alone or in combination

(3) Warnings/Precautions

- (a) Hyperthyroidism
- (b) Cardiovascular disease
- (c) Arrhythmias
- (d) Diabetes mellitus

(4) Adverse effects

- (a) Fine tremor
- (b) Tachycardia
- (c) Hypokalemia

(5) Short-acting: used for quick relief of asthma symptoms

(a) Albuterol (Proventil HFA, Ventolin HFA)

- (i) Typical adult dosage: 2 puffs q4–6h as needed

- (ii) Albuterol also available in nebulizer solution

(b) Levalbuterol (Xopenex)

- (i) Solution used in nebulizer (Figure 20-2)

- (ii) Treatments take 5–15 minutes, q6–8h

- (iii) Available in 0.31 mg, 0.63 mg, and 1.25 mg

- (iv) Inhaler: 1–2 puffs q4–6 hr as needed (typical adult dose)

(c) Pirbuterol (Maxair)

- (i) Typical adult dose: 2 puffs q4–6h as needed

(6) Long-acting: NOT for acute attacks

(a) Salmeterol (Serevent)

(b) Formoterol (Foradil)

- (c) Combination products: more likely to be prescribed (preferred) due to anti-inflammatory (corticosteroid) component for control of symptoms

- (i) Fluticasone/salmeterol (Advair Diskus)

- (ii) Budesonide/formoterol (Symbicort)

b. Methylxanthines

(1) Mechanism of action



Figure 20-2—Nebulizer. (From Hopper T: Mosby's pharmacy technician, ed. 2, St. Louis, 2007, Saunders)

- (a) Increase cAMP in bronchial smooth muscle cells by inhibiting phosphodiesterase, thereby causing bronchodilation
- (2) Used in children unable to use inhalers; adults with nocturnal symptoms; status asthmaticus (IV)
 - (a) Not used often
- (3) Contraindications
 - (a) Hypersensitivity
 - (b) Active peptic ulcer
 - (c) Uncontrolled seizures
- (4) Warnings/Precautions
 - (a) Cardiac disease
 - (b) Hypertension
 - (c) Hepatic impairment
- (5) Adverse effects
 - (a) Nausea
 - (b) Vomiting

- (c) Tremor
- (d) Insomnia
- (e) Tachycardia
- (6) Available oral and IV
- (7) Examples
 - (a) Oral: theophylline (Aerolate, Elixophyllin, Quibron-T, Resbid, Slo-bid, T-Phyl, Theolair, Theo-24, Theo-Dur, Theo-X, Uni-Dur or Uniphyll)
 - (b) IV: aminophylline
- (8) Therapeutic serum concentrations: 5–15 $\mu\text{g/mL}$
- 2. Long-term control: anti-inflammatory medications (asthma “controllers”)
 - a. Mast cell stabilizers
 - (1) Mechanism of action
 - (a) Stabilize mast cell membrane
 - (b) Prevent calcium ions from entering mast cells, thereby preventing release of inflammatory mediators
 - (2) Administered by metered-dose inhalers (maintenance therapy)
 - (3) Adverse effects
 - (a) Throat irritation
 - (b) Mouth dryness
 - (c) Dermatitis
 - (4) Examples
 - (a) Cromolyn (Intal)
 - (b) Nedocromil (Tilade)
 - b. Leukotriene inhibitors (Figure 20-3)
 - (1) Mechanism of action
 - (a) Inhibits leukotriene receptors by blocking 5-lipoxygenase activity. Examples: zafirlukast (Accolate), montelukast (Singulair)
 - (b) Leukotriene synthesis inhibitor: Example: Zileuton (Zyflo)
 - (2) Adverse effects
 - (a) Pharyngitis
 - (b) Headache

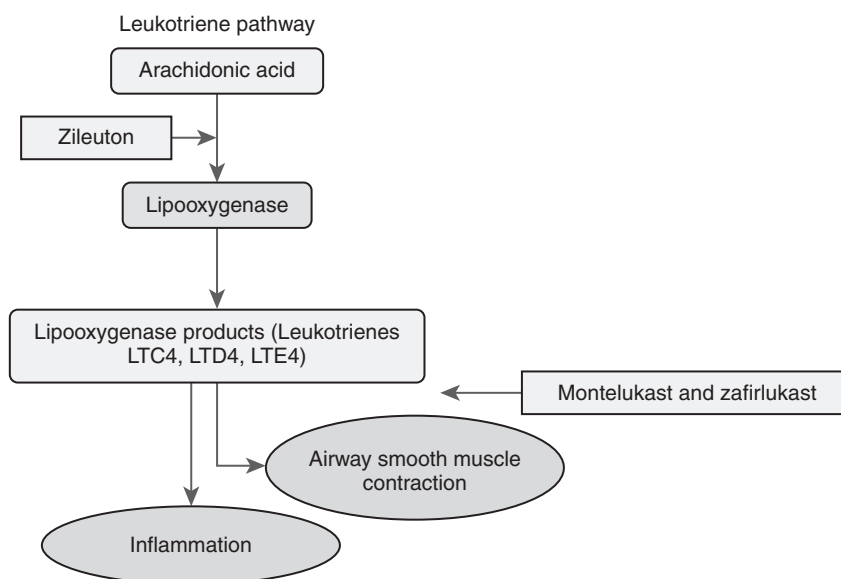


Figure 20-3—Leukotriene pathway. (From Moscou K, Snipe K: Pharmacology for pharmacy technicians. St. Louis, 2009, Mosby)

- (c) Rhinitis
- (d) Gastritis
- (e) Increases in liver enzymes
- c. Corticosteroids
 - (1) Mechanism of action
 - (a) Blocks production of cytokines by mast cells and eosinophils, thereby inhibiting inflammation of asthmatic airways
 - (b) No direct action on smooth muscle cells
 - (2) May be administered by oral, parenteral, or inhalation routes
 - (3) Adverse effects
 - (a) Adrenal suppression
 - (b) Osteoporosis
 - (c) Potential immunosuppression
 - (4) Examples
 - (a) Flunisolide (AeroBid), triamcinolone (Azmecort), beclomethasone (Beclovent or Vanceril), fluticasone (Flovent), budesonide (Pulmicort), betamethasone (Celestone Soluspan), dexamethasone (Decadron), methylprednisolone (Medrol), prednisone (Sterapred), prednisolone (Orapred, Pediapred or Prelone)

II. Chronic Obstructive Pulmonary Disease

A. Background

1. Chronic obstructive pulmonary disease (COPD) is a type of lung disease that involves damage to or obstruction of the airways of the lungs, which makes it difficult to breathe. COPD is an overall term referring to a group of chronic lung conditions, including chronic bronchitis and emphysema and possibly asthma or asthmatic bronchitis. Although chronic bronchitis and emphysema may occur separately, it is common for patients to have both diseases simultaneously.
2. The Centers for Disease Control and Prevention (CDC) report that COPD affects up to 24 million Americans. The main risk factor for COPD is smoking. COPD is most likely to develop in cigarette smokers, but cigar, pipe, and marijuana smokers also are susceptible. The risk of COPD is directly related to the number of years a person smokes and the amount smoked. Researchers estimate that smoking causes 80%–90% of COPD deaths. According to the American Lung Association, COPD is the fourth leading cause of death in the United States. Patients with COPD typically die from complications, such as severe lung infections, heart problems, or lung cancers. The American Lung Association also states that female smokers are nearly 13 times more likely to die from COPD than women who have never smoked and male smokers are nearly 12 times more likely to die from COPD than men who have never smoked.

B. Signs and symptoms

1. Symptoms of COPD usually develop gradually over many years and typically worsen over time.
 - a. Chronic bronchitis or emphysema (or both)
 - (1) Chronic bronchitis
 - (a) Chronic cough

- (b) Increased mucus that is yellow-greenish in color, frequent clearing of the throat, wheezing, and shortness of breath
- (c) Fatigue
- (2) Emphysema
 - (a) Shortness of breath, especially during activity (one of the earliest symptoms)
 - (i) Constant, even at rest
- b. Bluish discoloration of the lips and nail beds (cyanosis): occurs when there is not enough oxygen in the blood
- c. Headaches
- d. Weight loss

C. Treatment

1. There is currently no cure for COPD. Treatment focuses on reducing symptoms and preventing complications.
2. Anticholinergic agents
 - a. Mechanism of action
 - (1) Used as adjuncts to beta-2 adrenoceptor agonists for COPD
 - b. Contraindications
 - (1) Hypersensitivity to atropine related drugs
 - c. Precautions
 - (1) Glaucoma
 - (2) Prostatic hypertrophy
 - (3) Pregnancy
 - d. Adverse effects
 - (1) Dry mouth
 - (2) Systemic anticholinergic effects are rare
 - e. Examples: tiotropium (Spiriva), ipratropium (Atrovent)
 - (1) Combination products: albuterol and ipratropium (Combivent)
3. Bronchodilators (beta-2 adrenoceptor agonists, e.g., albuterol)
4. Corticosteroids
5. Leukotriene inhibitors

III. Cystic Fibrosis

A. Background

1. Cystic fibrosis (CF), also called mucoviscidosis, is an inherited life-threatening disorder that causes severe lung damage and nutritional deficiencies. CF causes the body to produce abnormally thick and sticky mucus, saliva, sweat, and digestive enzymes. In healthy individuals, these secretions serve as lubricants in the body. In patients with CF, however, the secretions are so thick that they plug up tubes and passageways in the body. The lungs and pancreas are the most commonly affected organs.
2. CF is most common among whites. Researchers estimate that 1 of 3,500 whites in the United States is born with CF. About 1 of 15,000 African Americans, 1 of 9,200 Latin Americans, and 1 of 31,000 Asian Americans are born with the disease in the United States.
3. Complications of CF, including lung infections and nutritional deficiencies, can be fatal. The average life expectancy of patients with CF is 35 years of age.

B. Signs and symptoms

1. Symptoms of CF vary among patients. Some patients experience severe symptoms that affect the lungs as well as the digestive and reproductive systems. Others may experience milder symptoms that affect fewer parts of the body. In some cases, severity of symptoms changes as patients get older.
2. In newborns, the first sign of CF may be a blockage of the intestines. Healthy babies normally pass greenish-black stools, called meconium, during their first couple days of life. However, if the infant has CF, the meconium may be too thick to move through the intestines. Other signs and symptoms include oily stools, failure to grow, and frequent lung infections.
3. Other symptoms
 - a. Increased amounts of salt in sweat
 - b. Oily stools
 - c. Thick sputum
 - d. Coughing
 - e. Difficulty breathing
 - f. Wheezing
 - g. Bowel obstructions

C. Treatment

1. There is currently no cure for CF. Patients receive treatment to help reduce symptoms and complications of the disease.
2. Antibiotics for treating respiratory infections; *Pseudomonas* species are common pathogens
 - a. Examples: Tobramycin (TOBI inhalation) or other aminoglycosides, ticarcillin/clavulanate (Timentin), piperacillin/tazobactam (Zosyn), imipenem/cilastatin (Primaxin), aztreonam (Azactam), ciprofloxacin (Cipro)
3. Bronchodilators
4. Pancreatic enzyme supplementation (examples: Creon, Pancrease, Ultrase)
5. Mucolytics
 - a. Dornase alfa (Pulmozyme, a recombinant human deoxyribonuclease [rh-DNase]); the enzyme helps break down viscous secretions and increase sputum clearance; typical dose is 2.5 mg via oral inhalation once or twice daily.

PATIENT PROFILE

Patient Initials: SV

Sex: Female

Age: 68

Height: 5' 3"

Weight: 74 kg

Race: White

Allergies: No known drug allergies (NKDA)

Patient Consultation: For recent exacerbations of COPD and community-acquired pneumonia, SV was hospitalized for 5 days and is discharged to home. SV goes to the pharmacy for new prescriptions from hospitalization. She does not understand the new medicine she has been given except for the antibiotics for her pneumonia. "My doctor also told me to stop my Zocor for now; do I not have high cholesterol anymore?"

Current Health Conditions:

Hypercholesterolemia

COPD (diagnosed 8 years ago)

Recent Laboratories of Note:

Cholesterol: 220 mg/dL

Serum creatinine: 1.1

Social History: Tobacco use: Former heavy smoker; quit 5 years ago when husband died of lung cancer

Alcohol use: None

Pharmacy Medication Profile:

Centrum Silver 1 tablet PO once daily

Spiriva Handihaler 1 capsule inhaled once daily in the morning

Simvastatin 40 mg PO once daily at bedtime

Mucinex 1 tablet PO twice daily

New Prescriptions:

Levaquin 500 mg once daily for 5 days (continuation of medication from hospital)

Clarithromycin 500 mg PO twice daily for 5 days (continuation of medication from hospital)

Advair inhaler 1 inhalation twice daily

PATIENT PROFILE QUESTIONS

1. What is the most likely reason that SV is asked to discontinue simvastatin at this time?
 - a. She does not actually have hypercholesterolemia; it was misdiagnosed
 - b. Her condition is now controlled with diet, and medication is no longer needed
 - c. The clarithromycin prescription could elevate her blood levels of simvastatin and thus the statin has been temporarily discontinued

Answer: c. Current recommendations are that simvastatin not be prescribed (is contraindicated) concurrently with clarithromycin due to a risk of rhabdomyolysis. A short discontinuation of the statin therapy will not be harmful and will help avoid a serious drug interaction.
2. Upon review of SV's medications, the pharmacist realizes that SV has become confused about her oral medications and her inhaled medications and has been taking the Spiriva capsules orally every morning in the past few weeks. Which of the following would be the most helpful tactic to encourage proper medication use and limit confusion?
 - a. She could prefill the Spiriva capsules into the inhaler the night before the needed dose.
 - b. She could store the inhaler medications in a different location on the counter in her home, separate from her oral medications
 - c. If she places the Spiriva in the refrigerator, she will prolong the shelf life, and this will limit confusion about her medications.

Answer: b. The best tactic from the above choices for this patient would be to keep medications that should be inhaled in a different area at room temperature than where she stores her oral medication bottles. Spiriva capsules should not be opened from the blister packaging or inserted into the inhaler device until the time of use. Spiriva should not be refrigerated.

3. To ensure adequate treatment with her antibiotic therapy, SV should be advised to do which of the following?
- Take clarithromycin tablets on an empty stomach.
 - Separate the Levaquin dose from that of the Centrum Silver by at least 2 hours.
 - Finish the course of therapy as prescribed even if she is feeling better.
- I only
 - II only
 - III only
 - I and III
 - II and III

Answer: e. Divalent cations from the minerals found in Centrum Silver could bind levofloxacin and prevent adequate oral absorption, leading to treatment failure. Completing the course of therapy for antibiotics is always important to ensure treatment success. Clarithromycin tablets do not need to be taken without food; they may be taken with or without food.

4. SV does not understand why she needs another inhaler. The pharmacist should explain which of the following points?
- The addition of Advair may help her stay out of the hospital.
 - The Advair acts differently than the Spiriva, and the two work well together.
 - The two together will make it easier to breathe, and Advair contains an agent to reduce inflammation, which may be a result of the recent pneumonia.
- II only
 - III only
 - II and III
 - I, II, and III

Answer: d. The combination of Spiriva (tiotropium, an anticholinergic agent) with a long-acting beta agonist and corticosteroid (e.g., Advair, salmeterol-fluticasone) may significantly improve lung function and reduce the risk of hospitalization in some patients with COPD, especially if tiotropium alone has not reduced hospitalization for the patient. The drugs' mechanisms act synergistically to help the patient breathe better, and the corticosteroid is helpful if inflammation is present (as is likely in the case of acute pneumonia). SV should know she is likely to feel better with the combination.

REVIEW QUESTIONS

(Answers and Rationales on page 375.)

- Which of the following medications can be used to treat asthma?
 - Isoproterenol
 - Epinephrine
 - Albuterol
 - I only
 - III only
- Which of the following statements regarding allergic rhinitis is FALSE?
 - It affects 40% of children.
 - It is least prevalent among young children.
 - It is associated with maternal smoking.
 - It is more common in males.
 - Incidence is lower among the elderly.
- What symptom of COPD is appropriately treated with ipratropium?
 - Bronchial inflammation
 - Bronchospasm
 - Mucus production
 - Ventilatory mismatch
 - All of the above
- All of the following are antihistamines (specifically H₁ antagonists) EXCEPT:
 - brompheniramine.
 - nizatidine.
 - meclizine.
 - dimenhydrinate.
 - hydroxyzine.
- Which of the following does NOT affect maintenance theophylline dosing?
 - Smoking
 - Renal insufficiency
 - Concomitant medications
 - Cor pulmonale
 - Hepatic failure
- Clearance of theophylline is decreased by:
 - Albuterol
 - Atropine
 - Ipratropium
 - Cimetidine
 - Epinephrine
- Which of the following is/are true about tiotropium?
 - Should only be taken orally
 - Short-acting bronchodilator
 - Muscarinic antagonist
 - I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
- Fexofenadine (Allegra):
 - has an onset of action of 60 minutes.
 - is nonsedating.
 - is an H₂ receptor antagonist.
 - a and b
 - a, b, and c

9. All of the following are potential side effects of atropine EXCEPT:
 - a. excessive salivation.
 - b. constipation.
 - c. mydriasis.
 - d. photophobia.
 - e. increase pulse.
10. Which of the following decreases theophylline clearance?
 - a. Ranitidine
 - b. Cimetidine
 - c. Ciprofloxacin
 - d. a and c
 - e. b and c
11. Which of the following is used to treat anaphylaxis?
 - a. Phenylephrine
 - b. Epinephrine
 - c. Dopamine
 - d. Clonidine
 - e. Terbutaline
12. Which of the following increases theophylline clearance?
 - a. Emesis
 - b. Activated charcoal
 - c. Nasogastric lavage
 - d. Induced diuresis
 - e. All of the above
13. Which of the following drugs is useful in COPD for its strong anticholinergic effects and low side-effect profile?
 - a. Albuterol
 - b. Atropine
 - c. Ipratropium
 - d. Cimetidine
 - e. Epinephrine
14. Which of the following drugs shows exclusively beta adrenergic effects?
 - a. Albuterol
 - b. Atropine
 - c. Ipratropium
 - d. Cimetidine
 - e. Epinephrine
15. What statement is correct regarding ipratropium therapy?
 - I. Dopamine Antagonist
 - II. Anticholinergic
 - III. Used to treat bronchitis and rhinorrhea
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
16. What statement is correct regarding levalbuterol?
 - I. Anticholinergic Agent
 - II. Available as a tablet and inhaler
 - III. Beta-2 Agonist
- a. I only
- b. III only
- c. I and II
- d. II and III
- e. I, II, and III
17. Which of the following is the most important factor in selecting a theophylline medication?
 - a. Age of the patient
 - b. Theophylline content of the medication
 - c. Concurrent medication
 - d. Presence of immunological disease
 - e. None of the above requires consideration.
18. A 15-year-old girl presents to the emergency department with an acute asthma exacerbation. Which of the following is the most appropriate initial treatment?
 - a. Inhaled corticosteroids
 - b. Antihistamine
 - c. Cromolyn sodium
 - d. Beta agonist
 - e. Theophylline
19. Which of the following is NOT a goal of asthma therapy?
 - a. Maintenance of normal daily activity
 - b. Prevention of acute exacerbations
 - c. Prevention of pulmonary destruction
 - d. Avoidance of adverse effects associated with medications
 - e. Prevention of chronic symptoms
20. Which of the following does NOT affect beta-adrenergic receptors?
 - a. Albuterol
 - b. Metaproterenol
 - c. Bethanechol
 - d. Terbutaline
 - e. a and c
21. Which of the following compounds could be responsible for this constellation of effects:
Tachycardia
Decreased diastolic pressure
Bronchial relaxation
No ocular effects
 - a. Alpha antagonist
 - b. Alpha agonist
 - c. Beta antagonist
 - d. Beta agonist
 - e. Muscarinic medication
22. Which of the following is NOT a direct-acting beta agonist?
 - a. Metaproterenol
 - b. Albuterol
 - c. Phenylephrine
 - d. Terbutaline
 - e. Isoetharine
23. Which of the following is true regarding isoproterenol?
 - I. Beta-1 and Beta-2 antagonist
 - II. Can treat bronchospasm
 - III. Can increase heart rate

- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
24. What is a toxic theophylline level?
- I. 15 mcg/ml
 - II. 25 mcg/ml
 - III. 35 mcg/ml
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
25. Which of the following is a mechanism associated with theophylline?
- a. Increased intracellular cyclic AMP
 - b. Blockage of adenosine receptors
 - c. Translocation of calcium
 - d. a and b
 - e. a, b, and c
26. Which of the following may occur with diphenhydramine toxicity?
- a. Hallucination
 - b. Blurred vision
 - c. Dry mouth
 - d. Sinus tachycardia
 - e. All of the above
27. Which of the following has the smallest bronchodilative effects?
- a. Norepinephrine
 - b. Epinephrine
 - c. Terbutaline
 - d. Isoetharine
 - e. a and b
28. A 70-year-old man with coronary artery disease is prescribed theophylline for emphysema-associated bronchospasm. Which of the following is NOT likely to occur in this patient?
- a. Arrhythmia
 - b. Agitation
 - c. Tremulousness
 - d. Nausea
 - e. Sodium retention
29. Which of the following antagonizes the effects of adenosine?
- a. Cromolyn
 - b. Terbutaline
 - c. Theophylline
 - d. Propranolol
 - e. Cortisol
30. Which of the following is a cholinergic antagonist?
- a. Ipratropium
 - b. Salmeterol
 - c. Ephedrine
 - d. Cromolyn
 - e. Isoetharine
31. Which of the following is NOT an effect of beta-2 bronchodilators?
- a. Tremors
 - b. Lethargy
 - c. Headache
 - d. Nervousness
 - e. Tachycardia
32. Which of the following is NOT a beta-2 selective agonist?
- a. Pirbuterol
 - b. Metaproterenol
 - c. Isoproterenol
 - d. Terbutaline
 - e. Albuterol
33. What is the action of cromolyn?
- a. Mast cell stabilization
 - b. Beta agonist
 - c. Bronchodilator
 - d. Anticholinergic
 - e. Beta blocker
34. Which of the following is a NOT sign of theophylline toxicity?
- a. Seizure
 - b. Tremor
 - c. Hyperkalemia
 - d. Vomiting
 - e. Tachyarrhythmia
35. Which of the following is safe to use in patients with asthma?
- a. Methacholine
 - b. Atropine
 - c. Bethanechol
 - d. Physostigmine
 - e. Propranolol

I. Osteoarthritis

A. Background

1. Osteoarthritis (OA), also called degenerative joint disease, is marked by the breakdown of cartilage that lines the ends of most limb bones. This type of cartilage is known as articular cartilage, and it serves to cushion the bones and allow painless joint movement. Because OA affects the articular cartilage, patients with OA experience pain and reduced mobility in their joints. OA may affect any joint in the body, but it occurs most often in fingers, spine, and weight-bearing joints. Individuals with OA often experience inflammation around the affected joint, which is caused by bits of cartilage that break off and aggravate the synovial tissue lining the joints.
2. Besides cartilage loss, OA is characterized by irregular thickening and remodeling of bone. The synovial tissue may bulge out of joints to form cysts (commonly known as Baker cysts), or become hardened with fibrous tissue overgrowth (a condition known as sclerosis). Bony protrusions, called *bone spurs* or *osteophytes*, may also form. These pathological changes result in increased blood flow and joint inflammation.

B. Risk factors

1. Age (older than 50 years)
2. Crystals in joint fluid or cartilage
3. High bone mineral density
4. History of immobilization
5. Joint injury
6. Joint hypermobility
7. Joint instability
8. Obesity
9. Peripheral neuropathy
10. Prolonged occupational or sports stress

C. Signs and symptoms

1. OA may affect any joint in the body; however, because it develops slowly, many patients do not experience symptoms right away. The pain and inflammation in OA is typically less severe and more localized than that of rheumatoid arthritis (RA), another form of arthritis that is more systemic.
2. Common symptoms of OA
 - a. Joint pain (arthralgia)
 - b. Swelling and/or stiffness in a joint (especially after not moving for a while); stiffness in morning lasts < 30 minutes.

- c. Joint discomfort before or during a change in the weather (such as conditions of low pressure and high humidity)
- d. Bony lumps on the fingers
- e. Loss of joint flexibility

3. When individuals have OA, the cells that form cartilage (called chondrocytes) cannot efficiently repair the damaged cartilage. Thus, OA represents a failure of the chondrocyte to maintain proper balance between cartilage formation and destruction. Instead, new bone grows alongside the existing bone, causing small lumps to form. Although these lumps cause minimal pain, they may be disfiguring and limit the joint's mobility.

D. Treatment

1. Nonpharmacologic

- a. Patient education
- b. Exercise: strengthening and range-of-motion exercises (physical/occupational therapy)
- c. Modification of activities of daily living
- d. Wedged shoe insoles (orthotics)
- e. Joint protection
- f. Weight loss
- g. Rehabilitation
- h. Heat or ice

2. Pharmacologic

- a. Acetaminophen (Tylenol): The American College of Rheumatology has recommended acetaminophen as first-line therapy for osteoarthritis of the hip or knee.
 - (1) Dose, maximum 4 g/day
 - (2) Adverse effects: Hepatotoxicity may occur.
- b. Nonsteroidal anti-inflammatory drugs (NSAID)
 - (1) Mechanism of action
 - (a) Decrease production of prostaglandins
 - (i) Nonselective inhibitors of cyclooxygenase (COX)-1 and COX-2
 - (b) Increase vascular permeability and sensitivity to the release of bradykinins
 - (c) Inhibits formation of prostacyclin and thromboxane, resulting in reduced platelet aggregation
 - (2) May be used if patients fail to respond to acetaminophen
 - (3) Adverse effects
 - (a) Abdominal pain

- (b) Gastrointestinal (GI) bleeding
- (c) Rash
- (d) Hypersensitivity reactions
- (e) Renal or hepatic impairment
- (f) Impaired bone marrow function
- (g) Platelet aggregation
- (4) Primarily metabolized in liver by cytochrome P-450 (CYP) 2C9 and excreted in urine
 - (a) Indomethacin, sulindac, and piroxicam undergo enterohepatic circulation resulting in a prolonged half-life (avoid in the elderly)
- (5) Contraindications
 - (a) Active peptic ulcer disease
 - (b) Renal disease
 - (c) Heart failure
 - (d) Cirrhosis
- (6) NSAID examples
 - (a) Salicylates (aspirin)
 - (b) Propionic acids (ibuprofen [Motrin], naproxen [Aleve, Naprosyn], oxaprozin [Daypro], ketoprofen [Orudis])
 - (c) Acetic acids (diclofenac [Voltaren], etodolac [Lodine], indomethacin [Indocin])
 - (i) Diclofenac is available for topical use.
 - (d) Oxicams (piroxicam [Feldene])
 - (e) COX-2 inhibitors (celecoxib [Celebrex])
 - (i) Mechanism of action: inhibits COX-2, thereby impairing the transformation of arachidonic acid to prostaglandins, prostacyclin, and thromboxanes
 - (ii) Rofecoxib (Vioxx) and valdecoxib (Bextra) were removed from marketing due to safety concerns.
 - (iii) Adverse effects: similar adverse event profile to other NSAID; linked to an increased risk of serious heart-related side effects, including heart attack and stroke. Selective COX-2 inhibitors have also been shown to increase the risk of stomach bleeding, fluid retention, kidney problems, and liver damage.
- c. Glucocorticoids
 - (1) Systemic glucocorticoids are not used for osteoarthritis
 - (2) Intraarticular injections may be used in patients who do not respond to NSAID or for whom NSAID are contraindicated.
 - (a) Examples: triamcinolone acetonide, triamcinolone hexacetonide, methylprednisolone
- d. Hyaluronic acids
 - (1) Used for osteoarthritis of the knee in patients who do not respond to NSAID

therapy or who have a history of gastric ulcer disease

- (2) Examples: sodium hyaluronate (Hyalgan, Supartz, Nuflexxa), hylan G-F 20 (Synvisc)
- e. Other analgesics
 - (1) Tramadol (Ultram): 50–100 mg can be administered as needed for pain relief every 4–6 hours, not to exceed 400 mg/day (immediate release)
 - (a) Mechanism of action: centrally acting synthetic analgesic
 - (b) Adverse effects: risk of seizure
 - (2) Opioids, such as codeine, oxycodone, or propoxyphene may be used short term in patients with acute pain exacerbations.
- f. Topical pain relievers

Used for localized pain control at a specific joint. Topical NSAID generally considered more effective than topical capsaicin.

 - (1) Capsaicin 0.025% cream
 - (2) Trolamine salicylate (e.g., Aspercreme, Sportscreme, Icy Hot, Ben-Gay)
 - (3) Methylsalicylate (e.g., Exocaine and Gordogesic)
 - (4) Topical NSAID: e.g., diclofenac (Voltaren Gel)
- g. Alternative therapies
 - (1) Glucosamine/chondroitin combination is most studied, particularly in patients with OA of the knee; may help with pain relief.
 - (a) Patients should be taking at least 1.5 g of glucosamine daily. Significant pain benefit may not occur in all patients. Does not appear to limit progression of OA in the joint.

II. Rheumatoid Arthritis

A. Background

1. Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects the peripheral joints in a symmetrical pattern. Although the exact cause is currently unknown, RA is thought to be due to autoimmune phenomena. These are characterized by abnormal immune responses against healthy host tissue. In RA, autoimmune reactions can cause joint inflammation and eventual degeneration.
2. Because RA is a type of autoimmune disorder, most patients have antibodies called rheumatoid factors. The presence of these antibodies in the blood confirms a diagnosis of RA, but it does not necessarily indicate the severity. Proinflammatory factors (such as tumor necrosis factor, interleukin, T cells, prostaglandins, and histamine) may also be elevated. Blocking these proinflammatory substances is the major target of most therapies for RA. The presence of chronic inflammation in the joints eventually leads to breakdown of synovial tissue, cartilage, and bone.

B. Risk factors

1. Sex (women more likely than men)
2. Age (most commonly between 20 and 50 years old)
3. Family history

C. Signs and symptoms

1. RA is marked by pain and swelling in the joints. Unlike OA, which affects only bones, cartilage, and synovial tissue, RA is an autoimmune disorder that may also cause swelling in other areas of the body, including the tear ducts, salivary glands, lining of the heart, lungs, and occasionally, the blood vessels. Furthermore, although osteoarthritis tends to be localized to a few joints, RA often affects many joints at the same time. The severity of symptoms varies among patients. Early nonspecific symptoms include fatigue, weakness, low-grade fever, loss of appetite, and joint pain.

D. Treatment

1. Treatment initially begins with NSAID, salicylates, or COX-2 inhibitors for relief of pain and inflammation, allowing for improvement in joint function while baseline assessments of joint damage, disease activity, and laboratory testing are completed.
2. Glucocorticoids may be used in dosages equivalent to or less than 10 mg of oral prednisone daily. Intraarticular injections may be effective for selected joints (Table 21-1).

Table 21-1 Oral Corticosteroid Equivalencies

Corticosteroid Agent	Equivalent Oral Dose (mg)
Cortisone	25
Hydrocortisone	20
Prednisone	5
Prednisolone	5
Triamcinolone	4
Methylprednisolone	4
Dexamethasone	0.75
Betamethasone	0.6

3. Disease-modifying antirheumatic drugs (DMARD) DMARD drugs are usually initiated within 3 months of RA diagnosis. DMARDs may reduce or prevent joint damage, preserve joint function, and may help financially to reduce care costs and preserve work status. The DMARDs most commonly used for RA include hydroxychloroquine, sulfasalazine, methotrexate (MTX), leflunomide, etanercept, infliximab, and anakinra (Table 21-2).

- a. Non-biologic DMARD: methotrexate (Rheumatrex), hydroxychloroquine (Plaquenil), sulfasalazine (Azulfidine)
- b. Biologic DMARD: infliximab (Remicade), etanercept (Enbrel), Anakinra (Kineret), abatacept (Orencia), rituximab (Rituxan)

- (1) Typically used only if insufficient response with nonbiologic DMARD; many agents added to existing MTX treatment.

- c. Immunosuppressants: leflunomide (Arava), azathioprine (Imuran), cyclosporine (Neoral, Sandimmune), cyclophosphamide (Cytosan)

Table 21-2 Common Medications Used in DMARD Therapy of RA

Drug	Typical adult maintenance dosage used in RA
Methotrexate	7.5–20 mg PO once weekly.
Hydroxychloroquine	200 mg PO twice daily
Sulfasalazine	1000 mg PO 2-3 times per day
Leflunomide	20 mg PO once daily if tolerated; otherwise, 10 mg/day
Etanercept	25 mg SC twice per week
Infliximab	3-10 mg/kg IV infusion given every 8 weeks
Anakinra	100 mg SC once daily
Adalimumab	40 mg SC every other week

III. Gout

A. Background

1. Gout is an intensely painful form of arthritis that causes the joints to become red, swollen, and stiff. Symptoms are most likely to develop in the big toe. It occurs when there is too much uric acid, a waste product that forms when the body breaks down purines found in red meat, poultry, and fish in the blood (hyperuricemia). Uric acid is carried through the bloodstream to the kidneys. If the body produces too much uric acid or if the kidneys do not eliminate adequate amounts, uric acid will build up in the blood. This condition is called *hyperuricemia*.

B. Signs and symptoms

1. Attacks occur suddenly, especially at night.
2. Joints become red, swollen, and stiff.
3. The big toe is most commonly affected; the symptom is often called podagra.
4. Other commonly affected joints include the ankles, heels, knees, wrists, hands, fingers, and elbows.
5. The pain may be so severe that a bed sheet touching the affected skin is unbearable.
6. Symptoms generally subside after 1–2 weeks.

C. Treatment

1. Nonpharmacologic therapy
 - a) Limit foods high in purines (e.g., red meat)
 - b) Maintain ideal body weight
 - c) Limit alcohol and drink appropriate amounts of fluids/water
2. Pharmacologic therapy
 - a. Colchicine (Colcris)
 - (1) Mechanism of action: blocks microtubule polymerization

- (2) Usual adult dose for acute attacks: 1.2 mg PO followed by 0.6 mg PO in 1 hour (total 1.8 mg)
 - (a) May be given 0.6 mg once or twice daily as maintenance regimen to prevent gout attack; may be combined with probenecid for maintenance treatment
- (3) Adverse effects: abdominal cramps, diarrhea, nausea, and vomiting. Gastric intolerance may indicate toxicity (decrease the dose or discontinue the drug). Other adverse reactions indicating toxicity include numbness or tingling in the extremities, unusual bleeding or bruising, feeling weak or tired, increased infections, and pale or gray color of the lips, tongue, or palms.
- (4) Be aware that concomitant use of P-glycoprotein (e.g., grapefruit juice) and strong CYP 3A4 inhibitors (e.g., erythromycin, clarithromycin) may cause severe drug interactions with colchicine, including death.
- b. Allopurinol (Zyloprim)
 - (1) Mechanism of action: xanthine oxidase inhibitor
 - (2) Usual adult dose: 200 to 300 mg/day PO for mild gout and 400 to 600 mg/day for those with moderate to severe tophaceous gout. If daily dose is >300 mg, administer in divided doses twice daily.
- c. Febuxostat (uloric)
 - (1) MOA: Same as allopurinol
 - (2) Usual adult dose: 40 to 80 mg PO once daily
- d. Sulfapyrazone: uricosuric agent
- e. Probenecid: uricosuric agent
- f. NSAID (ibuprofen, naproxen, indomethacin, sulindac)
- g. Corticosteroids

PATIENT PROFILE

Patient Initials: JN

Sex: Male

Age: 60

Height: 6' 1"

Weight: 81.8 kg

Race: White

Allergies: No known drug allergies (NKDA)

Patient Consultation: JN is a 60-year-old white man in overall good health who has just received a consultation with an orthopedic physician at the request of his family physician. He has increasing pain in his right knee with noted "creaking" feelings. The discomfort and stiffness are worse in the morning upon arising, and symptoms improve quickly as the patient gets up and "moves around." He sometimes has difficulty with going down large flights of stairs, such as at the football stadium. Most daily activities are not limited by the condition at this

time. He self-treated for several months with glucosamine/chondroitin but states "it did not help all that much."

Current Health Conditions:

Familial hypercholesterolemia

Gastroesophageal reflux disease (GERD); now on maintenance therapy

Recent Laboratories:

Cholesterol: 180 mg/dL

LDL cholesterol: 120 mg/dL

Serum creatinine: 0.9 mg/dL

Rheumatoid factor: negative

Notes from recent doctor visit:

Joint findings local to the right knee only; + crepitus, slight reduction in range of motion (ROM). Radiologic exam at orthopedic office noted narrowing of the joint space and some apparent calcification. No effusions or erosions are present.

Social History:

Tobacco use: None

Alcohol use: Occasional beer or wine when out to eat

Exercise: Avid runner in past; used to compete in marathons; still jogs for short distances a few times per week, but knee sometimes "gives way" and he has curtailed his running program in the past 6 months

Pharmacy Medication Profile:

Lipitor 20 mg PO once daily

Glucosamine/chondroitin supplement 500 mg PO three times per day

Prevacid 15 mg PO once daily in the morning

New Prescriptions:

Celebrex 100 mg PO twice daily

Physical therapy twice weekly for 2 weeks to learn quadriceps strengthening exercises; physician recommended moderate low-impact aerobic exercise (e.g., an aquatics program) in place of jogging to reduce impact on joints.

PATIENT PROFILE QUESTIONS

1. What symptoms does JN have that are consistent with a diagnosis of osteoarthritis (OA) versus rheumatoid arthritis?
 - I. Unilateral joint involvement of a large joint
 - II. Limited periods of morning stiffness (e.g., 30 minutes or less)
 - III. Crepitus
 - IV. Radiologic evidence
 - a. I and II
 - b. I and III
 - c. I, II, and IV
 - d. I, II, III, and IV

Answer: d. All of the above. Patients with osteoarthritis usually complain of symptoms in larger joints, and it is common that a unilateral joint is affected. Morning stiffness usually improves quickly upon arising as the patient moves about. Crepitus is a crackling sound of the joint that feels like a vibration on movement of the joint, which

indicates wear and tear. Radiographic evidence of OA includes joint narrowing with osteophyte formation and sometimes tissue calcification. There are no laboratory alterations specifically associated with OA. JN has relatively mild to moderate OA at this time, given the lack of usual interference with normal activities of daily living, such as bathing. The presentation of OA differs significantly from that of rheumatoid arthritis (RA). RA involves four of the following seven findings: 1) morning stiffness usually lasting >1 hour, 2) symptoms in three or more joints, 3) involvement of the joints in the hands, 4) symptoms in symmetric joints, 5) rheumatoid nodules on physical exam, 6) positive serum rheumatoid factor, and 7) radiographic evidence of joint erosions and bony deformities. JN does not have symptoms consistent with RA.

2. JN will receive added benefit by continuing to take the glucosamine/chondroitin supplement with his new prescriptions.

- a. True
- b. False

Answer: b. False. JN has stated he has received no apparent benefit from the use of the supplement and continued therapy is not recommended. There is no evidence to state that continuing this supplement with Celebrex will confer additional benefit. Many organizations recommend that such supplements be discontinued if no apparent benefit is noted after 6 months of supplementation.

3. Which of the following is true regarding Celebrex therapy for JN?
 - I. The Prevacid prescription is likely to reduce his risk for an NSAID-induced ulcer.
 - II. If JN had listed an allergy to sulfa, Celebrex would be contraindicated.
 - III. The initial drug of choice for treating osteoarthritis pain is a NSAID.
 - IV. The Celebrex dose for JN is incorrect and should be 200 mg PO once daily.

- a. I only
- b. I and II
- c. II only
- d. II and III
- e. II, III, and IV

Answer: b. Prevacid is one medication that can help prevent NSAID-induced gastrointestinal ulcers. Although JN does not have apparent risk factors for GI ulceration, it is an additional benefit conferred by his existing prescriptions. Celebrex contains a sulfa moiety in its chemical structure and is contraindicated in patients with a sulfa allergy. The initial medication recommended for treating the pain and symptoms of mild to moderate OA is usually acetaminophen; acetaminophen has been shown to be as effective as ibuprofen (NSAID) and poses less risk for side effects when taken

within appropriate adult limits (e.g., no more than 1 gram four times per day). Patients with moderate to severe symptoms typically respond better to prescription therapies. The dose of Celebrex for OA is either 200 mg PO once daily or 100 mg PO twice daily; the current prescribed dose is correct.

REVIEW QUESTIONS

(Answers and Rationales on page 377.)

1. The drug(s) of choice for controlling hyperuricemia include:
 - I. Allopurinol
 - II. Paroxetine
 - III. Nizatidine
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
2. Which of the following is a sign of colchicine toxicity?
 - a. Abdominal pain
 - b. Constipation
 - c. Photosensitivity
 - d. Oral rash
 - e. Anuria
3. Which of the following is an oral gold compound?
 - a. Aspirin
 - b. Corticosteroids
 - c. Ibuprofen
 - d. Penicillamine
 - e. Auranofin
4. Which of the following medications must be given on an empty stomach?
 - a. Corticosteroids
 - b. Ibuprofen
 - c. Aspirin
 - d. Auranofin
 - e. Penicillamine
5. Which of the following should NOT be combined with allopurinol?
 - a. Methotrexate
 - b. Mercaptopurine
 - c. Cyclophosphamide
 - d. Cisplatin
 - e. L-Asparaginase
6. Which of the following are considered uricosuric drugs?
 - I. Probenecid
 - II. Colchicine
 - III. Sulfinpyrazone
 - a. I only
 - b. III only
 - c. I and III
 - d. II and III
 - e. I, II, and III

7. Which of the following is/are drug(s) of choice for treating acute gout attacks?
- I. Indomethacin
 - II. Colchicine
 - III. Allopurinol
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
8. All of the following are true about rheumatoid arthritis EXCEPT:
- a. More common in men than in women
 - b. Onset occurs commonly between the ages of 40 and 60
 - c. Smoking increases risk
 - d. There may be a genetic component
 - e. It is a chronic disease and there is no cure
9. True or False: Colchicine is not an analgesic or uricosuric agent.
- a. True
 - b. False
10. Osteoarthritis involves which of the following tissues?
- I. Bone
 - II. Articular cartilage
 - III. Synovium
- a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III

I. Introduction/Definitions

- A. Seizure: A seizure occurs when these neurons generate electrical discharges that spread throughout the brain. This can occur with both normal and abnormal nerve cells.
- B. Epilepsy: Epilepsy is a group of disorders characterized by recurrent seizures. In epilepsy, brain cells (neurons) create abnormal electricity that causes seizures or jerking movements. In some cases, seizures cause a loss of consciousness, a period of confusion, a staring spell, or muscle spasms. A single seizure is not considered epilepsy. Individuals with epilepsy have repeated episodes of seizures. Different forms of epilepsy are either secondary to a particular brain abnormality or neurological disorder or are said to be idiopathic (without any clear cause).

II. Types of Seizures

A. Partial seizures

- 1. Partial, or focal, seizures begin in a focal or discreet area of the brain
- 2. They may be further divided into simple partial and complex partial
 - a. Simple partial
 - 1) No change in consciousness
 - 2) Activity localized in a specific portion of the brain
 - 3) Duration 20–60 seconds
 - 4) Twitching of the muscles or limbs, turning the head to the side, paralysis, visual changes, or vertigo (dizziness) may occur.
 - b. Complex partial
 - 1) Consciousness is altered or lost.
 - 2) Symptoms are similar to simple partial seizures but patients have changes in their ability to interact with the environment.
 - 3) Symptoms may be caused by abnormal electrical discharges between neurons in specific areas of the brain, such as the temporal lobe.
 - 4) Duration 30 seconds to 2 minutes

B. Generalized seizures

- 1. Involve larger areas of the brain, often both hemispheres (sides), from the onset. They are further divided into many subtypes. The more common types include tonic-clonic (grand mal), absence (petit mal), and myoclonic seizures.

a. Tonic-clonic (grand mal)

- 1) Loss of consciousness
- 2) Sustained muscle contraction (tonic), followed by alternating muscle contractions and relaxation (clonic)
- 3) An aura or an unusual feeling that often warns patients that they are about to have a seizure, usually immediately before the loss of consciousness
- 4. Average 5–20 minutes in duration

b. Absence (petit mal)

- 1) Only loss of consciousness occurs and there are no other associated motor symptoms, such as jerking
- 2) Staring, subtle body movements, brief lapses of awareness
- 3) Less than 10 seconds

c. Myoclonic

- 1) Brief jerking movement that arises from the central nervous system (CNS), usually involving both sides of the body
- 2) No loss of consciousness
- 3) Many different syndromes associated with myoclonic seizures, including juvenile myoclonic epilepsy, West syndrome, and Lennox-Gastaut syndrome (atonic seizures or drop attacks)

III. Signs and Symptoms

A. Symptoms vary depending on the type of seizure

1. Partial seizure

- a. Simple partial seizures do not result in loss of consciousness. These seizures may alter emotions or change the way things look, smell, feel, taste, or sound.
- b. Complex partial seizures alter consciousness, causing the individual to lose awareness for a period of time. Complex partial seizures often result in staring and nonpurposeful movements, such as hand rubbing, lip smacking, arm positioning, vocalization, or swallowing.

2. Generalized seizure

- a. Absence seizures (petit mal): characterized by staring, subtle body movements, and brief lapses of awareness
- b. Tonic-clonic seizures (grand mal): most common form of generalized seizures. They are also the most widely recognized epileptic seizure. In a tonic-clonic seizure, the person loses consciousness, the body stiffens, and the person falls to the

Table 22-1 First Generation (Conventional) Antiepileptic Drugs

Drug	AED Uses	Proposed AED MOA	Dosing (Adults)	Therapeutic Range	Adverse Effects	Kinetics and Interactions	Notes
Valproic acid and its derivatives (Depacon; Depakene; Depakote; Depakote ER; Depakote Sprinkle)	First-line option for all types of epilepsy May be used as monotherapy in mixed seizure types	↑ Gamma-aminobutyric acid	Initially 15 mg/kg per day. May increase by 5–10 mg/kg per day at weekly intervals (until therapeutic levels are achieved) Maximum 60 mg/kg per day	50–100 mcg/mL, but should be adjusted to patient response	GI irritation (use EC or ER to decrease effects), weight gain, hair loss, tremor, sedation, easy bruising, hyperammonemia Hepatic failure may occur; monitor liver function Increased risk of suicidal behavior	Inhibits CYP 2C9 and uridine 5'-diphosphate-glucuronosyl-transferases (UGT) (↓metabolism of lamotrigine) high plasma protein binding (PPB) (displaces phenytoin)	LFT and blood levels should be monitored Contraindicated with liver dysfunction or urea cycle disorders Lamotrigine levels significantly elevated by valproate use extreme caution when coadministering
Phenytoin (Dilantin; Phenytek) Fosphenytoin (Cerebyx) is a prodrug of phenytoin; more hydrophilic; IV or IM; phlebitis rare NOTE: Fosphenytoin dosing is always in phenytoin equivalents (PE)	Tonic-clonic Partial Maintenance of antiseizure effects in status epilepticus	Prolongs inactivation of Na ⁺ channels	Loading dose of 15–20 mg/kg (based on phenytoin serum concentrations); oral loading dose is given in 3 divided doses every 2–4 hours; maintenance dose of 300 mg per day or 5–6 mg/kg per day in 3 divided doses or 1–2 divided doses with extended release Fosphenytoin: Loading dose of 15–20 PE/kg IM/IV Maintenance dose of 4–6 PE/kg per day divided doses every 8–12 hours	Total phenytoin 10–20 mcg/mL or free phenytoin 1–2 mcg/mL Monitoring postload: IV >2 hours after end of infusion Oral 24 hours after end of load	Dose/concentration-related: CNS depression, nystagmus Dose/concentration-independent: coarsening facial features, hirsutism, folate deficiency, glucose intolerance, gingival hyperplasia, Stevens-Johnson syndrome Increased risk of suicidal behavior	Induces CYP 2C and 3A families and UGT Metabolized by 2C9 and 2C19 High PPB ↑ total phenytoin: amiodarone, cimetidine, fluconazole, fluoxetine, sulfonamides, ticlopidine, trimethoprim ↑ free phenytoin: valproic acid, salicylates, hypoalbuminemia, uremia, dialysis ↓ total phenytoin: antacids, carbamazepine, ciprofloxacin, rifampin	>400 mg/dose = decreased absorption and increased GI effects IV phenytoin C/I with sinus bradycardia or heart block (extreme hypotension) Do not coadminister with antacids

Carbamazepine (Tegretol; Carbatrol; Epitol; Equetro)	Tonic-clonic Partial	Prolongs inactivation of Na ⁺ channels	Oral: Initially, 400 mg per day in 2 divided doses (tablets, extended release tablets) or 4 divided doses (oral suspension); may increase by maximum of 200 mg per day at weekly intervals Average dose used 800–1200 mg per day Adjust to patient's response	6–12 mcg/mL	Serious skin reactions (Stevens-Johnson syndrome), drowsiness, dizziness, head- ache, GI irritation, hyponatremia (Syndrome of inap- propriate anti- diuretic hormone, [SIADH]) bone marrow suppression (monitor CBC at baseline, monthly for 3 months, then yearly; stop therapy if WBC <2.5 or ANC <1 Increased risk of suicidal behavior	Induces CYP 1A2, 2C9, 3A4, 2E1, and UGT (↓ efficacy of oral contraceptives, doxy- cycline, theophylline, warfarin) Metabolized by CYP 1A2, 2C9, 3A4 (autoinducer) CYP 2E1 induction can lead to acetamino- phen toxicity	Monitor LFT, CBC, serum sodium and carbamazepine levels
Phenobarbital (Luminal)	Tonic-clonic Partial Second-line choice in status if benzodiazepine and phenytoin are ineffective	Gamma- aminobutyric acid potentiation	Loading dose (IV): Initially for status epilepticus 300–800 mg, then 120–240 mg/dose at 20-minute intervals until seizure control Maintenance dose (oral, I.V) of 1–3 mg/kg per day in divided doses or 50–100 mg 2–3 times per day	10–40 mcg/mL	CNS depression (including respira- tory depression) can cause para- doxical excitation in children. Increased risk of suicidal behavior	Induces CYP 1A2, 2C family, 2D6, 3A4, and UGT Metabolized by CYP 2C9, 2C19 (autoinducer)	Reserved for patients who have failed other therapies

Continued

Table 22-1 First Generation (Conventional) Antiepileptic Drugs—cont'd

Drug	AED Uses	Proposed AED MOA	Dosing (Adults)	Therapeutic Range	Adverse Effects	Kinetics and Interactions	Notes
Ethosuximide (Zarontin)	Absence	Unknown but may be due to ↓ current of T-type Ca^{++} channels gamma-aminobutyric acid	Oral: Initially, 500 mg per day; increase by 250 mg as needed every 4–7 days to a maximum of 1.5 g per day in divided doses	40–100 mcg/mL	GI irritation, ataxia, rash, lethargy, headache, bone marrow suppression Increased risk of suicidal behavior	Metabolized by CYP 3A4	First choice for absence seizures only if patient has no other seizure types; in mixed seizure types, monotherapy may induce tonic-clonic seizure
Primidone (Mysoline)	Seizure disorders (grand mal, psychomotor, and focal) second-line for all but absence	Gamma-aminobutyric acid potentiation	Oral: Initially, 125–250 mg/day at bedtime; increase by 125–250 mg per day every 3–7 days; usual dose of 750–1500 mg per day in divided doses 3–4 times/day with maximum dosage of 2 g per day	3–12 mcg/mL	CNS depression (including respiratory depression) can cause paradoxical excitation in children. Increased risk of suicidal behavior	Induces CYP 1A2, 2C family, 2D6, 3A4, and UGT Metabolized by CYP 2C9, 2C19 (autoinducer)	
Clonazepam (Klonopin)	Second-line for absence, myoclonic	Gamma-aminobutyric acid potentiation	Oral: Initially, 1.5 mg in 3 divided doses; may increase by 0.5–1 mg every 3 days Not to exceed 20 mg per day.	Not established	Ataxia, sedation, anorexia	Metabolized by CYP 3A4	May be used in patients nonresponsive to ethosuximide Risk of seizures with abrupt withdrawal

AED, antiepileptic drug; C/I, contraindicated; CYP, cytochrome P-450; EC, enteric-coated dose form; ER, extended-release dose form; LFT, liver function test; MOA, mechanism of action; PPB, plasma protein binding.

Table 22-2 Second Generation Antiepileptic Drugs

Drug	AED Uses	Proposed AED MOA	Dosing (adult)	Therapeutic Range	Adverse Effects	Kinetics and Interactions	Notes
Lamotrigine (Lamictal)	Partial Adjunctive treatment of Lennox-Gastaut May be used as monotherapy in mixed seizure types	↓ Glutamate release	Oral: Usual maintenance dose of 100–500 mg per day in divided doses Dose used dependent on concomitant valproic acid	Not established	Dizziness, drowsiness, sedation, diplopia (double vision) *Rash especially early in treatment Increased risk of suicidal behavior	Induces UGT Metabolized by UGT ↓ levels with estrogen (oral contraceptives or pregnancy) ↑ levels with valproate ↑ levels of carbamazepine metabolite resulting in toxicity	Risk of rash decreased by slow titration (especially important when coadministered with valproate)
Topiramate (Topamax)	Tonic-clonic Lennox-Gastaut syndrome	Prolongs inactivation of Na ⁺ channels and may ↑ gamma-aminobutyric acid	Oral: Initially, 25 mg twice daily. May increase weekly by 50 mg per day in divided doses Maximum dose of 200 mg twice daily	Not established	Psychomotor slowing, oligohidrosis (lack of sweat), decreased appetite or weight loss, behavioral changes, metabolic acidosis, renal stones (when combined with other carbonic anhydrase inhibitors) Increased risk of suicidal behavior	May induce CYP 3A4 When combined with first generation, AED changes have been noted in the levels of both topiramate and other AEDs. 70% renally cleared	Reduce dose by 50% in renal failure Titrate slowly to decrease CNS effects
Oxcarbazepine (Trileptal)	Partial	Prolongs inactivation of Na ⁺ channels	Oral: Usual dose of 1200 mg per day in 2 divided doses	12–30 mg/L	Similar to carbamazepine More hyponatremia, less bone marrow suppression Increased risk of suicidal behavior	Induces CYP 3A4 and UGT Inhibits CYP 2C19 Metabolized by UGT	May need to adjust dose in renal impairment
Levetiracetam (Keppra)	Myoclonic Partial-onset Tonic-clonic	Unknown	Oral: Initially, 500 mg twice daily Usual recommended dose of 1500 mg twice daily	Not established	Sedation, fatigue, lack of coordination, psychosis, bone marrow suppression Increased risk of suicidal behavior	66% renally cleared Pharmacodynamic interaction with carbamazepine (increased toxicity without increased carbamazepine concentration)	Used in patients intolerant to phenytoin IV form available Adjust dose in renal impairment
Gabapentin (Neurontin)	Partial (adjunct)	↑ Gamma-aminobutyric acid availability	Oral: usual maintenance dose of 900–1800 mg per day in 3 divided doses; higher doses sometimes needed	Not established	Sedation, GI irritation, weight gain, behavioral changes Increased risk of suicidal behavior	100% renally cleared Do not coadminister with antacids or cimetidine	Divide dose to maximize absorption Titrate slowly to decrease sedation Decrease dose with renal impairment

Continued

Table 22-2 Second Generation Antiepileptic Drugs—cont'd

Drug	AED Uses	Proposed AED MOA	Dosing (adult)	Therapeutic Range	Adverse Effects	Kinetics and Interactions	Notes
Pregabalin (Lyrica)	Partial (adjunct)	↑ Gamma-aminobutyric acid availability	Oral: usual maintenance dose of 150–600 mg per day in divided doses	Not established	Sedation, ataxia, weight gain Increased risk of suicidal behavior	100% renally cleared	Titrate slowly to decrease sedation
Tiagabine (Gabitril)	Partial (adjunct)	↑ Gamma-aminobutyric acid availability	Oral: usual maintenance dose: of 32–56 mg per day in 2–4 divided doses	Not established	Irritability, ataxia, tremor, weakness, speech disorders, GI irritation Increased risk of suicidal behavior	98% PPB Metabolized by CYP 3A4	PPB displaced by valproate Titrate slowly to decrease adverse effects
Zonisamide (Zonegran)	Partial (adjunct)	Prolongs inactivation of Na ⁺ channels	Oral: Initially, 100 mg per day Usual maintenance dose of 200–400 mg per day	Not established	Psychomotor slowing, GI irritation, decreased cognition, kidney stones, rash, decreased sweating Increased risk of suicidal behavior	Metabolized by CYP 3A4 (major), 2D6, 2C19, and UGT 30% renally cleared	Sulfa allergy potential Do not use if CrCl <50 mL/min
Felbamate (Felbatol)	Last resort for Tonic-clonic or Partial	Unknown	Oral: usual maintenance dose of 2400–3600 mg per day	Not established	Aplastic anemia, hepatotoxicity, CNS stimulation (insomnia, decreased appetite, weight loss) Increased risk of suicidal behavior	Inhibits CYP 2C19 Metabolized by CYP 2E1, 3A4, UGT 40%–50% renally cleared Interacts with valproic acid, phenytoin, carbamazepine, phenobarbital	Only use if nothing else is effective Patients must sign informed consent before initiation therapy

AED, antiepileptic drug; CNS, central nervous system; CrCl, creatinine clearance; CYP, cytochrome P-450; GI, gastrointestinal; UGT, uridine 5'-diphosphate glucuronosyl transferase.

ground. This is followed by jerking movements. After a minute or two, the jerking movements usually stop and consciousness slowly returns.

- c. Myoclonic seizures: usually appear as sudden jerks of the arms and legs

IV. Treatment (Tables 22-1 and 22-2)

- A. Anticonvulsant medications are the treatment choice for epilepsy and seizure disorders. Treatment with one anticonvulsant agent is the goal, if possible.
- B. When initiating therapy for epilepsy, drugs should be chosen based on seizure type(s) and drug side effect profiles.
- C. AED and oral contraceptives
 1. Many AED induce the metabolism of estrogen. If breakthrough bleeding occurs, the ethinyl estradiol component of the oral contraceptive should be increased to 50 mcg/day per active pill.
 2. As folate metabolism is altered by many AED, folic acid should be added to limit birth defects in the event pregnancy occurs.
 3. Estrogen decreases lamotrigine concentrations.

V. Medications Associated with Decreasing Seizure Threshold

- A. Alkylating agents (e.g., busulfan, chlorambucil)
- B. Antimalarials (chloroquine, mefloquine)
- C. Antimicrobials/antivirals: in general, seizures are more likely with these agents when dosage adjustments are not made for renal impairment or other clinical parameters (e.g., imipenem, penicillins)
- D. Select pain medications (e.g., meperidine, tramadol)
- E. Natural products (e.g., ephedra or ma huang, ginkgo biloba)
- F. Immune system modulators (e.g., cyclosporine, tacrolimus, interferons)
- G. Psychotropic medications (e.g., bupropion, lithium)
- H. Radiographic contrast agents
- I. Methylxanthines (e.g., theophylline)
- J. Sedative-hypnotic drug withdrawal (e.g., benzodiazepine withdrawal in dependent patients, or the use of flumazenil in benzodiazepine-dependent patients)
- K. Psychostimulants (e.g., amphetamines, cocaine, methylphenidate)

VI. Status Epilepticus

- A. Medical emergency
- B. Prolonged, repetitive seizure activity that lasts more than 20–30 minutes, during which time the patient is unconscious. Status epilepticus is a medical emergency with a significantly poor outcome. It can result in death if not treated aggressively. Its causes include improper use of certain medications, stroke, infection, trauma, cardiac arrest, illicit drug overdose (such as cocaine or methamphetamine), and brain tumor.
- C. Treatment: The goal of treatment always should be immediate diagnosis and termination of seizures.

For an AED to be effective in status epilepticus, the drug must be administered intravenously (or rectally, as with diazepam, if IV access not immediately accessible) to provide quick access to the CNS without the risk of serious systemic and neurologic adverse effects.

D. Medications

1. Benzodiazepines (diazepam [Valium, Diastat], lorazepam [Ativan], midazolam [Versed]): drugs of choice for first-line management of status epilepticus
2. Hydantoins (phenytoin [Dilantin] or fosphenytoin [Cerebyx]) are typically added to maintain seizure control
3. Barbiturates (e.g., phenobarbital) may be used if benzodiazepines and hydantoins are ineffective or if allergy history prevents use of hydantoin.

PATIENT PROFILE

Patient Initials: BM

Sex: Male

Age: 18

Height: 6' 1"

Weight: 68 kg

Race: White

Allergies: Penicillin (Ampicillin, rash)

Medical History:

Generalized tonic-clonic seizure disorder, diagnosed at age 14 years

Social History:

Tobacco use: None

Alcohol use: None since diagnosed with epilepsy 4 years ago

Exercise: BMX biking competitions

Medication Profile:

Phenytoin 100 mg PO three times daily

Current medical problem: BM is sent to the hospital by his neurologist due to complaints of increasing seizure frequency over the past week despite stated compliance with his medication. His phenytoin level on admission is 5 mcg/mL. While he is in the emergency department, he has another seizure.

PATIENT PROFILE QUESTIONS

1. After an initial dose of lorazepam 4 mg IV, the emergency physician orders fosphenytoin 100 mg phenytoin equivalents (PE) to be given immediately in the emergency department to help raise the phenytoin level to the appropriate range (10–20 mcg/mL). The pharmacist prepares a standard intravenous infusion containing 25 mg PE per mL of fosphenytoin. If the infusion should be given no faster than 150 PE/min, how many milliliters can be given in 1 minute to deliver the dose safely, but quickly?
 - a. 16 mL
 - b. 1 mL
 - c. 4 mL

Answer: c. The dose ordered is 100 mg PE; 4 mL of the pharmacist-prepared 25 mg PE/mL solution contains the appropriate dose as ordered. Because 100 mg is less than 150 mg, the 4 mL dose can be administered during 1 minute without exceeding the maximum rate for safe administration for this young adult.

2. Once the patient is stabilized on the neurology unit, the neurologist decides to add carbamazepine to the existing phenytoin regimen. His phenytoin level is now 13 mcg/mL. Carbamazepine suspension is ordered with an initial dose of 200 mg PO twice daily. What are appropriate instructions to the nursing staff?
 - I. Use an oral syringe to measure the dose.
 - II. Shake the suspension well before each use.
 - III. Common adverse reactions at the start of treatment include dizziness, drowsiness, unsteadiness or ataxia, and nausea.
 - IV. If a rash is noted, notify the neurologist immediately.
 - V. Have the patient drink plenty of fluids to prevent kidney stones.
 - a. I and II
 - b. I, II, and III
 - c. I, II, III, and IV
 - d. I, II, III, and V

Answer: c. Carbamazepine does not cause kidney stones as a side effect. To prevent underdosage or overdosage, the nurses should shake the suspension well before each use and use a calibrated device to measure the needed dose. Common side effects during therapy initiation include those listed. Because carbamazepine is associated with serious skin rashes, a rash should be reported immediately, and the drug will likely be discontinued.

3. After several days, the neurologist is ready to send BM home. He changes the prescription of carbamazepine suspension to tablets. What is the appropriate dosage adjustment for the change in dosage forms?
 - a. The dosage should be increased by 25%.
 - b. The tablet dosage should remain the same as the suspension dosage.
 - c. The dosage should be decreased by 25%.

Answer: b. No dosage adjustment in the total daily dosage is necessary when switching from carbamazepine suspension to the immediate-release tablets. Both deliver roughly the same amount of drug to the systemic circulation.
4. At discharge, BM's carbamazepine level is 9 mcg/mL. Four weeks later, BM has a seizure, and a repeat drug concentration panel reveals his phenytoin level is 13 mcg/mL and his carbamazepine level is 4 mcg/mL. A review of the pharmacy profile and a discussion with his mother reveals that the patient appears to have been compliant with his medications. What is the most likely reason for the change in carbamazepine concentrations?
 - a. A drug interaction with phenytoin

- b. Auto-induction of its own metabolism by carbamazepine
- c. A nutrient interaction now that BM is home and receiving his normal diet

Answer: b. After 21–30 days, carbamazepine's effect on hepatic metabolism, and thus auto-induction, reaches a maximum. It is not uncommon for carbamazepine levels to decline in the first weeks of therapy, requiring upward titration of dosage to maintain therapeutic effect.

REVIEW QUESTIONS

(Answers and Rationales on page 377.)

1. Which of the following is a common side effect of anticonvulsants?
 - a. Gastric upset
 - b. Changes in appetite
 - c. Changes in body weight
 - d. Cognitive changes
 - e. All of the above
2. What are adverse effects of anticonvulsant therapy?
 - I. Teratogenicity
 - II. Withdrawal
 - III. CNS depression
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
3. Which of the following is a common adverse effect associated with phenytoin therapy?
 - a. Dehydration
 - b. Photosensitivity
 - c. Gingival hyperplasia
 - d. Weight gain
 - e. Renal insufficiency
4. A 7-year-old girl is diagnosed with absence seizures. Which of the following is the most appropriate initial therapy?
 - a. Phenytoin
 - b. Ethosuximide
 - c. Valproic acid
 - d. Fluoxetine
 - e. Phenobarbital
5. Dilantin may cause all of the following adverse effects EXCEPT:
 - a. bradycardia.
 - b. hypertension.
 - c. cardiac arrhythmia.
 - d. lupus erythematosus.
 - e. folic acid deficiency.
6. Which of the following types of seizure are NOT treated with phenytoin?
 - a. Absence
 - b. Grand mal

- c. Complex partial
 - d. Simple partial
 - e. Generalized tonic-clonic
7. What is/are the most common adverse effects of anticonvulsive drugs?
- a. Headache and dizziness
 - b. Gastrointestinal symptoms
 - c. Alternation of cognition
 - d. Adverse effects on appetite and body weight
 - e. All of the above
8. Which of the following statements about valproic acid is FALSE?
- a. It may cause pancreatitis.
 - b. It shows decreased serum levels with isoniazid treatment.
 - c. It is less than 50% protein bound in circulation.
 - d. It is excreted in urine.
 - e. It may increase the risk of suicide.
9. Drugs useful in the management of temporal-lobe epilepsy include:
- a. Trimethadione
 - b. Carbamazepine
 - c. Phenytoin
 - d. a and b
 - e. b and c
10. Which of the following serum phenytoin concentrations is within the therapeutic range?
- a. 15 mg/mL
 - b. 15 mcg/mL
 - c. 25 mg/mL
 - d. 25 mcg/mL
 - e. 5 mg/mL
11. What is a correct statement regarding gabapentin therapy?
- I. Treats neuropathic pain
 - II. Treats seizures
 - III. Causes fatigue, somnolence and dizziness
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
12. What is a correct statement regarding carbamazepine therapy?
- I. Treats partial seizures
 - II. Treats generalized tonic-clonic seizures
 - III. Treats mixed seizures
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
13. Which of the following statements is true regarding drug interactions of anti-seizure medications?
- a. Alcohol can reduce phenytoin efficacy
 - b. Phenytoin can reduce oral contraceptive efficacy
 - c. Valproate can increase phenobarbital levels
 - d. a and b
 - e. a, b, and c
14. Which of the following are common dose-related side effects of carbamazepine?
- a. Nausea
 - b. Ataxia
 - c. Diplopia
 - d. Headache
 - e. All of the above
15. Carbamazepine is indicated for which of the following condition(s)?
- I. Bipolar disorder prophylaxis
 - II. Treatment of acute mania
 - III. Trigeminal neuralgia
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
16. Which of the following anti-seizure drugs acts primarily at calcium channels?
- a. Carbamazepine
 - b. Phenytoin
 - c. Ethosuximide
 - d. Clonazepam
 - e. All of the above
17. Which of the following is the appropriate laboratory parameter to evaluate for phenytoin toxicity?
- a. Alkaline phosphatase (Alk Phos)
 - b. Gamma-glutamyl transpeptidase (GGT)
 - c. Glutamic pyruvic transaminase (SGPT)
 - d. Glutamic oxaloacetic transaminase (SGOT)
 - e. Lactic acid dehydrogenase (LDH)
18. Which seizures are classified as partial?
- I. Complex partial
 - II. Tonic-Clonic
 - III. Grand Mal
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
19. What is the appropriate initial management of a patient presenting with acute barbiturate overdose?
- a. Maintenance of airway
 - b. Gastric lavage
 - c. IV dextrose
 - d. Hemodialysis
 - e. Pentylenetetrazol

20. Which of the following seizures varies in presentation depending on which part of the cortex is affected, lasts between 20-60 seconds, and does not impair the patient's state of consciousness?
- Absence
 - Simple partial
 - Complex partial
 - Myoclonic
 - None of the above
21. Which of the following may be used to treat complex partial seizures?
- Ethosuximide or carbamazepine
 - Carbamazepine or phenobarbital
 - Phenytoin
 - Phenytoin or ethosuximide
 - Phenytoin, primidone, or carbamazepine
22. Which of the following is used for the treatment of petit mal seizures?
- Ethosuximide
 - Sodium valproate
 - Phenytoin
 - a and b
 - a and c
23. A patient with asthma is taking prednisone for a recent exacerbation. For a newly diagnosed seizure disorder, she is started on phenytoin. Two weeks later, she returns to the clinic and complains of increased asthma symptoms. What is the likely mechanism?
- Increased hepatic degradation of prednisone
 - Increased airway hyperreactivity
 - Inhibition of prednisone absorption
 - Prevention of prednisone diffusion into lung tissue
 - Increased renal excretion of prednisone
24. Which of the following is/are effective in terminating status epilepticus?
- IV diazepam
 - IV valproate
 - Primidone
 - a and b
 - None of the above
25. Hirsutism is associated with the chronic administration of which anti-seizure medication?
- Phenytoin
 - Valproate
 - Carbamazepine
 - Clonazepam
 - Primidone
26. Clonazepam is useful in treating:
- Absence seizures
 - Lennox-Gastaut syndrome
 - Myoclonic seizures in children
- I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
27. Which of the following has active metabolites?
- Primidone
 - Carbamazepine
 - Phenytoin
 - Phenobarbital
 - a and b
28. What statement is false regarding petit mal seizures?
- Treated with valproate
 - Treated with ethosuximide
 - Tonic clonic is another name for petit mal seizures
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
29. Which of the following is NOT an adverse effect associated with phenytoin?
- Leukemia
 - Lymphadenopathy
 - Hepatosplenomegaly
 - Folic acid deficiency
 - Macrocytic anemia
30. Which of the following is most specific for petit mal seizures?
- Primidone
 - Ethosuximide
 - Phenytoin
 - Carbamazepine
 - Gabapentin
31. What drugs is/are used for the management of epilepsy?
- Phenobarbital
 - Diazepam
 - Mephobarbital
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III

I. Osteoporosis

Osteoporosis is a condition in which bones have decreased density and altered structure; the weakened bones are prone to fractures. Osteoporosis is considered a silent disease because bone loss itself is gradual and painless. There are usually no symptoms until the bones weaken to the point of fracture.

A. Incidence

The incidence of osteoporosis increases with age and is more common among individuals with slender frames, such as Asians and Scandinavians. Africans and African Americans genetically have denser bones and it takes longer for denser bone mass to decrease to the level of osteoporosis. Osteoporosis can occur at any age, in all ethnic groups, and in both sexes, although it is much more common in women. Because vitamin D and calcium are essential for healthy bones, malnourished individuals, including those with eating disorders, may develop osteoporosis.

B. Pathophysiology

1. In normal bones, there is a regulated balance between the activity of cells that create bone and those that break it down, a process called *bone remodeling*. There are three main cell types that compose bone:
 - a. Osteoblasts are the cells primarily responsible for new bone formation and its mineralization.
 - b. Osteoclasts are responsible for breaking down old bone in a process called *resorption*.
 - c. Osteocytes are calcified osteoblasts that comprise the hard part of the bone structure.
2. Healthy bone remains stable because osteoblasts and osteoclasts are working at a similar rate, allowing bone to continuously remodel and heal when damaged. If osteoclast activity outpaces osteoblast activity, bones become weakened. In other words, if resorption is greater than formation, bone loss occurs.
3. By the mid-30s, most men and women gradually begin to lose bone strength. When bones become less dense and structurally weaker, this condition is known as osteopenia. Osteopenia refers to mild bone loss that is not as severe as osteoporosis. Individuals with osteopenia are at increased risk of developing osteoporosis. As the condition progresses, bones lose calcium, phosphorus, boron, and other minerals and they become lighter, less dense, and more porous. If untreated, osteopenia can progress painlessly to

osteoporosis, increasing likelihood of fracture. Although any bone is susceptible to fracture, the most common fractures due to osteoporosis occur at the spine, wrists, and hips. Spine and hip fractures in particular may lead to chronic pain, long-term disability, and even death.

4. Extracellular levels of calcium, vitamin D, and parathyroid hormone (PTH) are key regulators in maintaining bone remodeling. PTH enhances the release of calcium and stimulates bone resorption and formation. Estrogen is thought to have a direct effect on bone cells. It enhances bone formation by stimulating the estrogen receptors, which are located on the osteoblasts. There is a direct link between the estrogen loss after menopause and the development of osteoporosis. Low hormone levels that occur in early menopause can significantly increase the risk of osteoporosis. Using anti-inflammatory corticosteroids may also significantly affect bone health. Corticosteroids are commonly taken by women greater than 55 years of age for conditions such as arthritis but are known to directly lead to bone loss. It is estimated that 20% of all osteoporosis cases may be attributed to corticosteroid use.

C. Risk factors

1. Sex (women are twice as likely to break/fracture bones than men)
2. Age (elderly)
3. Ethnicity (caucasian)
4. Family history
5. Frame size (small boned)
6. Smoking
7. Estrogen levels: longer exposure to estrogen equals less chance of developing osteoporosis
8. Other hormone-related diseases: hyperthyroidism, hyperparathyroidism, Cushing's syndrome
9. Chronic use of corticosteroids
10. Other medications (e.g., > 2 years of use of medroxyprogesterone (Depo-Provera) for birth control)

D. Signs and symptoms

The early stages of bone loss are often not accompanied by any symptoms. Once bones have been weakened by osteoporosis, signs and symptoms may include back pain, which can be severe if a vertebra has fractured or collapsed; loss of height with an accompanying stooped posture; and fractures

(commonly wrists, hips, or vertebrae). Although some fractures (such as in the wrist or hip) are obvious, spinal fractures can be more difficult to diagnose. Spinal fractures may be painless; even if pain occurs from a vertebral fracture, it might be attributed to another cause besides a fracture. More obvious signs of spinal fractures are reduced height and kyphosis, which is the curved upper spine that is sometimes called a “dowager’s hump.”

E. Diagnostic tests

1. Bone mineral density (BMD)
2. Dual-energy x-ray absorptiometry (DEXA) (Table 23-1)

Table 23-1 DEXA Result Interpretation

	T-score
Normal	> -1
Osteopenia	-1 to -2.5
Osteoporosis	< -2.5

3. Peripheral dual-energy x-ray absorptiometry (pDEXA)
4. Dual photon absorptiometry (DPA)
5. Quantitative ultrasound
6. Quantitative computed tomography (QCT)
7. X-rays

F. Treatment

1. Lifestyle and nutrition
2. Adequate intake of calcium
 - a. Everyone older than age of 8 years, minimum calcium intake of 1000 mg/day
 - b. Individuals older than age of 50 years, minimum calcium intake of 1200 mg/day
 - c. Pre-teens and teens (9 to 18 years old), minimum calcium intake of 1300 mg/day
3. Adequate intake of vitamin D needed to help with absorption of calcium and maintain muscle strength
 - a. Until age 60 years: 400 international units (IU) of vitamin D per day
 - b. After age 60 years: 600–800 IU of vitamin D per day
4. Weight-bearing exercises
 - a. Weight-lifting, jogging, hiking, stair-climbing, step aerobics, dancing, racquet sports, other activities that require muscles to work against gravity
5. Medications
 - a. Therapies that increase BMD and prevent fractures
 - (1) Calcium
 - (a) Important for attaining peak bone mass and preventing osteoporosis, antiresorptive, beneficial effects enhanced with other therapies and exercise
 - (b) 1200–1500 mg of *elemental* calcium daily

- (c) Adverse effects: constipation, gas, and kidney stones (rare)
- (d) Caution needed with concomitant use with certain antibiotics (e.g., ciprofloxacin)

(2) Vitamin D supplements

- (a) Promote calcium absorption
- (b) 400–800 IU per day
- (c) Active form of vitamin D is calcitriol (1, 25-dihydroxycholecalciferol)
- (d) Consider use in kidney dysfunction
- (e) Not approved for osteoporosis treatment
- (f) Adverse effects: hypercalcemia (weakness, headache, somnolence, nausea, cardiac rhythm disturbance), hypercalciuria

b. “Bone-building” treatments

Without adequate calcium and vitamin D, the following treatments cannot improve bone architecture. Calcium and vitamin D are therefore prerequisites to the following therapies.

(1) Bisphosphonates

- (a) Mechanism of action: bisphosphonates adsorb to the bone, preventing osteoclasts from adhering to the same bone surfaces, thereby inhibiting osteoclast activity.
- (b) For the prevention and treatment of osteoporosis in postmenopausal women
- (c) Provide the greatest BMD increases, effect is dose-dependent, combination therapy with estrogen/hormone replacement therapy (HRT) results in greater increases in BMD
- (d) Examples
 - (i) Alendronate (Fosamax) taken orally once a week
 - (ii) Risedronate (Actonel) taken orally once a week
 - (iii) Ibandronate (Boniva) taken orally once a month; can also be given IV, once every 3 months
 - (iv) Zoledronic acid (Reclast) given IV once a year
- (e) Adverse effects: nausea, dyspepsia, abdominal pain, diarrhea; esophageal, gastric, or duodenal irritation, perforation, ulceration or bleeding, acid reflux; osteonecrosis of jaw
- (f) Considerations, if patient is taking medication orally
 - (i) Take on an empty stomach, with plain water only, first thing in the morning before having anything to eat or drink.
 - (ii) Patient must not lie down, eat, drink, or take other medications for at least 30 minutes. If patient wants to lie down after 30 minutes, the patient must eat

- breakfast first. These directions are necessary to avoid irritation of esophagus
- (iii) **Caution:** Use of bisphosphonates in women who are pregnant or breastfeeding is not well studied.
- (2) Hormone replacement therapy
- (a) Estrogen alone or estrogen plus progestin
 - (i) Mechanism of action: The bone-protective effects of estrogen may involve suppression of inflammatory chemicals called cytokines, as discussed previously. There are estrogen receptors on osteoblasts and osteoclasts. Estrogens decrease osteoclast recruitment and activity, inhibit PTH peripherally, increase calcitriol concentrations and intestinal calcium absorption, and decrease renal calcium excretion. Estrogens also decrease cytokine levels.
 - (ii) Consideration: The progestin component is added only in women with an *intact* uterus to prevent endometrial overgrowth and endometrial cancer.
 - (iii) **Caution:** Use is contraindicated in active/suspected estrogen-dependent cancer, abnormal vaginal bleeding, severe liver disease, and active vascular thrombosis. Relative contraindications include migraines, thromboembolic disease, hypertriglyceridemia, uterine fibroids, endometriosis, gallbladder disease, family history of breast cancer, and chronic hepatic dysfunction.
 - (3) Selective estrogen receptor modulators (SERM)
 - (a) Mechanism of action: mimic the positive effects of estrogen on bones without side effects such as breast cancer and stroke; raloxifene (Evista) decreases spine fractures in women and is approved for use only in women at this time.
 - (b) Examples: raloxifene (Evista), tamoxifen (Nolvadex)
 - (c) Adverse effects: hot flashes, leg cramps, thromboembolic events
 - (d) Consideration: Avoid in patients with history of blood clots.
- c. Medications that increase BMD only
- (1) Calcitonin (Miacalcin)
 - (a) Mechanism of action: inhibits activity of osteoclasts; thought to increase spine BMD. May also lessen pain from spinal fractures.
 - (b) Available as injection and nasal spray; nasal spray more commonly used.
 - (c) Adverse effects
 - (i) Intranasal: rhinitis, epistaxis, and nasal irritation
 - (ii) Subcutaneous: GI symptoms, injection-site pain, and flushing
 - d. Medications that increase bone formation
 - (1) Teriparatide (Forteo)
 - (a) Mechanism of action: a form of PTH that helps stimulate bone formation
 - (b) Side effects: dizziness/syncope, chest pain, rash, nausea, rhinitis, fatigue, leg/muscle cramps, arthralgia
 - (c) Considerations
 - (i) If patient's PTH levels are elevated or if the patient has ever had radiation therapy, may not be able to take this medication
 - (ii) Daily injection given subcutaneously and can be taken for a maximum of 2 years
6. Surgery
- a. Vertebroplasty
 - b. Kyphoplasty
- G. Prevention
1. Smoking cessation
 2. Alcohol in moderation
 3. Maintain healthy body weight
 4. Sunlight (some exposure necessary for adequate vitamin D)
 5. Diet
 6. Adequate calcium and vitamin D are essential for the prevention of osteoporosis in general, including postmenopausal osteoporosis. Postmenopausal women are especially susceptible to fractures of the hip, wrist, and spine; therefore, it is recommended by healthcare professionals for postmenopausal women to have about 1200–1500 milligrams of calcium and 800 IU of vitamin D daily.
 7. Exercising regularly (e.g., strength training, weight-bearing activities, walking, jogging)
 8. Avoiding hazardous falls
- II. Vaginitis due to Yeast Infection
- A. A yeast infection is a fungal infection called vulvovaginal candidiasis (VVC). It is rare before menarche. Incidence is likely after age 20, and 50% of women who have had a yeast infection before will have another yeast infection.
 - B. Yeast is part of the normal flora in the vagina. Usually, changes in the patient's vaginal environment triggers the infection. Changes include hormonal changes, such as in pregnancy, or the use of antibiotics, which disrupt the normal flora in the vagina.
 - C. The major pathogen is *Candida albicans*. With increasing use of over-the-counter (OTC) products,

short-course therapies, and the increased use of preventive or long-term maintenance therapy, there is an increased incidence of non-*albicans* candidiasis (e.g., *Candida glabrata*). A diagnosis for a yeast infection or VVC entails a positive vaginal culture for *Candida*.

- D. Yeast infections can be sporadic or recurrent. They could also be defined as *uncomplicated* sporadic infections, which most likely, will be susceptible to all forms of antifungal therapy regardless of the duration of treatment. *Complicated* or recurrent VVC occurs in immunocompromised patients or those who have uncontrolled diabetes. Therapy in these populations requires longer duration (10–14 days), regardless of the route of administration.
- E. Risk factors
1. Sexually active, but VVC is not an STD
 2. Oral-genital contact
 3. Diaphragm with spermicide
 4. Contraceptive sponge
 5. Intrauterine device (IUD)
 6. Oral contraceptives (OC), especially of higher dose
 7. Antibiotic use
 8. Diet (particularly excessive carbohydrates)
 9. Douching
 10. Tight-fitting clothing
 11. African American women appear to be at higher risk for VVC compared with white women.
- F. Symptoms generally worsen during menstruation because the hormonal changes provide a better environment for fungal growth.
1. Itching
 2. Watery or curd-like vaginal discharge that is white in color
 3. Vaginal erythema (reddening of the skin)
 4. Pain during sexual intercourse (dyspareunia)
 5. Painful urination
 6. Swollen labia and vulva
 7. Vaginal lesions
- G. Treatment
1. Nonpharmacological
 - a. Avoiding harsh soaps and perfumes to reduce irritation
 - b. Keeping the genital area clean and dry by avoiding tight clothing
 - c. Avoiding frequent or prolonged exposure to hot tubs
 - d. Using cool baths to soothe the skin
 - e. Eating yogurt containing *Lactobacillus acidophilus*
 2. Prescription antifungal suppositories/vaginal creams (Table 23-2)
 - a. Vaginal yeast infections are treated with antifungal medications that are inserted directly into the vagina as suppositories or as cream-filled applicators.
 - b. Adverse effects: minimal, include vaginal burning, stinging, or irritation

Table 23-2 Prescription Antifungals for Vaginal Conditions

Active Ingredient		Duration
Terconazole	0.4% cream	7 days
(Terazol, Zazole)	0.8% cream or 80 mg suppository	3 days
Nystatin	100,000 unit vaginal tablet	14 days

Table 23-3 OTC Medications for Vaginal Candidiasis

Active Ingredient		Duration
Butoconazole (Femstat)	2% cream	3 days
Clotrimazole (Gyne-Lotrimin, Mycelex, Canesten)	1% cream or 100-mg tablet	7 days
	2% cream or 200-mg tablet	3 days
	10% cream or 500-mg tablet	1 day
Miconazole (Monistat, Vagistat-3, Monistat-1 Ovule Pak)	2% cream or 100-mg suppository	7 days
	200-mg suppository	3 days
	1200-mg ovule	1 day
Tioconazole (Vagistat-1)	6.5% ointment or 300-mg ovule	1 day

3. Common OTC vaginal medications
 - a. Selection of product is based on patient's preference for the preparation used and the duration of treatment.
 - b. Adverse effects: minimal, include vaginal burning, stinging, or irritation
4. Prescription oral antifungals (Table 23-3)
 - a. Oral azole antifungal agents may also be used to treat vulvovaginal candidiasis or yeast infection as an alternative to using antifungal creams.
 - (1) Fluconazole (Diflucan): 150 mg PO for 1 day
 - (2) Ketoconazole (Nizoral): 200 mg PO bid for 5 days
 - (3) Itraconazole (Sporanox): 200 mg PO bid for 1 day
 - (4) Adverse effects: nausea, vomiting, or headache

D. Resistance

1. When persistent positive yeast cultures fail to respond to therapy despite patient adherence to therapy. Often occurs with *Candida glabrata*.
2. Treatment
 - a. Boric acid

- b. Initial 600 mg intravaginal capsule daily for 14 days
 - c. Maintenance: 1 capsule intravaginally twice weekly
 - d. Caution: toxic if administered orally
 - e. Requires extemporaneous compounding by pharmacist.
3. 5-Flucytosine
- a. 1000-mg cream inserted vaginally nightly for 7 days; product not commercially available in the United States; requires extemporaneous compounding.

III. Menopause

Menopause is when a woman's menstrual periods stop completely. It signals the end of the ovaries releasing eggs for fertilization. Menopause begins naturally when the ovaries start making less estrogen and progesterone, the hormones that regulate menstruation.

A woman is said to have completed menopause when her menses have stopped for an entire year. Menopause generally occurs between the ages of 45–55 years, although it can occur as early as the 30s or as late as the 60s. Progesterone (the hormone that prepares the body for pregnancy) levels drop and fertility declines. In the 40s, changes in menstrual patterns are experienced. The woman's period may become longer or shorter, heavier or lighter, and more or less frequent. Eventually, the ovaries cease to function and there are no more periods.

All women will experience menopause. Menopause is not considered a disorder and most women do not need treatment for it. However, if symptoms are severe, medications may be used to help alleviate symptoms.

A. Risk factors associated with early menopause

- 1. Smoking
- 2. Nulliparity (never carrying a child to full term)
- 3. Depression
- 4. Exposure to toxic chemicals (such as pesticides)
- 5. Treatment of childhood cancer with pelvic radiation or chemotherapy

B. Signs and symptoms

- 1. Change in menstruation (periods may be shorter or longer, lighter or heavier, with more or less time in between)
- 2. Hot flashes and/or night sweats
- 3. Trouble sleeping
- 4. Vaginal dryness
- 5. Mood swings
- 6. Trouble focusing
- 7. Hair loss on the head but increased hair on the face (less common)

C. Nonpharmacologic treatment

- 1. Smoking cessation
- 2. Reducing alcohol intake
- 3. Limiting caffeine intake
- 4. Weight control
- 5. Exercise
- 6. Balanced diet
- 7. Nonestrogenic vaginal creams

D. Pharmacologic treatment

- 1. Hormone replacement therapy (HRT)

Some women take hormone replacement therapy (HRT) to relieve the symptoms associated with menopause. HRT is medication containing one or

more female hormones, usually an estrogen plus progestin (synthetic progesterone); the progestin is added if the woman has an intact uterus. HRT may protect against osteoporosis. However, HRT also has risks. It can increase the risk of breast cancer, heart disease, and stroke. Certain types of HRT have a higher risk, and each woman's risks vary depending upon her health history and lifestyle.

- a. Can cause many short-term and long-term side effects; risks versus benefits should be weighed carefully and monitored closely by physician

- b. Common minor side effects include bloating, breast tenderness, cramping, irritability, mood changes or depression, menstrual bleeding

- c. More serious, long-term side effects

- (1) Breast cancer and cardiovascular disease (stroke, heart attack), especially in women who have not had a hysterectomy
- (2) Endometrial cancer (women who have NOT had the uterus removed are prescribed low doses of estrogen with progestin to protect against endometrial cancer.)
- (3) Increased risk for deep vein thrombosis (DVT) or blood clots

- d. Various types and forms of HRT are available. Need and symptom relief determine which is used.

- (1) Pills
- (2) Vaginal creams
- (3) Vaginal ring inserts
- (4) Implants
- (5) Injections
- (6) Transdermal patches

- e. Estrogen therapy is the most popular treatment for hot flashes due to menopause

- (1) Examples

- (a) Conjugated estrogens (Premarin; Cenestin)
- (b) Esterified estrogens (Estratab, Menest)
 - (i) Contain 75%–85% natural estrogens and 15%–25% equine estrogen
 - (ii) Used to treat hot flashes, atrophic vaginitis, and urethritis
- (c) Estradiol: the major estrogen type secreted during menstrual years, available in various forms
 - (i) Oral pill (Estrace)
 - (ii) Transdermal patch (Climara, Estraderm, Vivelle)
 - (iii) Vaginal tablet (Vagifem)
 - (iv) Vaginal cream (Estrace Vaginal Cream)
- (d) Estropipate (estrone): naturally produced from estradiol and a less potent estrogen
 - (i) Oral pill (Ogen, Ortho-Est)
 - (ii) Used to treat hot flashes and vaginal atrophy and to prevent osteoporosis

- (e) Vaginal estrogen
 - (i) Can help relieve vaginal dryness, discomfort with intercourse, and some urinary symptoms
 - (ii) Examples: Vaginal tablet (Vagifem), ring (Nuvaring), or cream (Premarin Vaginal Cream); releases a small amount of estrogen that is absorbed by the vaginal tissue
 - 2. Alternatives to HRT for treatment of menopausal symptoms
 - a) Antidepressants (low-dose)
 - (1) Used for hot flashes (off-label)
 - (2) Selective serotonin reuptake inhibitors (SSRI)
 - (i) Examples: fluoxetine (Prozac, Sarafem), paroxetine (Paxil), citalopram (Celexa), and sertraline (Zoloft)
 - (3) Selective serotonin and norepinephrine reuptake inhibitors (SSNRI)
 - (i) Example: venlafaxine (Effexor)
 - (ii) Adverse effects include drowsiness and fatigue.
 - (4) Gabapentin (Neurontin)
 - (i) Used for hot flashes
 - (ii) Adverse effects include drowsiness, sedation, blurred vision, nausea, vomiting, or tremor.
 - (5) Clonidine (Catapres)
 - (i) Used to reduce the frequency of hot flashes
 - (ii) Adverse effects include slow heart rate, low blood pressure, fatigue, dizziness, headache, constipation, nausea, vomiting, diarrhea, insomnia, or a dry mouth.
 - E. Dietary supplements provide modest benefit at best, but may be used initially before pharmacologic management to mildly reduce incidence and severity of hot flashes.
 - 1. Phytoestrogens
 - 2. Black cohosh
 - 3. Soy
 - 4. Red clover
- IV. Contraception
- A. Oral contraceptives (Tables 23-4 to 23-9)
 - 1. Consists of hormones, estrogen and progestin, in pill form to be taken daily. A 4-week cycle typically has 21 hormonally active pills followed by seven pills containing no hormones. Some packagings omit the inactive pills. Some regimens (e.g., Seasonique) allow for continuous dosing for 3 months.
 - 2. There are three categories of oral contraceptives. Before prescribing, the physician considers age, medical history, lifestyle, cost, and potential side effect profile. If one category is tried, but the patient experiences too many adverse effects, the doctor may switch to another category. The doctor may also try another brand, within the same category, but with a different dose.
 - a) Monophasic pills contain same amount of hormones (estrogen and progestin) in all active pills of pack. Because all pills have a uniform hormone level, monophasic pills are least likely to cause side effects due to fluctuating hormone levels in the body.
 - b) Biphasic pills contain two different doses of hormones in active pills of pack.
 - c) Triphasic pills contain three different doses of hormones in active pills of pack, changing every week during first 3 weeks.
 - (1) Biphasic and triphasic pills reduce the total hormone dosage a woman receives and are thought to better match the body's natural menstrual cycle.
 - 3. Mechanism of action
 - a) Prevent ovaries from releasing eggs by negative feedback
 - b) Thicken the cervical mucus, which prevents sperm from joining with an egg
 - c) Thin the lining of the uterus, preventing pregnancy by interfering with implantation of a blastocyst; applies only to combination and progestogen-only pills
 - 4. Advantages of oral contraceptive
 - a) Preventing pregnancy
 - b) Treating irregular menstrual periods
 - c) Manipulating menstrual cycle to avoid a period during certain events, such as vacations or weekends, by extending the number of intake days of hormonally active pills or by skipping the nonactive pill week
 - d) May help prevent certain conditions, such as benign breast disease, pelvic inflammatory disease (PID), polycystic ovary syndrome, and functional cysts
 - e) Prevent ectopic pregnancies
 - f) Can help treat acne, hirsutism, endometriosis
 - 5. Disadvantages and common side effects
 - a) Do not protect from sexually transmitted diseases (STD)
 - b) Nausea
 - c) Breast tenderness
 - d) Breakthrough bleeding or no periods
 - e) Headaches
 - f) Mood changes: depression, anxiety
 - g) Lower sexual desire
 - h) Weight gain
 - 6. More serious risks include blood clots, heart attack, stroke, or pulmonary embolism especially in women older than 35 years and women who smoke, have hypertension or hyperlipidemia, and are obese.
 - 7. Considerations
 - a) Depending on the oral contraceptive, a woman begins taking the first pill on the first day of her period or on the first Sunday after her period.
 - b) It is important to take the pill daily and consistently (same time every day).
 - c) When a woman stops taking birth control pills, there may be a few months before normal ovulatory cycle resumes.

TABLE 23-4 Monophasic Oral Contraceptives

Generic Components and Doses	Product Names
Ethinyl estradiol 30 mcg Desogestrel 0.15 mg	Desogen Ortho-Cept <i>Reclipsen</i> <i>Solia</i> <i>Apri</i>
Ethinyl estradiol 30 mcg Drospirenone 3 mg	Yasmin
Ethinyl estradiol 35 mcg Ethinodiol diacetate 1 mg	Demulen 1/35 <i>Zovia 1/35</i> <i>Kelnor 1/35</i>
Ethinyl estradiol 50 mcg Ethinodiol diacetate 1 mg	Demulen 1/50 <i>Zovia 1/50</i>
Ethinyl estradiol 20 mcg Levonorgestrel 100 mcg	Levlite Alesse <i>Aviane</i> <i>Lutera</i> <i>Lessina</i>
Ethinyl estradiol 30 mcg Levonorgestrel 150 mcg	Levlen Nordette <i>Levora</i> <i>Portia</i>
Ethinyl estradiol 35 mcg Norethindrone 0.4 mg	Ovcon-35 <i>Balziva</i>
Ethinyl estradiol 35 mcg Norethindrone 0.5 mg	Modicon Brevicon <i>Necon 0.5/35</i> <i>Nortrel 0.5/35</i>
Ethinyl estradiol 35 mcg Norethindrone 1 mg	Ovcon-50
Ethinyl estradiol 20 mcg Norethindrone acetate 1 mg	Loestrin 1-20 <i>Microgestin 1-20</i> <i>Junel 1/20</i>
Mestranol 50 mcg Norethindrone 1 mg	Ortho-Novum 1-50 Norinyl 1-50 <i>Necon 1-50</i>
Ethinyl estradiol 30 mcg Norgestrel 0.3 mg	Lo-Ovral <i>Low-Ogestrel</i> <i>Cryselle</i>
Ethinyl estradiol 50 mcg Norgestrel 0.5 mg	Ovral <i>Ogestrel</i>
Ethinyl estradiol 35 mcg Norgestimate 0.25 mg	Ortho-Cyclen <i>Sprintec</i> <i>Mononessa</i> <i>Previfem</i>
Ethinyl estradiol 20 mcg Norethindrone acetate 1 mg + ferrous fumarate 75 mg	Loestrin FE 1-20 <i>Microgestin FE 1-20</i> <i>Junel FE 1-20</i>
Ethinyl estradiol 30 mcg Norethindrone acetate 1.5 mg + ferrous fumarate 75 mg	Loestrin FE 1.5-30 <i>Microgestin FE 1.5-30</i> <i>Junel FE 1.5-30</i>

Note: **Bold** indicates originator product brand names; *italics* indicate generic name.

TABLE 23-5 Biphasic Oral Contraceptives

Generic Components and Doses	Product Names
Ethinyl estradiol 20 mcg Desogestrel 0.15 mg (21-day) Ethinyl estradiol 10 mcg (5-day)	Mircette <i>Kariva</i>
Ethinyl estradiol 35 mcg Norethindrone 0.5 mg Ethinyl estradiol 35 mcg Norethindrone 1 mg	Ortho Novum 10-11 <i>Necon 10-11</i>

Note: **Bold** indicates originator product brand names; *italics* indicate generic name.

TABLE 23-6 Triphasic Oral Contraceptives

Generic Components and Doses	Product Names
Ethinyl estradiol 25 mcg and desogestrel 100 mcg Ethinyl estradiol 25 mcg and desogestrel 125 mcg Ethinyl estradiol 25 mcg and desogestrel 150 mcg	Cyclessa <i>Velivet</i> <i>Vesia</i>
Ethinyl estradiol 30 mcg and levonorgestrel 0.05 mg Ethinyl estradiol 40 mcg and levonorgestrel 0.075 mg Ethinyl estradiol 30 mcg and levonorgestrel 0.125 mg	Triphasil Tri-levlen <i>Enpresse</i> <i>Trivora</i>
Ethinyl estradiol 35 mcg and norethindrone 0.5 mg Ethinyl estradiol 35 mcg and norethindrone 0.75 mg Ethinyl estradiol 35 mcg and norethindrone 1 mg	Ortho Novum 7-7-7 <i>Necon 7/7/7</i> <i>Nortrel 7/7/7</i>
Ethinyl estradiol 35 mcg and norethindrone 0.5 mg Ethinyl estradiol 35 mcg and norethindrone 1 mg Ethinyl estradiol 35 mcg and norethindrone 0.5 mg	Tri-Norinyl <i>Leena</i> <i>Aranelle</i>
Ethinyl estradiol 35 mcg and norgestimate 0.18 mg Ethinyl estradiol 35 mcg and norgestimate 0.215 mg Ethinyl estradiol 35 mcg and norgestimate 0.25 mg	Ortho Tri-Cyclen <i>Tri-sprintec</i> <i>Trinessa</i> <i>Tri-previfem</i>
Ethinyl estradiol 25 mcg and norgestimate 0.18 mg Ethinyl estradiol 25 mcg and norgestimate 0.215 mg Ethinyl estradiol 25 mcg and norgestimate 0.25 mg	Ortho Tri-Cyclen Lo
Ethinyl estradiol 20 mcg and norethindrone acetate 1 mg Ethinyl estradiol 30 mcg and norethindrone acetate 1 mg Ethinyl estradiol 35 mcg and norethindrone acetate 1 mg	Estrostep/ Estrostep FE

Note: **Bold** indicates originator product brand names; *italics* indicate generic name.

TABLE 23-7 Extended Cycle Oral Contraceptives

Generic Components and Doses	Product Names
Ethinyl estradiol 20 mcg and drospirenone 3 mg	Yaz 24/4
Ethinyl estradiol 20 mcg and norethindrone acetate 1mg + ferrous fumarate 75mg	Loestrin 24 Loestrin FE 24/4
Ethinyl estradiol 30 mcg and levonorgestrel 0.15 mg	Seasonique

Note: **Bold** indicates originator product brand names; *italics* indicate generic name.

TABLE 23-8 Progestin Only Oral Contraceptives

Generic Components and Doses	Product Names
Norethindrone 0.35 mg	Ortho-Micronor Nor-QD <i>Camila</i> <i>Errin</i> <i>Jolivet</i>

Note: **Bold** indicates brand name; *italics* indicates generic brand name.

TABLE 23-9 Emergency Contraceptive

Generic Component and Dose	Product Name
Levonorgestrel 0.75 mg	Plan B

Note: **Bold** indicates brand name.

PATIENT PROFILE

Patient Initials: RH

Sex: Female

Age: 49

Height: 5' 4"

Weight: 60 kg

Race: White

Allergies: Bandage adhesives (severe skin irritation)

Medical History:

Hypothyroidism

Social History: Tobacco use: None

Alcohol use: 1 glass of wine with dinner nightly

Family History:

Osteoporosis

Medication Profile:

Levoxyl 100 mcg once daily

Current pharmacy problem: The pharmacist knows RH well; she is a frequent visitor at the pharmacy. She comes seeking nonprescription advice for “hot flashes.” She is the mother of four children, the youngest of elementary-school age. For the past 4 months, her menstrual periods have been a bit erratic in flow and time of occurrence each month. She used to be much more regular. She has had a recent gynecological examination that was normal, and her thyroid parameters are under control. Lately, she has occasionally found herself in soaking sheets in the middle of the night, and sometimes finds herself with unusual intolerances to the balmy Florida weather, even in air conditioning. The hot flashes come and go daily and are uncomfortable. Her physician has told her that she is perimenopausal. She has not been willing to take hormonal birth control due to her age, and she has a non-hormonal IUD for contraception.

A friend recommended that RH try soy supplements or black cohosh products for her hot flash symptoms. She is willing to try these before talking with her doctor further regarding her options. She wants to know the pharmacist’s opinion of these products.

PATIENT PROFILE QUESTIONS

- Based on the evidence, which of the following statements is most true about the use of soy or black cohosh supplements in terms of efficacy?
 - The supplements may be tried as first option in patients with mild to moderate symptoms because there is little concern for safety or side effects in any woman and they have been proven efficacious at reducing hot flash episodes.
 - The North American Menopause Society (NAMS) 2007 guidelines state these may be reasonable first options in women with mild-moderate symptoms provided breast cancer risks and contraindications are not evident; however, trials of better evidence, such as the Herbal Alternatives for Menopause Trial (HALT study), do not support their efficacy.
 - Avoid these supplements because experts have completely recommended against their use.

Answer: b. Experts have not gone so far as to recommend against the use of alternative tactics for mild to moderate hot flashes; the NAMS statements have continued to include their use as initial strategies for selected patients with mild symptoms. The supplements have NOT been proven efficacious; trials of better study design, such as the HALT trial, have found the supplements do not sufficiently relieve vasomotor symptoms. Caution is recommended in employing black cohosh because liver problems and other reported potential adverse effects have not been thoroughly evaluated. Under current guidelines, both strategies may be tried for a limited period to see if they are helpful to a patient.

- RH tries a soy isoflavone supplement for several months with lifestyle changes. She returns to the pharmacy in 6 months stating symptoms are not really better and are “getting more pronounced and

frequent.” She has discussed her options with her physician. She will try estrogen-progestin hormone replacement therapy (HRT) for a few months. What type of HRT regimen might be the best choice for RH?

- Use a low-dose transdermal estrogen (e.g., 25 mcg/day estradiol-progestin patch).
- Use traditional dosing of conjugated estrogens 0.625 mg PO per day with either a sequential or continuous oral progestin.
- Use conjugated estrogen 0.3 mg PO daily in combination with either sequential or continuous oral progestin.
- Use oral estrogen alone in low dose (e.g., conjugated estrogen 0.3 mg PO daily).

Answer: c. Although answer a would also be acceptable in many patients, RH has a reliable history of skin irritation to adhesives and thus the transdermal patches are likely to cause irritation. An option not presented here is a topical estrogen gel or lotion combined with an oral progestin. That leaves oral therapy. The current medical approach is to use lower hormonal estrogen dosages, for a very short time (e.g., usually 2 years or less) to treat vasomotor symptoms. The use of estrogen alone is NOT an option; RH has an intact uterus and needs a progestin-containing regimen to lower the risk of endometrial proliferation. A peri-menopausal woman could also be a candidate for low-dose oral contraception to alleviate symptoms, but this patient indicated in her history that she did not want to take them. She also has a reliable birth control method (IUD).

- Several years later RH's menstrual periods have ceased, with confirmatory FSH level of >40 ng/mL indicating menopause. RH is no longer interested in hormones due to the potential health risks, particularly with regard to breast cancer and heart disease. She is now on regular calcium and vitamin D supplements. She wonders what is the best way to discontinue hormone replacement. True or False: RH should quit estrogen regimen “cold turkey” because vasomotor symptoms should not occur now that she is in menopause.
 - True
 - False

Answer: b. False. The statement is false because vasomotor symptoms will likely occur when the hormones are discontinued, even though the patient is already menopausal. The symptoms will be due to estrogen depletion as the replacement hormones are halted or tapered.

Discontinuation of therapy is an area of controversy. Most physicians advocate a tapering of hormones for several months in a stepped fashion and employing lifestyle strategies or alternative vasomotor treatments, such as serotonin modulators, if hot flashes become severe again. However, longer hormonal treatment may increase health risks, so some patients will choose to discontinue treatment without a long taper.

REVIEW QUESTIONS

(Answers and Rationales on page 379.)

- Which of the following underlying factors may be responsible for the development of osteoporosis in postmenopausal women?

- Increased osteoclast activity
- Increased interleukin 1 and 6 levels
- Decreased estrogen levels

- I only
- III only
- I and II
- II and III
- I, II, and III

- Which of the following is/are true regarding the mini-pill?

- Contains estrogen only
- A common side effect of progestin-only pills is spotting, or breakthrough bleeding
- Its major mechanism of action is to change the character of cervical and vaginal mucus

- I only
- III only
- I and II only
- II and III only
- I, II, and III

- Which of the following are adverse effects of hormone replacement therapy?

- Breast pain
- Nausea
- Fluid retention

- I only
- III only
- I and II only
- II and III only
- I, II, and III

- Which of the following drugs does NOT possess a steroidal nucleus?

- Norethindrone
- Liothyronine
- Ethinyl estradiol
- Prednisolone
- Fluoxymesterone

- Prostaglandins may be used to treat all of the following EXCEPT:

- delayed labor.
- premature labor.
- retained products of conception.
- impotence.
- Prostaglandins may be used to treat all of the above.

- Which of the following medications should be avoided in pregnant women due to ability to stimulate uterine contractions?

- Misoprostol
- Piroxicam
- Aspirin
- Tetracycline
- Phenytoin

- Which of the following is/are an appropriate use of testosterone therapy?

- Palliation of advanced breast cancer
- Erythropoiesis stimulation
- Treatment of constitutional pubertal delay

- d. a and b
 - e. a and c
8. Which of the following statements concerning antithyroid medications is FALSE?
- a. Propranolol decreases peripheral T3 formation.
 - b. Methimazole inhibits organification.
 - c. Lithium is first-line treatment for thyroid storm.
 - d. Iodide prevents dietary iodine uptake.
 - e. PTU inhibits organification.
9. Which of the following oral contraceptives contains progestin only?
- a. Jolivette
 - b. Lo-Ovral
 - c. Ortho-Novum
 - d. Loestrin
 - e. Nordette
10. Which of the following is an absolute contraindication to oral contraceptive use?
- a. History of DVT
 - b. Breast carcinoma
 - c. Abnormal genital bleeding
 - d. Ischemic heart disease
 - e. All of the above
11. Which of the following does NOT stimulate growth hormone release?
- a. Serotonin
 - b. Clonidine
 - c. Somatostatin
 - d. Growth hormone releasing hormone
 - e. Bromocriptine
12. All of the following are signs and symptoms of hyperthyroidism EXCEPT:
- a. Weight gain
 - b. Tachycardia
 - c. Nervousness
 - d. Increased appetite
 - e. Sweating
13. Which of the following is a mechanism of action of progestins?
- a. Causes a rise in body temperature at ovulation
 - b. Inhibits formation of endocervical secretion
 - c. Has inherent estrogenic activity
 - d. a and b
 - e. a, b, and c
14. The mini-pill can contain which of the following hormones?
- I. Ethinyl estradiol
 - II. Norethindrone
 - III. Norgestrel
- a. I only
 - b. III only
 - c. I and II
- d. II and III
 - e. I, II, and III
15. Which of the following is an appropriate indication for gonadotropin-releasing hormone analog therapy?
- a. Central precocious puberty
 - b. Endometriosis
 - c. Female infertility
 - d. Prostate cancer
 - e. All of the above
16. Which of the following has antiestrogen effects at the estrogen receptor?
- a. Norethynodrel
 - b. Tamoxifen
 - c. Goserelin
 - d. Ketoconazole
 - e. Aminoglutethimide
17. What statement is FALSE regarding the Gonadotropin-releasing hormone?
- I. GnRH regulates the secretion of FSH
 - II. GnRH regulates the secretion of LH
 - III. Contraindicated in endometriosis
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
18. What statement is TRUE regarding tamoxifen?
- I. Estrogen receptors are located in the breast
 - II. Estrogen antagonist
 - III. Treats breast cancer
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
19. Which of the following is NOT a component of oral contraceptives?
- a. Norgestrel
 - b. Mifepristone
 - c. Levonorgestrel
 - d. Ethyndiol diacetate
 - e. All of the above
20. Which of the following estrogen patches are applied twice weekly?
- a. Vivelle-Dot
 - b. Alora
 - c. Menostar
 - d. a and b
 - e. b and c
21. Which of the following is NOT a side effect of oral contraceptives?
- a. Hepatic adenoma
 - b. Chloasma

- c. Weight gain
 - d. Growth retardation
 - e. Thromboembolism
22. Which of the following is a side effect of gonadotropin releasing hormone therapy in women?
- a. Multiple births
 - b. Amenorrhea
 - c. Ovarian hyperstimulation
 - d. Menopausal symptoms
 - e. All of the above
23. Which of the following statement about the “mini-pill” (progestin-only pill) is true?
- a. It is less effective than combined oral contraceptives.
 - b. Ovulation does not occur when taken correctly.
 - c. It commonly causes breakthrough bleeding.
 - d. It acts primarily via thickening of cervical mucus.
 - e. All of the above

- I. Introduction: The immune system consists of physical and chemical barriers and specific and nonspecific mechanisms to eliminate antigens.
- II. Components of the Immune System
 - A. Antigen-presenting cells
 1. B cells
 - a. Produce antibodies
 2. Monocytes
 - a. Precursor cell to macrophages
 - b. Circulate in blood; migrate into tissues
 - c. Scavenge foreign cells
 3. Macrophages
 - a. Phagocytose and kill microorganisms; activation of T cells and initiation of immune response
 - b. Secrete cytokines
 - c. Present antigens to lymphocytes
 4. Dendritic cells
 - a. Activation of T cells and initiation of adaptive immune response
 - b. Star-shaped
 - B. Polymorphonuclear leukocytes or neutrophils (PML or PMN)
 1. Neutrophils
 - a. Phagocytose and kill microorganisms; first line of defense
 - b. Most abundant (40%–70% of white blood cells [WBC])
 - c. Effector cells of innate immunity
 - d. Short-lived (half-life of mature neutrophils is 2–3 days)
 2. Eosinophils
 - a. Kill antibody-coated parasites through release of toxic substances, major basic protein, eosinophil cationic protein, and several enzymes
 - b. ~5% of WBC
 - c. Protects against parasitic organisms
 - d. Major source of inflammatory mediators
 - e. Bind IgE
 3. Basophils
 - a. Rare (<5% of WBC)
 - b. Unknown function
 - c. Bind to IgE
 - d. Source of type I hypersensitivity reactions
 4. Mast cells
 - a. Function: expulsion of parasites from body through release of granules containing histamine and other active agents
 - C. Cytotoxic leukocytes
 1. Natural killer cells
 - a. Kills cells infected with certain viruses
 - b. Larger than lymphocyte with granular cytoplasm
 - c. Effector cell of innate immunity
 2. Lymphokine-activated killers (LAK)
 - a. Kill various tumor target cells and abnormal lymphocytes
 - D. Lymphocytes
 1. B cells: produce antibodies
 2. T cells: helper, cytotoxic
 - a. Helper T cells: regulate immune response
 - b. Cytotoxic T cells: kill altered cells (infected with viruses, tumor cells)
 - E. Antibodies
 1. Ig (immunoglobulin) G: most common antibody in blood
 - (1) Active in blood against bacteria and viruses
 - (2) Helps phagocytes eliminate antigens
 2. IgM: reacts with certain antigens; found in circulating body fluids
 3. IgA: plays a role in mucosal immunity
 4. IgD: found on B cells. not released from the cell
 - a. May be involved in B-cell activation
 5. IgE: involved in allergic reactions; stick to mast cells and release inflammatory substances
 - a. Rare in blood
 - F. Acute phase reactants
 1. Soluble mediators of the immune system
 2. Levels increase if infection or tissue damage is present
 3. Control tissue injury; increase host resistance to infection; promote tissue repair
 - G. Cytokines
 1. Interferons (IFN): important in controlling viral infections and augmenting immune response
 - a. Nonspecific immune system
 - b. Examples: INF- α , INF- β , Interferon- γ
 2. Tumor necrosis factors (TNF): produced by macrophages and T lymphocytes; regulate immune response and hematopoiesis
 - a. Examples: TNF- α , TNF- β

3. Interleukins (IL): mediators between leukocytes
 - a. Examples: IL-1, IL-2, IL-3, IL-4
 4. Chemokines: directed migration of leukocytes during immune response
 5. Transforming growth factor (TGF): involved in stem cell differentiation and other functions
 6. Hematopoietic colony-stimulating factors (CSF): important in maturation of leukocytes
- H. Active and passive immunity
1. Active immunity
 - a. Response to an infection
 - b. Immunization (vaccination)
 2. Passive immunity
 - a. Mother-to-baby
 - (1) IgG crosses placenta
 - (2) IgA in breast milk
 - b. Antibody injection into nonimmune person (antiserum)
- I. Innate versus adaptive defense system
1. Nonspecific defense mechanism (innate)
 - a. First line of defense: physical barriers (skin, mucosa)
 - b. Second line of defense: chemical barriers (phagocytes, natural killer cells, inflammation, fever, antimicrobial proteins)
 2. Specific defense mechanisms (adaptive)
 - a. Third line of defense: immune system (lymphocytes, antibodies)
 - (1) Protects against infectious agents and abnormal cells
 - (2) Responsible for most complement activation
- J. Antigens
1. Substance from a pathogen or foreign organism capable of inducing a specific immune response
 2. When the body is exposed to an antigen for the first time, antibody production is slow and at low levels. If the body is exposed to the same antigen again, the antibody response is more intense and rapid.
- III. Immunization/Vaccinations
- A. Basic Principles of Vaccination
1. Exposure to antigen will provoke an immune response.
 2. Repeated exposure to antigen produces immunological memory.
 3. Vaccine strategy: make a vaccine that gives a strong immune response—safely
 4. US Centers for Disease Control publish recommended vaccination schedules
- B. Common Vaccines (Figures 24-1 and 24-2)
1. Diphtheria, tetanus, pertussis (DTaP, DT, Rd, Tdap) vaccines
 - a. Daptacel (DTaP) diphtheria, tetanus toxoids, and acellular pertussis
 - (1) Indicated for infants and children, 6 weeks to 6 years old
 - (2) Dose is IM injection of 0.5 mL given at 2, 4, 6, and 15–20 months; booster at 4–6 years (total of 5 doses)
 - (3) How supplied: 0.5 mL suspension for injection
 - (4) Adverse effects: fever, pain and swelling at injection site, irritability, loss of appetite, drowsiness
 - b. Pediarix (DTaP-HBV-IPV) diphtheria, tetanus toxoids, and acellular pertussis, hepatitis B (recombinant), inactivated poliovirus vaccine
 - (1) Indicated for infants and children, 6 weeks to 7 years old
 - (2) Dose is IM injection of 3 doses of 0.5 mL each, at 6- to 8-week intervals; first dose at minimum age of 6 weeks; not used for booster doses
 - (3) How supplied: 0.5 mL vial
 - (4) Adverse effects: fever, pain and swelling at injection site, irritability, loss of appetite
 - (5) Diphtheria toxoid, tetanus toxoid, and pertussis antigens are the same as Infanrix
- c. Infanrix (DTaP; diphtheria, tetanus toxoids, and acellular pertussis)
 - (1) Indicated for infants and children, 6 weeks to 7 years old
 - (2) Dose is IM injection of 0.5 mL each at 2, 4, and 6 months; one booster at 15–20 months and another booster at 4–6 years of age (total of 5 doses)
 - (3) How supplied: 0.5 mL vial
 - (4) Adverse effects: fever, pain and swelling at injection site, irritability, loss of appetite, drowsiness
 - (5) Note: Diphtheria toxoid, tetanus toxoid, and pertussis antigens are the same as Pediarix and may be used to complete DTaP immunization with Pediarix.
- d. Adacel (Tdap) tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis
 - (1) Indicated for ages 11–64 years old as an active booster immunization (single-dose)
 - (2) Dose is IM injection of one dose of 0.5 mL; 5 years should pass since the last tetanus, diphtheria, or pertussis vaccine
 - (3) How supplied: 0.5 mL vial
 - (4) Adverse effects: fever, pain and swelling at injection site, headache, rash
- e. Boostrix (Tdap) tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis
 - (1) Approved for ages 10–64 years old as an active booster immunization (single-dose)
 - (2) Dose is IM injection of one dose of 0.5 mL; 5 years should have passed since the last tetanus, diphtheria, or pertussis vaccine
 - (3) How supplied: 0.5 mL vial
 - (4) Adverse effects: fever, pain and swelling at injection site, gastrointestinal upset, headache
2. *Haemophilus influenzae* vaccines
 - a. Combivax (*Haemophilus b* conjugate [meningococcal protein conjugate]) and hepatitis B [recombinant] vaccine
 - (1) Indicated for infants 6 weeks to 15 months for *Haemophilus influenzae*

- type b and hepatitis B virus (HBsAg-negative mothers)
- (2) Dose is IM injection at 2, 4, and 12–15 months (total of 3 doses)
 - (a) For best response, the interval between the second and third dose should be 8–11 weeks.
 - (3) How supplied: 0.5 mL vial
 - (4) Adverse effects: pain and swelling at injection site, fever, erythema, somnolence, rash, diarrhea, anorexia
 - (5) Note: May be administered concurrently with DTP, OPV, eIPV, Varivax, M-M-R II, and booster of DTaP
- b. Pedvax Hib (*Haemophilus* b conjugate vaccine [meningococcal protein conjugate])
- (1) Indicated for children 2–71 months for *Haemophilus influenzae* type b
 - (2) Dose is IM injection
 - (a) 2–10 months: 0.5 mL dose, followed by 0.5 mL dose 2 months later; booster at 12–15 months
 - (b) 11–14 months: 0.5 mL dose, followed by 0.5 mL dose 2 months later
 - (c) 15–71 months: 0.5 mL dose
 - (3) How supplied: 0.5 mL vial (does not contain thimerosal or lactose)
 - (4) Adverse effects: pain and soreness at injection site, irritability, diarrhea, erythema, otitis media, rash, upper respiratory tract infection, vomiting
 - (5) Note: May be administered concurrently with DTP, OPV, eIPV, Varivax, M-M-R II, or Recombivax HB
3. *Pneumococcal* vaccines
- a. Pneumovax 23 (PPV23), pneumococcal vaccine polyvalent
- (1) Indicated for 50 years and older, and children 2 years and older who are high risk
 - (2) Dose is SC or IM injection of 0.5 mL dose
 - (3) How supplied: single- or multiple-dose vial
 - (4) Adverse effects: fever, pain at injection site, erythema, warmth, swelling, and local induration
- b. Prevnar (PCV pneumococcal 7-valent conjugate vaccine [Diphtheria CRM₁₉₇ protein]) (capsular serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F)
- (1) Indicated for infants and toddlers, 6 weeks to 15 months old, and unvaccinated children through 9 years old
 - (2) Dose is IM injection of 4 doses; first dose at 2 months, then one at 4, 6, and 12–15 months
 - (3) How supplied: 0.5 mL vial
 - (4) Adverse effects: pain and irritation at injection site, fever, drowsiness, rash, weakness, vomiting, and seizures
4. Poliovirus vaccines
- a. IPOL (poliovirus vaccine inactivated, type 1 [Mahoney], type 2 [MEF-1], and type 3 [Saukett])
- (1) Indicated for infants as young as 6 weeks of age, up to adult
 - (2) Dose is SC or IM injection
 - (3) Infants: 3 doses of 0.5 mL at 2 month intervals, followed by a fourth dose of 0.5 mL at 12–15 months (and at least 2 months after the third dose)
 - (4) How supplied: 0.5 mL
 - (5) Adverse effects: irritability, erythema, fever, vomiting, anorexia, fatigue
- b. Orimune (oral live attenuated poliovirus [OPV], [Sabin strain types 1, 2, and 3])
- (1) No longer available in the United States
5. Influenza vaccines
- NOTE: Other TIV vaccine brands (Agrimflu, Flulaval, Fluarix) are available.
- a. Fluzone TIV (influenza virus trivalent inactivated vaccine, TIV)
- (1) Indicated for infants 6 months and older against influenza virus types A and B
 - (2) Dose is IM injection
 - (a) 6–35 months: one or two doses of 0.25 mL; two doses should be administered at least 1 month apart in children younger than 9 years old
 - (b) 3–8 years: one or two doses of 0.5 mL
 - (c) 9 years and older: one 0.5 mL dose
 - (3) How supplied
 - (a) 0.25-mL prefilled syringe (no preservative)
 - (b) 0.5-mL prefilled syringe (no preservative)
 - (c) 0.5-mL single-dose vial (no preservative)
 - (d) 5-mL multi-dose vial, contains thimerosal
 - (4) Adverse effects: pain at injection site, fever, malaise, myalgia
 - (5) Note: Use TIV vaccines with caution in patients with allergy to eggs; may cause anaphylaxis, asthma
- b. Fluvirin TIV (influenza virus trivalent inactivated vaccine, TIV)
- (1) Indicated for children, 4 years and older against influenza virus types A and B
 - (2) Dose is IM injection
 - (a) 4–8 years: one or two doses of 0.5 mL
 - (b) 9 years and older: one 0.5 mL dose
 - (3) How supplied
 - (a) 0.5-mL prefilled syringe, contains thimerosal
 - (b) 5-mL multi-dose vial, contains thimerosal
 - (4) Adverse effects: pain at injection site, fever, myalgia, malaise
 - (5) Note: Use TIV vaccines with caution in patients with allergy to eggs; may cause anaphylaxis, asthma

- c. FluMist LAIV (live attenuated influenza vaccine (LAIV) types A and B) intranasal spray
 - (1) Indicated for 2–49 years
 - (2) Dose is nasal spray
 - (a) Children 2–8 years not previously vaccinated: two doses, 1 month apart (one spray in each nostril); previously vaccinated: one dose (one spray in each nostril)
 - (b) Children and adults 9–49 years: one dose (one spray in each nostril)
 - (3) How supplied: 0.2 mL prefilled nasal spray; refrigerate
 - (4) Adverse effects: runny nose, nasal congestion, fever, sore throat
 - (5) Note: Do not use in patients with asthma or children younger than 5 years with recurrent wheezing
6. Measles, mumps, rubella (MMR) vaccine: live vaccine for measles, mumps, and rubella
 - a. M-M-R-II
 - (1) Indicated for 12 months and older
 - (2) Dose is SC injection of two doses, first dose at 12–15 months, second dose at 4–6 years; use within 30 minutes of reconstitution
 - (3) How supplied: 0.5 mL vial (lyophilized vaccine) and one 7 mL vial of diluent (sterile water for injection)
 - (4) Adverse effects: fever, syncope, headache, irritability, atypical measles, panniculitis
 - (5) Note: Use with caution in patients with egg allergy. However, studies have suggested that it is safe in children with severe egg allergy. It should be given 1 month before or after administration of other live vaccines and may be administered concurrently with Varivax or PedvaxHIB.
7. Varicella virus vaccine (chickenpox vaccine)
 - a. Varivax (live, attenuated virus vaccine [Oka/Merck strain of varicella])
 - (1) Indicated for 12 months and older
 - (2) Dose is SC injection
 - (a) Children 12 months to 12 years: 0.5 mL; if a second dose is administered, give a minimum of 3 months later; use within 30 minutes of reconstitution
 - (b) Children 13 years and older: 0.5 mL; second 0.5 mL dose 4–8 weeks later
 - (3) How supplied: 0.5 mL; reconstitute with diluent
 - (4) Adverse effects: pain and swelling at injection site, rash, erythema
8. Combined varicella and MMR vaccine
 - a. ProQuad (combined attenuated live virus vaccine [MMR and varicella])
 - (1) Indicated for children 12 months to 12 years
 - (2) Dose is SC injection of 0.5 mL; use within 30 minutes of reconstitution
 - (3) How supplied: 0.5 mL after reconstitution with sterile water
 - (4) Adverse effects: pain and swelling at injection site, rash, erythema
9. Meningococcal (meningitis) vaccines
 - a. Menomune MPSV4 (meningococcal polysaccharide serogroups A, C, Y, and W-135)
 - (1) Indicated for children 2 years and older
 - (2) Dose is SC injection of single dose of 0.5 mL; use within 30 minutes of reconstitution; protective antibody levels achieved within 7–10 days after vaccination
 - (3) How supplied: 0.5 mL vial with 0.78 mL diluent (no preservative); 0.5 mL (five per package) with 0.78 mL diluent (no preservative); 10 doses with 6 mL vial diluent (contains preservative) for administration with needle and syringe (not to be used with jet injector)
 - (4) Adverse effects: pain at injection site, erythema, chills, fever, headache
 - b. Menactra MCV4
 - (1) Indicated for children and adults, 2–55 years, to prevent meningococcal disease
 - (2) Dose is IM injection of single dose of 0.5 mL
 - (3) How supplied: latex free syringe: 0.5 mL BD Luer-Lok
 - (4) Adverse effects: pain at injection site, irritability, diarrhea, drowsiness, Guillian-Barré syndrome
10. Varicella zoster vaccine
 - a. Zostavax (live attenuated virus vaccine)
 - (1) Indicated for adults 60 years and older for prevention of herpes zoster (shingles)
 - (2) Dose is SC injection of 0.65 mL single dose; use within 30 minutes of reconstitution
 - (3) How supplied: 0.65 mL lyophilized powder (19,400 plaque-forming units [PFU])
 - (4) Adverse effects: pain and swelling at injection site, pruritus, erythema
 - (5) Do not use in patients with AIDS.
 - (6) Note: DOES NOT TREAT shingles or postherpetic neuralgia
11. Human papillomavirus vaccine (HPV vaccine)
 - a. Gardasil (human papillomavirus (HPV) quadrivalent (types 6, 11, 16, and 18) vaccine, recombinant)
 - (1) Indicated for girls and women (9–26 years)
 - (2) Dose is IM injection of three doses, 0.5 mL at 0, 2, 6 months
 - (3) How supplied: 0.5-mL single-dose vial; protect from light
 - (4) Adverse effects: pain and swelling at injection site, nausea, fever
 - (5) Do not use in pregnant women
 - b. Cervarix (HPV bivalent vaccine)
 - (1) Indicated in females age 10–25 years
 - (2) Dose in IM injection of three doses, 0.5 mL at 0, 2, 6 months

12. *Rotavirus* vaccines

- a. RotaTeq (rotavirus vaccine, live, oral, pentavalent)
 - (1) Indicated for infants and children for prevention of rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4
 - (2) Dose: Oral is three doses; first dose at 6–12 weeks, second and third doses at 4- to 10-week intervals
 - (3) How supplied: 2 mL oral solution; protect from light; do not reconstitute or dilute
 - (4) Adverse effects: diarrhea, bronchospasm, irritability, nasopharyngitis, otitis media, vomiting
 - (a) Warning: intussusception
- b. Rotarix (rotavirus vaccine, live, oral, of serotypes G1 and non-G2 (G3, G4, and G9))
 - (1) Indicated for infants and children for prevention of rotavirus gastroenteritis caused by G1 and non-G2 (G3, G4, and G9)
 - (2) Dose: Oral is two doses of 1 mL administered orally; administer first dose at 6 weeks of age; second dose after an interval of at least 4 weeks and before 24 weeks of age
 - (3) How supplied: 1-mL oral suspension
 - (4) Adverse effects: irritability, fever, runny nose, vomiting, fussing
 - (a) Warning: intussusception

13. Hepatitis A vaccines

- a. Vaqta (inactivated virus vaccine)
 - (1) Indicated for children and adults, persons 12 months and older
 - (2) Dose: IM injection
 - (a) Adults (19 years and older): 1 mL (50 units) with booster of 1 mL (50 units) 6–18 months later
 - (b) Children (12 months to 18 years): 0.5 mL (25 units) with booster of 0.5 mL (25 units) 6–18 months later
 - (3) How supplied
 - (a) Adults: Hepatitis A virus antigen 50 units/mL (1 mL) in injection or suspension (preservative free)
 - (b) Pediatric: Hepatitis A virus antigen 25 units/0.5 mL (0.5 mL) in injection or suspension (preservative free)
 - (4) Adverse effects: irritability, drowsiness, headache, fever, anorexia, pain and swelling at injection site, erythema, warmth
- b. Havrix (inactivated virus vaccine)
 - (1) Indicated for children and adults, 12 years and older
 - (2) Dose is IM injection
 - (a) Adults: 1-mL single injection at day 0 and 1-mL booster dose given between 6 and 12 months later
 - (b) Children 12 months to 18 years: 0.5 mL single injection and 0.5 mL booster given between 6 and 12 months later

(3) How supplied

- (a) Adults: 1 mL (1440 ELISA units of viral antigen)
 - (b) Children: 0.5 mL (720 ELISA units of viral antigen)
- (4) Adverse effects: irritability, drowsiness, headache, fever, anorexia, pain and swelling at injection site, erythema, warmth
 - (5) Note: Prefilled syringes contain dry natural latex rubber and may cause allergic reactions.

14. Combined hepatitis A and hepatitis B vaccines

- a. Twinrix (inactivated virus vaccine [recombinant], a combined hepatitis A and hepatitis B vaccine)
 - (1) Indicated for adults, 18 years of age or older, against disease caused by hepatitis A virus; active immunization against disease caused by hepatitis A virus and hepatitis B virus (all known subtypes)
 - (2) Dose is IM injection
 - (a) Adults: three doses of 1 mL each given on a 0-, 1-, and 6-month schedule. Alternatively, four doses on days 0, 7, and 21–30 followed by a booster dose at month 12 may be used.
 - (3) How supplied: 1 mL (720 ELISA units of inactivated hepatitis A virus and 20 mcg of hepatitis B surface antigen) prefilled Tip-Lok syringes
 - (4) Adverse effects: headache, fatigue, soreness and redness at injection site

15. Hepatitis B vaccines

- a. Engerix-B (recombinant)
 - (1) Indicated for all known subtypes of hepatitis B virus; it is expected that hepatitis D will be prevented by Engerix-B
 - (2) Dose is IM injection
 - (a) Adults (older than 19 years): three doses at 0, 1, and 6 months in a 20 mcg/mL suspension; first dose given on the elected date, second dose given 1 month later, third dose given 6 months after the first dose
 - (b) When used for immediate prophylactic intervention (e.g., administration to persons who are wounded in bombings or similar mass casualty events), vaccination should begin within 24 hours and no later than 7 days following the event
 - (c) Children, adolescents (birth to 19 years): three doses of 10 mcg/0.5 mL
 - (d) Infants: three doses, recommended to start at birth, second dose given at 1 month, third dose given at 6 months
- b. Recombivax HB
 - (1) Indicated for all known subtypes of hepatitis B virus

Vaccine ▼	Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B*		HepB	HepB			HepB						
Rotavirus*				RV	RV	RV*						
Diphtheria, Tetanus, Pertussis*				DTaP	DTaP	DTaP	See footnote*	DTaP				DTaP
Haemophilus influenzae type b*				Hib	Hib	Hib*	Hib					
Pneumococcal*				PCV	PCV	PCV	PCV				PPSV	
Inactivated Poliovirus*				IPV	IPV	IPV						IPV
Influenza*						Influenza (Yearly)						
Measles, Mumps, Rubella*							MMR		see footnote*			MMR
Varicella*							Varicella		see footnote*			Varicella
Hepatitis A*							HepA (2 doses)				HepA Series	
Meningococcal*											MCV	

Range of recommended ages for all children except certain high-risk groups

Range of recommended ages for certain high-risk groups

Range of recommended ages for all children except certain high-risk groups

Range of recommended ages for certain high-risk groups

*Please refer to the CDC website (<http://www.cdc.gov/vaccines/recs/schedules/>) to view specific comments regarding appropriate immunization schedule practices and limitations.

Figure 24-1 — Recommended immunization schedule for persons aged 0–6 years — United States, 2010. (From <http://www.cdc.gov/vaccines/recs/schedules/>)

Vaccine ▼	Age ►	7–10 years	11–12 years	13–18 years
Tetanus, Diphtheria, Pertussis*			Tdap	Tdap
Human Papillomavirus*		see footnote*	HPV (3 doses)	HPV Series
Meningococcal*		MCV	MCV	MCV
Influenza*		Influenza (Yearly)		
Pneumococcal*		PPSV		
Hepatitis A*		HepA Series		
Hepatitis B*		HepB Series		
Inactivated Poliovirus*		IPV Series		
Measles, Mumps, Rubella*		MMR Series		
Varicella*		Varicella Series		

Range of recommended ages for all children except certain high-risk groups

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

*Please refer to the CDC website (<http://www.cdc.gov/vaccines/recs/schedules/>) to view specific comments regarding appropriate immunization schedule practices and limitations.

Figure 24-2 — Recommended immunization schedule for persons aged 7–18 years — United States, 2010. (From <http://www.cdc.gov/vaccines/recs/schedules/>)

(2) Dose is IM injection

- (a) Adults (older than 19 years): three doses of a 10-mcg (1-mL) suspension at 0, 1, and 6 months
- (b) Birth to 19 years: three doses of 5 mcg (0.5 mL). Note: Two dose schedule is available for those 11–15 years old
- (c) Infants: three doses of 5 mcg (0.5 mL) recommended to start at birth, second dose given at 1 month, third dose given at 6 months

- (3) Adverse effects: flushing, hypotension, pain at injection site

PATIENT PROFILE

Patient Initials: SV

Sex: Female

Age: 68

Height: 5' 3"

Weight: 74 kg

Race: White

Allergies: No known drug allergies (NKDA)

Patient Consultation: For recent exacerbations of COPD and community-acquired pneumonia, SV was hospitalized for 5 days and just completed her antibiotic therapies as an outpatient. SV wonders if there are any strategies to help her stay healthy and prevent another hospital admission.

Current Health Conditions:
Hypercholesterolemia
COPD (diagnosed 8 years ago)

Recent Laboratories of Note:
Cholesterol: 220 mg/dL
Serum creatinine: 1.1

Social History:

Tobacco use: Former heavy smoker; quit 5 years ago when husband died of lung cancer

Alcohol use: None

Recent immunizations: None in the past 10 years

Pharmacy Medication Profile:

Centrum Silver 1 tablet PO once daily

Spiriva Handihaler 1 capsule inhaled once daily in the morning

Simvastatin 40 mg PO once daily at bedtime

Mucinex 1 tablet PO twice daily

Advair inhaler 1 inhalation twice daily

PATIENT PROFILE QUESTION

1. SV's pharmacist notes that key vaccinations are missing from her vaccination record and autumn is rapidly approaching. What are two vaccination strategies that could have a great impact on the health of SV and reduce the risk of respiratory-related hospitalizations?

- I. Receiving Pneumovax
- II. Receiving FluMist
- III. Receiving Fluzone
- IV. Receiving Zostavax

- a. I and II
- b. I and III
- c. I and IV

Answer: b. Annual influenza vaccination should be given to all patients with COPD. Influenza can lead to COPD exacerbations and respiratory failure. Morbidity and mortality may be decreased as much as 50%.

Currently, the best choice for influenza vaccination from the above choices would be immunization with the injectable inactivated virus vaccine Fluzone. FluMist contains live, attenuated virus and is inhaled through the nose; those with reactive airways or who are receiving chronic corticosteroid therapy may need to avoid this form of influenza vaccination. The current adult immunization schedule from the Centers for Disease Control and Prevention shows that the pneumococcal vaccine for all adults with COPD is recommended. A single dose of Pneumovax is sufficient for most patients. If the patient was younger than 65 years old at time of primary vaccination, a second dose is recommended after the age of 65 years. Although Zostavax (herpes zoster vaccine) immunization is also a consideration given her age, it would not be given to prevent respiratory-related illness.

REVIEW QUESTIONS

(Answers and Rationales on page 380.)

1. Which of the following cells produces histamine?
 - I. Mast cells
 - II. Basophils
 - III. Erythrocytes
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and III
2. Which of the following represents a normal white blood cell count?
 - a. 100–200 cells per cubic millimeter
 - b. 400–500 cells per cubic millimeter
 - c. 1200–3800 cells per cubic millimeter
 - d. 4300–10,800 cells per cubic millimeter
 - e. 32,000–56,000 cells per cubic millimeter
3. Which of the following cell type(s) is/are NOT involved in antibody mediated response?
 - a. Plasma cells
 - b. T-cytotoxic cells
 - c. T-helper cells
 - d. B lymphocytes
 - e. All of the above
4. Cells that produce and secrete antibodies are:
 - I. plasma cells.
 - II. T cells.
 - III. B cells.
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
5. Which of the following may cause elevated white blood cells?
 - a. Viral infection
 - b. Stress
 - c. Medication
 - d. Bacterial infection
 - e. All of the above
6. Leukocytes expressing CD-8 receptors are:
 - a. B lymphocytes.
 - b. T-cytotoxic cells.
 - c. RBC.
 - d. Natural killer cells.
 - e. None of the above
7. Which of the following are live vaccines?
 - I. Oral polio
 - II. Mumps
 - III. Measles
 - a. I only
 - b. III only

- c. I and II
 - d. II and III
 - e. I, II, and III
8. Intussusception is most likely to occur with the use of:
- a. RotaTeq
 - b. Prevnar
 - c. Comvax
 - d. Gardasil
 - e. Varivax
9. Which of the following vaccines need to be reconstituted?
- I. Menomune
 - II. M-M-R-II
 - III. Pneumovax 23
- a. I only
 - b. III only
- c. I and II
 - d. II and III
 - e. I, II, and III
10. Which of the following vaccines should not be administered to infants younger than 6 weeks of age?
- a. Rotavirus
 - b. DTaP
 - c. Hib
 - d. Pneumococcal
 - e. All of the above
11. The quadrivalent HPV vaccine contains which of the following pseudovirion antigens?
- a. HPV 6, HPV 11, HPV 16, HPV 18
 - b. HPV 1, HPV 2, HPV 3, HPV 4
 - c. HPV 16 and HPV 18 only
 - d. HPV 6 and HPV 11 only
 - e. None of the above

I. Antiproliferative Antimetabolites

A. Azathioprine (Imuran)

1. Prodrug converted to 6-mercaptopurine
2. Mechanism of action
 - a. Inhibits purine synthesis, incorporates into DNA as “false” purine
 - b. Inhibits synthesis and proliferation of T and B lymphocytes
3. Use
 - a. Renal transplant (adjunct; prophylaxis)
 - b. Rheumatoid arthritis
 - c. Inflammatory bowel disease (non-FDA approved)
4. Side effects (after 7–14 days of therapy)
 - a. Neutropenia
 - b. Anemia
 - c. Thrombocytopenia
 - d. Hepatotoxicity
 - e. Cholestasis
 - f. Pancreatitis
 - g. Infectious disease
5. Adult Dose is initially 3–5 mg/kg per day IV or PO. maintenance 1–3 mg/kg per day PO
 - a. White Blood Cell count (WBC) 3000–5000 → decrease dose by 50%
 - b. Dosage in renal failure: Patients with oliguria may have delayed elimination of azathioprine and may require lower doses.

B. Mycophenolate mofetil (CellCept)

1. Prodrug of mycophenolic acid (MPA)
2. Mechanism of action
 - a. Inhibits purine synthesis
 - b. Blocks activity of inosine monophosphate dehydrogenase (IMPDH)
 - c. Inhibits synthesis and proliferation of T and B lymphocytes
 - d. Minimal effect on cytokine production
3. Side effects
 - a. Neutropenia
 - b. Anemia
 - c. Diarrhea, heart burn, abdominal pain
 - d. Hypertension
 - e. Peripheral edema
 - f. Rash
 - g. Herpes
 - i. Hypercholesterolemia
 - j. Hyperglycemia
 - k. Hyperkalemia, hypocalcemia, hypomagnesemia
 - l. Viral infections (CMV)

4. Drug interactions

- a. Cyclosporine: ↓ MPA levels
- b. Steroids: ↓ MPA levels
- c. Tacrolimus: ↑ MPA levels

5. Dose

- a. IV 1 g twice daily (liver, kidney) or 1.5 g twice daily (heart)
- b. PO 1.5 g twice daily (heart, liver) or 1 g twice daily (kidney)
- c. Dosage in renal failure: Patients who had a renal transplantation with severe chronic renal impairment (Glomerular filtration rate [GFR] <25 mL/min/1.73 m²) should not receive doses greater than 1 gram twice a day.

II. Glucocorticoids

A. Mechanism of action

1. Blocks cytokine activation by binding to glucocorticoid response elements
 - a. Inhibits secretion of Interleukin (IL)-1, IL-2, IL-3, and IL-6, γ -interferon, Tumor Necrosis Factor (TNF)- α
2. Interferes with cell migration
3. Suppresses antibody and complement binding

B. Use: first-line therapy for treatment of acute graft rejection

1. High-dose methylprednisolone: 250–1000 mg daily for 3 days

C. Side effects: immediate (1–3 months)

1. Increased appetite, weight gain, Cushing-like features
2. Sodium and water retention
3. Hypertension
4. Hyperlipidemia
5. Diabetes
6. Acne
7. Hirsutism
8. Cataracts
9. Infections
10. Mood changes

D. Side effects: long-term

1. Osteoporosis
2. Avascular necrosis
3. Growth retardation
4. Skin atrophy

III. Calcineurin inhibitors

A. Cyclosporine (Sandimmune, Neoral, Gengraf)

1. Mechanism of action
 - a. Inhibits T-cell proliferation; inhibits IL-2 and IL-2-induced activation

- b. Binds to cyclophilin, inhibits antigenic response of helper T cells
- 2. Use
 - a. Prevention of allograft rejection in solid organ recipients of kidney, liver, or heart
 - b. Prevention of graft-versus-host disease in bone marrow transplant recipients
 - c. Management of autoimmune diseases
 - d. Severe recalcitrant plaque psoriasis in non-immunocompromised adults
- 3. Hepatic metabolism via cytochrome P-450 (CYP)
- 4. Side effects
 - a. **Nephrotoxicity (major side effect)**
 - b. Gingival hyperplasia
 - c. Hypertension
 - d. Hyperlipidemia
 - e. Diabetes mellitus
 - f. Neurotoxicity
 - g. Alopecia
 - h. Hyperkalemia
 - i. Hypomagnesemia
 - j. Hemolytic uremia syndrome
- 5. Typical adult dose
 - a. Various dosing regimens
 - b. Titrate based on trough levels
 - c. Sandimmune, Neoral, and Gengraf brands of cyclosporine are not bioequivalent and cannot be used interchangeably.
 - d. Patients with hepatic insufficiency or renal failure should receive doses at the lower end of the dosing recommendations.
- 6. Therapeutic drug monitoring
 - a. Concentration-based rather than dose-based
 - b. Narrow therapeutic window; range not absolutely defined (general range 100–400 ng/mL)
 - c. Monitor troughs
- B. Tacrolimus (Prograf)
 - 1. More potent than cyclosporine
 - 2. Similar activity to cyclosporine
 - 3. Mechanism of action: Inhibits the activity of calcineurin
 - a. Reduces production and release of IL-2
 - 4. Use
 - a. Prophylaxis of organ rejection in patients receiving liver transplants
 - b. Topical treatment of atopic dermatitis
 - c. Immunosuppressant after kidney transplant
 - d. May be used as rescue therapy for rejection
 - 5. Highly lipophilic
 - 6. Hepatic metabolism of CYP450 3A4
 - 7. Side effects (similar to cyclosporine)
 - a. Tremor, insomnia, paresthesia
 - b. Diarrhea
 - c. Hyperkalemia, hypomagnesemia
 - 8. Typical adult dose
 - a. More side effects occur when given IV
 - b. 0.03 to 0.1 mg/kg/day IV as a continuous infusion or 0.15 to 0.3 mg/kg/day orally, divided and given every 12 hours
 - c. Doses should be adjusted to maintain trough tacrolimus concentrations of 5 to 20 ng/mL.
 - d. Convert to oral as soon as possible if the patient is receiving IV administration
- 9. Converting from cyclosporine to tacrolimus
 - a. Discontinue cyclosporine 24 hours before starting tacrolimus
- 10. Therapeutic drug monitoring
 - a. Early after transplantation
 - b. Levels correlate with area under the curve concentration (AUC)
 - c. Target trough: 5–20 ng/mL (10 ng/mL)
- C. Sirolimus (Rapamune)
 - 1. mTOR inhibitor
 - 2. Mechanism of action
 - a. Inhibits delayed T-cell activation by inhibiting signal transduction
 - b. Blocks response of T and B cells to cytokines
 - 3. Use
 - a. Renal transplant
 - b. Combination use with cyclosporine and prednisone; withdrawal protocol in low-risk patients
 - 4. Half-Life ($T_{1/2}$): 60 hours; time to reach steady state is 12 days
 - 5. Drug interactions (similar to cyclosporine)
 - a. CYP 3A4
 - 6. Adverse effects
 - a. Similar to cyclosporine (less nephrotoxicity)
 - b. Infections (e.g., herpes simplex virus [HSV])
 - c. Peripheral edema
 - d. Hypertriglyceridemia
 - e. Hypertension
 - f. Hypersensitivity reactions
 - g. Thrombocytopenia
 - h. Constipation, abdominal pain, diarrhea, nausea
 - 7. Typical adult dose
 - a. Dose of 6 mg PO (loading) followed by 2–5 mg/day (maintenance)
 - b. Give 4 hours after morning dose of cyclosporine
 - 8. Therapeutic drug monitoring
 - a. Every 5–7 days
 - 9. Avoid with voriconazole, a potent CYP 3A4 inhibitor, which may ↑ sirolimus levels
- IV. Antilymphocyte globulins
 - A. Lymphocyte immune globulin (Atgam)
 - 1. Typical adult dose ~15 mg/kg per day
 - 2. Side effects

- a. Headache
 - b. Fever
 - c. Chills
 - d. Nausea
 - e. Serum sickness
 - f. Acute renal failure
 - g. Acute respiratory distress syndrome
 - h. Injection site reaction
 - i. Hemolytic anemia
 - j. Cytokine release syndrome (CRS) – may limit reaction by use of required premedication; slow infusion
- B. Antithymocyte globulin [rabbit] (Thymoglobulin)
- 1. Typical adult dose 1.5 mg/kg per day
 - 2. Side effects
 - a. Fever
 - b. Hyperkalemia
 - c. Hypertension
 - d. Leukopenia
 - e. Peripheral edema
 - f. Shivering
 - g. Cytokine release syndrome (CRS) may limit reaction by use of required premedication; slow infusion
 - 3. Benefits
 - a. Decreases and delays the onset of acute rejection
 - b. Delays introduction of calcineurin inhibitors
 - c. Predictable suppression of T cells
 - d. Better tolerated than Atgam
 - 4. Risks
 - a. CMV infections and malignancy risks comparable to Atgam
 - b. Serum sickness
 - c. Thrombocytopenia
 - d. First-dose reactions: “shake and bake”
 - e. Prevention medications: steroids, acetaminophen, antihistamine
- V. Monoclonal Antibodies
- A. Daclizumab (Zenapax)
- 1. Humanized monoclonal antibody (mAb)
 - 2. Mechanism of action: block alpha unit of IL-2 receptor on activated T cells; inhibits IL-2 binding and IL-2 activation
 - 3. Dose 1 mg/kg per dose
 - 4. Side effects: well tolerated, anaphylaxis
- B. Basiliximab (Simulect)
- 1. Chimeric mAb
 - 2. Mechanism of action: block alpha unit of IL-2 receptor on activated T cells; inhibits IL-2 binding and IL-2 activation
 - 3. Dose 20 mg per dose
 - 4. Side effects: well tolerated, anaphylaxis
- C. Muromonab CD-3 (OKT3)
- 1. Murine mAb
 - 2. Dose 2.5–5 mg/day
 - 3. Side effects
 - a. CRS “shake and bake” (fevers and chills)

PATIENT PROFILE

Patient Initials: DR

Sex: Male

Age: 33

Height: 5' 9"

Weight: 74 kg

Race: Caucasian

Allergies: No known drug allergies (NKDA)

Current Health Conditions:

Hypercholesterolemia

Hypertension

Kidney transplantation 2 years ago, secondary to familial kidney disease

Pharmacy Medication Profile:

Lipitor 20 mg PO once daily

Procardia XL 90 mg PO q_{AM}

Neoral solution 185 mg PO twice daily

Prednisone 40 mg PO once daily

Prilosec 20 mg PO once daily

PATIENT PROFILE QUESTIONS

1. What is/are common side effects of treatment with Neoral?

- I. High blood pressure
- II. Renal toxicity
- III. Anemia and neutropenia

- a. I only
- b. II only
- c. I and II
- d. I and III
- e. II and III
- f. I, II, and III

Answer: c. Cyclosporine has no effects on red blood cell counts or on white blood cell counts.

Cyclosporine inhibits T-lymphocyte proliferation for its immunosuppressant effect. Hypertension and a potential for nephrotoxicity are commonly recognized side effects; hypertension often requires medical management in these patients.

2. The Prilosec prescription is going to be therapeutically substituted with an H₂ antagonist on the family practice clinic formulary. Which of the following would be an appropriate choice for DR?

- I. Tagamet
- II. Pepcid
- III. Zantac

- a. I or II
- b. II or III
- c. I, II, or III

Answer: b. Although all the drugs listed are in the H₂ antagonists class of medications, Pepcid (famotidine) and Zantac (ranitidine) are the safest to give to DR due to a lack of drug interactions with his prescribed immunosuppressant drugs. Tagamet (cimetidine) exhibits many drug interactions with medications metabolized by hepatic cytochrome P450 isoenzymes and would not be a good choice for a patient stabilized on important medications to prevent transplantation rejection.

3. What are points that should be included in counseling a patient on appropriate Neoral administration?
- Take doses at the same time each day, with consistent intervals between doses.
 - Do not take Neoral with grapefruit juice.
 - Mixing the solution in milk will help it taste better.
 - The solution should be refrigerated.

- I only
- III only
- I and II
- II and IV
- I, II, III, and IV

Answer: a. Neoral should not be stored in a refrigerator. It is okay to mix Neoral in apple or orange juice at room temperature, but mixing in milk will result in an unpalatable taste. Doses are usually given twice daily and should be spread 12 hours apart and at consistent times of day each day. Grapefruit juice interacts with Neoral and this juice should be avoided.

REVIEW QUESTIONS

(Answers and Rationales on page 381.)

- Which of the following is considered an immunosuppressant?
 - Sirolimus
 - Cyclosporine
 - Demeclocycline
 - I only
 - III only
 - I and II
 - II and III
 - I, II, and III
- Which of the following is an adverse effect(s) associated with cyclosporine?
 - Nephrotoxicity
 - Hyperlipidemia
 - Gingival hyperplasia
 - Hypertension
 - All of the above are adverse effects.
- Which of the following statements about cyclosporine are true?
 - It inhibits T cell proliferation.
 - It has a narrow therapeutic window although the range is not absolutely defined.
 - Sandimmune, Neoral, and Gengraf brands of cyclosporine are bioequivalent and may be used interchangeably.
 - I only
 - III only
 - I and II only
 - II and III only
 - I, II, and III
- The mechanism of tacrolimus is similar to that of:
 - cyclophosphamide.
 - cycloserine.
 - cyclosporine.
 - All of the above
 - None of the above
- Which of the following are potential benefit(s) of using Thymoglobulin?
 - Better tolerated than ATGAM
 - Predictable suppression of T cells
 - The incidence of CMV infections less than ATGAM
 - I only
 - III only
 - I and II
 - II and III
 - I, II, and III
- Azathioprine may be used for which of the following?
 - Renal transplant (adjunct)
 - Rheumatoid arthritis
 - Inflammatory bowel disease
 - I only
 - III only
 - I and II
 - II and III
 - I, II, and III
- Which of the following are potential adverse effect(s) with methylprednisolone?
 - Weight gain
 - Cataracts
 - Osteoporosis
 - Growth retardation
 - All of the above
- Which of the following statements about tacrolimus (Prograf) are true?
 - It is highly lipophilic.
 - Target trough is between 5–20 ng/mL.
 - It is metabolized by CYP 3A4.
 - I only
 - III only
 - I and II
 - II and III
 - I, II, and III
- Which of the following statements about the mechanism of mycophenolate mofetil are true?
 - It inhibits purine synthesis.
 - It has minimal effect on cytokine production.
 - It blocks activity of inosine monophosphate dehydrogenase (IMPDH).
 - It inhibits synthesis and proliferation of T and B lymphocytes.
 - All of the above are true.
- Which of the following drugs is associated with hypertension?
 - Cyclosporine
 - Indapamide
 - Prazosin
 - None of the above
 - All of the above

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Nonprescription Products

26 CHAPTER

- I. Introduction
 - A. Nonprescription or over-the-counter (OTC) products are medicines that can be bought without a prescription. They are relatively safe and effective when directions on the label are followed and when used as the prescriber or health care professional directs.
 - B. These products are regulated by the Food and Drug Administration (FDA).
 - C. Reasons consumers self-diagnose and use OTC products
 - 1. Products readily available in pharmacies and grocery stores
 - 2. High insurance costs (for medication or doctor's visits) or **no** insurance
 - 3. Availability of information on the web (i.e., WebMD.com)
 - 4. Time constraints (e.g., doctor's visits, travel time, missed time from work)
 - D. There are more than 80 therapeutic categories of OTC drugs, ranging from acne drug products to weight-control drug products.
 - E. Common OTC products
 - 1. Cough and cold
 - 2. Otics
 - 3. Ophthalmics
 - 4. Pain, fever
 - 5. Sleep aids, stimulants
 - 6. Constipation, diarrhea, nausea, vomiting
 - 7. Smoking cessation
 - 8. First aid
 - 9. Topical (e.g., for jock itch, lice)
 - F. Special considerations when using OTC products
 - 1. Drug interactions (drug-disease, drug-drug, drug-food, drug-herbal)
 - 2. Pediatrics
 - 3. Pregnant, nursing
 - 4. Geriatrics
 - 5. Disease state
- II. Cough and Cold
 - A. The common cold may involve the nose, throat, sinuses, eustachian tubes (connects the ears to the throat), trachea (windpipe), larynx (voice box), and bronchial tubes (airways).
 - B. The cause of developing a cold is due to a viral infection, including rhinoviruses (most common), coronaviruses, adenoviruses, echoviruses, respiratory syncytial viruses (RSV), and coxsackieviruses.
 - C. In response to infection, the immune system triggers a series of events, including release of inflammatory cytokines (a group of proteins that help regulate inflammation, blood cell production, and immunity), such as interleukin-6 (IL-6), interleukin-8 (IL-8), and granulocyte-macrophage colony-stimulating factor (GM-CSF), fluid leakage (runny nose), mucous membrane swelling (stuffy nose), increased mucous production, and stimulation of sneeze and cough reflexes.
 - 1. Symptoms usually appear about 1 to 3 days after exposure to a cold virus. Nasal symptoms can begin as early as 2 hours after exposure; cough and sore throat symptoms usually begin 10–12 hours after exposure to the virus.
 - 2. Signs and symptoms may include runny or stuffy nose, itchy or sore throat, dry cough, facial pressure due to sinuses (hollow bones in the front of the face), slight body aches or a mild headache, sneezing, itchy, watery eyes, low-grade fever (less than 102 °F), and mild fatigue (tiredness).
 - 3. Nasal discharge may become thicker as the cold runs its course.
 - 4. Colds last on average for 1 week. Mild colds may last only 2 or 3 days; severe colds may last a maximum of 2 weeks. Cough due to a cold can last hours or days.
 - D. Risk factors
 - 1. Social activity
 - a) Being around children (teachers, day care workers)
 - b) Traveling in airplanes or buses
 - c) Being around people who are sneezing and coughing
 - d) Touching public railings and doors
 - e) Workplace
 - f) Healthcare workers

2. Age
 - a) Infants' immune systems not fully developed
 - b) Colds generally occur less frequently with age
 3. Seasonal changes
 - a) In cold months, air is dry and heating dries air even more.
 - b) In hot months, air conditioning dries air.
 - c) Dry air dehydrates the mucous membranes in the nose and throat, which are the first line of defense against the viruses. This allows the viruses to attack the tissue in the nose and throat.
 4. Environmental toxins
 - a) Injure airways and damage the cilia
 - (1) Cigarette smoke
 - (2) Industrial smoke
 - (3) Other air pollutants
 5. Lowered immunity
 6. HIV
 7. Cancer
 8. Medications (e.g., corticosteroids, chemotherapy)
 9. Stress
 10. Too much exercise
 11. Malnutrition
 12. Lack of sleep
- E. Treatment
1. There is no cure for the common cold.
 2. OTC cold preparations may be used for symptoms.
 - a) Annually Americans spend about \$2.9 billion on OTC drugs in addition to \$400 million on prescription medicines for symptomatic relief from colds.
- F. Pharmacological therapy
1. Pain relievers and fever reducers
 - a) Indication: fever, sore throat, body aches, and headache
 - b) Examples: acetaminophen (Tylenol), ibuprofen (Advil, Motrin)
 - c) Considerations
 - (1) Acetaminophen (Tylenol)
 - (a) Does not affect platelet function or increase blood clotting time
 - (b) Does not cause gastrointestinal (GI) irritation
 - (c) Analgesic-antipyretic of choice for children with viral infections or chicken pox (no risk for Reye syndrome)
 - (d) May be used in patients with gout taking probenecid
 - (e) Caution with use in patients with hepatic disease
 - (f) Acetaminophen can cause liver damage, especially if taken chronically, or in doses that exceed 4 grams daily
 - (2) NSAID (e.g., aspirin, ibuprofen)
 - (a) Upper GI disturbances are common
 - (b) Risk for increased bleeding
 - (c) Drug interactions: antacids, heparin, or oral anticoagulants
 - (d) Caution with use in patients with stomach ulcers, poor kidney function
 - (e) Duration of antipyretic effect may be slightly longer (3–4 versus 5 hours)
 - (f) It is recommended never to give aspirin to children ages 3 to 12 years old. Aspirin may play a role in causing Reye syndrome, a rare but potentially fatal illness in children with concomitant viral illness.
2. Decongestants help open swollen mucous membranes of the nasal passages so the individual can breathe easier.
- a) Indication: nasal or sinus congestion
 - b) Decongestants include tablets, sprays, inhalers, and nose drops.
 - c) Examples
 - (1) Oral decongestant pseudoephedrine (e.g., Sudafed)
 - (a) Considerations: alpha-adrenergic activity; avoid use in patients with cardiac disease, hypertension, etc.
 - (b) Not recommended in the pediatric population because of the potential for cardiac stimulation, hypertension, or neurologic complications
 - (2) Nasal spray oxymetazoline 0.05% (Afrin), phenylephrine 0.5% (Neo-Synephrine)
 - (a) Considerations: use should not exceed more than 72 hours because of a tolerance effect and possible rebound congestion; purulent secretions present in the nose should be removed before administration.
 - (3) Nasal inhaler propylhexedrine (Benzedrex)
 - (4) Nasal inhaler levmetamfetamine (Vicks Vapor Inhaler)
 - d) Side effects
 - (1) Stinging, burning, sneezing, increased nasal discharge, drying of the nostrils, and altered taste may occur.
 - (2) Other side effects include rapid or pounding heartbeat, dizziness, trouble sleeping, shaking of the hands, and tremors.
 - e) Caution
 - (1) Nasal decongestants are safe for most patients, except people with heart disease, high blood pressure, thyroid disease, glaucoma (increased pressure in the eyes), diabetes, seizure disorders, or enlarged prostate, or by individuals using a monoamine oxidase inhibitor (MAOI).
 - f) Contraindications

- (1) Nasal decongestants are not safe in individuals using a MAOI. Healthcare professionals recommend not using decongestants while pregnant or breastfeeding.
- g) Counseling points
 - (1) Over time, decongestant nose drops, inhalers, and sprays can actually cause rebound congestion, which means the nasal passages are not able to function normally without using these medications.
 - (2) Prolonged use can also cause chronic inflammation of the mucous membranes.
 - (3) Decongestant nasal drops and sprays are not to be used for more than 3 days, which helps to stop the potential of nasal rebound.
 - (4) If symptoms worsen, a doctor may need to evaluate the situation.
3. Antihistamines
 - a) Indications: symptoms like runny or stuffy nose, itchy or sore throat, sneezing, and itchy, watery eyes
 - b) Examples
 - (1) First-generation, nonselective antihistamines that cause sedation
 - (i) Diphenhydramine (Benadryl)
 - (ii) Clemastine (Tavist-1)
 - (iii) Chlorpheniramine (Chlor-Trimeton)
 - (iv) Brompheniramine (Dimetane)
 - (2) Second-generation, selective, nonsedating antihistamines
 - (i) Loratadine (Claritin)
 - (ii) Cetirizine (Zyrtec)
 - c) Side effects
 - (1) Anticholinergic (mostly with first generation)
 - (i) Dry mouth
 - (ii) Dry eyes
 - (iii) Urinary retention
 - (iv) Constipation
 - (v) Elevated heart rate
 - (vi) Sedation
 - d) Caution
 - (1) Antihistamines can cause confusion and increased risk of falls if administered to elderly patients, particularly first-generation agents
4. Cough syrups
 - a) Indication: for symptomatic relief of cough associated with a cold.
 - b) Examples (Figure 26-1)
 - (1) Various combinations of antihistamines, decongestants, and cough suppressants
 - (2) If the cough is productive (brings up mucus), the ingredient guaifenesin can help break up the chest congestion (water intake is also important).
 - (3) If the cough is dry and hacking, a cough suppressant (dextromethorphan) can stop the cough.
 - c) Considerations
 - (1) Dextromethorphan
 - (a) Can use in pregnancy
 - (b) Less constipation than with use of opiate
 - (2) Codeine
 - (a) Can use in pregnancy
 - d) Caution
 - (1) Many doctors strongly discourage the use of these combination cough syrups for any child younger than 2 years old, in whom accidental overdoses could be fatal.
 - e) Counseling points
 - (1) Coughs associated with a cold usually last less than 2–3 weeks. If a cough lasts longer than 3 weeks, the patient should see a doctor.
 - (2) Cough due to colds in adults may be safely treated for as long as 7 days.
 - (3) The American Academy of Pediatrics highly recommends the use of calibrated measuring devices for the administration of all liquid medications to children and infants.
5. Lozenges
 - a) Indication: sore throat caused by a cold
 - b) Examples
 - (1) Lozenges for sore throat contain active ingredients such as the anesthetics benzocaine, menthol, dyclonine, phenol/sodium phenolate, and hexylresorcinol.
 - (a) Phenol/sodium phenolate and hexylresorcinol also have antibacterial properties.
 - c) Side effects are rare
 - d) Counseling points
 - (1) Experts recommend not self-treating sore throat for more than 2 days.
 - (2) If a sore throat lasts more than 7 days, healthcare professionals recommend seeing a doctor.
- G. Nonpharmacological therapy can help reduce cold symptoms and is recommended by healthcare professionals for all infants younger than 9 months.
 1. Rest and increased intake of fluids
 2. Saline nasal drops
 3. Nasal bulb aspirator
 4. Elevating the head
 5. Humidification
 6. Petroleum jelly
- III. Otics
 - A. Otic preparations (ear drops) are commonly used in adults and children and may be used to relieve pain, itching, and inflammation in the ear caused by ear infections, for example. Otic preparations can also be used to remove cerumen (ear wax) and to clear water from the clogged ear (ear drying aid).
 - B. They are made as solutions and suspensions.
 - C. Anti-infective
 1. Indication: external ear infections, all are prescription-only medications

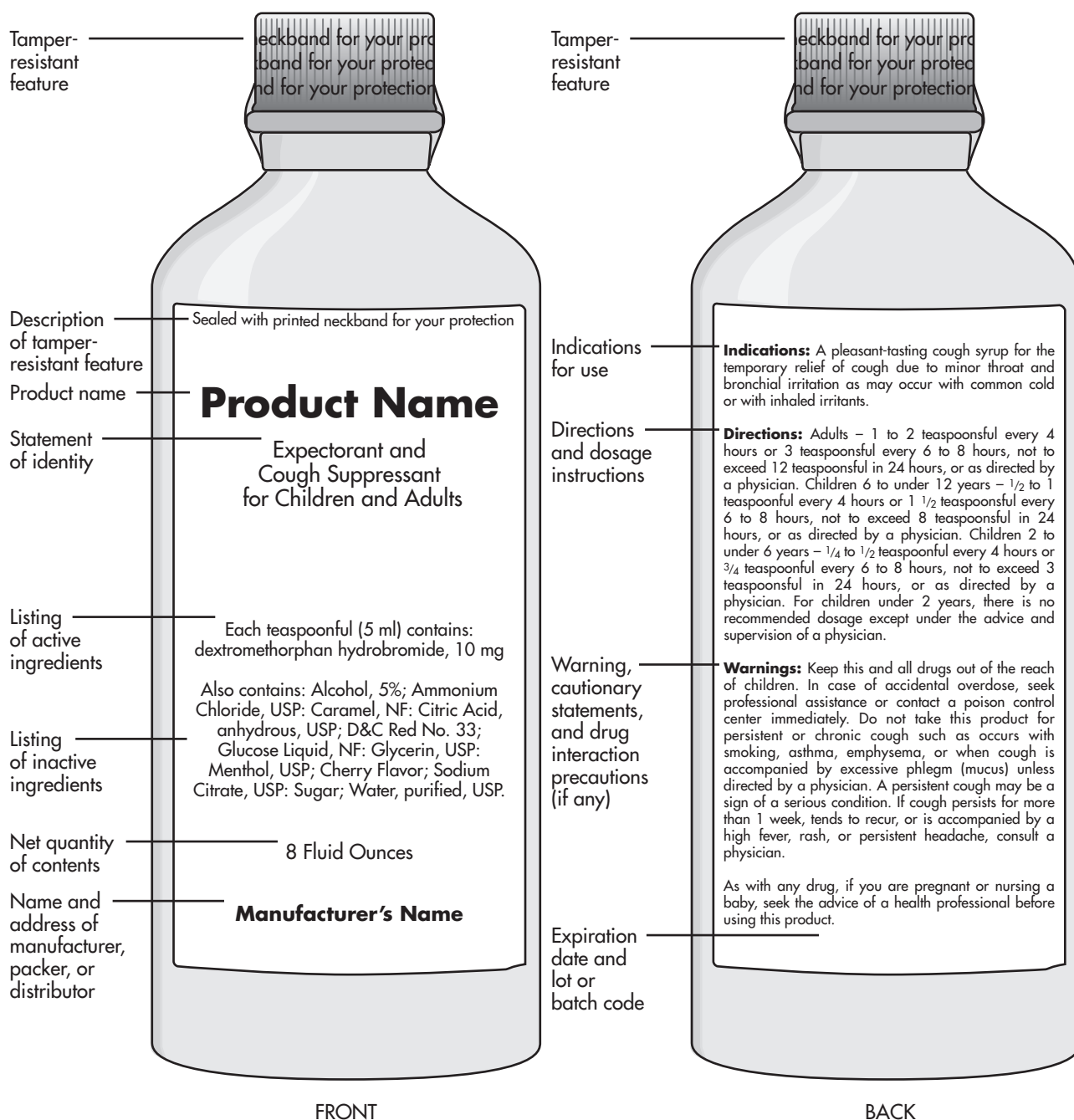


Figure 26-1 — **Sample front and back of cough expectorant product.** (From Donjon RP, Goeckner BJ: Mosby's OTC drugs: an over-the-counter drug resource for health professionals. St. Louis, 1999, Mosby.)

2. Examples

- Neomycin and polymyxin B (AK-Spore HC, Cortisporin, and Otocort)

D. Anesthetics

- Indication: ear pain, prescription only

2. Examples

- Benzocaine (Americaine Otic and Otocain)
- Combination of antipyrine (an anti-inflammatory) and benzocaine (Auralgan, Auroto, Otocalm)

E. Ear wax removal

- Indication: to soften, loosen, and remove excessive ear wax

2. Examples

- Carbamide peroxide (Murine, Debrox)
- Carbamide peroxide with anhydrous glycerin (Physicians' Choice Ear Drops Ear Wax Removal Kit)
- Hypertonic seawater (EARinse)

F. Ear drying aid

- Indication: water-clogged ear after swimming, showering, washing the hair

2. Examples

- Isopropyl Alcohol (95%) in Anhydrous Glycerin (5%) (Auro-Dri and Swim-Ear)

- G. Side effects
 - 1. Dry skin
 - 2. Itching
 - 3. Skin rash
 - 4. Redness
 - 5. Swelling or other sign of irritation in or around the ear not present before use of this medicine
- H. Counseling points
 - 1. It is best to warm the ear drops to body temperature (37 °C or 98.6 °F) by holding the bottle in the hand for a few minutes and gently rolling the bottle before using the medicine. This helps to lessen the pain in the ear.
 - 2. The individual must lie down or tilt the head so that the infected ear faces up.
 - 3. The earlobe is gently pulled up and back for adults (down and back for children) to straighten the ear canal.
 - 4. The medicine is then dropped into the ear canal as directed, keeping the ear facing up for approximately 5 minutes to allow the medicine to coat the ear canal.
 - a) For young children and other patients who cannot stay still for 5 minutes, keeping the ear facing up for at least 1 or 2 minutes may be best.
 - b) Watching television can also help keep children from moving around.
 - 5. Cotton may be placed in the ear canal to keep the medicine from running out.
 - 6. Keep the medicine as germ-free as possible, do not touch the dropper to any surface (including the ear), and keep the container tightly closed.
 - 7. To help clear up the infection completely, the patient should keep using this medicine for the full time of treatment, even if the symptoms have disappeared, and do not miss doses.
 - 8. Ask a doctor before use if a patient has:
 - a) Ear drainage or discharge
 - b) Ear pain
 - c) Irritation or rash in the ear
 - d) Dizziness
 - e) An injury or perforation (hole) of the eardrum
 - f) Recently had ear surgery
 - 9. Stop use and ask a doctor if:
 - a) A patient needs to use more than 4 days
 - b) Excessive earwax remains after use of this product

IV. Ophthalmics

- A. Ophthalmic products include eye drops and lubricants. They are commonly used to relieve redness, dryness, itching, and inflammation in the eye caused by seasonal allergies or from working in front of a computer, to name a few examples. Some ophthalmic products can also be used to rinse the eye of debris.
- B. Ocular decongestants
 - 1. Indication: redness of the eye
 - 2. Examples
 - a) Naphazoline (Clear Eyes, AK-Con, or Opcon)
 - b) Tetrahydrozoline (Visine AC)
 - c) Naphazoline/Pheniramine combination (Opcon-A)

- 3. Side effects
 - a) Uncommon
- 4. Counseling points
 - a) These medications provide quick relief, but the effects usually only last a few hours. However, long-term use may worsen symptoms.
 - b) Overuse may cause the eyes to become red.
- C. Antihistamines
 - 1. Indication: swelling, redness, and itching of the eye
 - 2. Examples
 - a) Ketotifen ophthalmic solution (Zaditor)
 - b) Antazoline phosphate (Vasocon-A)
 - c) Naphazoline HCl, pheniramine maleate (Opcon-A, Naphcon A)
 - 3. Side effects
 - a) These medications may cause mild burning or stinging when they are first applied to the eyes.
 - 4. Counseling points
 - a) These medications provide quick relief, but the effects usually only last a few hours.
- D. Lubricants
 - 1. Indication: For the temporary relief of burning, irritation, and discomfort due to dryness of the eye or exposure to wind or sun
 - 2. Examples
 - a) Hydroxypropylmethylcellulose (Lacrisert)
 - b) Polyethylene glycol 400 (0.25%) (Blink Tears)
 - c) Glycerin (0.50%), naphazoline hydrochloride (0.03%) (Clear Eyes Maximum Redness Relief)
 - d) Artificial teardrops (Polyvinyl Alcohol 1.4%) (Akwa Tears)
 - e) Carboxymethylcellulose Sodium (CMC) (1.0%) (Celluvise)
 - f) Hypromellose (0.3%) (GenTeal)
 - g) Mineral oil 42.5%; white petrolatum 56.8% (Refresh Lacri-Lube Lubricant Eye Ointment)
 - h) Glycerin (0.6%), Propylene glycol (0.6%) (Soothe)
 - 3. Considerations
 - a) Tear production may decrease with age so that fewer tears are available to keep the surface of the eye moist. Both of these changes explain why older people are more likely to have dry eyes.
 - 4. Counseling points
 - a) In treating dry eye, the first thing to do is to remove or reduce the cause. Reducing contact lens wear time and taking breaks from intense visual work are two examples.
 - b) If the individual has chronic dry eye, it is important to use the drops even when the eyes feel fine to keep them lubricated.
 - c) If the eyes dry out while sleeping, there are thicker lubricants, such as ointments, that can be used at night.



Figure 26-2—**Examples of giving eye medication.** A, Cleansing the eye from the inner to outer canthus prior to giving the eye medication. B, Insert the eyedrop into the lower conjunctival sac. C, Application. D, Applying gentle pressure against the nasolacrimal duct after application. (From Lilley LL, Harrington S, Snyder JS: Pharmacology and the nursing process, ed. 5. St. Louis, 2007, Mosby.)

E. Eye rinses

1. Sodium chloride

- Indication: Temporary relief of corneal edema
- Examples
 - Sodium chloride (5%) (Bausch & Lomb Muro 128® 5% ointment)

F. Counseling points

- The proper way for a patient to use eye drops or ointments is:
 - Wash your hands.
 - Shake the container.
 - Tilt your head back and look up.
 - Gently pull your lower lid away from the eye, forming a pouch (Figure 26-2).
 - Into the pouch place one drop or 1/4 to 1/2 inch of ointment. Do not touch the eye or eyelid with the container or dropper.
 - For drops
 - For 5 minutes the patient should:
 - Either close an eye, or with the eye open press a finger against the inner corner of the eyelid and the side of the nose (see Figure 26-2).

This prevents the medication from entering the tear duct and draining away.

g) For ointment

- Simply close the eye. Vision may be blurred for several minutes.
- Repeat with the other eye if needed.
- Replace the cap or dropper on the bottle or tube; tighten.
- It takes 5 minutes for most of an eye drop to be absorbed into the eye. Wait at least 5 minutes before instilling a second drop or between applying other eye medications.

V. Pain and Fever

A. Fever

- For infants and very young children, even a slight increase in body temperature may indicate a serious infection. If a baby younger than 12 months old has a temperature higher than 100 °F, a healthcare provider should be consulted immediately.
- Adults and children who have temperatures higher than 102 °F that are not responding to medications, such as ibuprofen (Motrin,

Advil), aspirin, or acetaminophen (Tylenol), should visit their doctors.

B. Pain

1. OTC analgesics are indicated for mild to moderate pain.

C. Pharmacological therapy may include:

1. Acetaminophen (Tylenol)

a) Considerations

- (1) Acetaminophen can cause liver damage, especially if taken chronically, or in doses that exceed 4 g daily

2. Aspirin (Ecotrin, Bayer, Aspergum, Aspirin, Easpirin)

a) Considerations

- (1) Aspirin may interact with asthma, a bleeding disorder, congestive heart failure (CHF), diabetes mellitus (DM), gout, hemophilia, elevated blood pressure, kidney or liver disease, thyroid disease, or a peptic ulcer.
- (2) Alcohol intake should be limited when taking aspirin because it increases the risk of stomach irritation and bleeding.

3. Special populations

a) Pediatrics

- (1) Do not give aspirin to children younger than 16 years old unless instructed otherwise by health care provider because it may cause a life-threatening, but rare, condition called Reye's syndrome.

b) Pregnancy and breast feeding

- (1) Do not use aspirin during the last 3 months of pregnancy, unless prescribed by the health care provider. Aspirin passes into breast milk. Avoid aspirin or do not nurse.

c) Geriatrics

- (1) With aspirin, gastrointestinal bleeding and irritation are more likely to occur in older persons.

4. NSAID: ibuprofen (Motrin, Advil), naproxen (Naprosyn)

5. Pain patches

6. Hot and cold therapy

7. Rubs and ointments

D. Nonpharmacological therapy includes:

1. Application of ice and/or heat
2. Cool compress
3. Cool liquids
4. Sponge bath
5. Psychological measures (such as biofeedback and cognitive therapy)

VI. Sleep Aids and Stimulants

A. Sleep aids

1. Pharmacological therapy (for short-term use)

a) Diphenhydramine (Benadryl, Nytol, or Sominex)

b) Doxylamine (Unisom)

c) Consideration

- (1) OTC sleep aids are not intended for long-term use, because dependency can develop.

B. Stimulants

1. Pharmacological therapy

2. Caffeine

- a) Caffeine is a stimulant that is found in coffee and various teas, soft drinks, and energy drinks.
- b) Caffeine is also available in pill form (e.g., No-Doze).
- c) Caffeine has been used to decrease fatigue.
- d) It has been shown to increase alertness, reduce sleepiness, enhance mental performance, and improve mood.
- e) Adverse effects
 - (1) Restlessness
 - (2) Nervousness
 - (3) Excitement
 - (4) Insomnia
 - (5) Flushed face
 - (6) Diuresis
- f) Considerations: addictive

VII. First Aid

A. Burn first aid

1. To care for a burn victim with a first- or second-degree burn, first remove the burning agent to keep it from inflicting further damage.
 - a) For example, fires are extinguished, and smoldering clothing that may be covered with hot tar or soaked with chemicals is immediately removed.
 - b) Any constricting jewelry, such as rings, are removed.
2. It is important to note that all third-degree burns and complicated location burns, such as the airway and eyes, need immediate evaluation by a doctor, and burnt clothing and/or burning agents should not be removed without the supervision of a healthcare provider.
3. It is recommended by healthcare professionals not to use butter or oils on a burn. The affected area should be doused with cool water as soon as possible.
4. Affected area can be cleansed gently with an antiseptic solution, if a first degree (mild) burn.
5. It is recommended by healthcare professionals to not apply ice or cool to near-freezing temperatures; this can cause additional tissue injury.
6. First-degree thermal burns can be treated with local skin care such as aloe vera. Many topical antibiotics (such as Neosporin or Bacitracin) and antiseptics are available.
7. Keeping the burned area clean is important because the damaged skin is easily infected.
 - a) Cleaning may be accomplished by gently running water over the burns periodically.
 - b) Wounds are cleaned and bandages are changed one to three times per day.
 - c) Bandaging
 - (1) The burn can be covered with a sterile gauze bandage.

- (2) The gauze should be wrapped loosely to avoid putting pressure on burned skin.
- (3) Bandaging keeps air off the burned skin, reduces pain, and protects blistered skin.
8. Minor burns usually heal without further treatment.
 - a) They may heal with pigment changes, meaning the healed area may be a different color from the surrounding skin.
9. It is recommended by healthcare professionals to watch for signs of infection, such as increased pain, redness, fever, swelling, or oozing. Seek medical help if infection develops.
10. Avoid re-injuring or tanning if the burns are less than a year old.
 - a) Tanning may cause more extensive pigmentation changes.
- B. Wound antiseptics and antibiotics
 1. Hydrogen peroxide
 2. Povidone-iodine (povidone-iodine 10%, equal to 1% available iodine)
 3. After cleaning the wound, apply a thin layer of an antibiotic cream or ointment such as Neosporin or Polysporin to help keep the surface moist.
 - a) The products do not make the wound heal faster, but they can discourage infection and allow the body's healing process to close the wound more efficiently.
 - b) Certain ingredients in some ointments can cause a mild rash in some individuals. If a rash appears, stop using the ointment.
 4. Bacitracin
 5. Benzalkonium chloride (0.13%) + lidocaine hydrochloride (2.5%) (Bactine)
 6. Betadine (povidone-iodine 10%, equal to 1% available iodine)

VIII. Topical Agents for Common Skin Conditions

A. Acne

1. Topical products for acne may dry up the oil, kill bacteria, and promote sloughing of dead skin cells. Generally, these medications are useful for people with mild acne. They help to open up clogged pores and have some antibacterial activity.
 - a) Benzoyl peroxide (Clean & Clear, Persa-Gel, Oxy 10 Spot Treatment)
 - b) Salicylic acid (Biore Blemish Bomb, ClearasilStay Clear, Zone Control Clearstick)
 - c) Adverse effects: dryness
 - d) If products containing salicylic acid and benzoyl peroxide do not work well, products with sulfur and/or resorcinol (Clearasil Adult Care) may be used.
 - (1) Adverse effect: noticeable color and odor
2. Considerations
 - a) It can take several weeks to see an improvement in symptoms.

B. Skin rashes

1. Oral and topical antihistamines like diphenhydramine (Benadryl) have been used to treat skin rashes caused by an allergic reaction.
 - a) Antihistamines decrease redness and itchiness associated with the rash.
 2. Baking soda
 - a) A solution of baking soda and water may help treat allergic skin reactions caused by poisonous plants.
 - b) Three teaspoons of baking soda can be mixed with one teaspoon of water and applied to affected areas of the skin.
 3. Calamine lotion
 - a) Calamine lotion (Calamox) can be applied to the skin to reduce itching and blistering caused by exposure to a poisonous plant.
 4. Cool compress
 - a) Applying a cool compress to affected areas of the skin may help relieve itching and swelling associated with rashes.
 5. Topical corticosteroids
 - a) Topical corticosteroids are the most common and effective treatments for rashes caused by atopic dermatitis. They are used until the rash clears. Low-strength topical corticosteroids should be used on the face.
 - b) Hydrocortisone (Bactine, Cortaid, Dermolate, or Aveeno anti-itch cream) is a low-strength corticosteroid cream that has been used to treat young children.
 6. Zinc oxide creams
 - a) Ointments that contain zinc oxide (like Desitin or Diaparene) may help relieve diaper rash in babies. The ointment is applied to affected areas of the skin each time the baby's diaper is changed.
- ##### C. Itching
1. Hydrocortisone cream has been applied to the affected area to temporarily relieve itching associated with allergic reactions and exposure to poisonous plants.
 2. Hydrocortisone 1% cream, which is available OTC, has anti-inflammatory effects and relieves swelling and redness in addition to itching.
 3. Prescription hydrocortisone has been used to relieve itching, redness, dryness, crusting, scaling, inflammation, and discomfort associated with the reaction.
- ##### D. Dry skin
1. Ammonium lactate
 - a) Used for dry, scaly skin conditions like xerosis and ichthyosis vulgaris
 - b) A thin layer should be applied to the affected areas of the skin, usually twice daily.
 - c) It should be rubbed thoroughly into the skin.
- ##### E. Poison ivy
1. Aloe vera gel
 - a) Applied to affected areas of the skin to relieve itching and help rashes heal
 - b) Should not be applied to open cuts, blisters, or sores on the skin

2. Baking soda
 - a) A solution of baking soda and water may help treat allergic skin reactions caused by poisonous plants.
 - b) Three teaspoons of baking soda can be mixed with one teaspoon of water and applied to affected areas of the skin.
 3. Calamine lotion
 - a) Calamine lotion (Calamox) can be applied to the skin to reduce itching and blistering.
 4. Cool showers
 - a) Taking cool showers can help relieve itching associated with the allergy.
 - b) Also, soaking affected areas in cool water with baking soda or oatmeal may help reduce itching and dry blisters.
 - (1) Colloidal oatmeal (Aveeno Oatmeal Bath) has been shown to relieve itching a maximum of 7 hours.
 5. Cool compress
 - a) Applying a cool compress to affected areas of the skin may help relieve itching.
 6. Hydrocortisone
 - a) Hydrocortisone cream may be applied to the affected area to temporarily relieve itching.
 - b) Hydrocortisone 1% cream, which is available OTC, has anti-inflammatory effects and relieves swelling and redness in addition to itching.
 - c) Prescription hydrocortisone has been used to relieve itching, redness, dryness, crusting, scaling, inflammation, and discomfort associated with the reaction.
- IX. Antihistamines
- A. Indications: symptoms like runny or stuffy nose, itchy or sore throat, sneezing, itchy, watery eyes
 - B. Examples
 1. First-generation, nonselective antihistamines that cause sedation
 - a) Diphenhydramine (Benadryl)
 - b) Clemastine (Tavist)
 - c) Chlorpheniramine (Chlor-Trimeton)
 - d) Brompheniramine (Dimetane)
 2. Second-generation, selective, nonsedating antihistamines
 - a) Loratadine (Claritin)
 - b) Cetirizine (Zyrtec)
 - C. Side effects
 1. Anticholinergic (mostly with first generation)
 - a) Dry mouth
 - b) Dry eyes
 - c) Urinary retention
 - d) Constipation
 - e) Elevated heart rate
 - f) Sedation (cetirizine more than loratadine)
 - D. Considerations
 1. First generation agents are less expensive compared to newer agents.
 2. Best when taken ~1–2 hours before exposure to offending allergen.
 3. If patient becomes tolerant, switch to an antihistamine in a different class.
- E. Caution
1. Antihistamines can cause confusion and increased risk of falls if administered to elderly patients, especially first generation agents
 2. Caution with use in patients with increased intraocular pressure, hyperthyroidism, and cardiovascular disease.
- X. Constipation, Diarrhea, Nausea, Vomiting
- A. Antidiarrheals
 1. Antimotility
 - a) Loperamide (Imodium)
 - (1) Loperamide hydrochloride slows down the speed at which fluids move through the bowels.
 - (2) Adverse effects
 - (a) Drowsiness
 - (b) Abdominal cramps
 - (c) Dizziness
 - (3) Caution
 - (a) Because it can cause toxic megacolon, it should not be used in young children or patients with severe colitis.
 2. Adsorbents
 - a) Polycarbophil
 - (1) FDA recommends as effective adsorbent
 - (2) Adsorbs 60× its weight in water
 - (3) Treats both diarrhea and constipation
 - (4) 500-mg chewable tablets
 - (5) Nonabsorbable, safe, may be taken 4 times per day, to a maximum of 6 g in adults
 - b) Kaolin
 - c) Pectin
 - d) Methylcellulose
 - e) Activated attapulgit
 - f) Considerations
 - (1) Nontoxic
 - (2) Nonspecific in action: they adsorb nutrients, toxins, drugs, and digestive juices
 - g) Caution
 - (1) Coadministration with other drugs reduces the drugs' bioavailability
 3. Antisecretory agent
 - a) Enzymes (lactase)
 - (1) Helpful for patients with lactose intolerance
 - (2) Lactase is needed for carbohydrate digestion and is needed for patients who have diarrhea after eating dairy products,.
 - (3) To be used each time a dairy product is eaten, such as milk or ice cream
 - b) Bacterial replacement
 - (1) *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*
 - (2) Replaces colonic microflora; restores intestinal functions; suppresses the growth of pathogenic microorganisms

- c) Bismuth subsalicylate (Pepto-Bismol, Bismatrol, or Kaopectate)
 - (1) Bismuth subsalicylate balances the way fluids move through the digestive tract. It also binds to harmful bacterial toxins, causing the toxins to be flushed out with the stool.
 - (2) 262-mg chewable tablets or 262 mg/5 mL liquid
 - (a) Two tablets or 30 mL every 30 minutes to 1 hour to a maximum of eight doses per day
 - (3) Adverse effects may include darkening tongue and stools with repeat administration.
 - (4) Considerations
 - (a) Might be toxic if given excessively to prevent or treat diarrhea
 - (b) May interact with anticoagulants or cause effects of salicylism (tinnitus, nausea, and vomiting)
 - (c) Can interfere with intestinal absorption of tetracycline
 - (d) Can induce gout attacks in patients with gout
- 4. Nonpharmacologic
 - a) Stopping solid foods for 24 hours
 - b) Avoiding dairy products
 - c) Start bland diet as bowel movements decrease
 - d) Oral rehydration fluids
- B. Laxatives
 - 1. Bulking agents
 - a) First-line treatment for chronic constipation
 - b) Considerations
 - (1) Must be consumed with fluid or else results in obstruction of esophagus, stomach, small intestine, and colon; caution in patients with intestinal stenosis
 - (2) Should be used daily and continued indefinitely in most patients, especially in those with chronic constipation
 - c) Caution
 - (1) Fiber should be avoided in bedridden patients who are cognitively impaired.
 - d) Effect seen in 1–3 days
 - (1) Hydrophilic colloids
 - (2) Methylcellulose
 - (3) Psyllium seeds
 - (4) Bran
 - (5) Polyethylene glycol
 - (6) Sorbitol
 - (7) Lactulose
 - 2. Agents that cause watery evacuation
 - a) Effects seen in 1–6 hours
 - (1) Magnesium sulfate
 - (2) Magnesium hydroxide
 - (a) Milk of magnesia used for acute constipation.
 - 3. Aloe
 - 4. Polycarbophil
 - (1) FDA recommends as effective adsorbent
 - (2) Adsorbs 60× its weight in water
 - (3) Treats both diarrhea and constipation
 - (4) 500-mg chewable tablets
 - (5) Nonabsorbable, safe, may be taken four times per day, to a maximum of 6 g in adults
- 5. Irritants and stimulants
 - a) Effects seen in 6–12 hours
 - b) Not recommended for regular daily use
 - (1) Senna
 - (2) Phenolphthalein
 - (3) Bisacodyl
- 6. Castor oil
 - a) Bowel movement within 1–3 hours after use
 - b) Caution
 - (1) Because it has a strong purgative action, it should not be used regularly.
- 7. Stool softeners
 - a) Emollient: surfactant agents
 - (1) Docusate sodium
 - (2) Increase water and electrolyte secretion in the small and large bowel
 - (3) To prevent, not treat, constipation
 - (4) Effect seen in 1–3 days
 - b) Lubricants
 - (1) Mineral oil
 - (a) Coats stool and allows easier passage; it inhibits colonic absorption of water, thereby increasing stool weight and decreasing stool transit time
 - (b) Effect seen 2–3 days after use
 - (c) Adverse effects
 - (i) Mineral oil may leak from the anal sphincter, causing pruritus and soiling of clothes
 - (d) Caution
 - (i) May be absorbed systemically
 - (ii) May decrease absorption of fat soluble vitamins (A, D, E, and K)
 - (iii) Because it can be aspirated when given orally, avoid use in bedridden patients
 - (e) Consideration
 - (i) Do not use before bedtime or when patient is recumbent because it can be aspirated when ingested orally.
 - (f) Effect seen in 1–3 days
- 8. Glycerin suppositories are used for acute constipation
 - a) Effect seen in 30 minutes
 - b) Considered to be a safe laxative but can sometimes cause rectal irritation
- 9. Enemas
- 10. Nonpharmacologic
 - a) Tap water enema used for acute constipation; bowel movement can be seen in 30 minutes
 - b) Regular exercise
 - c) Dietary measures such as increasing fiber (20–35 g each day including more fruits and uncooked vegetables), more water, and more whole grain breads and cereals are helpful.

- d) For individuals who get gas or bloating from whole grains, a fiber substitute such as psyllium (a natural soluble fiber) may help. If gas is still a problem, methylcellulose (Citrucel) or polycarbophil (FiberCon) may be beneficial. These products do not undergo bacterial fermentation, therefore creating less gas.

XI. Smoking Cessation

A. There is evidence that combining the nicotine patch with nicotine gum or nicotine nasal spray increases long-term quit rates compared with using a single type of nicotine replacement therapy. Nicotine gum, in combination with nicotine patch therapy, may also reduce withdrawal symptoms better than either medication alone. A doctor or pharmacist can provide more information.

B. Pharmacological therapy

1. Nicotine gum

- a) 2 mg recommended for patients who smoke <25 cigarettes per day
- b) 4 mg recommended for patients who smoke >25 cigarettes per day
- c) Side effects
 - (1) Bad taste in the mouth
 - (2) A tingling feeling on the tongue while chewing the gum
 - (3) Hiccups
 - (4) Upset stomach (nausea) or heartburn
 - (5) Nausea and light-headedness are possible signs of overdose and warrant dose reduction.
- d) Counseling points
 - (1) Nicotine gum might not be appropriate for people with temporomandibular joint (TMJ) disease, or popping of the jaw, or for those with dentures or other dental work such as bridges.
 - (2) Nicotine gum is generally used for 12 weeks.
 - (3) It should be chewed slowly until a peppery or minty taste emerges and then parked between the cheek and the gums for absorption through the oral mucosa. The gum should be chewed slowly and intermittently and parked for about 30 minutes or until the taste dissipates.

2. Nicotine lozenge

- a) Nicotine lozenge comes in the form of a hard candy and releases nicotine as it slowly dissolves in the mouth. Eventually, the quitter uses fewer and fewer lozenges during the 12-week program until he or she is completely nicotine-free.
- b) Side effects
 - (1) Soreness of the teeth and gums
 - (2) Indigestion
 - (3) Throat irritation
 - (4) Nausea and light-headedness are possible signs of overdose and warrant dose reduction.

c) Counseling points

- (1) There is no eating or drinking within 15 minutes before using or while the lozenge is in the mouth.
- (2) Each lozenge will last about 20–30 minutes, and nicotine will continue to leach through the lining of the mouth for a short time after the lozenge has disappeared.
- (3) No more than five lozenges in 6 hours, or more than 20 lozenges total per day are used.
- (4) One lozenge after another is not used because this may cause hiccups, heartburn, nausea, or nervousness.
- (5) Biting or chewing the lozenge will cause more nicotine to be swallowed quickly and may result in indigestion and/or heartburn.

3. Nicotine patches

- a) Nicotine patch looks like an oversized adhesive bandage. The outer part of the patch sticks to the skin, while the inner portion presses against and slowly releases nicotine into the skin.
- b) Side effects
 - (1) Sleep disruption
 - (2) Skin irritation because of the adhesive, not the nicotine
 - (3) Nausea and light-headedness are possible signs of overdose and warrant dose reduction
- c) Counseling points
 - (1) The patch is used on a clean, dry, nonhairy area of skin on the upper body or the outer part of the arm.
 - (2) Skin that is very oily, burned, broken out, cut or irritated in any way may cause the patch not to stick.
 - (3) Men with excess hair can apply the patches on the underside of the arms or clip excess hair from the back or chest.
 - (4) The patch may stay in place if it is placed over joints, such as the shoulder.
 - (5) Most individuals prefer the patch placed on an area that is not visible to others.
 - (6) The patch should not be removed from the sealed, protective pouch until it is ready to be used.
 - (7) There are instructions in the package regarding opening, such as where to cut the package so as not to cut the patch.
 - (8) After opening the package, the patch is immediately applied to the skin, pressing firmly against the skin with the palm for about 10 seconds.
 - (9) Healthcare professions recommend rotating the site of patch application.

- (10) Apply the patch on a different place on the skin daily.
- (11) The nicotine patch may not be a good choice for individuals with skin problems or allergies to adhesive tape.
- (12) It should not be worn for more than 24 hours because it may irritate the skin.
- (13) Leaving a patch on for 24 hours may cause sleep disturbance, such as difficulty sleeping or vivid dreams.
- (14) Removing the patch in the evening around 8 p.m. may stop sleep problems.
- (15) Use of nicotine patches usually lasts 8 to 10 weeks, but this can vary with the individual and the brand of patch.
- (16) There appears to be little benefit in using the patch for more than 8 weeks.

C. Nonpharmacological therapy

1. "Cold turkey"
2. Support and counseling

PATIENT PROFILE

Patient Initials: BH

Sex: Female

Age: 28

Height: 5' 6"

Weight: 90 kg

Race: White

Allergies: No known drug allergies (NKDA)

Current Health Conditions:

No chronic health conditions

Family History:

Obesity

Heart disease

Diabetes

Pharmacy Medication Profile:

No current active medications

Pharmacy Consult: BH is seriously trying to lose weight after several failed efforts with diet and exercise alone. She would like more information regarding orlistat (Alli). She recently had an appointment with a registered dietician at the hospital where she works as a nurse and joined a Weight Watchers support group. The dietician encouraged her to consider Alli treatment as an adjunct to diet and exercise.

PATIENT PROFILE QUESTIONS

1. What is BH's body mass index (BMI)?
 - a. 44 kg/m²
 - b. 32 kg/m²
 - c. 28 kg/m²

Answer: b. The BMI is a calculated index that uses the patient's weight and height. A common formula to calculate BMI is:

$$\text{BMI} = \frac{\text{Weight (in pounds)} \times 703}{\text{height squared (inches}^2\text{)}}$$

Obesity is defined as a BMI >30 kg/m². BH is considered obese.

2. Is Alli, which is a nonprescription diet aid, an appropriate treatment option for BH?
 - a. Yes
 - b. No

Answer: b. Nonprescription use of Alli is aimed at those who are mild or moderately overweight (BMI 25–28 kg/m²). BH should be encouraged to talk to her doctor about treatment options, including prescription use of orlistat.
3. BH confers with her doctor, who agrees that a trial of Alli, combined with current weight loss strategies, is warranted, rather than expose BH to potentially intolerable prescription strength doses of orlistat (Xenical). What are important counseling points for BH before taking Alli?
 - I. Gastrointestinal side effects include loose or frequent stools that may be hard to control, an urgent need to go to the bathroom, and flatulence that may cause oily spotting.
 - II. Side effects should diminish with time but may recur if the patient is not compliant with a reduced fat intake in the diet.
 - III. Take one Alli capsule three times per day with each main meal containing fat. If a meal is skipped, that dose of Alli should also be skipped.
 - IV. It may take several months for noticeable results.
 - V. A multivitamin containing the fat-soluble vitamins A, D, E, and K is recommended; however, the dose should be separated from a dose of Alli by at least 2 hours.
 - a. I and II
 - b. I, II, and III
 - c. I, II, III, and V
 - d. All of the above

Answer: d. All of the above are pertinent counseling points. Patients should note that for some patients, weight loss with Alli might not be significantly greater than that obtained with diet and exercise efforts alone. Compliance with dietary recommendations is essential for weight loss and for limiting embarrassing and uncomfortable side effects. Although short-term treatment with orlistat at nonprescription doses has not reduced the absorption of fat-soluble vitamins, experts generally recommend multivitamin supplementation.

REVIEW QUESTIONS

(Answers and Rationales on page 381.)

1. Which of the following is the preferred form of iron for the treatment of iron deficiency anemia?
 - a. Ferric salts
 - b. Elemental iron
 - c. Ferrous iron
 - d. b or c
 - e. A combination of b and c
2. OTC products containing minoxidil include:
 - I. solutions.
 - II. gel.
 - III. tablets.

- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
3. True or False: Clotrimazole is available for administration as an oral troche, topical cream, topical solution, and vaginal cream.
- a. True
 - b. False
4. Clotrimazole:
- a. is excreted predominantly in the feces.
 - b. is absorbed into systemic circulation after topical application.
- c. has a time to peak serum concentration of 1–2 days after oral troche.
- d. a and b
- e. a, b, and c
5. True or False: Oxymetazoline nasal spray should be used for at least 2 weeks in order for the patient to experience relief.
- a. True
 - b. False

- I. Definition
 - A. **Nutrition** is the provision of the materials necessary to nourish the body and sustain life (Box 27-1).
 - B. **Malnutrition** is the lack of adequate intake of nutrients induced by altered dietary intake or nutrient utilization resulting from consuming too little food, lack of vital nutrients, or impaired absorption or metabolism due to disease.
 1. Type
 - a. Marasmus
 - 1) Reduced calorie intake
 - 2) Extremely thin/emaciated; skin hangs on skeletal bones
 - b. Kwashiorkor
 - 1) Lack of protein intake
 - 2) Fat stores in the abdomen and face
- II. Types of Delivery of Nutritional Support
 - A. Enteral nutrition
 - B. Parenteral nutrition
 1. Peripheral parenteral nutrition (PPN)
 2. Total peripheral nutrition (TPN)
- III. Enteral Nutrition
 - A. Involves the gastrointestinal tract and requires a functioning small intestine
 - B. Oral or feeding tube
- IV. Parenteral Nutrition
 - A. Parenteral nutrition is the use of intravenous nutrients. Patients with a nonfunctioning gastrointestinal tract receive therapy to ensure they are adequately nourished.
 - B. Goals
 1. Maintain or restore nutritional integrity
 2. Restore the body's protein metabolism
 3. Prevent malnutrition
 4. Diminish rate of weight loss/maintain body weight
 5. Promote wound healing
 6. Replace nutritional deficits
 - C. Indications
 1. Short bowel syndrome, massive bowel resection
 2. Active inflammatory disease of the intestine
 3. Severe malabsorption
 4. Intractable vomiting or diarrhea
 5. Severe acute pancreatitis
 6. High output fistula (>500 mL/day)
 7. Severe malnutrition with intolerance to enteral tube feedings
 8. Enteral feeding access not possible due to upper GI obstruction
 9. Enterocutaneous fistula with high output
 10. Lower birth weight infants (premature)
 11. Bone marrow transplant with graft versus host disease (GVHD) of the gut
 - D. Contraindications
 1. Functional gastrointestinal tract
 2. Patients do not want to eat
 3. Venous access is not available
 4. Awaiting flatus or bowel sounds after surgery
 5. Expected duration of parenteral nutrition is less than 5 days
 6. Terminal illness
 - a. The prognosis does not warrant the use of nutritional support (the benefits do not outweigh the risks).
 - E. Administration
 1. PPN
 - a. Use of small veins in the extremities
 - b. Used when central line access is not available
 - c. Short-term use only
 - d. Osmolarities greater than 900 mOsm/L may irritate the peripheral vein.
 - 1) PPN solutions must be isotonic to prevent damage to veins.
 - e. Glucose concentration of PPN is lower than that of central TPN.
 - f. Do not use in patients requiring fluid restrictions.
 2. Central (TPN)
 - a. Use of larger veins in the trunk
 - 1) Subclavian, internal jugular, and femoral
 - b. Osmolarity generally 1000–2000 mOsm/L
 - F. TPN components
 1. Carbohydrates (dextrose)
 - a. Caloric value 3.4 kcal/gm
 - b. Maximal carbohydrate utilization
 - 1) 4–5 mg/kg per minute; do not exceed 7 mg/kg per minute or 202–205 kcal/kg per day
 - c. Common dextrose TPN concentrations: 5%, 10%, 15%, 20%, 35%
 2. Fats (lipid emulsion [Intralipids, Liposyn])
 - a. Caloric value 9 kcal/g
 - b. Most concentrated source of calories
 - c. Fat emulsions available: 10% (1.1 kcal/mL) or 20% (2.0 kcal/mL)
 - d. Liposyn
 - 1) Prevents fatty acid deficiencies
 - 2) Contains 5% safflower oil, 5% soybean oil, up to 1.2% egg phospholipids
 - 3) In a 10% solution, each mL provides 1.1 kcal

Box 27-1

2005 Focus Areas of the *Dietary Guidelines for Americans*

1. Adequate Nutrients within Calorie Needs
 - Consume a variety of nutrient-dense foods and beverages within and among the basic food groups while choosing foods that limit the intake of saturated and trans fats, cholesterol, added sugars, salt, and alcohol.
 - Meet recommended intakes within energy needs by adopting a balanced eating pattern, such as the USDA Food Guide for the DASH Eating Plan.
2. Weight Management
 - To maintain body weight in a healthy range, balance calories from foods and beverages with calories expended.
 - To prevent gradual weight gain over time, make small decreases in food and beverage calories and increase physical activity.
3. Physical Activity
 - Engage in regular physical activity and reduce sedentary activities to promote health, psychological well-being, and a healthy body weight.
 - Achieve physical fitness by including cardiovascular conditioning, stretching exercises for flexibility, and resistance exercises or calisthenics for muscle strength and endurance.
4. Food Groups to Encourage
 - Consume a sufficient amount of fruits and vegetables while staying within energy needs. Two cups of fruit and 2½ cups of vegetables per day are recommended for a reference 2000-calorie intake, with higher or lower amounts depending on the calorie level.
 - Choose a variety of fruits and vegetables each day. In particular, select from all five vegetable subgroups (dark green, orange, legumes, starchy vegetables, and other vegetables) several times a week.
 - Consume 3 or more ounce-equivalents of whole-grain products per day, with the rest of the recommended grains coming from enriched or whole-grain products. In general, at least half the grains should come from whole grains.
 - Consume 3 cups per day of fat-free or low-fat milk or equivalent milk products.
5. Fats
 - Consume less than 10% of calories from saturated fatty acids and less than 300 mg/day of cholesterol, and keep trans fatty acid consumption as low as possible.
 - Keep total fat intake between 20% and 35% of calories, with most fats coming from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts, and vegetable oils.
 - When selecting and preparing meat, poultry, dry beans, and milk or milk products, make choices that are lean, low-fat, or fat-free.
 - Limit intake of fats and oils high in saturated and/or trans fatty acids, and choose products low in such fats and oils.
6. Carbohydrates
 - Choose fiber-rich fruits, vegetables, and whole grains often.
 - Choose and prepare foods and beverages with little added sugars and caloric sweeteners, such as amounts suggested by the USDA Food Guide and the DASH Eating Plan.
 - Reduce the incidence of dental caries by practicing good oral hygiene and consuming sugar- and starch-containing foods and beverages less frequently.
7. Sodium and Potassium
 - Consume less than 2300 mg (approximately 1 tsp of salt) of sodium per day.
 - Choose and prepare foods with little salt. At the same time, consume potassium-rich foods, such as fruits and vegetables.
8. Alcoholic Beverages
 - Those who choose to drink alcoholic beverages should do so sensibly and in moderation—defined as the consumption of up to one drink per day for women and up to two drinks per day for men.
 - Alcoholic beverages should not be consumed by some individuals, including those who cannot restrict their alcohol intake; women of childbearing age who may become pregnant, pregnant, and lactating women; children and adolescents; individuals taking medications that can interact with alcohol; and those with specific medical conditions.
 - Alcoholic beverages should be avoided by individuals engaging in activities that require attention, skill, or coordination, such as driving or operating machinery.
9. Food Safety
 - To avoid microbial foodborne illness:
 - Clean hands, food-contact surfaces, and fruits and vegetables. Meat and poultry should be washed or rinsed.
 - Separate raw, cooked, and ready-to-eat foods while shopping, preparing, or storing foods.
 - Cook foods to a safe temperature to kill microorganisms.
 - Chill (refrigerate) perishable food promptly and defrost foods properly.
 - Avoid raw (unpasteurized) milk or any products made from unpasteurized milk, raw or partially cooked eggs or foods containing raw eggs, raw or undercooked meat and poultry, unpasteurized juices, and raw sprouts.

*The 2005 *Dietary Guidelines* remain the current guidance until the 2010 *Dietary Guidelines* are published.

From the US Department of Health and Human Services, US Department of Agriculture: *Dietary guidelines for Americans 2005: Key recommendations*, Washington, DC, 2005, Authors. Retrieved March 22, 2006, from www.health.gov/dietaryguidelines/dga2005/recommendations.htm.)

- 4) Emulsion appears cloudy, with a milky appearance
- e. Patients with severe egg allergies may not tolerate lipids
3. Protein (amino acids)
 - a. Caloric value 4 kcal/g
 - b. Restrict in patients with end stage renal and/or liver disease
 - c. Protein requirements increase depending on health of patient
 - 1) Normal: 1 g/kg per day
 - 2) Mild stress: 1.3 g/kg per day
 - 3) Moderate stress (major surgery): 1.5 g/kg per day
 - 4) Major stress (major trauma or burns): >2.0 g/kg per day
 - e. Ideal amino acid solution is 50:50 ratio of essential to nonessential amino acids.
 - f. Nitrogen balance studies dictate appropriate protein intake in critically ill patients.
 - 1) $N_2 \text{ balance} = N_2 \text{ intake} - N_2 \text{ loss}$
 - 2) $N_2 \text{ intake} = \text{grams protein consumed} / 24 \text{ hours} / 6.25$
 - 3) $N_2 \text{ loss} = \text{grams urine urea nitrogen} + 4 \text{ (nonurinary losses)}$
 - (a) Positive N_2 balance between +2 and +4 is optimal.
4. Water (30 mL/kg per day)
5. Vitamins
 - a. Fat-soluble vitamins: A, D, E, K
 - b. Water-soluble vitamins: e.g., Vitamins B₁, B₂, B₆, B₁₂
6. Trace minerals
 - a. Examples: zinc, copper, chromium, manganese and selenium
7. Electrolytes
 - a. Recommended maximum electrolyte concentrations per liter of standard TPN
 - 1) Na: 130 mEq
 - 2) K: 80 mEq
 - 3) Mg: 8 mEq
 - 4) Ca: 10 mEq (general estimates, the calcium-to-phosphate ratio is also important in avoiding precipitation and maintaining solution compatability)
 - 5) Phos: 25 mM (general estimates, the calcium-to-phosphate ratio is also important in avoiding precipitation and maintaining solution compatability)
8. Some medications may be safely added to parenteral nutrition solutions.
 - a. H₂-receptor antagonists (cimetidine, ranitidine, famotidine)
 - b. Insulin
 - c. Heparin
- G. Monitoring
 1. Intake and output
 2. Body weight
 3. Electrolytes
 4. Nitrogen balance
 5. Chemistry screens
 6. Triglycerides
7. Complete blood count (CBC) with differential and prothrombin time
8. Albumin level
- H. Complications
 1. Catheter-related
 - a. Pneumothorax
 - b. Air embolism
 - c. Catheter embolization
 - d. Venous thrombosis
 - e. Catheter occlusion
 - f. Improper location of catheter
 - g. Phlebitis
 - h. Catheter-related sepsis
 2. Gastrointestinal
 - a. Fatty liver
 - b. Cholestasis
 - c. Gut atrophy
 3. Metabolic
 - a. Nutrition alterations
 - 1) Overfeeding
 - 2) Refeeding syndrome
 - 3) Altered mineral balance
 - 4) Altered vitamin balance
 - b. Hyperglycemia
 - c. Rebound hypoglycemia
 - d. Hyperammonemia
 - e. Hypertriglyceridemia
 - f. Electrolyte imbalances
 - 1) Sodium, normal = 135–145 mEq/L
 - a) Hypernatremia
 - (i) Causes: dehydration, diabetes insipidus, excess sodium intake
 - (ii) Intervention: ↑ fluid intake, ↓ sodium intake
 - b) Hyponatremia
 - (i) Causes: diuretics, excess fluid, gastrointestinal, skin, renal losses, syndrome of inappropriate antidiuretic hormone (SIADH)
 - (ii) Intervention: decrease fluid intake, varies depending on cause
 - 2) Potassium, normal = 3.5–5.0 mEq/L
 - a) Hyperkalemia
 - (i) Causes: diuretics (potassium-sparing), metabolic acidosis, renal failure, insulin deficiency, chemotherapy, burns, excessive potassium intake
 - (ii) Intervention: ↓ potassium intake, correct metabolic acidosis, identify and correct underlying cause
 - b) Hypokalemia
 - (i) Causes: diuretics, anabolism, vomiting, diarrhea, metabolic alkalosis
 - (ii) Intervention: ↑ potassium intake, check for magnesium deficiency
 - 3) Calcium, normal = 8.5–10.5 mg/dL
 - a) Hypercalcemia
 - (i) Causes: dehydration, malignancy
 - (ii) Intervention: ↑ fluid intake, ↓ calcium intake
 - b) Hypocalcemia

- (i) Causes: chronic renal failure, hypoalbuminemia
- (ii) Intervention: calculate estimated serum calcium concentration; correct for hypoalbuminemia; adjust calcium intake when necessary
- 4) Magnesium, normal = 1.5–2.0 mEq/L
 - a) Hypermagnesemia
 - (i) Causes: renal dysfunction, excessive magnesium intake
 - (ii) Intervention: ↓ magnesium intake, check renal function
 - b) Hypomagnesemia
 - (i) Causes: diarrhea, malabsorption, anabolism, parathyroid disease; drugs that deplete magnesium
 - (ii) Intervention: ↑ magnesium intake, check for refeeding syndrome
- 5) Phosphorus, normal = 3.0–4.5 mg/dL
 - a) Hyperphosphatemia
 - (i) Causes: renal dysfunction, hypoparathyroidism, excessive phosphorus intake, chemotherapy
 - (ii) Intervention: ↓ phosphorus intake, identify and treat underlying cause
 - b) Hypophosphatemia
 - (i) Causes: antacids and drugs that bind phosphorus, anabolism, phosphate-free dialysate, burn recovery, respiratory alkalosis, diabetic ketoacidosis, alcoholism
 - (ii) Intervention: discontinue any agents that bind phosphate, ↑ phosphorus intake, check for refeeding syndrome
- I. Fatty liver
- II. Hyperglycemia
- III. Pneumothorax
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
- 4. Renal failure may cause which of the following electrolyte imbalances?
 - a. Hypermagnesemia
 - b. Hypocalcemia
 - c. Hyperphosphatemia
 - d. Hyperkalemia
 - e. All of the above
- 5. Which of the following acronyms refer(s) to a type of parenteral nutrition?
 - I. PPN
 - II. PNM
 - III. TNA
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and II
- 6. Parenteral administration of 1 L of 10% dextrose in water provides the patient with approximately how many kcal of energy?
 - a. 100–150 kcal
 - b. 150–200 kcal
 - c. 300–350 kcal
 - d. 400–450 kcal
 - e. 700–750 kcal

REVIEW QUESTIONS

(Answers and Rationales on page 381.)

1. Which of the following medications may be safely added to parenteral solutions?
 - I. Ranitidine
 - II. Insulin
 - III. Heparin
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
2. Which of the following statements regarding peripheral parenteral nutrition is true?
 - a. It is used when central line access is not available.
 - b. It is for long-term use only.
 - c. Isotonic solutions should be avoided.
 - d. It must be infused through a large vein, such as the superior vena cava.
 - e. All of the above
3. Which of the following is a possible complication of administering parenteral nutrition solutions?
 - I. Fatty liver
 - II. Hyperglycemia
 - III. Pneumothorax
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
4. Renal failure may cause which of the following electrolyte imbalances?
 - a. Hypermagnesemia
 - b. Hypocalcemia
 - c. Hyperphosphatemia
 - d. Hyperkalemia
 - e. All of the above
5. Which of the following acronyms refer(s) to a type of parenteral nutrition?
 - I. PPN
 - II. PNM
 - III. TNA
 - a. I only
 - b. III only
 - c. I and II only
 - d. II and III only
 - e. I, II, and II
6. Parenteral administration of 1 L of 10% dextrose in water provides the patient with approximately how many kcal of energy?
 - a. 100–150 kcal
 - b. 150–200 kcal
 - c. 300–350 kcal
 - d. 400–450 kcal
 - e. 700–750 kcal
7. A nutritional product is said to contain 12 g of protein, 24 g of carbohydrate, and 6 g of fat in each 100-mL serving. What is the caloric content of a serving?
 - a. 122.4 kcal
 - b. 183.6 kcal
 - c. 177.9 kcal
 - d. 368.6 kcal
 - e. 426.2 kcal
8. What caloric density value (kcal/g) should be used when calculating the amount of amino acids in infusion solutions?
 - a. 4 kcal/g
 - b. 9 kcal/g
 - c. 3.4 kcal/g
 - d. 6.2 kcal/g
 - e. None of the above
9. The fatty acid emulsion, Liposyn II:
 - a. provides calories.
 - b. causes the final solution to be cloudy.
 - c. prevents fatty acid deficiencies.
 - d. contains safflower oil, soybean oil, and egg phosphatides.
 - e. All of the above

10. Before the patient is administered a fat emulsion such as Liposyn II, the pharmacist should determine if the patient has an allergy to:
- I. eggs
 - II. peanuts
 - III. shellfish
- a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III

Basic Pharmacokinetics

28
CHAPTER

Pharmacokinetics is the study of the rate of movement of drugs within biological systems, or the study of what the body does to the drug, as characterized by drug absorption, distribution, metabolism, and excretion (ADME). It establishes a time course of the drug in the body and helps optimize drug therapy (Figure 28-1).

I. Absorption

- A. The rate at which the medication enters the systemic circulation
- B. Drug characteristics that affect absorption
 1. Formulation (e.g., enteric coating may prevent the drug from dissolving until it reaches small intestine)
 2. Solubility (water soluble or lipid soluble)
 3. Molecular weight
 4. Ionization
- C. Patient factors that affect absorption
 1. Route of administration (e.g., drug absorption is instantaneous with IV administration)
 2. Gastric pH
 3. Content of the GI tract
 4. Other concurrent medications
- D. Bioavailability is the fraction (F) of the dose that reaches systemic circulation
 1. Absolute bioavailability is the estimation of F for other routes of administration compared to IV administration (100% bioavailability or $F = 1$)
 2. Relative bioavailability is the estimation of F of a particular drug compared with another formulation of the same drug

E. Loading doses

1. Loading dose refers to the higher concentrations of a drug that may be administered at the initial course of treatment. It allows for a rapid achievement of therapeutic serum levels.

II. Distribution

- A. The movement of drug to the body's tissues
- B. Mechanisms
 1. Solubility in lipid (lipophilicity) as opposed to water (hydrophilicity)
 - a) Lipophilic drugs accumulate in adipose tissue.
 2. Affinity for various body tissues
 3. Blood flow to each of these tissues

4. Plasma protein binding

- a) Major plasma protein: albumin
 - (1) Acidic (anionic) drugs, including phenytoin, warfarin, and ibuprofen, bind to albumin.
 - (2) Basic drugs, including lidocaine and quinidine, bind to globulins.
- b) Factors that determine the degree of binding
 - (1) Amount of available binding sites
 - (2) Affinity of drug for plasma protein

C. Volume of distribution is the extent of drug distribution

III. Metabolism

- A. The removal of drug from the body by transforming the drug to less-active forms and other compounds
- B. Liver is the primary site of metabolism; other sites include blood and lungs
- C. Typically, drugs undergo two phases of drug metabolism (phase I and phase II)
 1. Phase I
 - a) Cytochrome P-450 (CYP) is the most important enzyme system of Phase I.

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Figure 28-1 — **Concentration and time of drug action.** (Reprinted by permission from Macmillan Publishers Ltd: *International Journal of Impotence Research*, 19:253-264, Sept. 21, 2006.)

- (1) CYP 450 enzymes may be induced or inhibited by other substances and are involved in many drug interactions.
- b) Reaction types
 - (1) Hydrolysis
 - (2) Oxidation
 - (3) Reduction
 - (4) Demethylation
 - (5) Methylation
 - (6) Alcohol dehydrogenase metabolism
2. Phase II
 - a) Conjugation reactions
 - (1) Acts on parent drug or phase I metabolite
 - b) Introduces highly polar conjugates
 - c) Conjugates readily excreted in urine
 - (1) More water soluble compared with parent compound
 - d) Reaction types
 - (1) Glucuronidation most common
 - (2) Acetylation
 - (3) Sulfoconjugation
- IV. Elimination
 - A. Removal of drug from the body as excreted into urine, lungs, bile, or sweat
 1. Pulmonary, expired in the air
 2. Bile, excreted in feces
 - a) Enterohepatic circulation
 3. Renal
 - a) Glomerular filtration
 - b) Tubular reabsorption
 - c) Tubular secretion
- V. Clearance
 - A. The volume of blood or plasma cleared of the drug per unit of time expressed as mL/min.
 - B. Most drugs are cleared through the kidneys by glomerular filtration, active tubular secretion, and passive tubular reabsorption.
- VI. Linear Pharmacokinetics
 - A. When the area under the curve (AUC) is proportional to the dose, the drug is said to follow linear kinetics. Increases in dosage result in proportional increases in plasma drug levels. Most drugs follow linear pharmacokinetics.
 - B. At steady state, the rate of drug administered is proportional to the amount of drug eliminated within one dosing interval, and the body reaches an equilibrium or constant serum or blood level.
 - C. Drugs that have a short half-life, such as gabapentin, reach steady state rapidly; drugs with a longer half-life, such as digoxin, require more time to reach steady state. Half-life is the time required for the body to decrease the amount of drug by half (50%). Generally, it takes 4–5 half-lives for the dosing of the drug to reach steady state.
- VII. Nonlinear Pharmacokinetics
 - A. When drugs do not change proportionally with the dose and the rate of elimination is constant regardless of amount of drug present, the drug is said to follow nonlinear pharmacokinetics (e.g., phenytoin).
 - B. When enzymes responsible for metabolism and elimination are saturated or occupied and the

result is nonproportional increases in drug levels, the occurrence is known as Michaelis-Menten kinetics (e.g., phenytoin).

REVIEW QUESTIONS

(Answers and Rationales on page 382.)

1. What is the correct definition for steady state?
 - I. Fraction of drug that reaches systemic circulation unchanged
 - II. Time required for half of the drug to be eliminated from the body
 - III. The rate of drug entering the body equals the rate of elimination
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
2. What is the half-life of a drug with a $V_d = 310/L/70\text{ kg}$, $CL = 72\text{ L/h/70 kg}$, and $F = 52$?
 - a. 1.5 hrs
 - b. 2 hrs
 - c. 3 hrs
 - d. 4 hrs
3. Drug absorption in patients with renal failure may be altered due to which of the following?
 - a. Gastric pH changes in gastrointestinal emptying time
 - b. Changes in gastrointestinal emptying time
 - c. Edema of the gastrointestinal tract
 - d. All of the above
4. What does “first pass effect” mean?
 - a. The process by which drug diffuses or is transferred from intravascular space to extravascular space (tissues)
 - b. The release of the drug from its dosage form
 - c. The elimination of unchanged drug or metabolite from the body
 - d. The hepatic metabolism of oral drugs before reaching systemic circulation
 - e. The movement of drug from the site of administration to the blood circulation
5. True or False: A phenytoin serum level does not have to be adjusted when serum albumin is reduced because it is highly protein bound.
 - a. True
 - b. False
6. CYP 450 enzymes are responsible for what type of metabolism reaction?
 - a. Oxidation
 - b. Methylation
 - c. Conjugation
 - d. Acetylation
7. True or False: Drug metabolism is a mechanism for elimination of drugs from the body.
 - a. True
 - b. False

8. Amphetamine is a weak base with a pK_a of 9.8. The urine of an overdose victim was found to have a pH of 8.0. What percentage of amphetamine would be ionized at this pH, and should the urine be acidified or alkalized to increase renal clearance?
 - a. 1.56%, acidified
 - b. 98.44%, acidified
 - c. 1.56%, alkalized
 - d. 98.44%, alkalized
9. A 64-year-old man has been taking phenytoin for 2 years and has come in for routine blood work. What is his adjusted phenytoin level and should he be given a loading dose to reach therapeutic range? (Height = 5' 10", weight = 187 lbs, phenytoin = 7.6 mcg/mL, albumin = 3.1 g/dL, SCr = 1.2 mg/dL)
 - a. 7.6 mcg/mL, requires loading dose
 - b. 10.56 mcg/mL, requires loading dose
 - c. 10.56 mcg/mL, does not require loading dose
 - d. 7.6 mcg/mL, does not require loading dose
10. A patient is given a 300-mg bolus of a drug and the initial concentration is determined to be 4.6 mg/L. What is the apparent volume of distribution of this drug in this patient?
 - a. 6.52 L
 - b. 65.2 L
 - c. 5.43 L
 - d. 54.3 L
11. If a 58-year-old, 176-lb (Height = 74 inches; IBLO = 81 kg) male patient has a serum creatinine of 2 mg/dL. What is the patient's estimated creatinine clearance?
 - a. 46 mg/dL
 - b. 58 mg/dL
 - c. 64 mg/dL
 - d. 66 mg/dL
12. Which statement is true regarding drug-drug interactions?
 - a. The effect of concomitant use of two separate drugs within the body
 - b. Not rarely encountered with modern drugs
 - c. Rarely of a serious nature
 - d. Only identified in patients with preexisting conditions
 - e. Almost always avoidable by ingesting drugs at different times during the day
13. Which of the following steady-state serum phenytoin concentrations is within the therapeutic range?
 - a. 15 mg/mL
 - b. 15 mcg/mL
 - c. 25 mg/mL
 - d. 25 mcg/mL
 - e. 5 mg/mL
14. Which of the following lithium levels is within the therapeutic range during initiation of therapy?
 - a. 0.4 meq/L
 - b. 0.6 meq/L
 - c. 1.2 meq/L
 - d. 2.0 meq/L
 - e. 2.4 meq/L
15. A patient is referred to a psychiatrist for major affective disorder. Which of the following medications will provide the onset of clinical activity?
 - a. Chlorpromazine
 - b. Lithium
 - c. Isocarboxazid
 - d. Protriptyline
 - e. None of the above
16. What statement is true regarding first order kinetics?
 - I. Drug is metabolized at a rate that is constant over time
 - II. Aspirin is metabolized via first order kinetics
 - III. $V = V_{max}[C]/K_m$
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
17. What drug undergoes phase II methylation?
 - a. Digoxin
 - b. Acetaminophen
 - c. Morphine
 - d. Diazepam
 - e. Dopamine
18. What is the correct definition for half-life?
 - I. Time required for half of the drug to be eliminated from the body
 - II. Fraction of drug that reaches systemic circulation unchanged
 - III. The rate of drug entering the body equals the rate of elimination
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
19. What factors influence drug bioavailability?
 - a. First pass effect
 - b. Solubility
 - c. Brand vs. Generic formulation
 - d. a and b
 - e. a, b, and c
20. Phase I reactions can be categorized into the following?
 - I. Oxidation
 - II. Reduction
 - III. Hydrolysis
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III
21. Solubility is LEAST affected by which of the following?
 - a. Sulfation
 - b. Hydroxylation

- c. Glutathione conjugation
d. Glucuronidation
e. a and d
22. Which of the following dosing routes would be chosen for limited first-pass effect and extended duration of action?
I. Transdermal
II. Rectal
III. Inhalation

a. I only
b. III only
c. I and II
d. II and III
e. I, II, and III
23. Which of the following routes of administration would avoid first-pass metabolism?
a. Oral
b. SC
c. IM
d. IV
e. b, c, and d
24. Clearance of theophylline is decreased by which of the following?
a. Albuterol
b. Atropine
c. Ipratropium
d. Cimetidine
e. Epinephrine
25. What drugs are substrates for cytochrome P-450 3A4 (CYP 3A4)?
I. Verapamil
II. Ethinyl estradiol
III. Quinidine

a. I only
b. III only
c. I and II
d. II and III
e. I, II, and III
26. What drug does NOT undergo glucuronidation?
a. Digoxin
b. Acetaminophen
c. Morphine
d. Diazepam
e. Dopamine
27. Which of the following dosing routes could be the most painful and can be administered in a depot preparation?
I. Transdermal
II. Rectal
III. Intramuscular

a. I only
b. III only
c. I and II
d. II and III
e. I, II, and III
28. Which of the following statements about first-order elimination is/are true?
a. Doubling the rate of administration of a first-order elimination drug will double the steady-state plasma concentration.
b. A constant amount of drug is eliminated per unit of time.
c. The amount of serum protein binding affects the volume of distribution.
d. a and b
e. a and c
29. What is the correct definition for bioavailability?
I. Time required for half of the drug to be eliminated from the body
II. The rate of drug entering the body equals the rate of elimination
III. Fraction of drug that reaches systemic circulation unchanged

a. I only
b. III only
c. I and II
d. II and III
e. I, II, and III
30. Which of the following statements regarding elimination half-life is/are INCORRECT?
a. It always increases with decreasing clearance.
b. It can be used to estimate time required to reach steady state concentration.
c. It is the time required for the total body amount of drug to be decreased by 50%.
d. a and b
e. b and c
31. Which of the following is a phase II reaction?
a. O-methylation
b. N-acetylation
c. Hydrolysis
d. Glucuronidation
e. a, b, and d
32. Rifampin induces CYP 3A4 enzymes.
a. True
b. False
33. Which of the following are alternative routes of administration to avoid first-pass effect?
I. suppository
II. sublingual
III. Intramuscular

a. I only
b. III only
c. I and II only
d. II and III only
e. I, II, and III
34. Phenobarbital induces cytochrome P-450 2C9 (CYP 2C9) enzymes.
a. True
b. False

35. Which does NOT affect the removal of a drug from plasma during hemodialysis?
- Protein binding
 - Volume of distribution
 - Bioavailability
 - Molecular size
36. Which of the following statements about elimination half-life is true?
- If total body clearance is doubled, elimination half-life is decreased.
 - If volume of distribution is doubled, elimination half-life is increased.
 - If total body clearance and volume of distribution are both decreased to the same degree, there will be no effect on elimination half-life.
 - All of the above
 - None of the above
37. Of the following, which strategy would best to minimize adverse drug events in patients with impaired renal function is to:
- Give smaller doses of the drug at the normal dose interval
 - Give the normal doses of the drug but prolong the dose interval
 - Minimize the number of medications given
 - Measure peak and trough drug levels after the third dose
38. Which of the following decreases theophylline clearance?
- Ranitidine
 - Cimetidine
 - Ciprofloxacin
 - a and c
 - b and c
39. Which of the following does NOT affect theophylline clearance?
- Ciprofloxacin
 - Warfarin
 - Erythromycin
 - a and c
 - b and c
40. Which of the following does NOT affect maintenance theophylline dosing?
- Smoking
 - Renal insufficiency
 - Concomitant medications
 - Cor pulmonale
 - Hepatic failure
41. Which of the following increases theophylline clearance?
- Emesis
 - Oral activated charcoal
 - Nasogastric lavage
 - Induced diuresis
 - All of the above
42. What is the half-life of digitoxin?
- 12 hours
 - 24 hours
 - 48 hours
 - 5 days
 - 7 days
43. Drug A is given as a rapid, single intravenous (IV) infusion to a 50 kg patient. The volume of distribution (V_d) for drug A is 2 L/kg. What is the predicted initial concentration (C_0) in plasma if a 500 mg dose is administered?
- 1 mcg/mL
 - 3 mcg/mL
 - 5 mcg/mL
 - 12 mcg/mL
 - 15 mcg/mL
44. Which 5-HT_{1B/1D} agonist has the lowest oral bioavailability?
- Amerge
 - Imitrex
 - Zelnorm
 - Axert
 - Frova
45. When a loading dose is administered, the initial drug concentration is dependent on which of the following?
- Elimination rate constant
 - Elimination half-life
 - Volume of distribution
 - Clearance
 - None of the above

I. Introduction

- A. Pharmacogenomics is the study of how interindividual genetic variations affect the response to drug therapy, including the influence of these variations on drug disposition (pharmacokinetics) and desirable or undesirable drug effects (pharmacodynamics). The term pharmacogenetics is closely related to pharmacogenomics, and the terms are often used interchangeably.¹
- B. There are small variations in genetic sequencing among humans. Genetic polymorphisms are DNA sequencing variations that occur with at least a frequency of 1% in the population; polymorphisms are responsible for significant alterations in the way a given person responds to a given drug. The effects may be pharmacokinetic or pharmacodynamic in nature; examples are given in the following review.
 1. **Pharmacokinetic effects:** Several genetic polymorphisms affecting drug metabolism via changes in enzymatic activity or transport proteins have been identified. Well-known examples include genetically-induced alterations in the activity of cytochrome P-450 (CYP) 2D6, CYP 2C19, and thiopurine methyltransferase. Many common drugs are affected by such alterations, including warfarin, codeine, antiarrhythmic agents, antidepressants, phenothiazine antipsychotics, and thiopurines such as mercaptopurine and azathioprine.
 2. **Pharmacodynamic effects:** Identifying expression of certain genetic traits within the context of a disease may result in more specifically targeted drug therapy with improved response rates and lowered risk for toxicity. Targets are often cellular receptors or signal transduction modulators. A well-known example is the development of the drug trastuzumab (Herceptin) and its activity in cancers (particularly breast cancer) where the over-expression of the ERBB2 (HER2/neu) oncogene is present in the tumor. Other examples include the recent findings that certain human leukocyte antigen (HLA) expressions predispose some patients to serious hypersensitivity reactions of specific medications. HLA proteins play a role in recognizing foreign substances in the body and in the subsequent immune responses.

Examples of drugs where HLA subtype expression plays a role in hypersensitivity include abacavir, allopurinol, carbamazepine, and phenytoin. Testing individuals for the expression of these HLA subtypes before selecting drug therapies may prevent serious adverse consequences in susceptible individuals. Certainly, genetic differences may also account for the presence of certain traits or diseases that may affect pharmacodynamic responses to drugs. Examples include Factor V Leiden mutations, which may predispose female patients with the mutation to be at risk of thromboembolism while taking oral contraceptives.

II. Benefits of Identifying Pharmacogenomic Variables

The field of pharmacogenomics is in its infancy. However, important and tangible recommendations for personalized prescribing are beginning to emerge. Pharmacogenomic variables are now identified for a few commonly prescribed drugs. Recommendations regarding laboratory testing and prescriber actions are now incorporated into the official prescribing literature for these drugs (Table 29-1). For other drugs, recommendations are not yet defined (Table 29-2). Pharmacogenomics is a rapidly changing discipline, and many factors, including health care costs, patient preferences, and the overall health of the patient will ultimately influence the individualization of any therapy.¹

A. Benefits that can be derived via better understanding of pharmacogenomics:

1. Identify populations at risk for significant allergy or toxicity; avoid risky medications in populations in which risk outweighs benefit
2. Potential for greater overall safety in the use or dosing of a particular drug, allowing drugs to remain marketed rather than pulled from market for safety
3. Ability to individualize drug therapy, increasing disease response rates via appropriate drug selection

III. Testing for Pharmacogenomic Data

A. There are two categories of pharmacogenomic tests.

1. FDA approved (not common)
2. Clinical Laboratory Improvement Amendments (CLIA)-compliant: independent laboratory test regulation program to ensure quality of testing

TABLE 29-1 Example Drugs With Known Pharmacogenomic Variables and Well Defined Recommendations in U.S. Product Labeling

Drug/Drug Class Generic (Trade Name)	Biomarker	Clinical Effect	Recommended Guidance from Package Label	Populations Affected (if known)
Abacavir (<i>Ziagen, Epzicom, Trizivir</i>)	HLA-B*5701	Increased risk of fatal/serious hypersensitivity reactions, which patients with allele are 114 times more likely to have	If biomarker present, starting or reinitiating an abacavir-containing regimen is not recommended ^{2,3}	No data available
Atomoxetine (<i>Strattera</i>)	CYP 2D6	Poor metabolizers have greater likelihood of adverse reactions; rapid metabolizers may have treatment failure	If poor metabolizers, initiate at lower starting dose; only increase to usual target dose if fail to improve after 4 weeks and initial dose well tolerated ⁴	Estimates of poor metabolizers: Caucasians 7% Asian 1%–2% Kun San Bushmen 18.8% African American 2%–3% See mercaptopurine notes
Azathioprine (<i>Imuran</i>)	Thiopurine methyltransferase (TPMT)	Patients with TPMT deficiency experience serious myelosuppression even with normal doses	Consider alternative if have low or absent TPMT; use caution in heterozygous patients; dosage reduction for those with reduced TPMT activity; monitor CBC closely ⁵	
Carbamazepine (<i>Carbatrol, Equetro, Tegretol</i>)	HLA-B*1502	If allele is present, increased risk of serious hypersensitivity reactions, such as Stevens-Johnson syndrome or toxic epidermal necrolysis (TENS)	Do not use in patients with positive biomarker unless treatment benefit clearly outweighs risk of potentially fatal skin reaction ⁶	Variation is found almost exclusively in persons of Asian descent, estimated as follows: 15% in Hong Kong, Thailand, Malaysia, and Philippines 10% in Taiwan 4% in North China Roughly 2%–4% in South Asia (e.g., India) <1% in Japan and Korea Rapid metabolizer estimates: Chinese 0.5%–1% Japanese 0.5%–1% Hispanic 0.5%–1% Caucasian 1%–10% African American 3% Ethiopians, North Africans, Arabs 16%–28%
Codeine (<i>Tylenol with codeine, others</i>)	CYP 2D6	Greater risk of adverse drug reaction (ADR) in rapid metabolizers or in breast-fed infants whose mothers are rapid metabolizers; rapid metabolism of codeine results in higher than expected serum morphine levels (morphine is the metabolite); a specific CYP 2D6*2x2 phenotype is responsible; may cause extreme sleepiness, confusion, or shallow breathing Poor metabolizers may have treatment failures	Choose the lowest effective dose for the shortest period of time and inform patient/caretaker about these risks and the signs of morphine overdose in patients, including breast-fed infants ⁷	

Continued

TABLE 29-1 Example Drugs With Known Pharmacogenomic Variables and Well Defined Recommendations in U.S. Product Labeling—cont'd

Drug/Drug Class Generic (<i>Trade Name</i>)	Biomarker	Clinical Effect	Recommended Guidance from Package Label	Populations Affected (if known)
Irinotecan (<i>Camptosar</i>)	UGT1A1	Patients with deficiency of UGT1A1 are at risk of severe toxicities (GI and neutropenia)	If homozygous for UGT1A1*28 allele, starting dose reductions are specified ⁸	Roughly 10% of North Americans are homozygous for UGT1A1*28
6-Mercaptopurine (<i>Purinethol</i>)	Thiopurine methyltransferase (TPMT)	Patients with TPMT deficiency experience serious myelosuppression even with normal doses	Patients with inherited little or no TPMT activity require substantial dose reduction; some patients with heterozygous TPMT deficiency require dose reduction ⁹	3 alleles—TPMT*2, TPMT*3A, and TPMT*3C—account for 95% of those with reduced TPMT activity; those homozygous for these alleles are deficient; those heterozygous have variable TPMT (low or intermediate) activity
Thioguanine (<i>Tabloid</i>)	Thiopurine methyltransferase (TPMT)	Patients with TPMT deficiency experience serious myelosuppression even with normal doses	Patients with inherited little or no TPMT activity require substantial dose reduction ¹⁰	See mercaptopurine notes
Trastuzumab (<i>Herceptin</i>)	ERBB2 (HER2/neu) oncogene	Drug targets tumors that overexpress this genetic	Drug is used only if oncogene is present ¹¹	25%–30% of primary breast cancers express the oncogene
Warfarin (<i>Coumadin</i> , <i>Jantoven</i>)	CYP 2C9	Slow metabolizers (those with CYP 2C9*2 or *3 variants) may need a lower dose or take longer to achieve target maintenance dosing; may be at increased risk of bleeding	Consider lower initiation doses for patients with certain genetic variations in CYP 2C9; essential to monitor the patient's prothrombin time (PT) and international normalized Ratio (INR) and adjust doses accordingly ¹²	Specific data not available
Warfarin (<i>Coumadin</i> , <i>Jantoven</i>)	Vitamin K epoxide reductase (VKORC1)	Patients with variants of VKORC1 may be at increased risk of bleeding; lower doses may be needed with closer monitoring of treatment	Consider lower initiation and maintenance doses for patients with certain genetic variations in VKORC1; essential to monitor the patient's PT and INR and adjust doses accordingly ¹²	Specific data not available

Table 29-2 Other Drugs with Pharmacogenomic Variables*

Drug/Drug Class	Biomarker	Potential Clinical Effect
Antidepressants Antipsychotics Antiarrhythmics Beta blockers	CYP 2D6	For selected drugs in classes only Greater likelihood of ADR or need for dose reduction in poor metabolizers; possible treatment failures in rapid metabolizers
5-Fluorouracil or capecitabine	Dihydropyridine dehydrogenase (DPD)	Rare, unexpected, and severe toxicity (e.g., stomatitis, diarrhea, neutropenia, and neurotoxicity) attributed to deficiency of DPD activity
Other chemotherapy agents	Various (e.g., tyrosine kinase, CYP variants)	Results in prolonged clearance of these chemotherapies Targeting of cells with various markers results in increased chemotherapy efficacy
General anesthetics	Ryanodine receptor (RyR1)	Poor metabolizers may have risk for drug toxicity Increased risk of malignant hyperthermia if biomarker is present
Oral contraceptives (OC) or tamoxifen	Factor V Leiden mutations	May increase risk for deep vein thrombosis or other blood clots
Proton pump inhibitors (PPI)	CYP 2C19	Rapid metabolizers may experience treatment failures

*Defined action may be available in future, currently prescriber actions not well defined.

B. As of early 2009, the following pharmacogenomic tests were FDA approved

1. Amplichip (tests for CYP 2D6, CYP 2C19)
2. Invader Assay (tests for UGT1A1)

C. FDA approval of other tests is currently pending. Several tests can also be ordered from independent CLIA-compliant laboratories. There is a searchable database for these laboratory tests at <http://www.fda.gov/cdrh/clia>.

IV. Conclusion

Pharmacists and other health care providers are encouraged to familiarize themselves with current guidance and rapid changes occurring in the field of pharmacogenomics. Current guidance has resulted in strong recommendations for screening before initiation of drug therapy or for the adjustment of drug dosages during therapy for selected drugs. Continuing education programs are available through organizations such as the American Medical Association and Food and Drug Administration.¹³

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REVIEW QUESTIONS

(Answers and Rationales on page 384.)

1. Which of the following statements about codeine would indicate that a patient is a poor metabolizer of CYP 2D6?
 - a. "I took codeine once after surgery. It worked very well and fast, but I got dizzy and pretty sleepy."
 - b. "I took codeine once after surgery, and to be honest, it did not seem to do that much for me. They switched my medication to morphine and that was much better."
 - c. "Codeine worked for me just fine, and I did not have any side effects."

2. Which of the following best describes the proper use of trastuzumab for breast cancer?
 - a. In patients with positive estrogen receptors
 - b. In patients who overexpress the ERBB2 (HER2/neu) oncogene
 - c. To target a tumor necrosis factor (TNF) within the tumor
3. A young male patient with newly diagnosed HIV infection is being considered for treatment with an abacavir-containing regimen to increase compliance. His genetic testing comes back positive for the HLA-B*5701 allele. What is the best course of action for this patient?
 - a. Initiate abacavir at a low dosage and monitor for side effects
 - b. Choose an alternative to abacavir for this patient
 - c. Continue with abacavir regimen as planned
4. A lower starting dosage is recommended for patients who take warfarin and have reduced activity of:
 - I. CYP 2C9
 - II. CYP 3A4
 - III. CYP 2D6
 - IV. VKORC1
 - a. Both I and IV
 - b. II only
 - c. Both II and III
 - d. IV only

- I. Basic Definitions
 - A. Toxicology refers to the study of poisons and toxins and how they interact with the body, both internal and external.
 - B. Clinical toxicology focuses on the toxic effects of therapeutic agents and nontherapeutic agents including drugs of abuse, household products, pesticides, metals, radiation, and other chemicals entities.
- II. General Approach
 - A. ABCs and D
 1. Airway
 2. Breathing
 3. Circulation
 4. Decontamination
 - B. Medical history
 1. Medications (Prescription, over-the-counter [OTC], herbals, supplements, vitamins, illicit drugs)
 2. Alcohol use
 3. Allergies
 4. Occupation
 - C. Physical examination
 1. Vital signs: blood pressure, heart rate, respiratory rate, temperature
 2. Mouth
 3. Pupils
 4. Breath sounds
 5. Bowel sounds
 6. Skin
 7. Urination
 8. Neurologic exam
 - D. Laboratory tests and imaging
 1. Complete blood cell (CBC) count
 2. Electrolytes
 3. Urinalysis
 4. Blood glucose
 5. Blood urea nitrogen (BUN)
 - E. Diagnosis, antidotes
 1. Decontamination
 - a. Skin
 1. Protect yourself
 2. Remove clothing
 3. Flush with water or normal saline
 - b. Eye
 1. Remove contact lens and discard it
 2. Flush with water or normal saline
 - c. Inhalation
 1. Observe for airway obstruction
 2. Intubate if necessary
- d. Gastrointestinal
 1. Induce emesis
 - a. Syrup of ipecac
 - 1) Consume within minutes of ingestion (30 mL repeated after 20 minutes if ineffective)
 - 2) Contraindicated when the patient is comatose, lethargic, having convulsions, unable to protect his/her airway, caustic or alkali ingestions
 - 3) Rarely given; no longer recommended by the American Association of Poison Control Centers
 2. Gastric lavage
 - a) Use for ingestions of highly toxic substances and substances not well absorbed by active charcoal (lithium, lead, iron); patients with altered mental status or alertness
 3. Activated charcoal
 - a) Cannot bind acids, bases, ethanol (EtOH), methanol, ethylene glycol, hydrocarbons, iron, lead, lithium, potassium, mercury
 - b) Commonly used for poisonings with carbamazepine, phenytoin, salicylates, digitalis, and theophylline
 - c) Multiple dosing: 1 g/kg every 2–6 hours
 - d) Most effective when given within 2 hours of ingestion
 - e) Most useful for poisons that are enterohepatic recycled
 - f) Adverse effects: chemical pneumonitis caused by charcoal aspiration
 4. Cathartics
 - a) Purgative agent used to evacuate the bowels
 - b) Example: sorbitol
- III. Specific Toxins and Management
 - A. Acetaminophen
 1. Narrow therapeutic range. Maximum dose: 4 g daily or 90 mg/kg daily (children); lower in patients with hepatic disease or with concomitant alcohol use.
 2. Presentation
 - a. Stage I (0–24 hours): nausea, vomiting (primarily asymptomatic)

- b. Stage II, latent stage (24–48 hours): increase in liver function tests (e.g., Alanine Aminotransferase [ALT], Aspartate Aminotransferase [AST], and bilirubin)
 - c. Stage III, hepatic stage (3–4 days): liver failure, jaundice, vomiting, hypoglycemia, renal failure, metabolic acidosis
 - d. Stage IV, recovery stage (4 days–2 weeks): resolution of hepatic dysfunction
 3. Influential factors of toxicity
 - a. Chronic alcoholics and the elderly are at an increased risk for hepatic disease even at therapeutic doses
 - b. Glucose 6 phosphate dehydrogenase (G6PD) deficiency
 4. Management
 - a. GI decontamination with activated charcoal
 - b. Antidote: in patients with toxic blood levels, *N*-acetylcysteine 140 mg/kg loading dose, then 70 mg/kg every 4 hours for 17 doses
 - B. Anticholinergics
 1. Agents with anticholinergic properties
 - a. Atropine
 - b. Antihistamines (e.g., diphenhydramine, meclizine, promethazine)
 - c. Antipsychotics (e.g., clozapine, thioridazine)
 - d. Antispasmodics (e.g., dicyclomine, oxybutynin)
 - e. Tricyclic antidepressants (e.g., amitriptyline, imipramine)
 - f. Mydriatics (e.g., homatropine)
 - g. Botanicals (e.g., *Atropa belladonna*, *Datura stramonium*)
 2. Presentation: dry mucous membranes, altered mental status, flushed skin, mydriasis, fever, tachycardia, hypertension, urinary retention, seizures
 3. Laboratory evaluation: no specific diagnostic studies exist
 4. Management
 - a. ABCs
 - b. GI decontamination
 - c. Activated charcoal
 - d. Supportive care
 - 1) Tachycardia: crystalloid infusions
 - 2) Agitation: benzodiazepines
 - 3) Fever: fluids, antipyretics
 - e. Antidote: physostigmine 2 mg IV at a slow, controlled rate (no faster than 4 minutes)
 - C. Benzodiazepines
 1. Presentation: drowsiness, slurred speech, nystagmus, ataxia, hypotension, coma with respiratory depression
 2. Management
 - a. Gastric lavage
 - b. Antidote: flumazenil (Romazicon)
 - 1) Used in severe overdose (i.e., comatose patient) and patients with significant cardiorespiratory depression
 - 2) IV dose: 0.2 mg IV in 30 seconds; repeat doses of 0.3 mg in 30 seconds at 1-minute intervals
 - 3) Do not exceed 3 mg in 1 hour
 - 4) Avoid in patients with mixed overdose particularly those who have taken tricyclic antidepressants; flumazenil may induce seizures
 - D. Digoxin
 1. Presentation: nausea, vomiting, diarrhea
 - a. Acute: asymptomatic for hours followed by gastrointestinal symptoms; bradydysrhythmias or supraventricular with AV block, high digoxin levels, hyperkalemia, visual changes (halos, blurred vision, changes in color perception)
 - b. Chronic: altered mental status, flu-like symptoms, gastroenteritis, dysrhythmias, lower potassium levels
 2. Complications: hyperkalemia, arrhythmias (initially as sinus bradycardia, followed by atrial tachyarrhythmias with or without heart block)
 3. Laboratory evaluation
 - a. Potassium
 - 1) After acute poisoning, potassium may become dangerously elevated.
 - 2) Temporary elevated potassium levels are acceptable in chronic toxicity.
 - 3) High potassium levels may offer protection because hypokalemia increases glycoside binding to the Na-K pump and worsens poisoning of the pump.
 - b. Digoxin levels
 - 1) Therapeutic level: 0.5–2 ng/μL
 - c. Renal and hepatic function
 4. Management
 - a) Activated charcoal
 - b) Manage hyperkalemia or hypokalemia
 - c) Sinus bradyarrhythmias and AV block: atropine
 - d) Ventricular tachycarrythmias: IV phenytoin
 - e) Digoxin-specific Fab antibodies (Digibind)
- Dose (vials [40mg]) = (ingested digoxin[mg]) (0.81)/0.6
OR
Dose (vials) = (digoxin concentration [ng/mL]) (body weight[kg])/100
- 1) Adverse effects: hypokalemia from rapid digoxin removal, cardiogenic shock, hypersensitivity reactions (rare)
- E. Salicylates
 1. Presentation: tachypnea, tachycardia, hyperthermia, altered serum glucose, dehydration, abdominal pain, nausea/vomiting, tinnitus, lethargy, altered mental status, seizures, respiratory alkalosis, metabolic acidosis
 2. Toxic dose: 160 mg/kg
 3. Lethal dose: 480 mg/kg
 4. Complications: hypokalemia, hyperglycemia, pulmonary edema, acute renal failure, GI bleed, hypoprothrombinemia
 5. Management
 - a. ABCs

- b. Activated charcoal with sodium bicarbonate
 - c. Urinary alkalinization (initiate when serum level is > 35 mg/dL) achieved by administration of sodium bicarbonate
 - d. Dialysis for severe acidemia, volume overload, pulmonary edema, cardiac or renal failure, seizures, coma, or levels of more than 100 mg/dL in acute ingestion or more than 60–80 mg/dL in chronic ingestion
- F. Cyclic antidepressants
- 1. Examples: amitriptyline, doxepin, imipramine
 - 2. Presentation: dry mouth, blurred vision, sinus tachycardia, urinary retention, myoclonic jerking, agitation, hallucinations, quinidine-like arrhythmias, hypotension, convulsions, coma
 - 3. Management
 - a. Activated charcoal
 - b. Alkalinization
 - c. Benzodiazepines (diazepam) or phenytoin to control seizures
- G. Sympathomimetics
- 1. Examples: amphetamines, cocaine, PCP, LSD
 - 2. Presentation: tremor, agitation, moist skin (sweating), mydriasis, hypertension, delirium, seizure
 - 3. Laboratory evaluation: electrolytes, BUN, creatinine, blood glucose, creatinine kinase (CK) levels, urine drug screening
 - 4. Management
 - a. Supportive care: ABCs
 - b. For agitation, benzodiazepines (diazepam, lorazepam) may be used.
 - c. Butyrophenones (e.g., haloperidol) are NOT recommended as they may lower seizure thresholds and prolong QT duration
 - d. For hypertension, an easily titrated agent such as nitroprusside may be used.
 - e. For QRS prolongation, ventricular arrhythmias, and hypotension, intravenous sodium bicarbonate is used.
- H. Warfarin
- 1. Presentation: bleeding, nosebleeds, bleeding of gums, vomiting blood, dark brown urine, red or black color in stool, unusual pain or swelling, headache, dizziness, weakness
 - 2. Laboratory evaluation
 - a. Prothrombin time (PT), international normalized ratio (INR), bleeding time
 - 3. Management
 - a. Acute
 - 1) Activated charcoal
 - 2) Gastric lavage
 - 3) If the PT is elevated, treat with vitamin K. Patients with acute hemorrhage may be administered fresh frozen plasma (FFP).
 - b. Chronic
 - 1) If INR is higher than therapeutic levels but less than 6 and the patient is not bleeding, withhold warfarin for 2–3 days and restart when the INR approaches the therapeutic range.
 - 2) If INR is between 6 and 10 and the patient is not bleeding, administer 5–10 mg of vitamin K₁ orally.
 - 3) If the INR is higher than 10 and the patient is not bleeding, a higher dose of vitamin K₁ may be administered.
 - 4) If INR $>$ or $= 9.0$ and bleeding, vitamin K is given parenterally. Consult hematology. May require fresh frozen plasma.
- I. Beta blockers
- 1. Presentation: hypotension, bradycardia, lethargy, bronchospasm (rare), seizures
 - 2. Laboratory evaluation
 - a. Blood glucose, electrolytes (potassium), electrocardiogram
 - 3. Management
 - a. Activated charcoal, gastric lavage
 - b. Glucagon (adults): 3–10 mg IV bolus followed by 2–5 mg/h infusion
 - c. Benzodiazepines if seizures occur
- J. Calcium channel blockers
- 1. Presentation: hypotension, bradycardia, altered mental status, seizures
 - 2. Laboratory evaluation
 - a. Blood glucose, arterial blood gas (ABG)
 - 3. Management
 - a. Activated charcoal
 - b. Gastric lavage
 - c. Glucagon 5–15 mg IV bolus followed by infusion of 10–15 mg/h
 - d. Calcium chloride bolus of 1–2 grams (10–20 mL 10%) plus continuous infusion of 20–40 mg/kg per hour (0.2–0.4 mL/kg per hour 10%)
- K. Cyanide
- 1. Presentation: tachypnea, bradypnea, tachycardia, bradycardia, hypoxia, hypotension, mydriasis, shock, seizures
 - 2. Laboratory evaluation: cyanide levels, blood gases, serum lactate, hemoglobin, electrolytes
 - 3. Management
 - a. Hydroxocobalamin: 50 mg/kg IV in 30 minutes or 5 g IV in 30 minutes (faster if patient is in cardiac arrest); may repeat dose once. Do not exceed total dose of 15 g; when repeated, infusion should be slow, lasting 8 hours.
 - b. Amyl nitrite: one ampule crushed and inhaled every 30 seconds until IV access is available for administration of sodium nitrite
 - c. Sodium nitrite: 10 mL of 3% solution slow IV push during 2–5 minutes
 - d. Sodium thiosulfate: 50 mL of a 25% solution (12.5 g) IV infused at 5 mL/min; 25 mL of solution may be administered 30 minutes after first dose
- L. Ethylene glycol (antifreeze)
- 1. Ingredient in radiator fluid
 - 2. Presentation
 - a. Stage 1, neurological (30 minutes to 12 hours after ingestion): nausea, vomiting, transient inebriation, euphoria, coma associated with hypotonia, hyporeflexia, occasional seizures, and meningismus

- b. Stage 2, cardiopulmonary (12–24 hours after ingestion): tachycardia, hypertension, compensatory hyperventilation
 - c. Stage 3, renal (24–72 hours after ingestion): oliguria, flank pain, acute tubular necrosis, renal failure, bone marrow suppression (rare)
 3. Laboratory test: calcium level, arterial blood gas, urinalysis
 4. Management
 - a. Gastric lavage within 30 minutes of ingestion
 - b. Fomepizole: Loading dose: 15 mg/kg IV in 30 minutes; maintenance dose: 15 mg/kg IV every 12 hours until patient is asymptomatic with a normal pH level and the ethylene glycol level is <20 mg/dL
 - c. Ethanol (EtOH) (when fomepizole is not available):
 - 1) Loading dose (IV): 7.6–10 mL/kg IV of 10% ethanol (v/v) in dextrose 5% in water during 30 minutes to achieve blood EtOH concentration of 100–130 mg/dL (21.7–28.2 mmol/L)
 - 2) Loading dose (oral): 0.8–1 mL/kg PO of 95% ethanol in 6 oz of orange juice during 30 minutes
 - 3) Maintenance doses (PO/IV): 0.15 mL/kg per hour PO of 95% EtOH; 1.4 mL/kg per hour IV of a 10% solution
 - a) Add Pyridoxine 100 mg IV four times daily for 2 days
 - b) Add Thiamine 50 mg IV four times daily for 2 days
- M. Iron**
1. Presentation: somnolence, hyperventilation from acidosis, cardiovascular collapse, abdominal tenderness, muscle rigidity, loose stool, pulmonary edema, altered mental status
 2. Laboratory evaluation: serum iron concentration, CBC, electrolytes, renal profile, liver function tests, PT/INR, acid-base measurements
 - a. Iron levels drawn more than 6 hours after ingestion may not accurately portray level of toxicity due to ferritin-binding and iron redistribution
 3. Management: deferoxamine mesylate
 - a. Indication: peak serum iron level greater than 500 mcg/dL, shock, lethargy/coma, persistent diarrhea or vomiting, anion gap acidosis, or a significant number of pills visualized on radiograph
 - b. Dose: 1000 mg IM, followed by 500 mg 4 and 8 hours later; based on the response of the patient, 500 mg may be administered every 4–12 hours IM; do not exceed 6000 mg in 24 hours
- N. Opioids**
1. Presentation: drowsiness, euphoria, depressed consciousness, CNS depression, respiratory depression, papillary miosis, ventricular arrhythmias, seizures, mydriasis
 2. Laboratory evaluations
 - a. ABGs
 - b. Toxicology screen
 - c. CBC
 - d. Metabolic panel
 3. Management
 - a. Naloxone (Narcan)
 - 1) Opioid antagonist
 - 2) Short half-life
 - 3) Dose: 0.1–2 mg/dose IV/IM (dose varies depending on the circumstance); may repeat in 1- to 2-minute intervals following IV use and 10-minute intervals after IM administration
 - 4) Discontinue treatment as soon as desired degree of opioid reversal achieved
- O. Organophosphates**
1. Presentation: cholinergic stimulation (SLUDGE = salivation, lacrimation, urination, diarrhea, GI upset, emesis) and DUMBELS (diaphoresis and diarrhea; urination; miosis; bradycardia, bronchospasm, bronchorrhea; emesis; excess lacrimation; and salivation)
 2. Laboratory evaluation: RBC cholinesterase
 3. Management
 - a. Decontamination
 - b. Atropine: 1–2 mg IV bolus, repeat every 3–5 minutes as needed for desired effects (drying of pulmonary secretions and adequate oxygenation)
 - c. Pralidoxime (2-PAM): 1–2 g IV in 100 mL isotonic sodium chloride solution/D5W in 15–30 minutes; repeat in 1 hour. If muscle weakness is not relieved, repeat every 3–8 hours if signs of poisoning reoccur
 - d. Benzodiazepines (e.g., diazepam): for treatment of seizures

REVIEW QUESTIONS

(Answers and Rationales on page 384.)

1. A 62-year-old African American man presents to the emergency department complaining of weakness, palpitations and dizziness; he also has low blood pressure. The patient has prolonged QRS complex. It appears that the patient has ingested a toxic amount of amitriptyline. The patient should receive which of the following?
 - a. Sodium bicarbonate
 - b. Ipecac
 - c. Calcium chloride
 - d. Epinephrine
 - e. None of the above
2. Which of the following may be used in treatment of cyanide overdose?
 - I. Amyl nitrite
 - II. Sodium thiosulfate
 - III. Hydroxocobalamin
 - a. I only
 - b. III only
 - c. I and II
 - d. II and III
 - e. I, II, and III

3. A 22-year-old woman presents to the emergency department 3 hours after ingesting 50 acetaminophen tablets (500 mg). Her initial acetaminophen level was 122 mcg/mL approximately 4 hours after ingestion. What is the most appropriate treatment for this patient?
- Forced hyperventilation
 - Sodium bicarbonate
 - Lorazepam
 - Esmolol
 - N*-Acetylcysteine repeated in 4 hours
4. An elderly woman presents to the pharmacy inquiring about ipecac. She would like to keep a bottle in her daughter's house in case of an emergency. What is the most appropriate response?
- Providing her the phone number of a poison control center
 - Informing her that ipecac is no longer recommended by the American Association of Poison Control Centers
 - Dispensing a bottle of ipecac that is kept behind the counter
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
5. What is/are the major effect(s) of anticholinergic toxicity?
- Tachycardia
 - Dry mucus membranes
 - Urinary retention
- I only
 - III only
 - I and II
 - II and III
 - I, II, and III
6. A 28-year-old woman with a history of depression and post-traumatic stress disorder presents to the emergency department 5 hours after ingesting 500 tablets of aspirin (325 mg each) as a suicide attempt. She denies ingesting any other chemical or drug. Vital signs: heart rate 118 beats per minute; blood pressure 112/60 mm Hg; respiratory rate 22 breaths per minute; temperature 99°F. Serum drug screen reveals a salicylate level of 630 mcg/mL. What is the most appropriate initial treatment for this patient?
- N*-Acetylcysteine
 - Vitamin K
 - Sodium bicarbonate
 - Charcoal and sorbitol
 - Ipecac
7. Which of the following agents would NOT be used for ethylene glycol toxicity?
- Ethanol (EtOH)
 - Fomepizole
 - Pyridoxine
 - Atropine
 - Thiamine
8. Which of the following is the antidote for morphine overdose?
- Sodium bicarbonate
 - Naloxone
 - Thiamine
 - Haloperidol
 - Diazepam
9. Flumazenil is used as an antidote for which of the following circumstances?
- Cocaine overdose
 - Acetaminophen overdose
 - Amitriptyline overdose
 - Alprazolam overdose
 - Iron overdose
10. A 72-year-old woman (80 kg) with normal renal function has accidentally been taking twice the prescribed dose of digoxin. Her digoxin serum concentration is 4.1 ng/mL. What is the appropriate dose of Digibind for this patient?
- 2 vials
 - 4 vials
 - 6 vials
 - 8 vials
 - 10 vials

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Drug Interactions

A

APPENDIX

Drug-drug interactions are a subset of adverse drug events that account for 3%–5% of medication errors. An interaction occurs when the effects of a medication are changed by the reaction with another drug, food, dietary supplement, or environmental chemical. The drug affected by the interactions is the “object drug.” The drug that causes the interaction is considered the “precipitant drug.” Drug interactions can cause toxic effects, enhance therapeutic effects, or be clinically insignificant.

Drug interactions typically arise in one of two ways: *pharmacokinetic* or *pharmacodynamic* interactions. With pharmacokinetic interactions, the absorption, distribution, metabolism, or excretion of a drug is altered by another. Blood levels of given drugs may be lowered or raised, depending on the type of interaction. With pharmacodynamic interactions, the pharmacologic response to one drug is altered by the coadministration of another; synergistic or antagonistic effects can occur.

PHARMACOKINETIC DRUG INTERACTIONS

ABSORPTION

One type of pharmacokinetic interaction involves a change in the absorption of a drug from the gastrointestinal (GI) tract. For example, bile acid sequestrants such as cholestyramine and colestipol can bind and impair the absorption of many concurrent drugs, especially warfarin, levothyroxine, digoxin, and thiazide diuretics. The absorption of some drugs, such as fluoroquinolones, is reduced when administered with multivalent cations, including those found in antacids such as aluminum, magnesium, and calcium. Other drugs have pH-dependent absorption and may be increased or decreased by drugs that alter stomach pH. An alteration in pH by antacids, for example, can alter the absorption of other drugs. For example, itraconazole requires an acidic environment for proper oral absorption; administration with antacids decreases itraconazole serum concentrations.

ENZYME INHIBITION AND INDUCTION

The liver is the principal site of drug metabolism. The gastrointestinal tract, skin, kidney, and lung are other sites of metabolism. Drug metabolism is carried out by enzyme systems. The hepatic cytochrome P-450 (CYP 450) enzyme superfamily is responsible for the metabolism of numerous compounds. The major families involved in drug metabolism are CYP 1A2, CYP 2C19, CYP 2C9, CYP 2D6, CYP 2E1, and CYP 3A. More than one isoform may play a role in metabolism of a drug. The CYP 3A enzyme family is

responsible for the greatest number of drug-drug interactions (Table A-1).

Many drug interactions are a result of the inhibition or induction of the CYP enzymes by a precipitant drug (the drug causing the inhibition or induction) and the resulting effect on the object drug (the affected substrate). Enzyme inhibition typically involves competition with another drug for the enzyme binding site. Drugs that inhibit CYP may increase plasma concentrations of other concurrently used drugs. For example, ketoconazole strongly inhibits CYP 3A4, the enzyme responsible for metabolism of triazolam in the gut wall and the liver. When these two drugs are given concomitantly, the metabolism of triazolam is decreased to such a degree that the patient is exposed to approximately 17 times more drug. If a substrate is metabolized to an active metabolite, CYP enzyme inhibition may result in less active metabolite formed and a reduced clinical effect.

Enzyme induction occurs when a drug stimulates the synthesis of more enzyme protein, thereby increasing the metabolism of substrates and generally leading to decreased drug effect. However, increased drug effect can occur if a substrate is metabolized to an active metabolite; enzyme induction for such substrates results in more active metabolite.

DRUG EFFLUX

Many drug interactions may also be linked to the modulation of P-glycoprotein (P-gp), an adenosine triphosphate (ATP)-dependent intracellular tissue-specific transport system. A drug that inhibits or induces P-gp affects its ability to transport a substrate drug or affects the exposure of the drug to metabolizing enzymes. For example, cyclosporine is an inhibitor of CYP 3A4 and of P-gp and may increase plasma concentrations of the “statin” cholesterol medications, which are substrates for P-gp. This interaction may lead to myalgia, weakness, and rhabdomyolysis. When concurrently administered with cyclosporine, the dosage of the statins should be reduced according to label recommendations.

RENAL ELIMINATION

The renal tubules are an important part of elimination for some drugs such as dofetilide. Renal elimination of dofetilide involves both glomerular filtration and active tubular secretion (via the cation transport system). The cation transport system within the renal tubule can be inhibited by medications such as cimetidine, leading to substantial dofetilide toxicity. As a result, dofetilide must not be used with any medications that inhibit active renal

Table A-1 Substrates, Inhibitors, and Inducers of CYP 450 Isoforms

CYP Isoform	Substrates	Inhibitors	Inducers
CYP 1A2	Amitriptyline, clomipramine, imipramine, propranolol, theophylline, tacrine, R-warfarin	Amiodarone, fluoroquinolones, fluvoxamine	Omeprazole, phenobarbital, phenytoin, cigarette smoking, charcoal-broiled meat
CYP 2C9	NSAID, phenytoin, S-warfarin, torsemide	Amiodarone, clopidogrel, fluconazole, fluvastatin, lovastatin, metronidazole, ritonavir, voriconazole, zafrilukast	Rifampin, carbamazepine, phenobarbital
CYP 2D6	Antidepressants (amitriptyline, clomipramine, fluoxetine, venlafaxine), antipsychotics (haloperidol, risperidone), beta blockers (metoprolol, propranolol, timolol), codeine, tramadol	Amiodarone, cimetidine, fluoxetine, paroxetine, fluphenazine, haloperidol, thioridazine	
CYP 2E	Acetaminophen, ethanol	Disulfiram	Ethanol, isoniazid
CYP 3A	Amitriptyline, benzodiazepines (alprazolam, triazolam, midazolam), calcium channel blockers, carbamazepine, cisapride, dexamethasone, erythromycin, ethinyl estradiol, glyburide, imipramine, ketoconazole, lovastatin, nefazodone, terfenadine, sertraline, theophylline, venlafaxine, protease inhibitors (ritonavir, saquinavir, indinavir, nelfinavir)	Protease inhibitors, azole antifungals (ketoconazole, itraconazole), amiodarone, cimetidine, diltiazem, erythromycin, grapefruit juice	Barbiturates, glucocorticoids, carbamazepine, efavirenz, nevirapine, phenytoin, pioglitazone, rifampin, St. John's wort

Hansten PD, Horn JR: Cytochrome P450 Enzymes and Drug Interactions, Table of Cytochrome P450 Substrates, Inhibitors, Inducers and P-glycoprotein, with Footnotes. In: *The Top 100 Drug Interactions - A guide to Patient Management*. 2008 Edition. Freeland, WA: H&H Publications; 2008:142–157.

tubular secretion. Metformin is another medication heavily dependent on renal tubular secretion; any medications competing for or reducing renal tubular secretion capacity of metformin may result in metformin accumulation and lactic acidosis.

PHARMACODYNAMIC DRUG INTERACTIONS

SYNERGISTIC EFFECTS

When the effect of two drugs is greater than the effects predicted by the individual compounds, a synergistic pharmacodynamic effect occurs. For example, concurrent use of zidovudine with lamivudine and abacavir produces a greater antiviral effect against HIV.

ADDITIVE EFFECTS

If the effect of two drugs is the sum of the effects of each, an additive pharmacodynamic effect occurs. For example, acetaminophen and narcotic analgesics are used together to provide added pain relief.

ANTAGONISTIC EFFECTS

An antagonistic effect occurs when drugs oppose each other and the effect of two drugs is less than the sum of their individual effects. For example nonsteroidal anti-inflammatory drugs (NSAID) may increase blood pressure and may inhibit the antihypertensive effect of such drugs as angiotensin-converting enzyme (ACE) inhibitors.

CATEGORIES OF DRUG INTERACTIONS

DRUG-DRUG INTERACTION

As stated, a drug-drug interaction is an alteration of the effect of a drug when administered with another drug. This includes prescription and over-the-counter (OTC) medications.

DRUG-HERB/DIETARY SUPPLEMENT INTERACTION

A supplement can be a vitamin, mineral, herb, or other nutritional ingredient taken in addition to normal dietary

intake. Most herbs and supplements have not been thoroughly tested for interactions. For example, calcium, which is found in antacids (e.g., Tums) or dietary supplements, may limit the absorption of various drugs through chelation. In particular, calcium may reduce the efficacy of fluoroquinolone and tetracycline antibiotics, which increases the risk of antibiotic failure. Patients may be advised to discontinue the supplement during the antibiotic course of therapy or separate the doses of medications and supplements by at least 2 hours. Herbal products may also interact with conventional medications. This may be due to lack of standardization, variations of strength of the active ingredient, contamination and adulteration. For instance, numerous interactions have been reported between St. John's wort and various drugs. St. John's wort induces CYP enzymes in the liver (specifically 1A2, 2C9, and 3A4) and P-gp. Concurrent use of drugs metabolized by these CYP enzymes and St. John's wort can lead to lower blood concentrations of these drugs and reduced therapeutic effect.

DRUG-NUTRIENT INTERACTION

A drug-nutrient interaction occurs when a drug interferes with the body's ability to absorb nutrients (the essential chemicals that are taken in from the diet and used in metabolism to provide energy and regulate body processes). For example, bile acid sequestrants such as cholestyramine can interact with fat soluble vitamins (A, D, E, K) and decrease vitamin absorption.

DRUG-FOOD INTERACTION

Food may delay, enhance, or reduce the absorption of a drug. The bioavailability, metabolism, and excretion of drugs may also be altered by food. Grapefruit juice, particularly in large quantities (>32 oz per day) can inhibit CYP 3A4 in the intestine, thereby reducing the metabolism of drugs metabolized by this pathway and increasing the drug's bioavailability. For example, concurrent use of grapefruit juice and 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMG-CoA reductase) inhibitors (statins) can lead to increased blood levels of the statins and increase the risk of statin-related side effects, including myalgia, myopathy, and rhabdomyolysis. Vitamin K, present in many vegetables, promotes the production of blood clotting factors that may reduce the effectiveness of anticoagulants such as warfarin.

DRUG-DISEASE INTERACTIONS

Drugs may worsen or exacerbate certain diseases. Conditions that place patients at high risk for drug interactions are asthma, cardiac arrhythmia, diabetes, epilepsy, hypothyroidism, and renal and hepatic impairment. For example, drugs such as nonselective beta blockers used for high blood pressure have strong effects on the bronchial tubes, can cause bronchoconstriction, and can trigger an asthma attack.

DRUG-LIFESTYLE INTERACTIONS

Lifestyle factors are those factors that are within the control of the patient, such as tobacco smoking, caffeine use, and ethanol intake. Numerous drug interactions

exist with smoking, as an example. Cigarette smoking can affect drug therapy by pharmacokinetic and pharmacodynamic mechanisms. Smoking increases theophylline clearance, shortens the drug's half-life, and significantly lowers plasma concentrations of theophylline by induction of CYP 1A2. Theophylline levels should be monitored if smoking is initiated, discontinued, or changed.

Alcohol may also interact with various drugs. Metronidazole is reported to cause disulfiram-like effects after alcohol intake, via inhibition of aldehyde dehydrogenase (ALDH).

ROLE OF THE PHARMACIST

There are many types of drug interactions with a range of severity and significance. The pharmacist can counsel the patient and inform him or her of appropriate steps to limit or avoid an interaction, thus improving therapeutic outcomes and limiting adverse events. Patients may not think to disclose information to their pharmacists about the use of all medications (especially if they use different pharmacies) including non-prescription (OTC) drugs, dietary, supplements, and herbal products. Pharmacists should ask the patient and update the patient's profile as needed. Patients should also be advised to use one pharmacy to obtain their prescription drugs to reduce the risk of interactions.

Resources for the Pharmacist

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Federal Pharmacy Law

B

APPENDIX

- I. Federal Controlled Substance Act
 - A. Regulates controlled substances
 1. Manufacturers or distributors of controlled substances must register annually in order to carry out these actions.
 2. Pharmacists or any person who dispenses or prescribes controlled substances must also register.
 - a. Registrations generally last 1 year but not more than 3 years after approval.
 3. Activities that require registration
 - a. Manufacturing controlled substances
 - b. Distributing controlled substances
 - (1) DEA Form 222 must be used for schedule II drugs
 - c. Prescribing controlled substances
 - d. Dispensing controlled substances
 - e. Exporting controlled substances
 - f. Importing controlled substances
 - g. Conducting research or chemical analysis with controlled substances
 - h. Compounding controlled substances
 - B. Controlled substances are divided into five categories
 1. Schedule I
 - a. Highest potential for abuse
 - b. No currently accepted medical use in the United States
 - c. Examples: opiate derivatives (e.g., heroin); hallucinogens (e.g., lysergic acid diethylamide [LSD])
 2. Schedule II (CII or C-II)
 - a. High potential for abuse including severe psychological and physical dependence
 - b. Accepted medical use
 - c. Examples: morphine, codeine (alone), methylphenidate
 3. Schedule III (CIII or C-III)
 - a. Lower potential for abuse than schedule II
 - b. Accepted medical use
 - c. Examples: secobarbital, pentobarbital, codeine with other ingredients (e.g., Tylenol-3)
 4. Schedule IV (CIV or C-IV)
 - a. Lower potential for abuse than schedules I through III
 - b. Accepted medical use
 - c. Examples: alprazolam, phenobarbital, diethylpropion
 5. Schedule V (CV or C-V)
 - a. Lowest potential for abuse
 - b. Example: 2.5 mg diphenoxylate and not less than 25 mcg of atropine sulfate per dosage unit, some codeine-containing cough syrups
 - C. Pharmacists dispensing a schedule II drug must affix a label that shows the date of filling. If the drug is a schedule III, IV, or V, the label must show the date of initial filling.
 - D. Prescribers must include their DEA registration number on each prescription for controlled substance.
 1. DEA registration number is a nine-character alphanumeric code consisting of two letters followed by seven digits.
 2. May begin with the letters A, B, C, or M (for midlevel practitioners [e.g., physician assistants, nurse practitioners])
 3. Second letter is usually the first letter of the registrant's last name
 4. The next six positions represent a computer-generated number unique to each registrant.
 5. The final seventh number is a computer-calculated check digit or verifying number.
 6. To confirm the DEA registration number
 - a) Add the first, third, and fifth digits together
 - b) Then add the second, fourth, and sixth digits and multiply that sum by 2
 - c) The right-most digit of the sum of these two calculations will correspond with the final, or seventh, digit number
 - E. Labeling of Schedule II, III, IV, and V prescriptions
 1. Labels should include
 - a) Pharmacy name and address
 - b) Serial number of prescription
 - c) Name of patient
 - d) Name of prescriber
 - e) Directions for use and cautionary statements
 - f) Date of filling
 - g) For schedule II, III, and IV drugs, the label should also include: "Caution: Federal law prohibits the transfer of this drug to any person other than the person for whom it was prescribed."
- II. Federal Food, Drug, and Cosmetic Act of 1938
 - A. Authorized the Food and Drug Administration (FDA) to manage the safety of food, drugs, and cosmetics
 - B. Passed after a disaster in which people died from consuming a toxic sulfanilamide elixir
 - C. No drug may be marketed or sold unless proven to be both safe and effective.

D. Definitions

1. Food

- a. Articles used for food or drink for humans or other animals, chewing gum, and articles used for components of any such article

2. Drug

- a. Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or other animals
- b. Articles (other than food) intended to affect the structure or any function of the body of humans or other animals

3. Dietary supplement

- a. Product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients
 - 1) Vitamin
 - 2) Mineral
 - 3) Herb or other botanical
 - 4) Amino acid
 - 5) Dietary substance for use by humans to supplement the diet by increasing the total dietary intake
 - 6) Concentrate, metabolite, constituent, extract, or combination of the above

E. Provides protection from adulterated or misbranded drugs

1. Misbranded

- a. Labeling false or misleading
- b. Does not provide adequate directions for use or warn patients about potential harm

2. Adulterated

- a. Consists in whole or in part of any filthy, putrid, or decomposed substance
- b. Prepared, packed, or held under insanitary conditions

F. Durham-Humphrey Amendment of 1951

- 1. "Caution: Federal law prohibits dispensing without a prescription."
- 2. Establishes two classes of drugs
- 3. Authorizes prescription refills

G. Kefauver-Harris Amendment of 1962

- 1. Also called the Drug Efficacy Amendment
- 2. Drug manufacturers must provide proof of the effectiveness and safety of their drugs *before* approval.
- 3. Established Good Manufacturing Practice (GMP) requirements

H. Prescription Drug User Fee Act of 1992

- 1. Requires manufacturers to pay fees for applications and supplements when the FDA needs to review clinical studies

I. Nutrition Labeling and Education Act of 1990

- 1. Mandates nutrition labeling on food

J. Dietary Supplement Health and Education Act of 1994

- 1. Defines dietary supplements
- 2. Permits certain support claims
- 3. See Chapter 7, Herb and Dietary Supplements, for additional information

L. Federal Food, Drug, and Cosmetic Act of 1938 was amended in 1997 to include Fast Track Products (section 506)

- 1. Addresses medical needs not met for a particular rare condition (e.g., no existing therapy)

- 2. Intended to treat a serious or life-threatening condition (e.g., product that could ameliorate serious adverse effects of other treatments)

III. Omnibus Budget Reconciliation Act of 1990 (OBRA '90)

A. The goal of OBRA '90 was to save government money

B. Requirements for the states and ways to improve understanding of medications for Medicaid patients

C. Pharmacy activities required under OBRA '90

1. Prospective drug use review (DUR)

- a) Screen prescriptions to determine if necessary and appropriate

- (1) Therapeutic duplication

- (2) Over-or-under utilization

- (3) Drug-disease interactions

- (4) Drug-drug interactions (including non-prescription over-the-counter [OTC] drugs)

- (5) Incorrect dosage or duration of treatment

- (6) Drug allergies

- (7) Clinical abuse or misuse

2. Patient information

- a) Name

- b) Address

- c) Phone number

- d) Age or date of birth (DOB)

- e) Sex

- f) Significant disease states

- g) Drug profile

- h) Known allergies or prior drug reactions

- i) List of drugs and devices previously used by patient

- j) Pharmacist comments relevant to individual's therapy

3. Patient counseling

- a) Name and description of medication

- b) Dosage form, dose, route, duration of therapy

- c) Intended use and expected action

- d) Common side effects

- e) Techniques for self-monitoring

- f) Potential drug-drug or drug-food interactions or interactions with other therapies

- g) Refill information

- h) Proper storage

- i) What to do if a dose is missed

IV. Poison Prevention Act of 1970

- A. Child-resistant closures must be on prescription containers unless the prescription is for an exempted drug or if the patient has authorized easy-open packaging.

V. Health Insurance Portability and Accountability Act of 1996 (HIPAA)

- A. Passed in 1996 to improve health insurance

- B. Addressed the public concerns over security and confidentiality of health information

- C. Privacy Rule provides standards for protecting the confidentiality of health information

- D. No health information may be disclosed without the individual's consent or authorization
 - E. Gives patients more control over their health information
 - F. Privacy Rule applies to a person's health information when this data is used, disclosed, or created by a healthcare provider, health plan, healthcare clearinghouse
- VI. Study Resources for the Multistate Pharmacy Jurisprudence Exam (MPJE)
 - A. The individual candidate should study applicable state and federal drug laws and regulations.
 - B. The National Association of Boards of Pharmacy website, *www.nabp.net*
 - C. Barry S. Reiss and Gary D. Hall, authors. *Guide to Federal Pharmacy Law*, 6th ed. 2009; Apothecary Press. Boynton Beach, FL.

Foreign Pharmacy Graduate Equivalency Examination



APPENDIX

The Foreign Pharmacy Graduate Equivalency Exam (FPGEE) is one part of a certification process managed by the Foreign Pharmacy Graduate Equivalency Committee (FPGEC) of the National Association of Boards of Pharmacy (NABP). The FPGEC Certification declares to the state boards of pharmacy that the applicant's foreign licensure and/or registration are valid and that his or her training and education meets the United States (US) standard. The FPGEC Certification is not a license to practice pharmacy in the US. To become licensed to practice pharmacy in the US the applicant must receive FPGEC certification first, apply to the individual state boards of pharmacy, and pass the licensing examinations of the selected state or jurisdiction.

To begin the certification process the applicant must be eligible, complete an application to the FPGEC, and provide appropriate documentation of education, degree, and foreign licensure (Table C-1). If the applicant meets these requirements, the FPGEC will send a letter inviting the applicant to take the FPGEE. In addition to taking the FPGEE, the applicant must take the English as a Foreign Language examination(s). The table below lists general requirements for certification. The applicant should seek additional detailed information from the FPGEC.

PRE-FPGEE

The optional pre-examination is an opportunity to practice answering questions in a similar format to the actual FPGEE. The pre-examination is shorter than the FPGEE, consisting of 66 questions administered over 85 minutes. The pre-examination is computer-based and provides a score immediately after examination completion. Passing scores on the pre-examination cannot guarantee passing scores on the FPGEE. Additionally, the applicant may choose to take a review course or attend review classes for further preparation.

FPGEE OVERVIEW AND EXAM OUTLINE

The exam is computer based and has 250 multiple-choice test questions administered over 5 ½ hours. It is offered twice per year at Pearson VUE testing centers in the United States. The comprehensive exam has nationally uniform content and structure and tests the applicant in four major content areas. Refer to the official NABP FPGEE

Study Guide for a detailed description of the following categories.

Basic Biomedical Science (21%)

- Anatomy and Physiology
- Pathology and Pathophysiology
- Microbiology
- Immunology
- Biochemistry and Biotechnology
- Molecular Biology and Genetics
- Biostatistics

Pharmaceutical Sciences (29%)

- Medicinal Chemistry
- Pharmacology
- Pharmacognosy and Alternative and Complementary Treatments
- Toxicology
- Bioanalysis and Clinical Chemistry
- Pharmaceutics and Biopharmaceutics
- Pharmacokinetics and Clinical Pharmacokinetics
- Pharmacogenomics and Pharmacogenetics
- Extemporaneous Compounding, Parenterals, and Enterals

Social, Behavioral, and Administrative Pharmacy Sciences (15%)

- Health Care Delivery Systems
- Economics and Pharmacoeconomics
- Practice Management
- Pharmacoepidemiology
- Pharmacy Law and Regulatory Affairs
- History of Pharmacy
- Ethics
- Professional Communication
- Social and Behavioral Aspects of Practice

Clinical Sciences (35%)

- Pharmacy Practice and Pharmacist-Provide Care
- Medication Dispensing and Distribution Systems
- Pharmacotherapy: Practice Guidelines and Clinical Trials
- Pharmacotherapy: Health Promotion and Disease Prevention
- Pharmacotherapy: Pharmaceutical Care
- Pharmacist-Provided Care for Special Populations
- Drug-Information
- Medication Safety
- Literature Evaluation and Research Design
- Patient Assessment Laboratory

Table C-1 Requirements for FPGE Certification

Foreign Pharmacy Graduate	The applicant must be a pharmacist with a pharmacy degree from a school outside of the United States, the District of Columbia, and Puerto Rico • If graduated before January 1, 2003 must have completed a four-year pharmacy curriculum • If graduated on or after January 1, 2003 must have completed a five-year pharmacy curriculum	
Documentation of Licensure Applications	Documentation of unrestricted ability to practice in foreign country or jurisdiction To the FPGE • FPGE Certification Application (to request application go to www.nabp.net/indexfpegc.asp) • Official documentation of licensure/registration or credentials • Two, full-face photographs taken within 3 months of the application (1 photo affirmed and notarized by appropriate official on application) • Initial application fee (\$800 USD) To the Educational Credential Evaluators, Inc (ECE) • ECE Application (to request application go to www.ece.org) • Official pharmacy school transcripts • Official documentation of pharmacy degree • General Evaluation Report Fee (\$85 USD)	
Test of English as a Foreign Language-Internet Based Test (TOEFL iBT) or TOEFL and Test of Spoken English (TSE)	Passing scores for TOEFL: • Reading (21) • Listening (18) • Speaking (26) • Writing (24)	Passing scores TOEFL: • 550 (paper-based) • 213 (computer-based) Passing score for TSE: 50
	*All sections must be completed in one session and a passing score achieved for all sections to qualify for FPGE certification	*A passing score must be achieved for each exam to qualify for FPGE certification
FPGEE	Passing Scaled Equated Score: 75	

USEFUL RESOURCES FOR EXAM PREPARATION

NABP's FPGEE Informational Website

Foreign Pharmacy Graduate Equivalency Examination (FPGEE), Foreign Pharmacy Graduate Equivalency Examination Committee (FPGE) Certification Program. National Association of Boards of Pharmacy, 2009. Web. Accessed 11 Nov 2009. <<http://www.nabp.net/indexfpegc.asp>>

FPGE Application Bulletin

Foreign Pharmacy Graduate Equivalency Committee Certification Program: Application Bulletin. National Association of Boards of Pharmacy, 2009. Web. Accessed 11 Nov 2009. <<http://www.nabp.net/ftpfiles/bulletins/FPGEAppRegBulletin.pdf>>

FPGEE Study Guide

Foreign Pharmacy Graduate Equivalency Examination Study Guide. National Association of Boards of Pharmacy, 2007.

Web. Accessed 11 Nov 2009. <<http://www.nabp.net/ftpfiles/bulletins/FPGEestudyguide.pdf>>

Educational Credential Evaluators, Inc Informational Website

Evaluation Services. Educational Credential Evaluators, Inc., 2009. Web. Accessed 11 Nov 2009. <<http://www.ece.org>>

Testing of English as a Foreign Language Informational Website

The TOEFL Test—Test of English as a Foreign Language. Educational Testing Services, Inc., 2009. Web. Accessed 11 Nov 2009. <<http://www.ets.org/toefl>>

Test of Spoken English Informational Website

TSE—Test of Spoken English. Educational Testing Services, Inc., 2009. Web. Accessed 11 Nov 2009. <<http://www.ets.org/tse>>

Answers and Rationales

CHAPTER 2

1. C. Rationale: $10 \text{ mEq} / (5 \text{ mEq/mL}) = 2 \text{ mL} = 2 \text{ vials}$

2. B. Rationale: molecular weight of $(\text{FeSO}_4 \cdot 7\text{H}_2\text{O}) = 278$
 $55.9/278 = X \text{ mg}/150 \text{ mg}$
 $8385 = 278 X$
 $30 \text{ mg} = X$

3. C. Rationale: $130 \text{ lb} \times 3 \text{ mg/lb} = 390 \text{ mg}$ (norm dose)
Maintenance Dose = $(\text{CrClpt}/\text{CrClnorm}) \times \text{norm dose}$
 $\text{MD} = (40/120) \times 390 \text{ mg}$
 $\text{MD} = 130 \text{ mg} = 150 \text{ mg}$

4. B. Rationale: $130 \text{ lb}/2.2 = 59 \text{ kg}$
 $0.25 \text{ mg/kg/min} \times 59 = 14.8 \text{ mg/min}$
 $14.8 \text{ mg/min} \times 60 \text{ min/h} = 886.4 \text{ mg/h}$
 $886.4 \text{ mg/h} \times 500 \text{ mL}/3500 \text{ mg} = 126.6 \text{ mL/hr}$

5. E. Rationale: All are valid DEA numbers.

6. C. Rationale: There are 4 quarts in 1 gallon, so in 2 gallons there are 8 quarts.

7. D. Rationale: One quart is 32 fluid ounces.

8. C. Rationale: One pint is 94.6 teaspoons.

9. C. Rationale: $20 \text{ mEq}/(2 \text{ mEq/mL}) = 10 \text{ mL}$

10. C. Rationale: $10 \text{ mEq}/(2 \text{ mEq/mL}) = 5 \text{ mL}$

11. B. Rationale: Isotonic solution = 0.9% NaCl
 $100 \text{ mL water} = 100 \text{ g water}$
 $0.009 \times 100 \text{ g} = 0.90 \text{ g}$

12. B. Rationale: Isotonic solution = 0.9% NaCl
 $0.9 \text{ g}/100 \text{ mL} = 0.45 \text{ g}/X \text{ mL}$
 $45 = 0.9 X$
 $50 \text{ mL} = X$

13. A. Rationale: $1/900 = 0.001111 \times 100\% = 0.1\%$

14. A. Rationale: $1/5000 = 0.002 \times 100\% = 0.02\%$

15. B. Rationale: $40 \text{ mg/mL} \times 0.5 \text{ mL} = 20 \text{ mg}$

16. B. Rationale: $1 \text{ tsp} = 5 \text{ mL}$; $5 \text{ mL} \times 4 = 20 \text{ mL/d}$
 $200 \text{ mL} \div 20 \text{ mL/d} = 10 \text{ days}$

17. B. Rationale: $150 \text{ mg} \times 2 = 300 \text{ mg/d}$
 $200 \text{ mg}/5 \text{ mL} = 300 \text{ mg}/X \text{ mL}$
 $1500 = 200X$
 $7.5 \text{ mL} = X$

18. B. Rationale: $300 \text{ mg} \times 2 = 600 \text{ mg/d}$
 $600 \text{ mg/d} \times 10 \text{ days} = 6000 \text{ mg}$
 $6000 \text{ mg} \div 200 \text{ mg} = 30 \text{ vials}$

19. D. Rationale: $32 \text{ mEq} \times 75 = 2400 \text{ mg}$
 $2400 \text{ mg} \div 600 \text{ mg} = 4 \text{ tablets}$

20. C. Rationale: Celsius = $5/9 \times (102.2 - 32)$
Celsius = 39° C

21. B. Rationale: $500 \text{ mL} \times 0.15 = 75 \text{ mL methyl salicylate}$
 $75 \text{ mL}/1500 \text{ mL} = X\%/100\%$
 $7500 = 1500X$
 $5\% = X$

22. B. Rationale: $300 \text{ mg} \div (150 \text{ mg}/5 \text{ mL}) = 10 \text{ mL}$

23. D. Rationale: Amoxicillin $125 \text{ mg}/5 \text{ mL}$, dose is $7.5 \text{ mL/day} = 187.5 \text{ mg}$
Bottle is $100 \text{ mL} \times 125 \text{ mg}/5 \text{ mL} = 2500 \text{ mg}$
 $2500 \text{ mg bottle} \times \text{number of days}/187.5 \text{ mg} = 13.333$
13 days

24. D. Rationale: $250 \text{ g}/500 \text{ mL} = 0.5$
 $0.5 \times 100\% = 50\%$

25. B. Rationale: VIII = 8; X = 10
 $8 + 10 = 18$

26. C. Rationale: $10 \text{ mg} \times 4 \times 2 = 80 \text{ mg} \div 5 \text{ mg} = 16 \text{ tabs}$
 $10 \text{ mg} \times 3 \times 2 = 60 \text{ mg} \div 5 \text{ mg} = 12 \text{ tabs}$
 $10 \text{ mg} \times 2 \times 2 = 40 \text{ mg} \div 5 \text{ mg} = 8 \text{ tabs}$
 $5 \text{ mg} \times 3 \times 2 = 30 \text{ mg} \div 5 \text{ mg} = 6 \text{ tabs}$
 $5 \text{ mg} \times 2 \times 2 = 20 \text{ mg} \div 5 \text{ mg} = 4 \text{ tabs}$
 $16 + 12 + 8 + 6 + 4 = 46 \text{ tablets}$

27. D. Rationale: $2 \text{ tabs} \times 2 \times 3 = 12 \text{ tabs}$
 $1 \text{ tab} \times 2 \times 3 = 6 \text{ tabs}$
 $1 \text{ tab} \times 1 \times 3 = 3 \text{ tabs}$
 $0.5 \times 1 \times 3 = 1.5 \text{ tabs}$
 $12 + 6 + 3 + 1.5 = 22.5 = 23 \text{ tabs}$

28. A. Rationale: $1000 \text{ mL} \times 0.0045 = 4.5 \text{ g}$

29. B. Rationale: D5W = 5% dextrose
 $1000 \text{ mL} \times 0.05 = 50 \text{ g}$

30. B. Rationale: $X/500 \text{ mL} = 10 \text{ g}/100 \text{ mL}$
 $5000 = 100 X$
 $50 \text{ g} = X$

31. C. Rationale: $9 \text{ g}/1000 \text{ mL} = X/500 \text{ mL}$
 $4500 = 1000 X$
 $4.5 \text{ g} = X$

32. A. Rationale: $1\% = 1 \text{ g}/100 \text{ mL} = 1000 \text{ mg}/100 \text{ mL}$
 $1000 \text{ mg}/100 \text{ mL} = X/25 \text{ mL}$
 $25000 = 100 X$
 $250 \text{ mg} = X$

33. C. Rationale: $X/500 \text{ mL} \times 50 \text{ g}/1000 \text{ mL}$
 $500000 = 50 X$
 $25 \text{ g} = X$

34. E. Rationale: $25 \times 0.005 = 0.125 \text{ mL}$
 $600 \text{ mL}/0.125 \text{ mL} = 100\%/X\%$
 $0.0208\% = X$
 $1:4807 = 1:4800$

35. A. Rationale: $1 \text{ g} = 1000 \text{ mg}$
 $1000 \text{ mg}/250 \text{ mL} = 60 \text{ mg}/\text{h}/X \text{ mL}$
 $15000 = 1000 X$
 $15 \text{ mL}/\text{hr} = X$

36. A. Rationale: $25000 \text{ units}/250 \text{ mL} = 100 \text{ units}/\text{mL}$
 $17 \text{ mL}/\text{h} \times 100 \text{ units}/\text{mL} = 1700 \text{ units}/\text{h}$
 $1700 \text{ units}/\text{hr} \times 6 \text{ h} = 10200 \text{ units}/\text{hr}$

37. D. Rationale: $2.5 \text{ mill units}/X = 0.5 \text{ mill units}/1 \text{ mL}$
 $5 \text{ mL} = X$

38. B. Rationale: $1 \text{ mill units}/1 \text{ mL} = 5 \text{ mill units}/X \text{ mL}$
 $5 \text{ mL} = X$

39. C. Rationale: $250 \text{ mg}/5 \text{ mL} = X \text{ mg}/7.5 \text{ mL}$
 $1875 = 5 X$
 $375 \text{ mg} = X$

40. C. Rationale: $250 \text{ mg} = 0.25 \text{ g}$
 $0.25 \text{ g}/5 \text{ mL} = 0.5 \text{ g}/X \text{ mL}$
 $2.5 = 0.25 X$
 $10 \text{ mL} = X$

41. E. Rationale: $250 \text{ mg} = 0.25 \text{ g}$
 $0.25 \text{ g}/1.5 \text{ mL} = 2 \text{ g}/X \text{ mL}$
 $3 = 0.25 X$
 $12 \text{ mL} = X$

42. A. Rationale: $500 \text{ mg} = 0.5 \text{ g}$
 $0.5 \text{ g}/1.5 \text{ mL} = X \text{ g}/3 \text{ mL}$
 $1.5 = 1.5 X$
 $1 \text{ g} = X$

43. D. Rationale: $1 \text{ g}/4.5 \text{ mL} = 2.5 \text{ g}/X \text{ mL}$
 $11.25 \text{ mL} = X$

44. B. Rationale: $50 \text{ g}/100 \text{ mL} = X \text{ g}/4 \text{ mL}$
 $200 = 100 X$
 $2 \text{ g} = X$

45. C. Rationale: $50 \text{ g}/100 \text{ mL} = 7.5 \text{ g}/X \text{ mL}$
 $7500 = 50 X$
 $15 \text{ mL} = X$

46. A. Rationale: D5W contains no sodium; it is 5% dextrose.

47. B. Rationale: A grain is the same in both the apothecary and the avoirdupois systems.

48. D. Rationale: one microgram = 1×10^6
one nanogram = 1×10^9
 $(1 \times 10^6) \times 1000 = 1 \times 10^9$

49. C. Rationale: $120 \text{ mL}/30 \text{ min} = 4 \text{ mL}/\text{min}$
 $4 \text{ mL}/\text{min} \times 15 \text{ drops}/\text{mL} = 60 \text{ drops}/\text{min}$

50. B. Rationale: $25 \text{ drops}/\text{min} \times 60 \text{ min}/\text{h} = 1500 \text{ drops}/\text{h}$
 $1500 \text{ drops} \div 15 \text{ drops}/\text{mL} = 100 \text{ mL}$

51. C. Rationale: $50 \text{ mg}/\text{mL} \times 0.7 \text{ mL} = 35 \text{ mg}$

52. D. Rationale: $40 \text{ mg} \div 2.5 \text{ mL} = 16 \text{ mg}/\text{mL}$
 $16 \text{ mg}/\text{mL} \times 1.9 \text{ mL} = 30.4 = 30 \text{ mg}$

53. B. Rationale: $1.5 \text{ mg} \times 0.7 \text{ mL} = 1.05 \text{ mg}/\text{mL}/0.5 \text{ mL} = 2.1 \text{ mg}$

54. A. Rationale: $(\text{mEq} \times \text{MW})/\text{Valence} = (20 \text{ mEq} \times 75)/1 = 1.5 \text{ g} = 15 \text{ mL}/1.5 \text{ g} = 0.1 \times 100\% = 10\%$

55. C. Rationale: $5 \text{ mg} \times 90 \text{ sec} = (450 \text{ mg}/\text{sec})/60 \text{ sec} = 7.5 \text{ mg}$

56. A. Rationale: $5 \text{ mg}/\text{mL} \times 6.2 \text{ mL} = 31 \text{ mg}$

57. B. Rationale: $0.3 \text{ mg} \times 1 \text{ mL} / 0.4 \text{ mg} = 0.75 \text{ mL}$

58. A. Rationale: $40 \text{ mg}/5 \text{ mL} \times 2.6 \text{ mL} = (104 \text{ mg}/\text{mL})/5 \text{ mL} = 20.8 \text{ mg}$

59. C. Rationale: $300 \text{ mL water} = 300 \text{ g water}$
 $250 \text{ g}/550 \text{ g} = X\%/100\%$
 $25000 = 550 X$
 $45.45\% = X$

60. B. Rationale: $\frac{1}{2} \text{ grain} \times 64.8 \text{ mg}/1 \text{ grain} = 32.4 \text{ mg}$

61. A. Rationale: Avg. Adult BSA = 1.73 m^2
 $(0.8/1.73) \times 200 \text{ mg} = 92.49 \text{ mg}$

62. C. Rationale: $100 \text{ mcg} \times 6 \text{ mL} = (600 \text{ mcg}/\text{mL})/1 \text{ mL} = 600 \text{ mcg}$

63. A. Rationale: $(0.2 \text{ L} \times 0.95) + (1 \text{ L} \times 0.7) + (0.2 \text{ L} \times 0.8) = 1.05 \text{ L}/1.40 \text{ L} = 0.75 \times 100\% = 75\%$

64. C. Rationale: $500 \text{ mL of D5W} = 25 \text{ g dextrose}$
 $50 \text{ mL of D50\%W will supply the } 25 \text{ g dextrose.}$

65. A. Rationale:
Step 1: Sodium chloride needed to render the prescribed volume isotonic: $(0.9/100) \times 60 = 0.54$

Step 2: $0.02 \times 0.15 = 0.003$

Step 3: g of sodium chloride needed to make the solution isotonic: $0.54 - 0.003 = 0.54$ g or 540 mg

66. A. Rationale: $(55.9 \text{ Fe}) + 7(18 \text{ H}_2\text{O}) + (32.1 \text{ S}) + 4(16 \text{ O}) = 278 \dots$
 $(55.9 \text{ Fe}) / (278 \text{ Total}) = 0.201 \times 500 \text{ mg Tab} = 100.5 \text{ mg elemental Iron}$

67. C. Rationale: $0.5\% \times 100 \text{ ml} = 50 \text{ ml gentian violet}$
 $50 \text{ ml (gv)} / 1250 \text{ ml} = 0.04\% / 100\% = 0.0004$ 1/0.0004 = 2500

68. C. Rationale: Recommended Dose $168 \text{ mcg} \times 2 = 336 \text{ mcg} \times 90 \text{ days} = 30204 \text{ mcg}$
 Inhaler: $42 \text{ mcg} \times 200 = 8400 \text{ mcg}$
 $30204 / 8400 = 3.597 = 4$ inhalers

69. A. Rationale: $6.25 \text{ g boric acid} = 6250 \text{ mg} / 100 \text{ ml} = 62.5 \text{ mg/ml}$

70. C. Rationale: $50 \text{ ml} \times (4 \text{ g} / 100 \text{ ml}) = 2 \text{ g} / 150 \text{ ml} = 0.0133 \times 100\% = 1.33\%$

71. C. Rationale: $200 \text{ mg}\% / 100\% = 2 \text{ mg/ml}$

72. B. Rationale: $1/50 = 0.02 \times 100\% = 2\% \times 250 \text{ g} = 5 \text{ g of solute}$

73. C. Rationale: $(5 \text{ g} / 100 \text{ ml}) \times 50 \text{ ml} = 2.5 \text{ g or } 2500 \text{ mg}$

74. A. Rationale: $1/200 = 0.005 \times 100\% = (0.5 \text{ g} / 100 \text{ mg}) \times 100000 \text{ mg} = 500 \text{ mg}$

75. D. Rationale: $\text{MW} = 2(23) + 12 + 3(16) = 106$
 $(0.4 \text{ g} \times 106 \text{ g}) / 46 \text{ g} = 0.922 \text{ g} = 922 \text{ mg}$

76. B. Rationale: $46 \text{ g} / 106 \text{ g} = 0.434 \times 100\% = 43.4\%$

77. A. Rationale: $58.5 \text{ g/mole} = 58.5 \text{ mg/mmol} \times 2 \text{ mmol} = 117 \text{ mg}$

78. C. Rationale: $1 \text{ mol} \times 5 \text{ g} = (5 \text{ g/mol}) / 78 \text{ g} = 0.064 \text{ mol} \times (1000 \text{ mmol} / 1 \text{ mol}) = 64.1 \text{ mmol}$

79. C. Rationale: $(1 \text{ mol} \times 0.05 \text{ mol}) / 74.6 \text{ g} = 3.73 \text{ g KCl}$

80. A. Rationale: $1/200 = 0.005 \times 100\% = 0.5\% \text{ v/v}$

81. C. Rationale: $2/2000 = 0.001 \times 100\% = 0.1\% \text{ w/v}$

82. B. Rationale: $1/1000 = 0.001 \text{ g} = (0.1 \text{ g} / 100 \text{ ml}) \times 100 \text{ ml} = 0.1 \text{ g} = 100 \text{ mg}$

83. C. Rationale: $5 - 1 = 4$

84. C. Rationale: $(1 \text{ g} \times 5 \text{ ml}) / 0.125 \text{ g} = 40 \text{ ml needed}$

85. C. Rationale: $500 \text{ mg} / 50 \text{ ml} = 10 \text{ ml}$

86. C. Rationale: $(1000 \text{ ml} / 8 \text{ hr}) = (125 \text{ ml/hr}) = (2.08 \text{ ml/min}) = 2.08 \text{ ml/min} \times 20 \text{ drops/min} = 40 \text{ drops/min}$

87. D. Rationale: $(100 \text{ ml/hr}) = 1.67 \text{ ml/min} \times 20 \text{ drops/ml} = 33.4 \text{ drops/min}$

88. A. Rationale: $(1 \text{ L} / 12 \text{ hr}) = (1000 \text{ ml} / 12 \text{ hr}) \times (1 \text{ hr} / 60 \text{ min}) = (1.39 \text{ ml/min}) \times (20 \text{ drops/ml}) = 27.7 \text{ drops/min} = 28 \text{ drops/min} = 28 \text{ gtt/min}$

89. B. Rationale: $(4 \text{ mcg/kg/min}) \times 10 \text{ Kg} = (40 \text{ mcg/min}) = 0.04 \text{ mg/min} \times (60 \text{ min} / 1.2 \text{ ml}) = 2 \text{ mg/ml} \times 100 \text{ ml} = 200 \text{ mg}$

90. B. Rationale: $100 \text{ g Dex} / 150 \text{ ml} = 0.667 \times 100\% = 66.7\%$

91. C. Rationale: $(100 \text{ ml} / 5 \text{ ml}) = 20 \times 150 \text{ mg} = 3000 \text{ mg/ml} = (3 \text{ g} / 100 \text{ ml}) \times 100\% = 3\% \text{ (w/v)}$

92. D. Rationale: $(9/5 \times 37^\circ \text{ C}) + 32 = 98.6^\circ \text{ F}$

93. A. Rationale: $1/10,000 = 0.0001 \times 100\% = 0.01\%$

94. C. Rationale: $(0.5 \text{ mg/kg/min}) \times 50 \text{ kg} = (25 \text{ mg/min}) \times (60 \text{ min/hr}) = (1.5 \text{ g/hr}) \times (100/1 \text{ g}) = 150 \text{ ml/hr}$

95. D. Rationale:
 $2.54 \text{ g} \times 1000 \text{ mg} = 2540 \text{ mg}$
 1 gram

$$\frac{2540 \text{ mg}}{1000 \text{ tablets}} \times \frac{X \text{ mg}}{60 \text{ tablets}}$$

$x = 152.4$
 $\sim 150 \text{ mg}$

96. A. Rationale: $(200 \text{ g} / 1100 \text{ g}) = 0.182 \times 100\% = 18.2\%$

97. D. Rationale: $16 \text{ oz} \times (30 \text{ ml} / 1 \text{ oz}) = 480 \text{ ml} \times (1 \text{ tbsp} / 15 \text{ ml}) = 32 \text{ tbsp doses}$

98. B. Rationale: $1 \text{ tsp} = 5 \text{ ml} \times 2 = 10 \text{ ml/d}$
 $180 \text{ ml} / (10 \text{ ml/d}) = 18\text{d}$

99. D. Rationale: $5 \text{ mg/ml} \times 5 \text{ ml} = 25 \text{ mg}$

100. A. Rationale: $110 \text{ lb} = 50 \text{ kg} \times 2 \text{ mg/kg} = 100 \text{ mg}$

101. C. Rationale: $80 \text{ lb} / (2.2 \text{ lb/kg}) = 40 \text{ kg} \times 30 \text{ mg/kg/d} = 1200 \text{ mg/d}$

102. D. Rationale: $1200 \text{ mg} / 3 \text{ doses} = 400 \text{ mg dose} / (325 \text{ mg/ml}) = 1.23 \text{ ml}$

103. D. Rationale: The bag has 250 ml of NS, so divided over 2 hours (120 minutes) the rate is 2.08 ml/min. The microdrip set is 60 gtt/ml, and since we already know that the flow rate is 2.08 ml/min, $60 \text{ gtt/ml} \times 2.08 \text{ ml/min} = 125 \text{ gtt/min}$.

104. C. Rationale: First divide the 1250 ml bag over 3 hours (180 minutes).
 $1250 \text{ ml} / 180 \text{ min} = 6.94 \text{ ml/min}$
 The question asks for the ml/hr, so multiply 6.94 ml/min by 60 minutes (1 hour) and this equals an infusion of 416.4 ml/hr.

105. C. Rationale: First, get the weight of the patient in kg by dividing his weight in lbs by 2.2. His weight is 109.1 kg, so at a dose of 2 mg three times daily you get $109.1 \text{ kg} \times 2 \text{ mg/kg} \times 3 = 654.6$ or approximately 654 mg zidovudine.

106. D. Rationale: In this question, the weight of the patient and infusion rate is not relevant because it is only asking for the concentration of the bag. Since $1 \text{ mg} = 1000 \text{ mcg}$, multiply the concentration of dobutamine, which is in mg, by 1000 to convert it into mcg. Then divide this by the concentration of the bag, which is 500 ml. The equation: $(200 \text{ mg} \times 1000 \text{ mcg}) / 500 \text{ ml} = 400 \text{ mcg/ml}$

107. C. Rationale: $(1 \text{ mg/kg/min}) \times 68.2 \text{ kg} = (68.2 \text{ mg/min}) \times (60 \text{ min/hr}) = (4.1 \text{ g/hr}) \times (100 \text{ ml/5g}) = 82 \text{ ml/hr}$

108. E. Rationale: $\text{mOsm/L} = (\text{wt of substance/MW in g}) \times \# \text{ of species} \times 1000$. Normal saline is 0.9% so: $9/58.5 \text{ g} \times 2 \times 1000 = 308 \text{ mOsm/L}$.

109. A. Rationale: $\text{NaCl: } (2\text{mOsm}/58.5) = (X/1000 \text{ mg})$ $X = 34.18 \text{ mOsm}$.
 $\text{D5W: } 50 \text{ mg/mL} \times 100 \text{ mL} = 5000 \text{ mg}$. $(1 \text{ mOsmol}/198) = (X/5000 \text{ mg})$. $X = 25.25 \text{ mOsm}$
 $34.18 + 25.25 = 59.43 \text{ mOsmol}$

110. C. Rationale: $128 \text{ oz} \times 30 \text{ mL/oz} = 3840 \text{ mL}$. $0.25 \text{ g}/100 \text{ mg} \times 3840 = 96 \text{ g}$. $99.9 \text{ g}/100 \text{ mg} = 96 \text{ g/X}$. Cross multiply to get 9.6 as your answer.

111. C. Rationale: The concentration of the chemical in alcohol is $1 \text{ g}/10 \text{ mL} = 0.1 \text{ g/mL}$. Next, set up a ratio: $11.1/100 = 0.1/X$. $X = 0.9$

112. D. Rationale: $0.3 \text{ mL} \times 3 = 0.9 \text{ mL}$. $0.9 \text{ mL} \times 5/100 = 0.045$

113. B. Rationale: $\text{mEq} = (5.86 \text{ g}/74.6) \times 1 = 0.07855$.
 $0.07855 \times 1000 = 78.5 \text{ mEq}$

114. C. Rationale: $V_d = t_{1/2} \times \text{CL}/0.693 = 7.8 \text{ hr} \times 9 \text{ L/hr}/0.693 = 101 \text{ L}$

115. A. Rationale: $250 \text{ mg}/5 \text{ mL}$ would give 50 mg/mL , so you would need 3 mL to give 150 mg .

116. D. Rationale: A 0.5 difference between pKa and pH yields 75% ionization and 25% remaining unionized. This falls between the reference values of pKa = pH giving a 50/50 % ionized to unionized and the difference between pKa and pH of 1 giving a 90% ionization. Using these commonly used reference values we can determine the pKa to pH difference of 0.6 would give us 79.9% ionization.

117. C. Rationale: The pH of the human body is approximately 7.35 at normal homeostatic conditions. This being said, the difference between the pKa of the weakly basic drug and the solution it resides in is 1.25. Using the general rule of thumb that a difference of 1 increment between pH and pKa yields 90% ionization and that a difference of 2 increments gives 99% ionization we can tell that the drug would fall in between these values remaining unionized at around 5.9%.

118. D. Rationale: The patient is to receive 2 mg/min of a $2 \text{ mg}/3 \text{ mL}$ solution. Over 60 minutes the patient would receive 120 mg contained within 180 mL using a basic proportion of the concentration originally provided.

119. B. Rationale: The patient is to receive 4000 mL over 24 hours giving 166.7 mL/hour or 2.8 mL/min . Multiplying the 2.78 mL/min by the drip factor of 15 drops/mL would yield 42 drops/min .

120. A. Rationale: The prescription calls for one tablet every other day. Since the quantity is 100, the day supply would be 200.

121. A. Rationale: Erythromycin lactobionate is the only salt form available IV. Stearate and ethylsuccinate are both administered orally for the most part in tablet or oral suspension/solution forms.

122. A. Rationale: When dealing with hydrogen ion concentrations, the value of the negative exponent represents the pH. In this case 1×10 raised to the negative 8 yields a pH of 8.

123. D. Rationale: Milliequivalents simply refers to the amount of molecules of KCl in each mL of the solution. 3 milliequivalents equals 3 molecules times the molecular weight of each molecule being 74.5 equals 223.5 mg/mL .

124. D. Rationale: 10 mEq is calculated as 10 molecules weighing 74.5 each or the molecular weight of KCl or 745 mg total.

125. A. Rationale: First the patient's IBW is calculated using the formula for women $45.5 \text{ kg} + 2.3 \text{ kg}$ for every inch over 60 inches. This gives us 50.1 kg . The Cockcroft-Gault equation is used taking $(140 - \text{patient's age}) \times \text{weight in kg}$ all divided by $72 \times \text{SCr}$. If the patient is a woman, as in this case, the answer is then multiplied by 0.85. Using the patient-specific information given in the question yields an answer of 33.5 mL/min .

126. C. Rationale: First the patient's IBW is calculated using the formula for men $50 \text{ kg} + 2.3 \text{ kg}$ for every inch over 60 inches. This gives us 68.4 kg . The Cockcroft-Gault equation is used taking $(140 - \text{patient's age}) \times \text{weight in kg}$ all divided by $72 \times \text{SCr}$. Using the patient-specific information given in the question yields an answer of 65.6 mL/min .

127. B. Rationale: The corrected calcium formula is $(4.0 - \text{Albumin}) \times 0.8 + \text{Calcium levels}$. Using the patient-specific information of the question yields an answer of 9.34 mg/dL .

128. E. Rationale: Working backwards diluting 100 mL of a $1:4000$ strength solution would equal 25 mL of a $1:1000$ strength solution using a proportional equation. Using a second proportional equation we can determine that 800 mL of the $1:1000$ solution equals 100 mL of the $1:125$ solution. Therefore you would have to add 700 mL to the original 100 mL to give you 800 mL of the $1:1000$ solution to carry out the next dilution.

129. C. Rationale: The formula for ANC is $(\% \text{ segs} + \% \text{ bands}) \times \text{WBC}$. So 19.8% of 2000 gives 396 as an answer.

130. C. Rationale: Use the Henderson-Hasselbalch equation: $\text{pH} = \text{pKa} + \text{Log} [\text{Conjugate Base}]/$

[ConjugateAcid]. Using the provided variables with 0.25 M of acetic acid as the conjugate acid and 0.75 M sodium acetate as the conjugate base gives an answer of 5.24. Also, since we are using K_a instead of pK_a , the negative log of the K_a must be taken in place of the pK_a in the Henderson-Hasselbalch equation.

131. C. Rationale: Answer is simply calculated by taking the AUC of the tablet and dividing it by the AUC of the capsule. $76.3/84.2 = 0.91$.

132. B. Rationale:

$$BMI = \frac{\text{weight in pounds} \times 703}{(\text{height in inches})^2}$$

Body Mass Index (BMI) is used to assess a patient for overweight status or obesity. BMI >25 is overweight and ≥ 30 is obese. This patient's BMI is 22.2.

133. B. Rationale: 40 mg/hour $\times$ 24 hours gives 960 mg. This is multiplied by 0.8 salt conversion factor when switching from IV aminophylline to oral sustained-release theophylline. This dosage is then split in 2 for the sustained-release formulation given every 12 hours. The closest answer, as often times it is difficult to be exact because of different dosages and manufacturers, is approximately 400 mg every 12 hours.

134. B. Rationale: Drugs such as aspirin undergo zero order kinetics in which the drug is metabolized at a constant rate over time. In first order kinetics, drug metabolism is directly proportional to drug concentration. $V = V_{max}[C]/K_m$ is the Michaelis-Menten first order kinetics equation.

CHAPTER 3

1. C. Rationale: 300 mL water = 300 g water
 $250 \text{ g}/550 \text{ g} = X\%/100\%$
 $25000 = 550 X$
 $45.45\% = X$

2. B. Rationale: 1 tsp = 5 mL; $5 \text{ mL} \times 4 = 20 \text{ mL/d}$
 $200 \text{ mL} \div 20 \text{ mL/d} = 10 \text{ days}$

3. C. Rationale: $3.7 \text{ g/X mL} = 187 \text{ mg}/5 \text{ mL}$
 $3700 \text{ mg}/X \text{ mL} = 187 \text{ mg}/5 \text{ mL}$
 $187 X = 18500$
 $98.9 \text{ mL} = X$, so $\sim 100 \text{ mL}$

4. A. Rationale:

Step 1: Figure out how much HC is in 30 g of the 1% HC cream.

Answer: 0.3 g

Step 2: Figure out how much HC powder needs to be added to get a finished product of 2% HC cream.

(NOTE: Since you are trying to double the cream concentration, the finished product will contain roughly double the g of pure HC in the base.)

Solve the following problem for X, which will = 0.306 g = 0.31 g

$$\frac{(0.3 + X) \text{ g HC}}{30 \text{ g}(1\% \text{ cream}) + X} = \frac{2 \text{ g HC}}{100 \text{ g finished product}}$$

5. C. Rationale: Calculate the amount of ZnO in each product.

$$200 \text{ g} \times \frac{5 \text{ g ZnO}}{100 \text{ g ung}} = 10 \text{ g}$$

$$400 \text{ g} \times \frac{10 \text{ g ZnO}}{100 \text{ g ung}} = 40 \text{ g}$$

The final product will have 600 g total ung after mixing.

$$50 \text{ g}/600 \text{ g} \times 100\% = 8.3\%$$

6. C. Rationale: 50 ml maldroxyl + 50 ml diphen = 100 ml
 $200 \text{ ml} - 100 \text{ ml} = 100 \text{ ml}$

7. D. Rationale: 1 lb = 454 grams so since you have 1 lb of the 28% W/W solution you have 454 grams of it. To get the 10% W/W solution, divide 454 grams by the concentration of the solution, which is 0.10. Next, multiply by 0.28, the concentration of the original solution. This will give you 1271.2 grams, which can be rounded to 1271 grams.

8. E. Rationale: $500 \text{ g} \times 0.05 = 25 \text{ g}$. $25 \text{ g} \times 1 \text{ mL}/1.25 \text{ g} = 20 \text{ mL}$

9. E. Rationale: $10 \text{ g}/100 \text{ mL} \times 4000 \text{ mL} = 400 \text{ g}$. $36.8 \text{ g}/100 \text{ mL} = 400 \text{ g}/X$. Solve by cross multiplication to get $X = 1086.96 \text{ mL}$. 1087 mL. $1087 \text{ mL}/1.19 = 913 \text{ mL}$ stock solution needed.

10. E. Rationale: The stock ointment is 5% and we want a concentration of 2%. The ratio of this is $5/2 = 2.5$, so we want to divide the grams of solution by 2.5 to get the concentration we want. Since 1 lb = 454 grams and we need 2 lbs, this is 2×454 which equals 908 grams, which is the quantity we need to divide by our ratio of 2.5. So $908/2.5 = 363 \text{ grams}$ of 5% formulation that we should use to prepare this order.

11. D. Rationale: 80 jars at 2 oz each = 160 oz total volume

$$1 \text{ oz} = 28.35 \text{ g}, \text{ so } 160 \text{ oz} \times 28.35 = 4536 \text{ grams}$$

$$1 \text{ lb} = 454 \text{ g}, \text{ so } 4536 \text{ g}/454 = 10 \text{ lbs}$$

12. D. Rationale: #LX = 60
 $60 \times 500 \text{ mcg} = 30,000 \text{ mcg}$
 $1 \text{ mcg} = 1.0 \times 10^{-6}$, so $30,000 \text{ mcg} = 0.03 \text{ g}$

13. B. Rationale: #LX = 60
 $60 \times 250 \text{ mcg} = 15,000 \text{ mcg}$
 $1 \text{ mcg} = 0.001 \text{ mg}$
 $15,000 \text{ mcg} \times 0.001 = 15 \text{ mg}$

14. A. Rationale: Sodium fluoride is a caustic substance. Water solubility and small quantity of powder are not issues the pharmacist should anticipate with this prescription.

15. C. Rationale: For diphenhydramine: $50 \text{ mg} \times (1 \text{ mL}/800 \text{ mg}) = 0.0625 \text{ mL}$.
For acetaminophen: $325 \text{ mg} \times (1 \text{ mL}/850 \text{ mg}) = 0.382 \text{ mL}$
 $0.0625 \text{ mL} + 0.382 \text{ mL} = 0.445 \text{ mL}$
Capsule size of 0.5 mL - 0.445 mL = 0.055 mL.
Lactose $950 \text{ mg/mL} \times 0.055 \text{ mL} = 52.3 \text{ mg}$ for each capsule.

Since we want #30 capsules, multiple $52.3 \text{ mg} \times 30 = 1569 \text{ mg}$. $1569 \text{ mg} = 1.569 \text{ g}$ (which can be rounded to 1.57 g).

16. D. Rationale: Emulsions are two-phase systems that consist of two immiscible liquids, one of which is uniformly dispersed throughout the other as fine droplets. They may be classified as oil-in-water (o/w) or water-in-oil (w/o). There may also be multiple emulsions (e.g., w/o/w emulsion where a water droplet enclosed in an oil droplet is itself dispersed in water). They may be used internally to mask the bitter taste or odor of drugs or externally as creams or lotions.

17. E. Rationale: All of the statements are true except the last one. Room air is taken into the HEPA filter and blown in a laminar flow towards the pharmacy personnel. It does not pass through a separate filter.

18. A. Rationale: In a horizontal flow hood, items should not be grouped together since this may prevent the clean air from passing over them. They should be placed individually from left to right and equidistant from each other and the front and back of the work space to prevent any contamination.

19. E. Rationale: LVPs are single unit doses that exceed 100 mL. Typical LVPs include water, dextrose, salts, amino acids, and TPN components. All of the choices listed are available as large volume parenterals.

20. B. Rationale: Laminar flow hoods are used to provide a constant flow of clean air out of the work area to prevent room air from entering and to provide clean air for the work area. The room air is not passed through an additional filter.

21. B. Rationale: The correct order is to first draw up 5 mL of air into the syringe, place the needle onto the vial's rubber closure at a 45 degree angle, raise the needle to a 90 degree angle and push through the rubber closure of the vial and inject the air. Injecting the air will create a change in pressure and allow you to easily remove 5 mL of the solution.

22. C. Rationale: The luer-lok tip and plunger must be disposed of if they are touched since this can compromise sterility. Since the outside of the barrel never comes into contact with the solution inside, holding the needle by the barrel will not compromise sterility.

23. D. Rationale: The larger the gauge number, the finer the diameter of the needle. Needle length is measured in inches. Common needles range from 7 gauge, which is the largest, to 33 gauge, which is the smallest.

24. C. Rationale:

$$\frac{10 \text{ mL vancomycin} + 100 \text{ mL normal saline}}{60 \text{ min}} = 110 \text{ mL}/60 \text{ min} = 110 \text{ mL}/\text{hour}$$

25. A. Rationale: $120 \text{ mL} \times \frac{75 \text{ g sucrose}}{100 \text{ mL}} = 90 \text{ g sucrose}$

$$90 \text{ g sucrose} \times \frac{100 \text{ mL}}{50 \text{ g sucrose}} = 180 \text{ mL}$$

180 mL total volume – 120 mL 75% w/v sucrose syrup – 60 mL of water to add

26. A. Rationale: 70% v/v isopropyl alcohol swabs are used to prevent contamination of vials. However, the correct technique is to use firm strokes in the *same* direction, using different portions of the swab.

27. E. Rationale: A pyrogen is a bacterial endotoxin that can be internal or external. Pyrogens are metabolic products of living microorganisms that cause a pyretic response (fever) upon injection.

28. E. Rationale: All of the choices are methods used to sterilize pharmaceutical products.

29. A. Rationale: A 5 micron filter straw is much too large to use when preparing an ampule, a 0.22 micron in-line filter is an appropriate size.

30. A. Rationale: Nitroglycerin adsorbs to PVC and this is why it must always be prepared in glass.

31. C. Rationale: Both nitroglycerin and insulin are adsorbed to the inner linings of intravenous containers and tubing.

32. D. Rationale: Neomycin and Polymyxin B Sulfates solution is a sterile antibiotic solution that once diluted is used for urinary bladder irrigation. Ringer's, sodium chloride, and sterile water are all used as irrigation solutions; dextrose is not.

33. D. Rationale: Ointments are oleaginous systems intended for topical application to the skin or mucous membranes. Hydrophilic petrolatum is an example of an ointment. Bentonite is an emulsifying agent. VEEGUM 6% and methylcellulose are suspending agents.

34. E. Rationale: Omeprazole, a proton-pump inhibitor, is commonly combined with sodium bicarbonate, an antacid. There is a brand name formulation available of the product known as Zegerid®. No alcohol is necessary in this recipe, since it is an oral preparation made for a child. This is why none of the choices are correct answers.

35. C. Rationale: One tsp = 5 mL. $10 \text{ mg omeprazole}/5 \text{ mL} = 2 \text{ mg/mL}$

36. E. Rationale: Since the concentration is 2 mg/mL and the requested quantity is 200 mL, $2 \times 200 = 400 \text{ mg}$ needed to prepare the solution.

37. C. Rationale: Codeine and diphenhydramine are both weak bases. Phenobarbital is a weak acid.

38. C. Rationale: 2% w/v means 2 g (weight) over 100 mL (volume).

39. B. Rationale: The notation $\bar{a}\bar{a}$ signifies that starch and talc are in a 1:1 ratio in the prescription. Since there are 5 g of talc, this means the amount of starch needed is also 5 g.

40. E. Rationale: Sterile Water for Injection, USP, is sterile, nonpyrogenic, distilled water that meets the same standards for presence of total solids as Purified Water, USP. No antimicrobial or other substances are permitted to be added to the sterile water, but it can be used to reconstitute antibiotics. It may also be used as a diluent. The USP 23 monograph states that water for injection is water purified by distillation or reverse osmosis.

41. E. Rationale: Limewater is made by mixing excess calcium hydroxide with distilled water. The mixture is shaken and then left to settle. This is why the term limewater is used interchangeably for calcium hydroxide.

42. A. Rationale: Woolfat is lanolin. Since lanolin is a fat, it is oleaginous.

43. B. Rationale: Hydrophilic ointment is an absorption.

44. D. Rationale: Lubriderm is an oil-in-water emulsion. Generally, lipophilic creams are classified as water-in-oil (w/o) emulsions and hydrophilic creams are classified as oil-in-water (o/w) emulsions.

45. D. Rationale: Eucerin is an oil-in-water emulsion. Generally, lipophilic creams are classified as water-in-oil (w/o) emulsions and hydrophilic creams are classified as oil-in-water (o/w) emulsions.

46. B. Rationale: #XC = 90
 $90 \times 250 \text{ mcg} = 22,500 \text{ mcg}$
 $1 \text{ mcg} = 0.001 \text{ mg}$
 $22,500 \text{ mcg} \times 0.001 = 22.5 \text{ mg}$.

47. D. Rationale: The larger the gauge number, the finer the diameter of the needle. Needle length is measured in inches. Common needles range from 7 gauge, which is the largest, to 33 gauge, which is the smallest.

48. C. Rationale: All of the choices are correct except choice "c" because if the ampule neck is broken towards the laminar flow hood, this might damage or contaminate the hood.

49. B Rationale:

$$\frac{120 \text{ mL}}{60 \text{ min}} \times \frac{20 \text{ gtt}}{\text{mL}} = 40 \text{ gtt/min}$$

50. D Rationale:

Lactose displacement:

Estriol:

$$\frac{250 \text{ mg}}{300 \text{ mg}} \times \frac{4 \text{ mg}}{x} = 3.33 \text{ mg lactose}$$

Estradiol:

$$\frac{180 \text{ mg}}{300 \text{ mg}} \times \frac{0.5 \text{ mg}}{x} = 0.3 \text{ mg lactose}$$

Total amount of lactose displaced:

$3.33 \text{ mg} + 0.3 \text{ mg} = 3.63 \text{ mg}$

Amount of lactose per capsule:

$300 - 3.63 = 296.37 \text{ mg}$

$$\frac{4 \text{ mg estriol}}{1 \text{ capsule}} \times 100 \text{ capsules} = 400 \text{ mg estriol}$$

$$\frac{0.5 \text{ mg estradiol}}{1 \text{ capsule}} \times 100 \text{ capsules} = 50 \text{ mg estradiol}$$

$$\frac{296.37 \text{ mg lactose}}{1 \text{ capsule}} \times 100 \text{ capsules} \times \frac{1 \text{ g}}{1000 \text{ mg}} = 29.637 \text{ g lactose}$$

51. D. Rationale: Vertical flow hoods blow air from the top down to maintain sterility and protect the worker, which is useful when dealing with potentially carcinogenic chemotherapy agents. Air blowing towards the worker is an example of a horizontal or laminar flow hood.

52. E. Rationale: Lactose, microcrystalline cellulose, and starch are all commonly used as a diluent or filler to provide bulk and cohesion of the powder blend. Active and inactive components will conglomerate together making the transfer into capsule shells much smoother.

53. E. Rationale: The density of the substance being placed in the capsule plays a role on exactly what capsule size to work with. Assuming a density close to 1, size #2 holds 370 mg and size #3 holds 300 mg. So either of these choices could be appropriate, depending on powder volume and density. Capsule #1 can hold 500 mg and capsule #5 can hold 130 mg.

54. C. Rationale: 200 mg three times a day is 600 mg and for 4 days is 2400 mg total. The vials contain 25 mg/mL times 20 mL gives 500 mg per vial. Thus, 500 mg times 5 vials gives you 2500 mg, giving enough theophylline to cover the 2400 mg required for the prescription.

55. E. Rationale: The prescription is accurately written. All other choices listed do not hold true.

56. D. Rationale: Sintering is a process in which powdered materials are heated to form a coherent mass. It may be employed when making tablet triturates.

57. D. Rationale: Magnesium stearate and sodium lauryl sulfate are both used as tablet/capsule lubricants. Sodium benzoate is most often used as a preservative.

58. C. Rationale: Methylparaben and sodium benzoate are both used as antimicrobial preservatives. Alcohol, although sometimes used for its preserving and sterilizing properties, is not considered by the USP-NF to be an antimicrobial preservative.

59. C. Rationale: 50 grams of coal tar would bring the total weight of the ointment to 500 grams. 50 grams is 10% of 500. This calculation does not take density into consideration.

60. C. Rationale: A 0.22 micron filter can fine enough to filter out glass particles and bacteria, but viruses are still too small to be filtered out. A micron filter of 0.02 is required for the filtering of all viruses.

61. B. Rationale: A simple proportional equation of $60 \text{ mL}/0.5\% = X \text{ mL}/2\%$ yields a result of 15 mL. 15 mL plus an additional 45 mL NS would give you 60 mL of the 2% solution required.

CHAPTER 4

1. C. Rationale: ConsumerLab.com independently evaluates nutritional supplements through lab tests and provides this information to both health professionals and consumers. ConsumerReports.org is an independent nonprofit organization that evaluates a variety of products, including diet and nutrition products. ASHP Essentials provides drug information including dosing, interactions, pharmacokinetics, and dosage forms, but does not include information about specific 'brand name' products.

2. E. Rationale: FDA.gov does not test herbal supplements for quality, purity, or safety and would not be able to provide a recommendation. ConsumerLab.com independently evaluates nutritional supplements through lab tests and provides this information to both health professionals and consumers. ConsumerReports.org is an independent nonprofit organization that evaluates a variety of products, including diet and nutrition products. USP.org is an official public-standards setting authority and wide number of drugs and over-the-counter medications, as well as dietary supplements and sets standards for quality, purity, and strength of dietary supplements. NSF.org is involved in testing dietary supplements and provides product certification for dietary supplements.

3. D. Rationale: Drug Facts & Comparisons is organized by therapeutic use.

4. A. Rationale: The Handbook of Injectable Drugs is organized alphabetically by generic name.

5. E. Rationale: Lexi-Comp, Drug Facts and Comparisons, and USP Volume 1 all provide unlabeled uses for drugs.

6. E. Rationale: Natural Standard does not provide a drug identifier. Clinical Pharmacology, Facts and Comparisons eAnswers, and WebMD provide a drug identifier tool within their online products.

7. B. Rationale: Harriet Lane provides separate age, height, and weight charts for boys and girls. Neofax and Identidex do not contain height and weight charts.

8. E. Rationale: FDA Medwatch is a service where both consumers and health care professionals can report product quality problems, use errors, adverse reactions, and therapeutic inequivalence/failure. These reports can be submitted online, by phone, or by submitting the MedWatch 3500 form by mail or fax.

9. A. Rationale: Primary literature is original research published for the first time. Secondary literature is derived from primary literature and includes analyzing, condensing, and synthesizing primary literature. Tertiary

literature is derived from primary and secondary literature and includes reference books.

10. E. Rationale: ISMP (Institute for Safe Medical Practices) is devoted to medication error prevention and safety and provides a list of sound-alike look-alike drugs.

11. B. Rationale: PubMed can be searched without MeSH terms.

12. C. Rationale: A PMID is a PubMed Identifier, which is a unique number assigned to a citation found in PubMed. Using the PMID in PubMed yields the abstract of the article you are looking for. Using a PMID in Micromedex, EMBASE, or Ovid would not yield this result since the PMID is not made for these search engines.

13. A. Rationale: Reporting adverse events to MedWatch is voluntary, and all adverse events that occur may not be reported.

14. B. Rationale: MedWatch publishes safety-related drug labeling.

15. A. Rationale: P&T stands for Pharmacy and Therapeutics, is usually composed of both pharmacists and physicians from multiple specialties, and reviews drugs for addition to the formulary.

16. B. Rationale: The P&T committee does not review, monitor, or approve and disapprove research. The P&T committee reviews medications for addition to the formulary.

17. D. Rationale: Therapeutic interchange is the substitution of a drug that is chemically different but therapeutically similar to the medication prescribed. Generic substitution is the substitution of a generic medication for a brand name medication. Pharmaceutical alternatives contain the same therapeutic moiety, but are different salts, esters, or complexes of that moiety or are different dosage forms (tablets versus capsules) or strengths. Pharmaceutical equivalents have the same active ingredients, are the same dosage form, have the same route of administration, and are identical in strength or concentration.

18. A. Rationale: Retrospective data has no impact on clinical outcome because it only looks at medical records of patients; it is usually collected from databases not real practice settings. There are multiple resources available to find retrospective data, depending on the subject being researched, and retrospective trials take less time because they do not need to have actual patients in clinical practice settings.

19. A. Rationale: The study result is statistically significant because $p < 0.05$ and it is clinically significant because a decrease in blood pressure by 10 mmHg can have a significant impact on a patient's health.

20. D. Rationale: Phase III trials usually include only several hundred to several thousand people from the

general population who are relatively healthy and last, on average, 3 years.

21. A. Rationale: Type A adverse drug reactions are usually dose dependent and predictable. Typically, they are recognized before a drug is marketed. Type B reactions are those that are unrelated to known pharmacological actions and are typically caused by immunological mechanisms. Type A reactions have a pharmacokinetic basis.

22. D. Rationale: Meta analysis takes different studies that address the same research topic and combines the results. RCT, Cohort, and Case Studies are all individual types of study designs, and results are not combined with other similar studies

23. B. Rationale: Surrogate measures are substitutes for real clinical outcome measures and are often chosen because they are easily detected versus a future marker such as mortality. However, for a disease like sepsis, which has a high mortality rate, the clinical endpoint of mortality is easy to assess and is a primary indicator of drug efficacy.

24. C. Rationale: Nominal data are categorical and are not placed in any particular order. In the study, people have either died by day 28 or they have not, leaving only two possible options. Ordinal data are categorical data that are placed in a logical order. Continuous data is data that can be measured on a scale.

25. B. Rationale: Martindale is the only option that includes information on foreign drugs. Red Book Drug Topics, Lexi-Comp, and AHFS do not deal with foreign drugs, instead they focus on drug information, side effects, and product and pricing information within the United States.

26. E. Rationale: In a triple-blind study the investigators, the experimental subjects, and the statistician are blinded or unaware of the nature of the treatment the participant is receiving.

27. C. Rationale: VAERS is the vaccine adverse event reporting system. MedWatch reports to the FDA voluntarily of adverse events and reactions from medications and medical devices. The Naranjo criteria classify the probability that an adverse event is related to drug therapy.

28. A. Rationale: A meta-analysis is a type of research study that combines the results of several studies to address a research hypothesis. This is done by identifying common study characteristics and primary endpoints among the trials collected to come to a larger and significant conclusion. Randomized controlled trials, cross-over studies, case-control studies, and cohort studies are all individual studies.

29. C. Rationale: An open label trial is a clinical trial in which both participants and researchers know which treatment is being administered, so both the Rosenthal

and Hawthorne effects can come into play. In a single blind trial, the participants do not know which treatment they are being administered but the researchers do. And in a double blind trial, neither participants nor researchers know which treatment is being administered, so it has the least risk of potential bias.

30. B. Rationale: A Type I (α) error is when the researcher falsely rejects the null hypothesis, which is what was done in this question. A Type II (β) error is when the researcher accepts the null hypothesis but the null hypothesis is false.

31. A. Rationale: MedLine is the largest component of PubMed and is accessible free of charge.

32. C. Rationale: Primary literature consists of original clinical trial publications. Secondary literature consists of databases or articles about an original study that have been modified or interpreted. For example, PubMed is a resource for secondary literature. Tertiary resources generally provide an overview of a topic by summarizing the results of several studies; examples of tertiary literature are textbooks and drug information databases.

33. A. Rationale: The National Institutes of Health and the National Library of Medicine worked to develop DailyMed. The information found on the DailyMed website includes FDA approved drug labeling (or the “package insert”).

34. C. Rationale: The PDA counterpart of Micromedex is mobileMicromedex.

35. E. Rationale: PubMed is a service of the US National Library of Medicine available free to the public.

36. C. Rationale: The truncation symbol in PubMed is * (e.g., premature* retrieves premature, prematurity, etc). When a truncation symbol is used, PubMed will not attempt to map the term.

37. B. Rationale: The primary reason for the Peer Review Process is to ensure accuracy and quality of content and clarity of each piece.

38. C. Rationale: The National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as “any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer . . . related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.”

39. D. Rationale: Privacy refers to personally identifiable information about an individual; the “state of being free from unsanctioned intrusion.”

40. D. Rationale: Copyright law is a subsection of intellectual property law. Other types of intellectual

property include trademarks, patents, industrial design rights and trade secrets in some jurisdictions.

41. C. Rationale: Data is considered continuous if the values can take on any value and be ordered or measured. For example, blood pressure, temperature, height, and weight are all continuous data.

42. A. Rationale: Plagiarism is copying or stealing the words or ideas without giving credit for the original idea or language.

43. A. Rationale: The Digital Object Identifier (DOI) a unique alphanumeric string assigned to a digital object (e.g., an electronic journal article or book chapter).

44. C. Rationale: Resources that may be used to check the compatibility of a drug with another drug or the stability of a drug include Trissel's Handbook of Injectable Drugs and King's Guide to Parenteral Admixtures.

45. A. Rationale: An adverse effect is defined as any undesirable effect associated with the use of a drug at normal dose.

46. D. Rationale: Primary literature is original research published for the first time that describes research methodology and scientific results that lead to therapeutic conclusions. It is the most current information.

47. A. Rationale: Both researcher and patient are not made aware of who is receiving placebo or study drug. It removes internal bias.

48. B. Rationale: A well conducted study will have both internal and external validity.

49. A. Rationale: If the confidence interval does not cross 0, the results are statistically significant.

50. A. Rationale: Confidence intervals are used in addition to p values to determine if statistically significant results are clinically significant.

51. E. Rationale: Continuous data can be measured on a scale and can have almost any numeric value on that scale, and it can also be divided into smaller increments. Mortality and gender cannot be described in this way and thus are not continuous.

52. C. Rationale: Using keywords and Boolean terms (AND, NOT, OR) to link search terms together is usually the most efficient way to search. The keyword "or" will yield the highest number of results.

53. C. Rationale: King Guide to Parenteral Admixtures is beneficial for determining compatibility and stability of injectable medications.

54. B. Rationale: Yahoo.com is a search engine that allows users to search websites and indexes information that is found.

55. B. Rationale: The Weber effect is a phenomenon that states that the number of reported adverse reactions for a drug increases until the middle to end of the second year of marketing.

56. B. Rationale: Ideally, a well conducted study would have both internal and external validity, which would make its results the most general.

57. C. Rationale: After the drug is approved and is being marketed, the drug's maker may conduct clinical trials called Phase IV or Post-Marketing Surveillance study to evaluate side effects, risks, and benefits over a long period of time.

58. B. Rationale: A type II error occurs when one rejects the alternative hypothesis (fails to reject the null hypothesis) when the alternative hypothesis is true. The probability of a type II error is denoted by β .

59. D. Rationale: Statistical power of a study can be used to calculate the sample size needed for the study results to have statistical significance and is determined before enrollment.

60. E. Rationale: A medication use evaluation is an evaluative method, reviewing practitioner prescribing, pharmacist dispensing and patient use of medications is considered. It is an ongoing, systematic process designed to maintain the appropriate and effective use of drug and improve quality of care for patients.

61. A. Rationale: Nominal data can be counted but not put into any order or measured. Therefore order is not important and it cannot be a measurement.

62. E. Rationale: Ethical issues when conducting a study include informed consent issues, institutional review board (IRB) approvals, and confidentiality issues, as well as power of the study.

63. A. Rationale: Therapeutic Interchange infers switching from one drug in a class to a similar drug in the same class do to formulary restrictions. Prevacid is not the generic equivalent to Protonix. Pharmaceutical alternative and equivalence do not pertain to what the question is asking.

64. E. Rationale: The role of a pharmacist in evidence-based medicine includes accurately integrating medical literature, evaluating levels of evidence from clinical studies, and performing a comprehensive review of the literature.

65. C. Rationale: A formulary is a regularly updated list of medication used in the diagnosis, prophylaxis, or treatment of disease.

66. B. Rationale: Intent to treat analysis "includes all randomized patients in the groups to which they were randomly assigned, regardless of their adherence with the entry criteria, regardless of the treatment the actually received, and regardless of subsequent withdrawal from treatment or deviation from protocol."

67. B. Rationale: Pharmacy and Therapeutics Committee (P&T) is a committee that oversees the policies and procedures related to all aspects of medication use within an institution.

68. A. Rationale: Guided-use strategies are additions to the formulary with additional processes in place to improve therapeutic outcomes.

69. D. Rationale: Off-label use should be based on comprehensive and balanced review of scientific evidence and patient safety. The P&T committee should establish a protocol guiding its use.

70. B. Rationale: A prospective medication use evaluation involves the pharmacist evaluating the patient's planned drug therapy before dispensing the medication.

71. C. Rationale: The patient has slight bradycardia, but his pulse is still > 50 bpm. Bradycardia is a common side effect of beta blockers such as atenolol, and it is important to assess if the patient also has orthostatic hypotension. If so, then the physician may need notification. If the patient is not symptomatic, he should continue to take his medication and monitor his pulse daily. The patient should not be advised to discontinue the medication since abrupt withdrawal can cause acute tachycardia, ischemia, and/or hypertension.

72. A. Rationale: Nexium is proton pump inhibitor used for GERD that should be taken daily before breakfast. It does not cause sedation, has no antifungal effects, and no effects on lowering blood pressure.

73. D. Rationale: A meta-analysis is a method of combining results of previous and similar research to determine a single estimate of treatment. The purpose is to increase sample size and decrease the chance of a type II (beta) error.

74. C. Rationale: Cochran's Q statistic is calculated from simulated measurements data with binary responses. It is the most common tool employed to assess how dissimilar data are in a meta-analysis.

75. A. Rationale: Gender (male/female) is an example nominal data or categorical data. Likert scales and visual analog scales are ordinal data, data that reflect ranking. Blood glucose is an example of continuous data, a value within a defined range.

76. B. Rationale: Phase I trials only include healthy volunteers to get a true baseline for toxicology, metabolism, and pharmacologic activities and to give some early evidence of effectiveness. By design Phase I trials include fewer than 100 subjects, and the study usually goes for less than 1 year. Patients for whom the drug was intended are usually accepted in Phase II.

77. C. Rationale: Medline is the only database listed that is free to the public. The rest require a fee for subscription and/or can only be accessed by professionals and institutions that have access.

78. B. Rationale: The answer is calculated by taking 75 patients that developed breast cancer in the HRT group and dividing by the 38 in the control group that developed breast cancer giving the answer of 1.97. This is stating that 1.97 patients taking HRT will develop breast cancer for every 1 patient in the control group that develops breast cancer.

79. B. Rationale: Trissel's Handbook on Injectable Drugs is used for drug compatibility and stability. Remington's is for compounding information. Martindale's is a complete drug reference. Brigg's is focused on drugs during pregnancy and lactation. Merck Index is a comprehensive collection of drug monographs.

80. A. Rationale: Historically USP DI Vol I contained information for the healthcare professional. USP DI Vol II contained advice for the patient. USP Vol III contained approved drug products and legal requirements. USP-NF contains standards for medicines, dosage forms, drug substances, excipients, medical devices, and dietary supplements.

81. A. Rationale: Brigg's deals with drugs during pregnancy and lactation. Merck Index is a comprehensive collection of drug monographs. Trissel's Handbook on Injectable Drugs is used for drug compatibility and stability. PDR provides specialty focused clinical resources.

82. B. Rationale: IPA is a database of literature abstracts making it secondary literature. All others listed are tertiary literature sources.

83. D. Rationale: Remington's should be used to obtain information on pharmaceutical compounding. Trissel's Handbook on Injectable Drugs is used for drug compatibility and stability. Martindale's is a complete drug reference. AHFS is a drug information database. Hansten and Horn's deals with drug interactions and their mechanisms.

84. C. Rationale: Martindale's is a drug information database that does contain information on foreign drugs. Trissel's Handbook on Injectable Drugs is used for drug compatibility and stability. Remington's is for compounding information. Martindale's is a complete drug reference. Brigg's deals with drugs during pregnancy and lactation.

85. A. Rationale: Hansten and Horn's deals with drug interactions and their mechanisms. Remington's should be used to obtain information on pharmaceutical compounding. Brigg's deals with drugs during pregnancy and lactation. Index Nominum contains area-specific information for medicinal preparations in 133 countries.

86. B. Rationale: Red Book Drug Topics does not deal with foreign drugs; instead it focuses on product and pricing information. The other sources listed do deal with foreign entities.

87. C. Rationale: PDR is the only source listed that actually contains manufacturer's package inserts. The other sources listed are useful drug information, products, and pricing sources, but only PDR contains the actual package insert.

88. A. Rationale: MEDMARx was developed by the USP to report and evaluate medication errors. MedWatch is similar, but was developed by the FDA for reporting drug misadventures. VAERS is used for reporting adverse events related to vaccinations.

89. D. Rationale: Multi-center pertains to study sites where a clinical study is conducted. Blocked, Cluster, and Stratified are all different ways of how to randomize patients in a study.

CHAPTER 5

1. B. Rationale: Maxair® is the brand name for pirbuterol, a beta-2-adrenergic agonist with a similar structure to albuterol.

2. C. Rationale: Norvasc® comes in 2.5 mg, 5 mg, and 10 mg oral tablets.

3. D. Rationale: Xalatan® is the brand name for latanoprost. It should be refrigerated before opened and can be kept at room temperature once opened for up to 6 weeks, but should never be frozen. It may discolor the iris, but not urine.

4. C. Rationale: Selegiline is contraindicated within 14 days of sertraline use because the combination increases the risk of serotonin syndrome, a potentially life-threatening condition characterized by symptoms such as increased heart rate, tremor, mental status changes, and hyperthermia. The physician should be notified in order to switch the patient's medications.

5. C. Rationale: Meperidine use is contraindicated within 14 days of selegiline use because the combination increases the risk of serotonin syndrome, a potentially life-threatening condition characterized by symptoms such as increased heart rate, tremor, mental status changes, and hyperthermia. The meperidine should be switched to another pain medication that does not interact with selegiline.

6. D. Rationale: NPH insulin is cloudy in appearance. Regular insulin should be clear in appearance.

7. B. The generic name of Invirase® is saquinavir, and it is a protease inhibitor. The brand name of ritonavir is Norvir®, the brand name for nelfinavir is Viracept®, and the brand name for indinavir is Crixivan®.

8. C. Rationale: Lantanoprost is used in patients with glaucoma or ocular hypertension. Pantoprazole is in the same class of proton pump inhibitors as lansoprazole and is available generically, making it the best option to recommend. Aripiprazole is used to treat schizophrenia and bipolar disorder. Fluconazole is an antifungal agent.

9. B. Rationale: A daily dose of Lipitor® 10 mg is equal to 20 mg simvastatin. Simvastatin 10 mg does not have an equivalent Lipitor® dose. Rosuvastatin 5 mg is equivalent to Lipitor 20 mg and rosuvastatin 10 mg is equivalent to Lipitor® 40 mg.

10. B. Rationale: The generic name of Aciphex® is rabeprazole, which is a proton pump inhibitor. Aripiprazole is the generic name for Abilify®, an antipsychotic. Pantoprazole is the generic name for Protonix®, a proton pump inhibitor. Albendazole is the generic name for Albenza®, which is used to treat worm infestations.

11. A. Rationale: The generic name of Noxafil® is posaconazole, an antifungal medication. Methimazole is the generic name for Northyx®, a drug used in patients with hyperthyroidism. Voriconazole is the generic name for VFEND®, an antifungal medication. Albendazole is the generic name for Albenza®, which is used to treat worm infestations.

12. C. Rationale: Terazol® is the brand name for terconazole, an antifungal medication. Tramadol is the generic name for Ultram®, an opioid analgesic. Tioconazole is the generic name for Vagistat-1®, a vaginal antifungal agent. Miconazole is used in multiple different antifungal preparations and can be found under the brand names of Monistat®, Lotrimin®, and Micaderm®.

13. B. Rationale: The most appropriate recommendation would be to hold the tube feedings for 1 hour before and 1 hour after the phenytoin administration. Another option would be to increase the phenytoin dose to compensate for the lowered bioavailability due to the tube feeding. The other choices are not correct because they do not ensure proper phenytoin levels or adequate nutrition for the patient.

14. C. Rationale: Prevalite® and Questran® are both brand names for cholestyramine resin, a bile acid sequestrant that can be used in the treatment of pruritis associated with elevated bile levels. Megace® is the brand name for megestrol, a drug used in the palliative treatment of endometrial and breast cancers, not in biliary obstruction.

15. B. Rationale: Prazosin, an alpha-1 blocker, can cause significant orthostatic hypotension and syncope, especially with the initial dose, or if therapy is interrupted or increased quickly. All of the other medications can cause hypotension as well but none of them are alpha-1-blockers, which have the most potential of causing first dose hypotension.

16. A. Rationale: Benztropine has both antihistamine and anticholinergic properties, and is used to reduce the extrapyramidal side effects of phenothiazine, an antipsychotic that causes extra pyramidal symptoms (EPS) due to its antagonism of dopamine.

17. A. Rationale: The orbit and the area around it of the eye is an immunocompromised environment that can become rapidly infected with *Pseudomonas aeruginosa*.

and develop destructive lesions due to the infection. It is common for *Pseudomonas* to be resistant to antibiotics and in some cases, eye surgery may be necessary in order to remove the infected tissue.

18. B. Rationale: Filgrastim, which stimulates granulocyte production, is used to selectively increase neutrophil production in patients receiving chemotherapy. Thrombopoietin is not used therapeutically. Erythropoietin is used in patients with low hemoglobins to stimulate red blood cell production, and Interleukin 11 is a cytokine that improves platelet production in patients with chemotherapy-induced thrombocytopenia. Sagramostim is used to shorten time to neutrophil recovery in patients with acute myelogenous leukemia (AML).

19. D. Rationale: Intravenous saline and oral rehydration are both options that may be used in restoring fluids in a 5-year-old patient with diarrhea. Depending on the cause and severity of the diarrhea, antibiotics may also be used.

20. D. Rationale: Bulimia can cause many electrolyte imbalances including hypernatremia, hyponatremia, hypokalemia, and hypochloremia. The electrolyte losses and extent of losses depends on the extent of the bulimia and the fluid status of the patient. For example, if the patient becomes dehydrated due to the bulimia, most likely hypernatremia will result.

21. A. Rationale: Adderall® is a stimulant used to treat attention deficit hyperactivity disorder (ADHD).

22. C. Rationale: Prazosin is an alpha-1 blocker that can cause significant orthostatic hypotension, dizziness, and syncope, which is why if taken before bed, this side effect will be minimized.

23. D. Rationale: The active ingredient in both Claritin® and Alavert® is loratidine, so Alavert® may be substituted for Claritin®. The most common active ingredient in Sudafed® is phenylephrine. The active ingredient in Bonine® is cyclizine and the active ingredient in Allegra® is fexofenadine.

24. B. Rationale: Nitroglycerin is a vasodilator used in the treatment of angina, perioperative hypertensive emergency, pulmonary hypertension, and congestive heart failure. It is not used to treat chronic hypertension.

25. E. Rationale: Alcohol may delay the absorption and elimination of sulfonylureas, causing an adverse reaction. The mechanism of action of sulfonylureas is stimulating insulin release from the beta cells in the pancreas. Sulfonylureas, unlike metformin, carry a risk of hypoglycemia.

26. D. Rationale: Simethicone disperses and prevents gas pockets in the gastrointestinal system, providing relief from bloating, pressure, and discomfort from gas.

27. C. Rationale: Lexapro® is available in 5 mg, 10 mg, and 20 mg oral tablets.

28. A. Rationale: Metformin can cause lactic acidosis, patients with serum creatinine levels over ≥ 1.5 mg/dL in males or ≥ 1.4 mg/dL in females, or New York Heart Association (NYHA) Class III or IV heart failure are at increased risk for this complication. Due to risk of lactic acidosis, metformin is not safe to use in patients with renal failure. Metformin does not show first dose effects and is excreted mostly in the urine. Metformin works by decreasing hepatic glucose production, increasing insulin sensitivity, and decreasing absorption of glucose in the intestines. It does not stimulate insulin release.

29. E. Rationale: Acarbose is an alpha-glucosidase inhibitor has very low bioavailability and is less than 2% absorbed. Since it acts locally in the GI tract due to its low absorption, it is not safe to use in patients with chronic intestinal disease.

30. D. Rationale: Glyburide may cause a disulfiram-like reaction because alcohol may delay the absorption and elimination of it. The onset of action of glyburide is 15-60 minutes. Oral agents used to treat type 2 diabetes mellitus cannot be used in type 1 diabetics because their beta cells are non-functional and they need daily insulin injections, so glyburide cannot be used to treat type 1 diabetes mellitus.

31. E. Rationale: Ranitidine is a histamine-2 antagonist that can be used to treat peptic ulcer disease. It may cause dizziness and is eliminated both in the urine and feces. All of the above choices are correct.

32. B. Rationale: Oral agents used to treat type 2 diabetes mellitus cannot be used in type 1 diabetes, since type 1 diabetics need daily injections of insulin because their beta cells are non-functional, so metformin cannot be used to treat type 1 diabetes mellitus.

33. A. Rationale: *H. pylori* is believed to be responsible for the majority of peptic ulcers.

34. E. Rationale: Ultram® (tramadol) is not currently scheduled by the Drug Enforcement Association (DEA). None of the choices are correct.

35. B. Rationale: Captopril, an ACE-inhibitor, works by inhibiting the angiotensin converting enzyme.

36. A. Rationale: Percodan® contains oxycodone and aspirin. The combination of aspirin and Coumadin® increases bleeding risk and should not be used together unless carefully monitored by a physician. Demerol® and Dilaudid® do not contain aspirin and therefore do not have the risk of this interaction.

37. E. Rationale: Furosemide is a loop diuretic that inhibits the reabsorption of sodium and chloride in the ascending loop of Henle and the distal renal tubule.

38. A. Rationale: The current maximum adult daily dose of acetaminophen is 4 g. Each tablet of Darvocet-N 100® contains 650 mg of acetaminophen. So 4000 mg/650 mg = 6 tablets maximum a day. Note: The FDA is currently

considering lower maximum daily limits for acetaminophen dosing.

39. C. Rationale: Metoprolol, a beta blocker, is a selective inhibitor of beta-1 adrenergic receptors.

40. D. Rationale: Hydrochlorothiazide is a thiazide diuretic that blocks sodium in the distal tubule.

41. A. Rationale: Candesartan binds to the AT1 angiotensin II receptor and this prevents angiotensin II from binding. This is why candesartan is classified as an angiotensin receptor blocker (ARB).

42. C. Rationale: Tamoxifen competitively binds to estrogen receptors and inhibits the effects of estrogen. It is a cytostatic anti-estrogen, since it suppresses cell growth and multiplication.

43. E. Rationale: Glipizide is a sulfonylurea that works by stimulating insulin release from beta cells in the pancreas.

44. B. Rationale: Simvastatin competitively inhibits HMG-CoA reductase, the enzyme that is responsible for catalyzing the rate limiting step in the synthesis of cholesterol.

45. D. Rationale: Methylprednisone is a corticosteroid that affects a number of physiologic systems such as immunity, inflammation, and stress.

46. A. Rationale: Insulin Lispro is a rapid acting injectable insulin.

47. A. Rationale: Nedocromil is a mast cell stabilizer that inhibits a variety of inflammatory cells.

48. B. Rationale: Albuterol is a beta-2-adrenergic agonist.

49. E. Rationale: Diphenhydramine is an H1-receptor antagonist.

50. C. Rationale: Verapamil is a non-dihydropyridine calcium channel blocker that inhibits calcium from entering the 'slow channels' of vascular smooth muscle and myocardium. Cromolyn is a mast cell stabilizer. Albuterol is a beta-agonist. Diphenhydramine is an H1-antagonist. Ranitidine is an H2-antagonist.

51. D. Rationale: Ranitidine is an H2-antagonist that competitively inhibits histamine at H2 receptors in gastric parietal cells. Cromolyn is a mast cell stabilizer. Albuterol is a beta-agonist. Verapamil is a calcium channel blocker. Diphenhydramine is an H1-antagonist.

52. B. Rationale: Patients with asthma who are stabilized on corticosteroids should always have the steroid tapered when discontinuing or switching to a non-steroid controller agent. Patients may experience withdrawal symptoms if prednisone is not gradually discontinued. These symptoms include fatigue, weakness, decreased appetite, weight loss and nausea. The patient should be gradually tapered off of the prednisone.

53. D. Rationale: Flexeril® (cyclobenzaprine HCl) is available as both a 5 mg and a 10 mg tablet.

54. D. Rationale: Fluticasone is an inhaled corticosteroid. Diphenhydramine is an H1-antagonist. Ranitidine is an H2-antagonist. Albuterol is a beta-agonist. Metoprolol is a beta-antagonist.

55. A. Rationale: Guaifenesin is an expectorant that helps loosen phlegm and thin bronchial secretions to make coughs more productive. Montelukast is a leukotriene antagonist used for the treatment of asthma. Ipratropium is an anticholinergic agent that dilates the bronchi and bronchioles and is useful in asthma and COPD.

56. B. Rationale: Albuterol is a short-acting beta-agonist that relaxes smooth muscle and is the treatment of choice for relief of acute symptoms. Cromolyn sodium stabilizes mast cell function and is used as an alternative in patients who have mild, persistent asthma. Prednisone is a systemic corticosteroid that is used for moderate to severe exacerbations. Ipratropium is an anticholinergic that reduces vagal tone of the airway, and it is used in moderate to severe exacerbations.

57. D. Rationale: Guaifenesin is an expectorant that helps loosen phlegm and thin bronchial secretions to make coughs more productive.

58. C. Rationale: Brimonidine is an alpha2-agonist that reduces aqueous humor formation and is used to treat glaucoma.

59. D. Rationale: Finasteride is dosed at 5 mg daily. Dutasteride, another medication used to treat benign prostatic hyperplasia (BPH) is dosed at 0.5 mg daily.

60. D. Rationale: Naproxen is dosed at 750 mg initially for an acute gout attack, followed by 250 mg every 8 hours, and 500 mg twice daily for acute migraine and for rheumatoid arthritis.

61. B. Rationale: Diazepam is the most appropriate choice for status epilepticus due to its rapid onset of action (almost immediate). Phenytoin is used in status epilepticus as second-line treatment due to a longer onset of action (~30 min). Ethosuximide is used to treat absence seizures. Paraldehyde was formerly used for refractory status epilepticus but it has been removed from the market in the US. Glutethimide is used for the short term treatment of insomnia but is not currently available in the US.

62. C. Rationale: Hydralazine may cause a lupus-like reaction that is dose-related and includes: fever, arthralgia, lymphadenopathy, myalgia, chest pain, and pleuritic chest pain.

63. B. Rationale: Ibutilide (Corvert®) is a Class III antiarrhythmic agent not a calcium channel blocker; all the others are calcium channel blockers.

64. E. Rationale: The dosage of doxycycline does not need to be adjusted in patients with renal failure. Doxycycline

is eliminated mostly into bile and feces, with only about 10% of the clearance going through the kidneys. As a result of this unique elimination, doxycycline would not accumulate in the body of a man with renal insufficiency. Minocycline, demeclocycline, oxytetracycline and tetracycline may increase BUN in renal impaired patients and may accumulate systemically.

65. E. Rationale: According to the American Autonomic Society and the American Academy of Neurology, orthostatic hypotension is defined as a systolic blood pressure decrease of at least 20 mm Hg or a diastolic blood pressure decrease of at least 10 mm Hg within three minutes of standing. It may be caused by various types of drugs including alpha blockers like prazosin, sildenafil (Viagra®), and amitriptyline (Elavil®). Other antihypertensive drugs, diuretics, vasodilators, insulin, MAO inhibitors, tranquilizers, narcotics, phenothiazines, sympatholytics, sympathomimetics, and tricyclic antidepressants may also cause orthostatic hypotension.

66. B Rationale: Vyvanse® (lisdexamfetamine) is indicated for attention deficit hyperactivity disorder (ADHD).

67. B. Rationale: The smallest strength of Percocet® is 2.5 mg oxycodone HCl – 325 mg acetaminophen. There is no strength of Percocet® with 1 mg of oxycodone HCl.

68. E. Rationale: Cholestyramine binds some drugs in the intestine and prevents their absorption. These drugs include phenobarbital, chlorothiazide, and warfarin among others.

69. C. Rationale: Kantrex® is the brand name for kanamycin. Moxatag®, Trimox®, Amoxil®, and Wymox® are brand names for amoxicillin.

70. D. Rationale: Studies have shown that multiple anticonvulsant medications can reduce blood levels of folic acid. There is no evidence to show that anticonvulsants interfere with the metabolism of riboflavin, tyrosin, rennin, or pyridoxine.

71. E Rationale: Zyvox® (linezolid) is available as IV injection, tablets, and oral suspension.

72. B. Rationale: Staph infections most commonly result in skin infections that usually result in a localized collection of puss, known as a boil. Strep infections commonly result in sore throats and pneumonia. *Candida* infection commonly results in oral thrush, yeast infections, and jock itch. *Aspergillus* commonly causes lung infections. *Pseudomonas* infection commonly causes pneumonia, urinary tract infections, and bacteremia.

73. B. Rationale: Idoxuridine is an antiviral agent that has demonstrated efficacy against HSV infections and is available in an ophthalmic form. Mupirocin and bacitracin are antibacterial agents that would not be effective against a virus. Amphotericin B is an anti-fungal agent that would not be effective against a virus. Thiabendazole is an anthelmintic agent that has activity against parasitic infections, but not viral infections.

74. D. Rationale: Tolnaftate is an anti-fungal used for the treatment of tinea pedis, tinea cruris, and tinea corporis. Miconazole, nystatin, and clotrimazole are all used to treat Candidal infections.

75. C. Rationale: Methotrexate is used to treat psoriasis. The dose is 2.5 mg/dose every 12 hours for 3 doses given weekly.

76. E. Rationale: Corticosteroids block prostaglandin activity as well as interfere with enzymes involved in inflammation, thereby reducing inflammation. Corticosteroids suppress the immune system, therefore making the patient more susceptible to infection and masking infectious symptoms.

77. A. Rationale: Piroxicam is dosed once daily, compared to ibuprofen and naproxen that are dosed 2-4 times daily. Piroxicam may cause GI side effects and does not demonstrate cytoprotective effects. Compared to other NSAIDs, piroxicam has the same mechanism of action and is more expensive.

78. D. Rationale: Clomiphene citrate is used for the treatment of ovulatory failure, which can cause infertility. Clomiphene stimulates ovulation.

79. A. Rationale: E.P.T.® home pregnancy test detects levels of human chorionic gonadotropin, which is produced in pregnancy, soon after conception.

80. E. Rationale: NO is a biologic messenger that lines blood vessels and signals smooth muscle relaxation. NO also binds and activates guanylyl cyclase in the vascular smooth muscle, which is an enzyme that catalyzes the activation of c-GMP.

81. B. Rationale: Advair® is a combination of a long-acting beta2-adrenergic agonist, salmeterol, and a corticosteroid, fluticasone.

82. D. Rationale: INR is an internationally standardized ratio for reporting results of blood coagulation tests and standardizes variations in PT values. PT is prothrombin time, which can be highly variable from one institution to the next, and can yield different results if a patient has his or her blood tested at multiple sites. The PT can be used to monitor warfarin treatment but the PT has been largely replaced by INR monitoring. PTT is a partial thromboplastin time test used to monitor heparin, and as with the PT test, results are highly variable. Bleeding time measures platelet function, but is also highly variable due to variations in methods used.

83. D Rationale: InnoPran XL® is available as 80 mg and 120 mg capsules that contain sustained-release beads.

84. B. Rationale: Anhedonia is a symptom of major depressive disorder, as well as schizophrenia and other mental disorders. First generations antipsychotics commonly cause movement disorders, such as akathisia and tardive dyskinesia. Second generation antipsychotics commonly cause endocrine side effects, such as weight gain and diabetes.

85. C. Rationale: Latanoprost is a prostaglandin F₂-alpha analog that will not impact the patient's CHF and atrial fibrillation. Timolol blocks beta-adrenergic receptors and ocular administration can result in some systemic absorption. Beta blockers are used with caution in patients with CHF, and may worsen CHF symptoms. Epinephrine is rarely used for the treatment of glaucoma due to side effects, including high blood pressure and disturbances in heart rhythm.

86. B. Rationale: Oral corticosteroids can cause a variety of systemic side effects when used long term including osteoporosis, muscle wasting, hyperglycemia and mood changes. These side effects are not seen with inhaled corticosteroids. There is no improvement in efficacy or ease of use with inhaled corticosteroids.

87. D. Rationale: Lisinopril is an angiotensin converting enzyme inhibitor. Metoprolol is a beta blocker, doxazosin is an alpha-1 blocker, losartan is an angiotensin receptor blocker and furosemide is a diuretic.

88. A. Rationale: True. Cromolyn stabilizes mast cells and takes between 2-6 weeks to see maximum benefit in controlling chronic asthma.

89. A. Rationale: When compared to monotherapy, ACEI and ARB combinations can more effectively lower blood pressure.

90. A. Rationale: Antihypertensive drugs in different classes work by different mechanisms of action in different places in the body and therefore combining them may be beneficial in patient's refractory to monotherapy.

91. A. Rationale: Bicitra®, a medication that makes the urine less acidic, is the US brand name for sodium citrate and citric acid.

92. E. Rationale: Aprepitant (Emend®) is available as capsule and as an injection. The drug is a selective antagonist of human substance P/neurokinin 1 receptors. It is used to prevent nausea and vomiting associated with chemotherapy.

93. C. Rationale: Metformin works best in newly diagnosed type II diabetics and results in the greatest initial reduction of A1C of the oral medications available for diabetes. Insulin is usually initiated after metformin and other oral agents have been maximized. Acarbose is poorly tolerated due to GI side effects and most patients discontinue this medication due to the side effects. Pioglitazone may result in weight gain, and will not result in as much A1C lowering as metformin.

94. C. Rationale: Chlorpropamide (Diabinese®) is a first-generation sulfonylurea, and glipizide (Glucotrol®) is a second generation sulfonylurea used in the management of type 2 diabetes. Tolterodine is a muscarinic receptor antagonist used for overactive bladder.

95. E. Rationale: Type I diabetes is usually caused by an autoimmune disorder and is usually diagnosed in children

and young adults. Patients with type I diabetes cannot produce their own insulin and must take insulin. The most common symptoms of type I diabetes are polyuria, polydipsia, and polyphagia.

96. D. Rationale: Type II patients may still produce some insulin on their own, but are resistant to the effects of insulin. Therapy for patients with type II diabetes includes medications that increase receptor sensitivity to insulin, and does not necessarily have to be insulin. Type II diabetes tends to occur in overweight patients.

97. D. Rationale: Diagnosis of diabetes is confirmed by a fasting blood glucose greater than 126 mg/dL, a random plasma glucose greater than 200 mg/dL, or an oral glucose challenge with a 2 hr plasma glucose level greater than 200 mg/dL.

98. C. Rationale: Acetaminophen is not an NSAID; it reduces pain and fever but not inflammation. Celecoxib (Celebrex®) is an NSAID and selective COX-2 inhibitor. Ketorolac (Toradol®) is also an NSAID.

99. B. Rationale: False. Insulin glargine is a long-acting basal insulin analog with a slow onset of action. It starts lowering blood sugar in 1.5 to 2 hours.

100. B. Rationale: Prempro® contains conjugated estrogen and medroxyprogesterone and is used to treat the symptoms of menopause such as hot flashes and vaginal dryness.

101. C. Rationale: Viramune® (nevirapine) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) used to treat human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS).

102. E. Rationale: Epivir® (lamivudine), Ziagen® (abacarin) (Retrovir), Videx® (didanosine), and Norvir® (ritonavir) are available as syrup or oral solution

103. E. Rationale: Apidra® (insulin glulisine), Humalog® (insulin lispro), and Novolog® (insulin aspart) are rapid-acting insulins.

104. C. Rationale: Azopt® (brinzolamide) is a carbonic anhydrase inhibitor.

105. A. Rationale: Pravastatin (Pravachol®) is not metabolized by the cytochrome P450 system and is least likely to have drug interactions.

106. C. Rationale: Xopenex® is the brand name for levalbuterol. Ventolin® is brand name albuterol, Serevent® is salmeterol, and Flovent® is fluticasone.

107. D. Rationale: The dose of trazodone (Desyrel®) for depression is 150 mg per day in divided doses. The maximum dose of trazodone is 600 mg per day.

108. C. Rationale: Almotriptan (Axert®) belongs to a class of drugs called triptans and is available in two doses, 6.25 mg and 12.5 mg.

109. E. Rationale: Imitrex® belongs to a class of drugs called triptans and is available as a nasal spray, tablets, and injection.

110. B. Rationale: Ketorolac is an NSAID, aspirin is a salicylate, prednisone is a corticosteroid, morphine is an opioid, and diazepam is a benzodiazepine.

111. B. Rationale: The maximum daily dose of oral ketorolac for pain management is 40 mg.

112. C. Rationale: Ketorolac is not contraindicated in epilepsy. Ketorolac is contraindicated in renal failure due to volume depletion, in hemorrhagic diathesis due to possible inhibition of platelet functioning by ketorolac, in gastrointestinal perforation due to increased risk of GI perforation and in breast feeding since ketorolac enters the milk and could inhibit prostaglandin synthesis in neonates.

113. C. Rationale: Xalatan® is latanoprost. Toradol® is ketorolac. Accuset, Conista and Zerolast are all made up drug names.

114. C. Rationale: The correct daily dose of latanoprost for the treatment of glaucoma is 1.5 mcg (1 drop).

115. B. Rationale: Latanoprost has a peak effect at 8-12 hours. It has an onset of action of 3-4 hours, a volume of distribution of 0.16 L/kg, is excreted in the urine as metabolites, and has a half-life elimination of 17 minutes.

116. C. Rationale: Moduretic® is a combination of amiloride and HCTZ. Atenolol and chlorthalidone is Tenoretic. Triamterene and HCTZ is Dyazide. Losartan and HCTZ is Hyzaar. Clonidine and chlorthalidone is Combipres®.

117. E. Rationale: Combipres® is a combination of clonidine and chlorthalidone. Atenolol and chlorthalidone is Tenoretic. Triamterene and HCTZ is Dyazide. Amiloride and HCTZ is Moduretic. Losartan and HCTZ is Hyzaar.

118. A. Rationale: Tenoretic® is a combination of atenolol and chlorthalidone. Triamterene and HCTZ is Dyazide. Amiloride and HCTZ is Moduretic. Losartan and HCTZ is Hyzaar. Clonidine and chlorthalidone is Combipres.

119. B. Rationale: Dyazide® is a combination of triamterene and HCTZ. Tenoretic is a combination of atenolol and chlorthalidone. Amiloride and HCTZ is Moduretic. Losartan and HCTZ is Hyzaar. Clonidine and chlorthalidone is Combipres.

120. A. Rationale: Zosyn® contains piperacillin and tazobactam.

121. B. Rationale: Rosuvastatin is the generic name for Crestor®. Carvedilol is the generic name for Coreg®. Venlafaxine is the generic of Effexor®. Pioglitazone is the generic for Actos®.

122. D. Rationale: Primaxin® contains imipenem and cilastatin. Zosyn® is piperacillin and tazobactam. Unasyn®

is ampicillin and sulbactam. Synercid® is quinupristin and dalbopristin. Carbenin is panipenem and betamiron, a combination product available in Japan.

123. B. Rationale: Unasyn® contains ampicillin and sulbactam. Zosyn® is piperacillin and tazobactam. Synercid® is quinupristin and dalbopristin. Primaxin® is imipenem and cilastatin. Carbenin® is panipenem and betamiron, a combination product available in Japan.

124. B. Rationale: Cyclobenzaprine (Flexeril®) is a skeletal muscle relaxant. Diazepam is a benzodiazepine (BZD) and GABA receptor agonist. Amitriptyline is a tricyclic antidepressant (TCA), and phenobarbital is a barbiturate.

125. A. Rationale: The usual dose of cyclobenzaprine for treatment of pain is 15 mg daily, though some patients may require up to 30 mg/day.

126. B. Rationale: Cyclobenzaprine should not be used longer than 3 weeks, due to potential increased risk of side effects.

127. E. Rationale: The onset of action for cyclobenzaprine is ~1 hour and the duration of effect is 12-24 hours. The half-life elimination is 8-37 hours.

128. D. Rationale: Methocarbamol can be dosed as any of the following: 1.5 g PO qid, 1 g IM q8h, or 1-3 g IV q6h.

129. E. Rationale: Methocarbamol causes leukopenia, not leukocytosis. It also causes bradycardia, urticaria, vertigo, and jaundice.

130. D. Rationale: The correct initial dose of amlodipine is 5 mg once daily.

131. C. Rationale: The maximum daily dose of amlodipine is 10 mg once daily.

132. C. Rationale: Zolpidem is a hypnotic. Morphine is an opiate, citalopram is a selective serotonin reuptake inhibitor (SSRI), phenobarbital is a barbiturate, and phenelzine is an MAO Inhibitor (MAOI).

133. A. Rationale: The correct dosage of zolpidem is 10 mg.

134. A. Rationale: The maximum daily dose of zolpidem is 10 mg.

135. B. Rationale: Eszopiclone does not cause diplopia, but may cause nystagmus. Eszopiclone causes unpleasant taste, gynecomastia, hallucinations, and headache.

136. E. Rationale: Eszopiclone is indicated for insomnia.

137. A. Rationale: Terbutaline may cause hypokalemia in < 1% of patients, as beta2 agonists may decrease serum potassium.

138. A. Rationale: Methylphenidate is FDA approved for the treatment of narcolepsy.

139. B. Rationale: Aspirin is in FDA pregnancy risk category D. Acetaminophen is safe to use in pregnancy and is pregnancy category B.

140. C. Rationale: The initial dose of sulfasalazine in the treatment of ulcerative colitis is 1g PO 3-4 times/day. 0.5 g/day is initial treatment for rheumatoid arthritis.

141. A. Rationale: The brand name of sulfasalazine is Azulfidine®. Sulfonate is the name of a salt or ester of sulfonic acid.

142. C. Rationale: Seroquel® is quetiapine, Abilify® is aripiprazole. Elavil® is amitriptyline, Clozaril® is clozapine, and Risperdal® is risperidone.

143. B. Rationale: Abilify® is aripiprazole. Elavil® is amitriptyline, Seroquel® is quetiapine, Clozaril® is clozapine, and Risperdal® is risperidone.

144. C. Rationale: Patients with depression should be titrated to a maintenance dose of 300 mg/day of quetiapine. Studies have not shown added benefit in patients treated with 600 mg/day of quetiapine.

145. C. Rationale: Patients with schizophrenia should be initially titrated up to 300-400 mg/day in 2-3 divided doses. The usual maintenance range for quetiapine is 300-800 mg/day.

146. D. Rationale: Quetiapine does not cause bradycardia, rather it may cause tachycardia. Quetiapine can cause hypotension, somnolence, hypercholesterolemia, and fever.

147. A. Rationale: Carisoprodol is metabolized in the liver by CYP 2C19 to meprobamate.

148. A. Rationale: For schizophrenia, the initial dose of aripiprazole is 10-15 mg per day. Doses higher than 10-15 mg have not shown increased efficacy for the treatment of schizophrenia, so doses higher than 15 mg per day would be unnecessary.

149. A. Rationale: For bipolar disorder, the initial dose of aripiprazole is 15 mg per day; however, the dose may be increased to 30 mg per day if clinically indicated.

150. B. Rationale: Aripiprazole has an onset of action of 1-3 weeks.

151. B. Rationale: Olanzapine is not a FDA approved monotherapy for major depressive disorders. Olanzapine is FDA approved to be used in combination with fluoxetine for depression associated with bipolar disorder and for treatment resistant depression.

152. A. Rationale: Olanzapine may cause postural hypotension. Olanzapine is available as injection for intramuscular use only. It is also available in orally disintegrating tablets, and tablets for oral use. It is not, however, available as an oral suspension. It should never be given IV. The drug is an atypical antipsychotic and not

a serotonin agonist. It is 93% bound to plasma proteins and has a long half life ranging from 21 to 54 hours.

153. B. Rationale: The recommended, FDA approved, initial PO dose for clonidine in hypertension is 0.1 mg bid. JNC7 recommended total maximum daily dose is 2.4 mg for hypertension. The 5 mg and 10 mg are overdoses and can lead to hypotension, 0.1 mcg is a subtherapeutic dose, and 1 mg is not used during initial dosing.

154. A. Rationale: True. Drowsiness/sedation has been reported in up to 3% of patients using the transdermal dosage form, and is commonly reported with use of oral clonidine.

155. D. Rationale: Rituximab is a monoclonal antibody directed at CD-20 surface antigens of B cells and increases antibody-dependent cellular toxicity through complement directed at B cells. Pharmacodynamic/kinetic shows B-cell recovery occurs roughly 6 months after completing treatment, and returns to normal in a year. Rituximab has been approved for use in Rheumatoid Arthritis (RA), and angioedema has been reported in 11% of patients.

156. D. Rationale: Memantine mimics endogenous N-methyl-D-aspartate (NMDA) to uncompetitively antagonize NMDA types of glutamate receptor. It has no direct effect on acetylcholinesterase, dopamine, norepinephrine, or serotonin.

157. D. Rationale: The recommended initial adult dose is 5 mg/day. Memantine comes in a 5 mg and 10 mg dosing form; 2 mg qd and tid, and 0.5 mg/day are not FDA approved dosing regimens. The 5 mg bid is a step up in titrating the dose to 20 mg, and is not a recommended initial dose.

158. C. Rationale: Paroxetine (Paxil®) is a selective serotonin reuptake inhibitor (SSRI) antidepressant used for depression, obsessive compulsive disorder, and panic disorder.

159. E. Rationale: Singulair® is available in 4 mg granules and chewable tablets, a 5 mg chewable tablet, and a 10mg tablet.

160. A. Rationale: OTC Minoxidil is available as a solution and as a foam for stimulating hair growth. OTC tablets are not available; they are prescription only. No gel form is available.

161. A. Rationale: Diflunisal (Dolobid®) is classified as an NSAID. Penicillamine, hydroxychloroquine, methotrexate, sulfasalazine are all classified as DMARDs.

162. B. Rationale: The recommended initial dose approved by the FDA for depression using transdermal selegiline is 6 mg/24 hr period.

163. A. Rationale: Donepezil noncompetitively antagonizes centrally acting acetylcholinesterase, but is reversible. It has no activity or any direct effect on GABA, serotonin, or dopamine.

164. A. Rationale: Donepezil comes in 5 mg and 10 mg tablets only.

165. C. Rationale: Donepezil is approved by the FDA for mild to severe dementia associated with Alzheimer disease.

166. A. Rationale: Chloroquine is one of the FDA approved treatments for extraintestinal amebiasis. The preferred treatment of mild to moderate extraintestinal amebiasis is a nitroimidazole, and then luminal amebicide.

167. E. Rationale: Chloroquine has been classified as an aminoquinoline (antimalarial). Aminoquinidine is an amino group attached to quinidine (antiarrhythmic). Chlorhexidine is an antiseptic, and n-alpha-quinine is a metabolite of selegiline metabolism.

168. D. Rationale: In adults, 500 mg per week is the FDA approved initial prophylaxis treatment. There are no other approved dosing regimens for prophylaxis.

169. A. Rationale: Anturane® is the US brand name for sulfinpyrazone.

170. C. Rationale: FDA approved omeprazole dose for treatment of symptomatic GERD is 20 mg/day for 4 weeks. 50 mcg, 2 mg, and 4 mg a day are subtherapeutic regimens, and do not effectively treat GERD. 50 mg a day is not an approved regimen and gives little additional benefit over the 40 mg/day dose based on pharmacodynamic/kinetic profiles.

171. A. Rationale: Omeprazole is extensively metabolized by the liver to inactive metabolites, and 77% of drug is excreted via kidneys as metabolites. Very little active drug is excreted via the kidneys.

172. E. Rationale: Tinidazole is an antiprozoal/antibacterial classified under the pharmacologic categories of nitroimidazole and amebicide.

173. B. Rationale: FDA approved tinidazole dose for treatment of bacterial vaginosis is 2 g per day for 2 days. A regimen of 2 g for 5 days adds no additional benefit over 2 day course of treatment. 20 g and 200 g per day for 5 and 2 days are overdoses and increase the risk for serious adverse effects. 200 mg a day for 5 days is a subtherapeutic dose, and may not achieve optimal bacteria killing.

174. C. Rationale: Amphotericin B can cause anemia not polycythemia. Hypotension, tachypnea, hypokalemia/magnesemia have all been adverse effects noted in clinical use.

175. B. Rationale: FDA approved clotrimazole prophylactic dose for treatment of oropharyngeal candidiasis is 10 mg troche tid for 14 days. 10 mg qd and 10 mg single dose are subtherapeutic doses and may not effectively prevent oral thrush. 10 mg 5 times daily is the correct dosage for patients who actively have oral thrush, but not prophylaxis. 10 mg 6 times daily is not an FDA approved treatment regimen, and may not add any additional benefit.

176. C. Rationale: FDA approved clotrimazole for active treatment of oropharyngeal candidiasis is 10 mg troche 5 times daily for 14 days. 10 mg QD and 10 mg single dose are subtherapeutic doses and may not effectively prevent oral thrush. 10 mg TID is the correct dosage for prophylaxis against oral thrush, but not treatment. 10 mg 6 times daily is not a FDA approved treatment regimen, and may not add any additional benefit.

177. A. Rationale: Clotrimazole comes in many dosage forms due to the nature and where fungal infections tend to occur. Clotrimazole also comes in combination with other medications.

178. A. Rationale: Clotrimazole is excreted in the feces as metabolites. Pharmacodynamic/kinetic data shows very minimal levels are absorbed systemically after topical application. The peak serum concentration of an oral troche is roughly 3 hours if the troche is allowed to dissolve in the mouth for 30 minutes.

179. A. Rationale: Auxiliary labels are required by law on all DEA schedule II to IV because of the abuse potential. The transfer label states that it is illegal for anyone other than whom it was prescribed to take the medication.

180. A. Rationale: Pregabalin (Lyrica®) is structurally related to gabapentin and used for neuropathic pain associated with diabetes and fibromyalgia.

181. C. Rationale: Thiopental is a barbiturate that affects the respiratory center of the brain, and follows linear kinetics. Barbiturates decrease cerebral activity due to effect on inhibitory neurotransmitters. It has the ability to depress the sensory cortex as a hypnotic, and does not alter the perception of pain. It can be used for seizure control, anesthesia induction, and can be used to treat elevated intracranial pressure.

182. C. Rationale: Lotrel® is a combination product of amlodipine and benazepril. Prinzipide® or Zestoretic® is a combination of lisinopril and hydrochlorothiazide. Caduet® is a combination of amlodipine and atorvastatin. BiDil® is a combination of hydralazine and isosorbide dinitrate.

183. A. Rationale: Prevpac® is a combination product of amoxicillin, clarithromycin, and lansoprazole. There are no products that contain a combination of ampicillin, a macrolide (azithromycin/clarithromycin), and a proton pump inhibitor (PPI) (lansoprazole/omeprazole). There is no approved combination product that contains amoxicillin and azithromycin with a PPI.

184. A. Rationale: Tacrolimus is generic for Prograf®, finasteride is generic for Propecia®, and proscar, pantoprazole is generic for Protonix®.

185. D. Rationale: Lamictal® (lamotrigine) and Mysoline® (primidone) are classified as antiepileptic agents. Kaletra® is a combination of lopinavir and ritonavir used for HIV.

186. B. Rationale: Alosetron can cause constipation because it antagonizes 5HT-3 (serotonin) receptors in the GI tract, which slows colon transit and secretions. Alosetron is used to treat irritable bowel syndrome (IBS) with predominant diarrhea in women that fail other therapies. It does not need to be renally dosed, and the only disease-related concern is with hepatic function.

187. E. Rationale: Tussionex® is a combination product of hydrocodone 10 mg and chlorpheniramine 8 mg per 5 mL (teaspoonful).

188. A. Rationale: The manufacturer reports Hibiclens® OTC contains 4% Chlorhexidine Gluconate as the active ingredient. There is no other formulation on the market called Hibiclens® with a higher concentration.

189. D. Rationale: Mupirocin is generic for Bactroban®, hydroxyzine is generic for Vistaril®, cetirizine is generic for Zyrtec®, and homatropine is generic for Isopto®.

190. B. Rationale: Tolterodine is generic for Detrol®, torsemide is generic for Demadex®, tolazamide is generic for Tolinase®, topiramate is generic for Topamax®, and tolmetin is generic for Tolectin®.

191. C. Rationale: About 90% of metformin is excreted via the kidneys as active drug. Metformin can also cause increases in lactic acid leading to lactic acidosis, which can increase the risk of renal failure. It is considered a hypoglycemic agent because it lowers blood glucose. The maximum dose reported by the manufacturer is 2500 g per day in younger adults because there is little additional benefit versus risk at higher doses.

192. A. Rationale: Glyburide is the generic for Glynase®, acarbose is generic for Precose®, rosiglitazone is generic for Avandia®, glimepiride is generic for Amaryl®, and chlorpropamide is generic for Diabinese® (discontinued product).

193. B. Rationale: Dorzolamide/timolol is generic for Cosopt®, brimonidine/timolol is generic for Combigan®, and epinephrine/pilocarpine is generic for Pilopine HS/Isopto Carpine/Pilocar/ or Adorbocarpine®. There is no combination drug using carbachol and dorzolamide.

194. B. Rationale: Oxymetazoline nasal spray should be discontinued after 3 days due to risk of rebound congestion, and exacerbation of nasal symptoms.

195. A. Rationale: Conjunctivitis is a common side effect that has been reported by patients. The duration of action reported by the manufacturer is roughly 4 hours, and the peak effect after topical application ranges from 1-2 hours.

196. C. Rationale: The manufacturer recommends NOT to refrigerate Biaxin® due to the possibility the solution will gel. Zithromax® can be refrigerated or NOT refrigerated for up to 10 days. Augmentin® MUST be refrigerated as reported by manufacturer due to stability issues.

197. A. Rationale: Ovulation is triggered when there is a surge, or rise, of Luteinizing Hormone (LH) marking the first day the egg is released. Folicle Stimulating Hormone (FSH) surges on day 1 of menses, and is not a predictor of ovulation. Human Chorionic Ganadotropin (hCG) is produced during pregnancy. Thyroid Stimulating Hormone (TSH) is a marker of thyroid function.

198. A. Rationale: Misoprostol is classified as and can be used in conjunction with mifepristone as an abortifacient up to 49 days after conception. Piroxicam and aspirin can cause the premature closure of the ductus arteriosus if given in the third trimester, but are not abortifacients. Phenytoin can cause congenital defects and possible hemorrhage at birth. Tetracycline can affect and discolor teeth, but can also effect bone growth during the second trimester.

199. D. Rationale: Trental® (pentoxifylline) and Pletal® (cilostazol) are used for the treatment of intermittent claudication. Diovan® (valsartan) is an ARB used for hypertension.

200. C. Rationale: The generic name for Cozaar® is losartan.

201. A. Rationale: The active ingredients in Symbyax® are olanzapine and fluoxetine.

202. B. Rationale: Enbrel® (etanercept) is used in the treatment of autoimmune diseases by interfering with the tumor necrosis factor (TNF) receptor.

203. E. Rationale: Azithromycin (Zithromax®) is available as oral tablets and suspension as well injection.

204. C. Rationale: The tetanus booster vaccine should be administered every 10 years.

205. A. Rationale: Naprosyn® (naproxen) is available as oral suspension containing 125 mg/5 mL of naproxen.

206. C. Rationale: The generic name for Norflex® is orphenadrine.

207. E. Rationale: Atacand® (candesartan cilexetil) is an angiotensin II receptor antagonist.

208. C. Rationale: Parnate® (tranylcypromine) is an MAO inhibitor used for depression. Eldepryl® (selegiline) is a selective MAO-B inhibitors used in Parkinson's disease.

209. C. Rationale: Actos® (pioglitazone) is available in oral dosage strengths of 15 mg, 30 mg, and 45 mg.

210. A. Rationale: Flunisolide (Aerobid®) is available as a metered dose inhaler (MDI). Serevent®, Advair®, and Foradil® are drugs available for dry powder inhalation (DPIs). Pulmicort® is available as a turbuhaler.

211. B. Rationale: The dose of Accolate® (zafirlukast) for asthma is 20 mg twice daily.

CHAPTER 6

1. E. Rationale: Insulin can be kept out of the refrigerator for up to 28 days at temperatures $<30^{\circ}\text{C}$ (86°F); preservatives will keep the insulin from spoiling for this period of time. Smoking raises blood sugar levels, making it harder to control blood sugar; people with diabetes who smoke are more likely to die of cardiovascular disease compared with nonsmokers with diabetes. Cloudy insulin should be rolled to mix; shaking can cause the insulin to clump.

2. A. Rationale: Nexium® should be taken once daily at least 1 hour before a meal.

3. A. Rationale: Atenolol causes a decrease in heart rate in addition to decreasing blood pressure. Patients may experience some bradycardia, but the patient should not be alarmed by a blood pressure of 132/78 and heart rate of 54 beats per minute.

4. E. Rationale: Asking patients for what conditions they take their medications verifies that patients know why they are taking the medication. Asking patients how they take the medications and what kinds of problems they have allows the pharmacist to determine patient compliance and any unwanted adverse effects.

5. C. Rationale: Metamucil® should be mixed with 8 oz water, stirred to dissolve granules, and drank immediately to ensure effectiveness. The entire dose is needed, so the patient should drink the entire glass.

6. B. Rationale: Rifampin may cause the urine to appear red/orange in color. Rifampin does not cause joint stiffness or photosensitivity.

7. C. Rationale: A COPD patient would use Atrovent® on a regular schedule, usually 2 puffs 4 times per day.

8. C. Rationale: Combivent® is typically dosed as 2 inhalations 4 times daily with additional doses as needed for wheezing. Spiriva® is dosed once daily, and the capsules must be inhaled from the HandiHaler® device.

9. B. Rationale: Diovan® causes dizziness in 2%–17% of patients in clinical trials. Diovan® does not cause bladder spasms or constipation but causes diarrhea in some patients. Diovan® may lead to blurred vision but does not cause vision to turn yellow.

10. A. Rationale: Abilify® is indicated as treatment for schizophrenia, adjunct treatment for bipolar disorder, and adjunct treatment for major depressive disorder. Abilify® is not FDA approved for obsessive compulsive disorder, postherpetic neuralgia, or diabetic peripheral neuropathy.

11. C. Rationale: Asking patients how the medications should be taken ensures that patients know how to take their medications and opens the discussion of adherence, storage, therapy duration, and any additional instructions. “What OTC medicines do you take?” and “Do

you have any allergies?” are preliminary questions that should be asked to determine what interactions or contraindications patients may have.

12. D. Rationale: Food decreases the absorption of alendronate and levothyroxine. Saquinavir, however, should be taken with food because food increases its absorption.

13. E. Rationale: Frequent diaper changes lessen the irritation from prolonged skin exposure to feces and urine. Breathable diapers or exposing the skin to open air prevents the warm and moist conditions perfect for microbial and yeast growth. Barrier creams prevent chaffing or rubbing that breaks down the skin.

14. E. Rationale: “What did the doctor tell you the medication is for?”, “How did the doctor tell you to take this medication?”, “What did the doctor tell you to expect when taking this medication?” are important questions to ask patients when dispensing new prescriptions.

15. E. Rationale: If a patient feels as if he or she has low blood sugar, he or she should test blood sugar. If the blood sugar level is below normal, a drink that contains sugar such as orange juice may help raise blood sugar level fast. Patients should wait about 10 minutes to let the sugar work. Within 30 minutes after the symptoms subside, a light snack may be eaten.

16. B. Rationale: MOA is to stimulate pancreas beta cells to release insulin and to lower PPG. Taking on an empty stomach or after missing a meal can cause hypoglycemia. It does not cause drowsiness.

17. E. Rationale: Shaking the container for 5–10 seconds ensures drug is homogeneously suspended in the aerosol vehicle. Holding breath increases drug contact time with tissues. Closing lips around mouth piece ensures no medicine escapes. Tilting head back repositions the tongue, and inhaling slowly helps lessen drug contact with tissues of the mouth.

18. D. Rationale: When administering eye drops, with the forefinger, pull down the eyelid to form a pocket. Hold the medication between the thumb and forefinger of opposite hand, brace the remaining fingers on the side of nose, and place the dispenser close to the eye without touching the eye. Nasolacrimal occlusion prevents or limits any systemic absorption.

19. D. Rationale: Before using a peak flow meter, the lungs should be fully inflated by taking a deep breath. Put the mouthpiece of the peak flow meter into the mouth. In one breath, blow out as quickly and as hard as possible.

20. D. Rationale: Gaviscon® may be taken as 2–4 tablets 4 times daily after meals or at bedtime with a half glass of water. It should not be used more than 2 weeks. Patients with dairy allergy do not need to avoid Gaviscon®.

21. E. Rationale: Aspirin therapy can cause some minor bleeding and should be avoided before using EZ Detect®

Fecal occult testing. Urine may contain trace amounts of blood and give false positive; and toilet cleaners can interact with the test leading to a false positive.

22. D. Rationale: Niaspan® should be given at bedtime with a low-fat snack. Because Niaspan® may cause flushing, it is recommended that patients take aspirin 325 mg approximately 30 minutes before taking the drug. Alcohol and hot beverages may worsen feelings of flushing.

23. D. Rationale: Weight-bearing exercises increase muscle and bone strength and should be recommended to patients at risk for osteoporosis. Patients should also consume 1200 mg of calcium and 800–1000 IU of vitamin D. Alcohol consumption should be limited because it can deplete calcium stores and inhibit calcium absorption.

24. E. Rationale: Fosamax® should be taken while the patient is sitting upright for at least 30 minutes. Fosamax® can cause serious damage to the stomach and esophagus. DO NOT chew. It should be taken first thing in the morning on an empty stomach with a full glass of water. Food reduces the bioavailability.

25. C. Rationale: Miacalcin® should be discarded after 30 doses. Unopened bottles should be refrigerated. It should be primed before the first use of a new bottle, not before each daily dose.

26. E. Rationale: Serevent® diskus is a dry powder inhaler (DPI) with individually measured doses of the powder for each inhalation. This is why it has a dose indicator so the patient knows how many doses are left. Because it is a dry powder, breathing out into the mouthpiece can cause the drug to become exposed to moisture and the patient will not be able to inhale the drug. Closing the diskus after use also prevent moisture from entering the device.

27. C. Rationale: Emergency contraception is less effective than regular birth control, which is why it should not be a primary form of contraception. Emergency contraception is sold in the United States and must be taken *within* 72 hours of unprotected sexual intercourse to be effective. Plan B works primarily by stopping the release of an egg from the ovary, thus delaying ovulation. Progesterone only formulations are usually well tolerated, compared to estrogen/progestin formulations.

28. B. Rationale: Risedronate is a bisphosphonate used to treat osteoporosis and is available by the brand name of Actonel®. It is not used to treat Parkinson disease. Risedronate can lodge in the esophagus and potentially cause esophageal ulcers, which is why it should be taken with a glass of water and in an upright sitting or standing position. However, because it has poor bioavailability when taken with food, it is recommended to take it on an empty stomach.

29. B. Rationale: Betaseron® is an interferon used in the treatment of multiple sclerosis; it does not treat Parkinson

disease or depression. Interferons have many side effects which include flu-like symptoms, increased risk of infection, and psychiatric adverse events such as psychosis, depression, and mania.

30. A. Rationale: Cytarabine is pregnancy category D and has been found to be teratogenic in animal studies. Case reports in humans have also found cytarabine to cause birth defects. The WHO recommends to avoid breastfeeding while on cytarabine.

31. C. Rationale: Levemir® should be stored in the refrigerator. Opened pens are stable at room temperature for up to 42 days. Opened pens should be stored in a cool, dark place.

32. B. Rationale: It is a pharmacist's responsibility to offer counseling to patients picking up their prescriptions. Patients do not need to have insurance coverage for this free service. However, if a patient does not understand the terminology the pharmacist is using or is either hearing or visually impaired, the patient may not understand the pharmacist; education level and physical impairment are correct choices because they are both potential barriers to a thorough oral consultation.

33. B. Rationale: The American Lung Association classifies three zones on a peak flow meter. These zones are the colors of a traffic light, with the green zone 80%–100%, yellow zone 50%–80%, and red zone less than 50% of peak flow.

34. C. Rationale: Ketorolac is a potent NSAID that has more safety concerns than other NSAID, so only short term use of less than 5 days is recommended. It should be taken with food or milk to help prevent GI discomfort.

35. C. Rationale: Xenical® is one brand name for orlistat, a lipase inhibitor used for the management of obesity. It has gastrointestinal side effects such as oily spotting and abdominal pain, which usually decrease over time with continued use. Xenical® should be taken 3 times daily with each meal. Multivitamin supplements containing fat-soluble vitamins should be taken once daily at least 2 hours before or after Xenical®.

36. C. Rationale: Plendil® should be taken without food. It is also a substrate of CYP 3A4, of which grapefruit juice is a potent inhibitor. It causes headache in about 11%–15% of patients.

37. E. Rationale: Patients taking MAO inhibitors should avoid foods containing tyramine such as aged cheese, draft beers, sauerkraut, cured meats and fish, fava beans, and soy sauce.

38. C. Rationale: Simvastatin, like all statins, has a risk of rhabdomyolysis, a condition characterized by the rapid breakdown of skeletal muscle with symptoms such as muscle pain and weakness. It is also a substrate of CYP 3A4, of which grapefruit juice is a potent inhibitor. It should be taken in the evening for maximum efficacy with or without food.

39. E. Rationale: Tri-Levlen® (ethinyl estradiol and levonorgestrel) is an oral contraceptive combination of female hormones. All three choices are logical counseling points that could be made to the patient. Taking with food or at bedtime would reduce nausea. Antibiotics can reduce the effectiveness of oral contraceptives, so utilizing a secondary method would be a good idea when taking antibiotics. Also, oral contraceptives generally cause weight gain and may cause headaches or breakthrough bleeding.

40. C. Rationale: Ibandronate (Boniva®) should be taken on an empty stomach and swallowed whole for adequate and efficient absorption. Patients should remain standing or sitting upright for at least 30 minutes after taking the medication to help prevent reflux and potential damage to the esophagus.

41. E. Rationale: All three of the choices are likely nonpharmacological methods that could reduce the frequency and severity of menopausal hot flashes.

42. E. Rationale: All three choices are potential side effects/adverse occurrences that could result from the use of bismuth subsalicylate.

43. E. Rationale: Cimetidine is an H-2 antagonist aimed at reducing the amount of stomach acid. All choices are likely nonpharmacological methods to aid in this reduction of reflux.

44. B. Rationale: Patients on warfarin should ensure consistent intake of vitamin K. Vitamin K decreases the effects of warfarin. Large amounts of vitamin K are found in foods such as liver, broccoli, brussel sprouts, spinach, Swiss chard, coriander, collards, cabbage, and other green leafy vegetables.

45. D. Rationale: Chlorpropamide is a sulfonylurea used for diabetes. Alcohol not only raises blood sugar to begin with but in combination with chlorpropamide can cause rapid flushing of patients' faces. The other choices have little to no effect on the use of chlorpropamide.

46. C. Rationale: Not eating or drinking before taking the lozenge is important to promote proper absorption of the lozenge through the subbuccal method. Nicotine gum works faster than the patch because the patch is designed to be a slow, gradual release of nicotine throughout the day. The patch should be worn all day to ensure steady levels of nicotine reaching the bloodstream throughout the day.

47. C. Rationale: The DASH diet includes limiting the intake of saturated fats and cholesterol and emphasizing 4–5 servings of fruits and vegetables daily. The DASH diet limits red meat intake but does not entirely restrict it.

48. E. Rationale: Increased thirst, headache, and fatigue are all signs of high blood sugar that should be mentioned when counseling a patient with diabetes.

49. E. Rationale: Metronidazole and alcohol can cause a disulfiram reaction leading to violent vomiting. Diphenhydramine and alcohol can lead to excessive sedation. Warfarin and alcohol can lead to excessive blood thinning and raise INR levels too high. Patients taking any of these three medications should be counseled to avoid alcohol consumption.

50. A. Rationale: Iron supplementation can result in black or greenish stools. Taking with food actually decreases absorption since most iron supplements are recommended on an empty stomach. Enteric-coated preparations are usually not recommended because of poor bioavailability, leading to inadequate clinical response.

CHAPTER 7

1. E. Rationale: The Dietary Supplement Health and Education Act of 1994 (DSHEA) defines dietary supplements and dietary ingredients, provides for use of claims and nutritional support statements, required ingredient and nutrition labeling and establishes good manufacturing practice regulations.

2. B. Rationale: Kava has been shown to cause severe liver injury including hepatitis, cirrhosis, and liver failure. Alcohol can increase the risk of liver toxicity. Kava has not been shown to have nephrotoxic effects. Kava is used to treat insomnia and anxiety.

3. D. Rationale: NCCAM, National Center for Complementary and Alternative Medicine; ODS, Office for Dietary Supplements; CFSAN, Center for Food Safety and Applied Nutrition; ASHP Essentials, American Society of Health-System Pharmacists.

4. D. Rationale: Echinacea is frequently recommended by experts in natural medicine for treatment of the common cold and for other conditions requiring immune stimulation. Valerian is popularly used to treat insomnia. Chamomile is used as a mild sedative. Chasteberry is used to treat hyperprolactinemia and menstrual disorders. Kava is used to treat anxiety.

5. A. Rationale: Comfrey has small but significant risk of toxicity, particularly hepatotoxicity. Topical comfrey products intended to be used on broken skin have been removed from the market in the US. As a result of its toxicity, comfrey-containing products are not recommended to be used.

6. E. Rationales: Vitamins K, A, D, and E are all stored in the liver and fatty tissues.

7. A. Rationales: Licorice is commonly used for treating ulcers. St. John's Wort is commonly used to treat depression. Saw palmetto is used for the treatment of BPH. Ginseng and alpha-lipoic acid are used to treat diabetes. Chondroitin and glucosamine are used to treat osteoarthritis.

8. C. Rationales: Grapefruit inhibits cytochrome P450 (CYP) 3A4 in the intestinal wall. Kava may significantly inhibit multiple CYP enzymes. Ginkgo may induce or

inhibit CYP 450 enzymes. St. John's Wort may induce CYP 3A4.

9. B. Rationale: Grapefruit interacts with medications through inhibition of cytochrome P450 3A4 in the intestinal wall. Grapefruit does not cause major interactions with medications through CYP 2D6.

10. C. Rationale: Saw palmetto is commonly used to treat urinary symptoms associated with BPH and in numerous controlled trials has been shown to be superior to placebo for these symptoms.

11. D. Rationale: Saw palmetto has been shown to be superior to placebo for treatment of BPH in numerous controlled trials. Further, some trials have shown possible equivalence to finasteride, a drug of choice in the treatment of BPH.

12. C. Rationale: Black cohosh is commonly used to treat menopausal symptoms including hot flashes, mood disturbances, diaphoresis, palpitations, and vaginal dryness. There have been case reports of hepatotoxicity, and concern remains that use of black cohosh can result in liver toxicity. Black cohosh does not appear to have an effect on CYP 450 metabolism.

13. D. Rationale: Yohimbine can be used for impotence; however, there is limited data to support it. MAOI when taken with foods containing tyramine can induce hypertensive crisis. There are no studies to support Yohimbine as a stimulant.

14. B. Rationale: Phytochemicals are chemicals that plants produce naturally and have some effect on health. Botanochemicals are plant products that can be used to synthesize and replace petroleum needed chemical. Phytomedicinals are medicines made from plant materials for medicinal purposes and include phytochemicals. Aetheroleum are obtained from plants as aromatic products and refers to the essential/volatile oil.

15. D. Rationale: All are products that are produced and found in plants that can have some effect on health.

16. D. Rationale: Phytoestrogens are plant-produced estrogens. Antiandrogens either inhibit the release or the biological effect of an androgen. Isoestrogens differ in amino acid structure from estrogen, but can initiate the same chemical process. Benzyl estrogens have a Benzyl group attached to estrogen.

17. E. Rationale: Some studies have shown that Vitamin B6, B12, and Folic acid can have effect on decreasing homocysteine levels.

18. D. Rationale: Glucosamine and chondroitin are made from shellfish and animal cartilage, and used to replenish a person's own cartilage. They do not have an effect on the immune system, inflammatory process, or pain.

19. A. Rationale: Food increases acid secretion, which is needed for calcium carbonate absorption.

20. D. Rationale: Most glucosamine is sourced from shellfish and animal cartilage. Legumes, tree nuts, and dairy are not used in the manufacturing process.

21. C. Rationale: Hypericum is the genus to which St. John's Wort belongs. Bitter orange, hydrangea, and hyoscyne are not found in the Hypericum genus.

22. D. Rationale: Hyperforin content found in St. John's wort plays an important role in induction of CYP 3A4. St. John's is an inhibitor of CYP 2C9 and 2D6, and has no known effect on CYP 2C8.

23. E. Rationale: Oral contraceptives may enhance the effects of pyridoxine. Isoniazid can reduce the effectiveness of pyridoxine. Pyridoxine can reduce the effectiveness of Levodopa.

24. B. Rationale: Yohimbine can be used for impotence; however, there is limited data to support it. Saw palmetto can be used for BPH and loss of libido. Kava works effectively for anxiety. Black cohosh can be used primarily for menopausal symptoms.

25. A. Rationale: Bleeding related to oral garlic use has been reported in case studies. Muscle pain, blurred vision, and increased blood pressure have not been reported.

26. B. Rationale: The FDA regulates dietary supplements pursuant to DSHEA. The DSHEA, which was passed in 1994, gave the FDA the responsibility to regulate good manufacturing practice for dietary supplements.

27. A. Rationale: Fenugreek is used as a lactation stimulant and during pregnancy for labor induction. Yarrow, when applied to the skin, is used for cuts and wounds; it should not be taken during breastfeeding and has been used traditionally as an abortifacient. Cascara sagrada is used for constipation and bowel cleansing. The use of garlic for hyperlipidemia is promising, although its lipid-lowering effects were modest.

28. E. Rationale: Chronic alcohol abuse causes thiamine deficiency. Korsakoff's psychosis is a condition caused by chronic alcohol abuse so patients with this condition are likely to have some degree of thiamine deficiency as well. Chronic diarrhea causes malabsorption of vitamins, including thiamine.

29. C. Rationale: Dietary Supplements are required to be labeled with "supplement facts" and not "nutritional facts". The DSHEA of 1994 placed dietary supplements under the category of food, not drugs, and thus the FDA regulates them as such. Dietary supplements are not regularly tested by any government agency, so information on the chemical ingredients of products is only available from third-party testers such as ConsumerLab for a fee. The FDA requires that every dietary supplement be labeled as such, but cannot be represented as a conventional food.

30. C. Rationale: Valerian is used in alleviating insomnia, it decreases sleep latency and increases sleep quality.

Kava is an herb that caused hepatotoxicity and is now off the market. Hypericum, or St John's Wort, is used for depression. Ginkgo is used in dementia with mild success and ginseng has been used to lower blood pressure in diabetics and immune system enhancement.

31. A. Rationale: Cranberries contain proanthocyanidins (PACS) that prevent *E. coli*, which is the bacteria responsible for a large majority of UTIs, from adhering to uroepithelial cells. Although cranberries are acidic, the acidification of urine is not the mechanism by which they prevent UTIs. Cranberries do not act as probiotics and do not restore urogenital flora.

32. A. Rationale: Echinacea is widely used as an immune stimulant for upper respiratory infections and common colds. Ginseng has been used to lower blood pressure in diabetics. Melatonin is used for sleep enhancement and jet lag. Saw palmetto is used to treat symptoms of benign prostatic hypertrophy (BPH).

33. E. Rationale: Both Kava and Black Cohosh are associated with adverse liver events. Kava was used for anxiety but has had multiple cases of reported hepatotoxicity that have led it to be pulled off the market. Black cohosh is used for symptoms of menopause. Saw palmetto is used for symptoms of benign prostatic hypertrophy (BPH). Hypericum, or St. John's Wort, is used for depression.

34. A. Rationale: Ginseng has been used to increase mental energy, although it is evidence grade C for this indication. Melatonin is used for jet lag and sleep, Echinacea is used as an immune stimulant, and grapefruit has been used for a variety of conditions but lacks strong evidence for its use, as research has been conflicting. Garlic is used for lipid lowering effects in patients with hyperlipidemia.

35. A. Rationale: St. John's wort is associated with photosensitivity and drowsiness but not diarrhea, breath odor, heartburn, or hepatotoxicity.

36. C. Rationale: Feverfew has been found to be effective in the prevention of migraines; although there are currently no randomized control trials available to support this use.

37. A. Rationale: Drugs (not dietary supplements) must undergo FDA approval after clinical studies to determine effectiveness and safety.

38. B. Rationale: Calcium is the only listed mineral supplement. Biotin is considered a vitamin supplement, while choline is considered an elemental supplement.

39. E. Rationale: Tums EX®, Vivactiv®, and Os-Cal® contain calcium. Vivactiv® and Os-Cal® are actually taken for calcium supplementation, while Tums EX® is an antacid containing calcium carbonate.

40. A. Rationale: Ferrous salt forms with a $+2$ charge are more rapidly absorbed than ferric salt forms with a $+3$ charge because $+3$ charged iron salts have to undergo a

conversion step to the $+2$ form before being absorbed efficiently

41. B. Rationale: Both Centrum® and Centrum Silver® contain vitamin K. Unicap Senior® multivitamin does not contain vitamin K.

42. D. Rationale: Capsicum is used to relieve pain including pain from shingles and osteoarthritis.

43. E. Rationale: Ephedra was used primarily for its stimulating effects causing increased metabolism and weight loss. Unfortunately, it was removed from the market due to its plethora of cardiovascular side effects especially when combined with MAOIs since the interaction could cause excessive noradrenergic stimulation leading to a hypertensive crisis.

44. A. Rationale: Iodine is used to synthesize thyroxine (T4) and triiodothyronine (T3).

45. A. Rationale: Chasteberry is used for many gynecologic disorders. The German Commission E approves the use of chasteberry for irregularities of the menstrual cycle, cyclical breast discomfort, and PMS.

46. B. Rationale: Valerian would certainly cause drowsiness. Some patients even utilize it for this very effect as a sleep aid or relaxant. The other herbals listed raise blood pressure, have stimulant-like effects, and even contain caffeine themselves. This would make them all very unlikely to cause drowsiness.

47. D. Rationale: Chamomile has been used for generations in teas for its mild calming effects and as an aid for digestion. Peyote, reishi mushroom, and capsicum are not commonly found in teas.

48. E. Rationale: All of the products listed contain zinc, and recent studies have found that zinc can reduce the severity and duration of common cold symptoms.

49. B. Rationale: Chronic use and exposure of riboflavin (vitamin B 2) can in fact discolor the skin and urine. Differentiation between urine discoloration and concentrated yellow urine should be made since all the B vitamins tend to cause a bright yellow urine color.

CHAPTER 8

1. B. Rationale: Serum creatinine (choice I) is an indicator of kidney function and relates to GFR; tobramycin is an aminoglycoside that can affect kidney function since the main side effect is nephrotoxicity. Since tobramycin is also an antibiotic, looking at cultures and sensitivities (choice IV) for each patient gives an indication of the appropriateness of antibiotic chosen. Choices II and III would not be helpful, since these tests primarily look at liver function, and tobramycin does not affect hepatic processes.

2. C. Rationale: This answer explains why the doctor monitors HbA1c and educates the patient regarding the

benefit of the test. Answer A is incorrect, as is D, since the HbA1c is not a urine test, nor is it used to indicate acute hypoglycemia. Answer B is true, but does not counsel the patient as to the HbA1c's use to monitor his condition.

3. A. Rationale: The increase in total WBCs, along with the increase in bands (left shift), is consistent with a systemic bacterial infection and is common with pneumonia or sepsis. Answer B is not correct, since neutropenia would indicate a decreased WBC. Answer C is not correct, since small, localized infections do not normally raise the WBC count or produce the left shift. Answer D is not correct, since eosinophils are not raised and the patient's presentation is not consistent with likely allergen exposure.

4. C. Rationale: CK-MB, found in heart muscle, elevates quickly after myocardial damage. The LDH elevation, also found in heart tissue, can also help confirm heart damage from infarction. Hematocrit and albumin are not indicative of infarction, and alkaline phosphatase is produced primarily in liver and bones.

5. C. Rationale: The TSH elevation indicates that she is hypothyroid. With no other findings in a previously stable patient, it is probable that he or she is experiencing a drug interaction with the multivitamin/mineral supplement. The patient should be counseled to take his or her levothyroxine on an empty stomach with plenty of water and separated from the supplement or other medications. The TSH should normalize within 4 weeks.

CHAPTER 9

1. D. Rationale: Select third-generation cephalosporins, including ceftriaxone and cefotaxime, are beta-lactams of choice for the empiric treatment of meningitis. Macrolides (e.g., erythromycin), fluoroquinolones (e.g., gatifloxacin), vancomycin, and aminoglycosides (e.g., gentamicin) are not typically used as first-line empiric therapy for bacterial meningitis.

2. B. Rationale: Macrolides like azithromycin are the drugs of choice for treating Legionnaire's disease.

3. B. Rationale: Hepatitis A can be prevented by vaccination as well as good hygiene. Hepatitis A is spread through the fecal-oral route and it does not cause chronic hepatitis.

4. B. Rationale: Aminoglycosides display bactericidal action and are active against a wide range of aerobic gram-negative bacilli. Aminoglycosides are usually not used clinically for *Neisseria meningitidis* infection due to the risk of the patient going into shock from lipid A endotoxin found in certain gram-negative bacteria. The aminoglycoside would cause cell lysis and release of the endotoxin.

5. D. Rationale: Patients taking the antibiotic metronidazole should avoid alcohol to prevent an

adverse disulfiram-like reaction. Metronidazole is also contraindicated in the first trimester of pregnancy.

6. B. Rationale: Aminoglycosides, such as tobramycin, can cause nephrotoxicity. Serum creatinine levels can be evaluated to determine if the patient has renal impairments and if dosage adjustments are needed.

7. A. Rationale: *E. coli* is a gram-negative bacilli and the causative organism in several infections, especially urinary tract infections.

8. A. Rationale: *Herpes simplex labialis* leads to the development of cold sores or blisters on the skin around the mouth. Herpes simplex labialis is usually caused by the herpes simplex virus, type 1 (HSV-1), whereas the most common causative agent of genital herpes is herpes simplex, type 2 (HSV-2).

9. C. Rationale: Patients should be prescribed two or more antituberculosis agents if there is a possibility of treatment failure. Treatment failure can be due to nonadherence or drug-resistant bacilli.

10. B. Rationale: Trachoma is typically caused by *Chlamydia trachomatis*.

11. B. Rationale: A single 2 g dose of the azithromycin ER oral suspension (ZMax®) can be used for CAP. The azithromycin oral tablets are also an option for a total dose of 1.5 g over 5 days given as 500 mg PO on day 1, and 250 mg PO once daily days 2-5.

12. C. Rationale: Doxycycline (Vibramycin®) is a tetracycline antibiotic used to treat a variety of infections including uncomplicated gonococcal infections, syphilis, Lyme disease, chlamydia, and many others. It is not indicated for Syndrome of Inappropriate Antidiuretic Hormone (SIADH). Like other tetracyclines, doxycycline may cause photosensitivity. It may also impair the effectiveness of hormonal contraception.

13. C. Rationale: the usual etiology of bullous impetigo is *Staphylococcus aureus*. The primary treatment for bullous impetigo is oral dicloxacillin. The other drugs listed could be considered alternatives; however, with the exception of azithromycin, most are listed in the choices at dosages or dosage schedules that do not match recommended pediatric regimens.

14. B. Rationale: A typical shingles rash follows the path of certain nerves on one side of the body—generally on the trunk, buttocks, neck, face, or scalp.

15. C. Rationale: Fluoroquinolones are often used to treat patients with community acquired pneumonia (CAP) due to strains of *S. pneumoniae* that are resistant or intermediately susceptible to penicillin, or for empiric treatment of CAP. Certain fluoroquinolones like levofloxacin have enhanced activity against the organism *S. pneumoniae*. Ciprofloxacin is not as clinically effective as the other quinolones for treatment of *S. pneumoniae*.

16. C. Rationale: Diabetic foot infection that is limited in extent can be treated with either clindamycin, Augmentin®, or an oral first generation cephalosporin. Of the choices provided clindamycin 300 mg PO qid is an effective treatment and dosage option for diabetic foot infection.

17. E. Rationale: No antibiotic treatment is warranted at this time. The patient has symptoms more consistent with chronic obstructive pulmonary disease (COPD). Chronic cough can develop in patients who smoke, often due to underlying COPD. The patient can be counseled on smoking cessation and evaluated for treatments for COPD.

18. D. Rationale: Amoxicillin/clavulante can be prescribed as a preferred second-line agent for this patient since a first-line treatment, including amoxicillin, is not providing relief. Treatments for sinusitis are often similar to those recommended for otitis media, since the causative organisms are similar. Levofloxacin and other quinolones are generally third-line agents. Erythromycin could be used but is generally a drug of choice in treatment guidelines for sinusitis.

19. E. Rationale: Alternative therapies for the treatment of *Strep. pharyngitis* for patients who are allergic to penicillin include macrolides, clindamycin, and oral second generation cephalosporins. The adult dosing regimen for azithromycin can be prescribed as a Z-pak® which is 500 mg PO for one dose, followed by 250 mg PO once daily for 4 days.

20. C. Rationale: Replacing the amoxicillin with an extended oral antibiotic, such as cefuroxime, is an appropriate second-line option of those presented. The regimen should be continued for 10 days after the switch. Continuing amoxicillin (choice a or b) is not appropriate. The patient has not responded to either amoxicillin or erythromycin therapy within 3 days and continues to have the same severity of symptoms, including fever. Replacing with a parenteral drug (choice d or e) is not appropriate, since otitis media should respond well to an appropriately chosen non-injectable second-line treatment.

21. E. Rationale: Penicillins are active against gram-positive bacilli. Aminoglycosides combined with penicillins provide a synergistic effect in the treatment of infections.

22. C. Rationale: Trimethoprim/sulfamethoxazole and ampicillin are not effective in treating *P. aeruginosa* while moxifloxacin is somewhat effective and not recommended. Ciprofloxacin for a duration of 2 weeks can be used for the treatment of complicated UTI for hospitalized patients.

23. C. Rationale: The quinolone drug of choice for patients who failed trimethoprim/sulfamethoxazole is ciprofloxacin. Ciprofloxacin for 3 days has similar treatment efficacy as the 7 day therapy.

24. E. Rationale: Azithromycin is a macrolide antibiotic indicated for mild-to-moderate pneumonia, otitis media,

sinusitis, and skin and soft tissue infections. It has a long duration of action (about 68 hours). Possible side effects include diarrhea, abdominal pain, nausea, elevated ALT and AST, and vomiting.

25. B. Rationale: Clostridial soft tissue infections include cellulitis, myositis, and clostridial myonecrosis; usually occur after trauma; and are treated with surgical debridement and with penicillin.

26. C. Rationale: Cellulitis is most often caused by group A beta-hemolytic Streptococci (e.g., *Strep pyogenes*) or *Staphylococcus aureus*. *Staph. epidermis* can cause skin infection but it is a less common cause of cellulitis, and *Pasteurella multocida* is a cause of cellulitis due to cat bite. *E. coli* and *Clostridium* typically inhabit the GI tract and are associated with diarrhea.

27. D. Rationale: Penicillin is the drug of choice and should be given immediately for severe cellulitis. The addition of clindamycin may also be beneficial.

28. D. Rationale: Risk factors for cellulitis include skin abnormalities (e.g., trauma, ulceration, fungal infection, other skin barrier compromise due to preexisting skin disease), which are common in patients with chronic venous insufficiency or lymphedema. Scars from saphenous vein removal for cardiac or vascular surgery are common sites for recurrent cellulitis, especially if tinea pedis is present.

29. E. Rationale: Therapeutic monitoring is required for gentamicin because it can cause nephrotoxicity. Older age, concomitant use with other nephrotoxic drugs (cisplatin and amphotericin B), and chronic renal insufficiency increase the risk of nephrotoxicity.

30. A. Rationale: A complicated UTI caused by *P. aeruginosa* can be treated with methenamine and fluoroquinolones. Trimethoprim-sulfamethoxazole is used as empiric therapy for uncomplicated UTI.

31. D. Rationale: Pyridoxine (vitamin B 6) can be prescribed to prevent peripheral neuropathy caused by large doses of isoniazid.

32. B. Rationale: Bactroban® (mupirocin) nasal ointment can be applied intranasally to treat methicillin-resistant *S. aureus*.

33. E. Rationale: Metronidazole (Flagyl) is used to treat a variety of infections including giardia infections of the small intestine, amebic liver abscess and amebic dysentery (infection of the colon causing bloody diarrhea), bacterial vaginosis, trichomonas vaginal infections, and carriers of trichomonas.

34. D. Rationale: Both cefepime and aztreonam have good activity against *P. aeruginosa*.

35. A. Rationale: Abelcet is amphotericin B lipid complex and is indicated as treatment in patients who have failed conventional amphotericin B therapy. Abelcet's antifungal

actions are used to treat serious and invasive fungal infections such as *Aspergillus* and *Candida*.

36. D. Rationale: Clarithromycin and azithromycin are both chemically related to erythromycin. The advantages of using these agents rather than erythromycin include a lower incidence of gastrointestinal adverse effects as well as greater oral bioavailability, less frequent dosing, and broader antimicrobial spectrum. Additionally, azithromycin has less potential for drug interactions compared to erythromycin.

37. E. Rationale: Famciclovir is indicated for the management of acute herpes zoster, recurrent genital herpes and prophylaxis of herpes in immunocompromised patients and dosage adjustment is needed for reduced renal function. Famciclovir is primarily excreted in the urine. Famciclovir is a prodrug that is metabolized to penciclovir, an active antiviral compound.

38. B. Rationale: Hydroxychloroquine can cause several visual disturbances including but not limited to blurred vision, difficulty focusing, retinopathy, and corneal changes.

39. D. Rationale: Amikacin is classified as an aminoglycoside antibiotic, not a penicillin antibiotic. Normal trough levels for amikacin are 10 mcg/mL. Possible side effects are nephrotoxicity and ototoxicity.

40. C. Rationale: Otitis media is generally caused by *H. influenzae* and *S. pneumoniae*.

41. E. Rationale: Cefoperazone, cefamandole, ceftriaxone, and cefotetan all have the potential to inhibit platelet aggregation.

42. E. Rationale: The patient has active influenza B. Zanamivir and oseltamivir are agents indicated for the treatment of both influenza A and B. Oseltamivir is the only agent currently approved for prophylaxis. Oral Oseltamivir is the best choice for a patient with asthma; inhaled zanamivir might aggravate asthma.

43. E. Rationale: The most appropriate IV empiric treatment for PID is cefotetan 2 g IV q12h plus doxycycline 100 mg IV bid. Clindamycin 900 mg IV q8h plus gentamicin can be used as an alternative therapy.

44. B. Rationale: Third generation cephalosporins like ceftriaxone are preferred agents for the treatment of meningitis. Also, it is the only parenteral drug in this list. Oral agents are not used for serious infection such as meningitis, which requires high and sustained systemic antibiotic levels. Ceftriaxone is highly lipid soluble and penetrate the blood brain barrier.

45. A. Rationale: Azithromycin has the longest duration of action (about 68 hours). The drug penetrates into phagocytes and has high tissue distribution. These properties contribute to drug antibacterial activity even after a regimen is halted.

46. C. Rationale: Generally, cephalosporins should be used with caution in patients with impaired renal function; many will require dosage adjustment in renal impairment. Cefaperazone does not require a dosage adjustment for renal impairment unless the patient also has active liver disease.

47. C. Rationale: Erythrocin® and Ilotycin® historically have been the brand names for the parenterally available preparations of erythromycin. Erycin is available as an oral tablet.

48. E. Rationale: Femstat®, Monistat®, Gyne-Lotrimin®, and Mycelex G® are all topical agents used as first-line therapy for vaginal yeast infections.

49. A. Rationale: Phenylketonuria (PKU) is a genetic disorder that is characterized by an inability of the body to utilize the essential amino acid, *phenylalanine*. The *cefprozil* suspension may contain phenylalanine, which should be avoided in patients with phenylketonuria (PKU) disorder.

50. E. Rationale: Diflucan® is available as oral tablet, injection, and oral suspension.

51. E. Rationale: Bactrim® (sulfamethoxazole/trimethoprim), Pentam® (pentamidine), and Mepron® (atovaquone) are indicated for the treatment of *Pneumocystis pneumonia* (PCP).

52. E. Rationale: Zithromax® (azithromycin), Biaxin® (clarithromycin), and Lamprene® (clofazimine) are used for the treatment of mycobacterium avium complex (MAC). Rifabutin (Mycobutin®), amikacin (Amikin®), ciprofloxacin (Cipro®), ethambutol (Myambutol®) may also be used.

53. D. Rationale: Rifabutin (Mycobutin®) is used to prevent infections caused by mycobacterium avium complex (MAC).

54. B. Rationale: Rifampin may cause hepatotoxicity. Patients with impaired liver function or jaundice should avoid rifampin use.

55. A. Rationale: Denavir® (penciclovir) is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and children 12 years of age and older.

56. C. Rationale: Combination therapy with a cell wall-active agent (e.g., ampicillin, vancomycin) and an aminoglycoside (e.g., gentamicin, streptomycin) is necessary to adequately treat enterococcal endocarditis.

57. A. Rationale: Seromycin (cycloserine) is an antitubercular agent. It is effective against *Mycobacterium tuberculosis*.

58. C. Rationale: *Bacteria* commonly implicated in *otitis externa* ("swimmer's ear") include *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Otitis media (middle ear infection) is usually caused by *H. influenzae* and *S. pneumoniae*.

59. E. Rationale: Doxycycline is a tetracycline antibiotic used for various diseases including acne vulgaris, Lyme disease, sexually transmitted diseases, and prevention of malaria. It is not a drug of choice for general pneumonia and is not used for leprosy.

60. A. Rationale: Metronidazole can cause an unpleasant metallic taste.

61. D. Rationale: Sulfonamides can cause hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

62. D. Rationale: Isoniazid, tetracycline, and rifampin may increase liver enzymes. Liver function tests should be performed at the initiation of treatment, and periodically thereafter if treatment duration is long.

63. E. Rationale: Erythromycin is commonly used in treating Legionnaire's disease, *Mycoplasma pneumoniae*, diphtheria, and chlamydial infections. It is also effective against gram-positive organisms including *Streptococcus pyogenes*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*.

64. B. Rationale: Aminoglycosides are effective primarily against gram-negative bacteria. They are not effective monotherapy against gram-positive organisms like *Streptococcus pneumoniae*.

65. A. Rationale: Telithromycin is a ketolide antibiotic derived from macrolides. It exerts its effects by reversibly binding to the 50s subunit of the bacterial ribosome. Telithromycin was developed for the treatment of respiratory tract infections. While it has been used for Lyme disease, the drug is now reserved for the treatment of serious respiratory infections (pneumonia), due to concerns regarding liver toxicity.

66. E. Rationale: Imipenem, a carbapenem beta-lactam antibiotic, which has broad antimicrobial coverage against many gram-negative, gram-positive, and anaerobic bacteria. A patient may have a hypersensitivity reaction to imipenem if the patient has a true penicillin allergy. *Pseudomonas* resistance can occur.

67. D. Rationale: The best answer is D. Bactericidal drugs kill bacteria whereas bacteriostatic drugs inhibit the growth and replication of bacteria. Penicillin and cephalosporins are bactericidal. Dependent on the organism and drug concentration, clindamycin can exhibit both bactericidal and bacterostatic effects.

68. A. Rationale: Cephalosporins are beta-lactam antibiotics classified according to their antibacterial activity and resistance to beta-lactamases into first, second, third, and fourth generations. Bacterial resistance can occur when bacteria secrete the enzyme beta-lactamase that can cause inactivation of cephalosporins. Cephalosporins depress beta-lactamase activity in some organisms. Third generation cephalosporins have more activity against gram-negative organisms but activity against gram-positive organisms is not as effective

compared to first and third generation cephalosporins. Cephalosporins have gram-positive activity; however, enterococcus is not susceptible.

69. E. Rationale: Drugs that can be used to treat MRSA include vancomycin, linezolid, and quinupristin/dalfopristin.

70. E. Rationale: Cefazolin is a parenteral first generation cephalosporin that can be administered IV or IM. It can be given every 8 hours with dosage adjustments required in patients with renal insufficiency. It is usually a low-cost antibiotic agent.

71. E. Rationale: Tetracycline antibiotics are bacteriostatic antibiotics that bind to the 30s subunit of the ribosome and inhibit protein synthesis. Tetracyclines have various uses including acne vulgaris, rosacea, Rocky Mountain spotted fever (rickettsia), Chlamydia.

72. D. Rationale: Ceftriaxone has little activity against anaerobes. Metronidazole, clindamycin, imipenem, and amoxicillin/clavulanate have excellent activity against anaerobes.

73. E. Rationale: Penicillin is excreted by the kidneys in the urine and has a 30 minute half-life. Penicillin does not penetrate the blood brain barrier well except in patients with inflamed meninges.

74. D. Rationale: A patient with a penicillin allergy may have a reaction to other beta-lactam antibiotics. There is a potential cross-sensitivity reaction that can occur in patients with penicillin allergies who are treated with cephalosporins.

75. D. Rationale: The antibiotic chloramphenicol can cause severe side effects that include pancytopenia, erythroid suppression of bone marrow, and gray-baby syndrome.

76. E. Rationale: Vancomycin's serious adverse effects are ototoxicity and nephrotoxicity. Dosage adjustment is required in renal impairment along with continuous therapeutic monitoring. Vancomycin should be reserved for the treatment of serious infections such as *C. difficile* (orally) and MRSA.

77. E. Rationale: Clinicians should be mindful of causative organism, resistance, appropriate diagnosis, and optimal dose, route, and duration of therapy when prescribing antibiotics. Inappropriate and poorly planned use can lead to antibiotic resistance, increased cost, adverse effects, increased infection rates, and disruption of the hospital's normal flora.

78. A. Rationale: Penicillin is first-line therapy for the treatment of Strep. pneumonia. Ceftriaxone, vancomycin and erythromycin are effective against Strep. pneumonia while gentamicin is ineffective.

79. E. Rationale: Aminoglycoside antibiotics are bactericidal and bind irreversibly to the 30S ribosomal

subunit inhibiting bacterial protein synthesis. Aminoglycosides are excreted by the kidneys and can cause serious nephrotoxicity. Ototoxicity is also a serious complication associated with aminoglycoside therapy.

80. E. Rationale: Clindamycin is an antibiotic with most activity against anaerobes and aerobic gram-positive organisms.

81. E. Rationale: Amphotericin is the drug of choice for serious and life-threatening fungal infections such as *aspergillosis* and *mucomycosis*. It binds to ergosterol altering cell membrane permeability in susceptible fungi, and thus causing cell death. It is a polyene antibiotic; polyenes are molecules that are both hydrophilic and lipophilic. *Nephrotoxicity* is the major dose-limiting toxicity of *amphotericin B*. Prior to starting treatment, a test dose should be given.

82. E. Rationale: Sulfonamides and trimethoprim inhibit folic acid synthesis and therefore act synergistically when used in combination. Sulfonamides are structurally similar to PABA. Sulfonamides inhibit the enzyme, dihydropteroate synthetase, that blocks PABA, which subsequently prevents the synthesis of folic acid in the bacteria. Sulfonamides do not affect mammalian cells.

83. A. Rationale: A maculopapular skin rash may be an early sign of allergic reaction to penicillin. Penicillin allergy may be activated with any exposure, including penicillins in food. Anaphylaxis is the most serious reaction. Nausea, vomiting, epigastric distress, diarrhea, and black hairy tongue are other common reactions.

84. E. Rationale: Aminoglycosides require dosage adjustment in renal insufficiency due to other nephrotoxic adverse effect. Aminoglycoside can be used in combination with other antibiotics to provide a synergistic effect in treating various conditions. Aminoglycosides are active against aerobic gram-negative and certain aerobic gram-positive organisms but are ineffective in treating anaerobic infections.

85. C. Rationale: Ciprofloxacin is available as oral tablets, intravenous solution, and eye and ear drops. It is not available as a topical ointment.

86. C. Rationale: Vancomycin is not a beta-lactam antibiotic. Meropenem, aztreonam, ceftriaxone, and ampicillin are beta-lactam or related antibiotics.

87. D. Rationale: Doxycycline is not effective against vancomycin-resistant *Enterococcus faecium*. Linezolid, daptomycin, tigecycline, and quinupristin-dalfopristin are used for *E. faecium* infections.

88. D. Rationale: Ciprofloxacin, a second generation fluoroquinolone, has the greatest activity against *Pseudomonas aeruginosa*.

89. D. Rationale: *Enterococcus faecalis* alters the composition of the peptide side chain of peptidoglycan to cause resistance to vancomycin.

90. A. Rationale: Enterococci are resistant to cephalosporins. Enterococcal infections are typically treated with penicillin along with an aminoglycoside. Vancomycin is used for penicillin-resistant strains.

91. A. Rationale: Ethambutol can cause dose-related optic neuritis. Visual status should be assessed before therapy and visual acuity and color discrimination should be monitored monthly.

92. C. Rationale: Tetracycline antibiotics are bacteriostatic antibiotics that bind to the 30S subunit of the ribosome and inhibit protein synthesis.

93. B. Rationale: Isoniazid's toxic metabolite may be responsible for the severe and potentially fatal hepatitis. The risk increases with older age, concomitant use with rifampin, and in patients who drink alcohol frequently.

94. E. Rationale: Kanamycin is an aminoglycoside. Systemic exposure can cause ototoxicity, which can result in hearing loss and nephrotoxicity.

95. A. Rationale: Ethambutol can cause dose-related optic neuritis, which may interfere with the patient's ability to detect the colors green and red. Visual status should be assessed before therapy and visual acuity and color discrimination should be monitored monthly.

96. B. Rationale: Isoniazid, an antitubercular drug, may cause systemic lupus erythematosus-like syndrome. Other drugs associated with lupus-like syndromes include hydralazine, methyldopa, chlorpromazine, quinidine, minocycline, and others. Drugs should be discontinued if the patient becomes symptomatic or develops hematological abnormalities including leukopenia or rising ESR.

97. D. Rationale: Isoniazid's toxic metabolite may be responsible for the severe and potentially fatal hepatitis. The risk increases with older age, concomitant use with rifampin, and in patients who drink alcohol frequently.

98. A. Rationale: Pyrazinamide is used with other drugs in the treatment of *Mycobacterium tuberculosis*. It is not used to treat other mycobacteria such as *Mycobacterium leprae* and *Mycobacterium avium*. Pyrazinamide is not effective against *Legionella* or *Rickettsia*.

99. D. Rationale: The antituberculosis drug, pyrazinamide, causes several adverse reactions including hyperuricemia.

100. C. Rationale: Isoniazid, an antimycobacterial drug, inhibits cell wall synthesis by interfering with mycolic acids in the cell wall.

101. B. Rationale: Ethambutol can cause dose-related optic neuritis. Visual status should be assessed before therapy and visual acuity and color discrimination should be monitored monthly.

102. B. Rationale: Treatment with isoniazid + pyrazinamide + rifampin + ethambutol or streptomycin are initiated in most patients with confirmed or suspected TB.

103. E. Rationale: Bactericidal drugs kill bacteria whereas bacteriostatic drugs inhibit the growth and replication of bacteria. Chloramphenicol, tetracycline, and spectinomycin are generally bacteriostatic.

104. C. Rationale: Famciclovir is an antiviral drug and is a prodrug of penciclovir. It is available as an oral tablet. Famciclovir is used for various herpesvirus infections, in particular herpes zoster. It is not used for CMV.

105. E. Rationale: Ganciclovir is available as an oral capsule, injection, and intravitreal implant.

106. E. Rationale: Primaquine is antimalarial drug that disrupts parasitic mitochondria and interferes with DNA functions.

107. A. Rationale: Amphotericin B is used to treat fungal infections caused by a wide variety of organisms including *Cryptococcus*.

108. B. Rationale: Clotrimazole exhibits its antifungal activity by binding with phospholipids in the fungal cell membrane to alter membrane permeability.

109. D. Rationale: Otitis media is most often caused by *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*.

110. A. Rationale: Patients diagnosed with UTI generally present with the symptoms of dysuria, frequency and urgency.

111. D. Rationale: The antifungal agents Itraconazole and amphotericin B are used to treat *Aspergillosis* caused by the fungus *Aspergillus*. Ketoconazole is not used for *Aspergillosis*.

112. A. Rationale: The primary agents used for tuberculosis are isoniazid and rifampin.

113. A. Rationale: First-line agents for the treatment of gonorrhea are cephalosporins such as cefixime or ceftriaxone. There is a potential cross-sensitivity reaction that can occur in patients with penicillin allergies who are treated with cephalosporins. Streptomycin or ofloxacin can be given as alternative therapy.

114. A. Rationale: Trimethoprim/sulfamethoxazole is active against *Pneumocystis pneumonia* (PCP) (caused by *P. jiroveci*), aerobic gram-positive, aerobic gram-negative, and several protozoa. TMP-SMZ is the drug of choice for PCP.

115. B. Rationale: *E. coli* is a gram-negative bacilli and the causative organism in several infections especially urinary tract infections.

116. E. Rationale: Penciclovir cream is used to treat herpes labialis and should be administered at the first sign of lesions. The cream can be applied to the affected area every 2 hours while awake for 4 days.

117. B. Rationale: Regimens for include proton pump inhibitors (e.g., omeprazole) + amoxicillin +

clarithromycin; metronidazole + bismuth subsalicylate + tetracycline + H2 blocker.

118. A. Rationale: Oral clindamycin can cause several adverse reactions and is known as being a drug to cause pseudomembranous colitis. Linezolid and ampicillin can be given orally and could cause this colitis, but oral clindamycin is well known to cause as a potential side effect. Ceftriaxone can cause but is given intravenously.

119. E. Rationale: Tetracycline antibiotics are bacteriostatic antibiotics (bactericidal at high concentrations) that bind to the 30S subunit of the ribosome and inhibit protein synthesis. Tetracyclines have various uses including Rocky Mountain spotted fever (rickettsia). It should be taken with food to avoid gastrointestinal upset. Phototoxic reactions are possible.

120. E. Rationale: Certain cephalosporins including cefoperazone, cefamandole, cefmetazole, and cefotetan are associated with disulfiram-like reactions with ethanol.

121. C. Rationale: Cefepime is a fourth generation cephalosporin. Cefdinir, ceftriaxone, cefixime, and ceftibuten are third generation cephalosporins.

122. D. Rationale: Management of HIV and TB can be complex due to the large number of medications used to treat both conditions and the potential drug-drug interactions. Hepatitis is a severe adverse effect of anti-TB therapy and requires close monitoring of symptoms and measurement of serum AST and bilirubin levels.

123. C. Rationale: *Pseudomonas aeruginosa* is a gram-negative bacteria. *Staphylococcus aureus*, *Streptococcus pyogenes*, *Bacillus anthracis*, and *Listeria monocytogenes* are gram-positive bacteria.

124. A. Rationale: The most common pathogens in CAP is *Streptococcus pneumoniae*. *H. influenzae*, *M. pneumoniae*, and *C. pneumoniae* are also common etiologies. Emerging drug resistance has made antibiotic treatment challenging.

125. C. Rationale: There are scoring systems that have been developed to stratify patients into risk categories to determine whether hospital admission is warranted. There are several indicators including comorbid illness (e.g., liver disease, renal disease), physical findings (e.g., altered mental status), laboratory findings (e.g., BUN > 40 mg/dL or SBP < 90 mmHG are high risk), and age (< 50 years considered low risk).

126. A. Rationale: Empirical therapy for outpatient management of CAP includes a macrolide or fluoroquinolone. Doxycycline can be considered as well.

127. B. Rationale: Azithromycin is a macrolide antibiotic that exerts its pharmacological effects through inhibition of RNA-dependent protein synthesis.

128. E. Rationale: Vancomycin is a bactericidal antibiotic that provides coverage for pseudomembranous colitis

and staphylococcus enterocolitis infections. Vancomycin treats severe infections when other antibiotics are ineffective. It does not treat atypical pneumonia, which is usually caused by *Mycoplasma*, *Legionella*, and other unusual species.

CHAPTER 10

1. E. Rationale: Furosemide (Lasix®) and ethacrynic acid (Edecrin®) are loop diuretics that promote the excretion of water and electrolytes by inhibiting sodium and chloride reabsorption in the kidney. Theophylline is a bronchodilator.

2. B. Rationale: Digitalis agents can have an inotropic and antiarrhythmic effect on the heart. Digitalis treatment can produce sympatholytic effects on the sinoatrial (SA) and atrioventricular (AV) nodes and increased conduction velocity which subsequently increases vagal tone. Digoxin (Lanoxin®) is a treatment for atrial flutter due to its ability to decrease AV node conduction rate.

3. C. Rationale: Digoxin inhibits sodium-potassium pump (Na/K ATPase), which causes an increase in intracellular sodium and calcium ultimately resulting in increased myocardial contraction.

4. A. Rationale: Reflex sympathetic discharge causes tachycardia and increased heart contraction.

5. D. Rationale: Digitalis is a treatment for atrial flutter due to its ability to decrease AV node conduction rate. Digoxin is used often used as the drug of choice in the treatment ventricular rate in patients with atrial fibrillation or flutter.

6. C. Rationale: Digoxin is available as oral tablets and injection. It is only slightly protein bound (20%–40%). Digoxin should be used with caution in patients with renal impairment. Renal impairment reduces the excretion of the drug and can cause toxicity.

7. A. Rationale: Quinidine (Quinidex®) is indicated for the treatment of premature ventricular arrhythmias (PVCs). Parenteral phenytoin is used to treat ventricular tachycardia, paroxysmal atrial tachycardia, and arrhythmias caused by digitalis intoxication. Digoxin immune antigen-binding fragments (FAB) is an antidote for digoxin toxicity that can be life-threatening. Lidocaine is used for the treatment of ventricular arrhythmias resulting from myocardial infarction.

8. E. Rationale: Digitalis improves diastolic filling time and increases cardiac output.

9. B. Rationale: A right side CVA will result in left side motor changes. A CVA on one side of the brain will affect the opposite side of the body because the nerve fibers cross in the spinal column.

10. A. Rationale: Digitalis toxicity has severe effects on the heart. Some of the more common toxic effects include premature ventricular contraction (PVC), second degree

AV block, third degree AV block, and atrioventricular junctional escape beats. Digoxin is used to treat ventricular rate control in atrial fibrillation.

11. B. Rationale: Nitroprusside (Nitropress®) causes serious toxic effects, which include cyanide toxicity, thiocyanate toxicity, methemoglobinemia, acidosis, and increased intracranial pressure. Thiocyanate toxicity can produce central nervous system (CNS) effects, seizures, and muscle spasms.

12. E. Rationale: Digoxin inhibits sodium-potassium pump (Na/K ATPase), which causes an increase in intracellular sodium and calcium ultimately resulting in increased myocardial contraction.

13. C. Rationale: Nitrates and nitrites can cause orthostatic hypotension. Symptoms of orthostatic hypotension include dizziness, weakness, and syncope.

14. A. Rationale: Digoxin contains a steroid nucleus within its chemical structure.

15. C. Rationale: Nitrates can cause decreased ejection time that can result in reduced myocardial oxygen requirements. Nitrates are vasodilating agents used in the treatment of cardiovascular diseases including angina, acute myocardial infarction, heart failure, and hypertension.

16. B. Rationale: Dopamine affects dopaminergic receptors in the kidney causing vasodilation, which can lead to diuresis.

17. A. Rationale: Nitroglycerin decreases intramyocardial tension by relaxing vascular smooth muscle, which results in decreased myocardial oxygen demand.

18. D. Rationale: Spironalactone is a potassium sparing diuretic that can raise potassium when the drug is started. If the patient already has a high potassium level, this may cause dangerous elevations in potassium.

19. D. Rationale: Digitalis decreases heart rate through stimulation of the medullary vagal center. Digitalis agents can have an inotropic and antiarrhythmic effect on the heart.

20. B. Rationale: Digitoxin is more extensively cleared by the liver than digoxin. Digitoxin also has higher oral availability, more plasma protein binding, and a longer half-life than digoxin.

21. A. Rationale: Digitalis decreases ventricular rate in patients with atrial fibrillation.

22. B. Rationale: Emesis is one of the gastrointestinal side effects that is a result of digitalis' ability to stimulate chemoreceptor trigger zones. This side effect can occur with all routes of administration.

23. C. Rationale: Digitalis therapy can cause life-threatening cardiovascular adverse effects like

arrhythmias that require immediate response. Discontinuing therapy and administering an antidote may be warranted if toxicity is present.

24. C. Rationale: A transient post-conversion arrhythmia can occur after administration of adenosine. Adenosine slows conduction and inhibits reentry pathways through the AV node. Adenosine is metabolized rapidly in the tissue to inactive metabolites.

25. C. Rationale: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), stage 2 hypertension is defined as 160/100 mm Hg or higher.

26. B. Rationale: A mild diuretic effect occurs within the first few days of starting the drug. After a few weeks, relaxation of the peripheral vascular system resulting in decreased afterload and lower blood pressure occurs.

27. E. Rationale: The standard IV dose of epinephrine for cardiac arrest is 1 mg and can be repeated every 3 to 5 minutes.

28. C. Rationale: Due to heparin's high risk of bleeding and high patient variability in response to heparin therapy, aPTT (activated partial thromboplastin time) is used to monitor heparin's effect and to make dosage adjustments. The earliest time the blood sample should be drawn and measured is around 6 hours after the bolus dose.

29. A. Rationale: Urokinase (Abbokinase®) exerts its thrombolytic action by directly converting plasminogen to plasmin. Anistreplase (Eminase®) and streptokinase (Streptase®) are indirect thrombolytics. Heparin is an anticoagulant and Epsilon-aminocaproic acid is used to treat excessive bleeding.

30. D. Rationale: Warfarin inhibits vitamin K epoxide reductase which prevents carboxylation of vitamin K dependent factors II, VII, IX, and X.

31. E. Rationale: Sulfonamides (e.g., trimethoprim/sulfamethoxazole) and salicylates (e.g., aspirin) can increase the risk of bleeding when administered with warfarin. Anticoagulant effects are decreased with the concomitant use of warfarin and rifampin. Drug-drug interactions have not been found with ranitidine and warfarin use.

32. D. Rationale: Heparin binds to antithrombin III (AT-III), which inactivates factors Xa, IIa, IXa, and XIIa. Factor Xa is much more sensitive to heparin than other serine proteases. Heparin is useful as prophylactic therapy for patients at risk for venous thromboembolism.

33. B. Rationale: Urokinase exerts its thrombolytic action by directly converting plasminogen to plasmin. Streptokinase is an indirect thrombolytic. Rash and development of antibodies are rare with tissue plasminogen activator (tPA) therapy.

34. C. Rationale: Drugs that reduce mortality in heart failure include beta blockers like carvedilol (Corg®) and angiotensin-converting enzyme (ACE) inhibitors. Spironolactone (Aldactone®) and angiotensin II receptor blockers may also reduce mortality. Drugs that have a neutral effect include digoxin and calcium channel blockers.

35. D. Rationale: Pulmonary fibrosis, hyperthyroidism, optic neuropathy, and elevated liver function tests are all adverse effects associated with amiodarone. Thrombocytopenia has not been noted with amiodarone use.

36. A. Rationale: Thrombotic diseases such as pulmonary embolism can be detected by the D-dimer screening test. D-dimer is a fibrin degradation fragment that is elevated in blood levels to indicate thrombosis.

37. A. Rationale: Warfarin is an anticoagulant that acts by inhibiting the hepatic synthesis of vitamin K-dependent clotting factors II, VII, IX, and X.

38. C. Rationale: The international normalized ratio (INR) goal range for antithrombotic therapy in patients with atrial fibrillation and mitral valve disease is between 2 and 3 with a target goal of 2.5.

39. E. Rationale: Atrial fibrillation, atrial flutter, ventricular fibrillation, and ventricular tachycardia can be caused by the reentry mechanism. Reentry is an abnormal impulse conduction and occurs when one impulse reenters the heart muscle more than once.

40. D. Rationale: Rhabdomyolysis is a rare but clinically important adverse event of HMG coenzyme A reductase inhibitor monotherapy or combination therapy.

41. E. Rationale: Several factors have been implicated in the pathogenesis of hypertension which include increased sympathetic nervous system activity, mineralcorticoid (e.g., aldosterone) excess, genetic influence, and renal insufficiency.

42. A. Rationale: African-American race, sedentary lifestyle, and the increasing rate of childhood obesity can contribute to hypertension in children.

43. E. The American College of Cardiology (ACC) and the American Heart Association (AHA) developed 4 stages to classify heart failure. Stage A is defined as patients who are at high risk of developing HF with no identified structural or functional abnormalities.

44. B. Rationale: Loniten® (minoxidil) is indicated for the treatment of severe hypertension. Due to minoxidil's ability to stimulate hair growth, it is available in a topical formulation as Rogaine® for treatment of alopecia.

45. E. Rationale: ACE inhibitors may cause orthostatic hypotension, therefore patients should be counseled to avoid sudden postural changes to prevent this side effect. Patients should report signs of infection due to ACE

inhibitor's ability to decrease WBC count (neutropenia), and patients should not take potassium salt substitutes due to the potential for hyperkalemia.

46. C. Rationale: Calcium channel blockers like Verelan® (verapamil) should be avoided in patients with congestive heart failure (CHF). Calcium channel blockers can worsen heart failure. Diuretics, vasodilators (e.g., angiotensin-converting enzyme [ACE]), beta-blockers, and inotropic agents (e.g., digoxin) are commonly used in CHF.

47. D. Rationale: One of the most commonly reported side effects of the calcium channel blocker, Verelan® (verapamil), is constipation. Peri-colace is a laxative that can relieve constipation.

48. E. Rationale: Digitalis toxicity can cause hypokalemia, hypercalcemia, and hypomagnesemia. Electrolytes should be monitored in patients receiving digitalis therapy.

49. A. Rationale: Nesiritide (Natrecor®) is contraindicated for use in patients with systolic blood pressure < 90 mm Hg.

50. B. Rationale: Metolazone (Zaroxolyn®) is a diuretic used to treat edema in patients with heart failure.

51. D. Rationale: The combined use of propranolol (Inderal®) and diltiazem (Cardizem®, Dilacor®, Tiazac®) can increase the therapeutic and adverse effects of both drugs. Some of these effects include decreased heart rate, decreased cardiac output and hypotension.

52. C. Rationale: Cardiac output is the volume of blood pumped by each ventricle per minute. Cardiac output depends on heart rate and stroke volume.

53. E. Rationale: Diltiazem (Cardizem®, Dilacor®, Tiazac®) is a class IV antiarrhythmic indicated for the treatment of supraventricular tachycardia and atrial fibrillation. Diltiazem is a calcium channel blocker that decreases conduction velocity and prolongs the refractory period.

54. A. Rationale: Beta-blockers with cardioselective B-1 activity will have less effect on B-2 receptors in the lungs. Acebutolol (Sectral®), metoprolol (Lopressor®, Toprol XL®), esmolol (Brevibloc®), and atenolol (Tenormin®) are examples of selective B-1 antagonists.

55. E. Rationale: Hypertension can have negative effects on the eye and cause retinopathy. Hypertension can negatively affect the brain and cause dementia.

56. B. Rationale: Thiazide diuretics induce excretion of sodium, chloride, and water due to its inhibition of tubular sodium transport. Thiazide diuretics can cause fluid and electrolyte imbalances such as hyperuricemia, hyperglycemia, hyponatremia, hypochloremia, hypercalcemia, and most commonly hypokalemia. Monitor electrolyte (e.g., potassium, glucose, and uric acid) and fluid imbalances.

57. C. Rationale: Preload is described as the initial stretching of a single cardiac myocyte prior to contraction. It is affected by venous blood pressure and the rate of venous return.

58. B. Rationale: The digitalis drug, digoxin, inhibits sodium-potassium pump (Na/K ATPase), which causes an increase in intracellular sodium and calcium ultimately resulting in increased myocardial contraction. Digoxin slows heart rate, decreases conduction velocity, and increases peripheral resistance. Digoxin could increase blood pressure, especially if given intravenously.

59. A. Rationale: Intravenous nitroprusside is a vasodilator that decreases preload and afterload (arteriole and venous dilation).

60. E. Rationale: Digoxin immune FAB is an antidote for digoxin toxicity, which can be life-threatening.

61. C. Rationale: Heart failure may affect the right ventricle, the left ventricle, or both sides. In right-sided heart failure, the right ventricle loses its pumping function, and blood may back up into other areas of the body, producing congestion. In right-sided heart failure, fluid accumulates in the feet, ankles, liver, and abdomen. Peripheral edema (swollen ankles or legs) and ascites (excess fluid in abdomen and abdominal organs) may be a result of right-sided heart failure. In left-sided heart failure, fluid accumulates primarily in the lungs.

62. C. Rationale: Low molecular weight heparin (LMWH) therapy should be continued for 3-6 months in cancer patients with deep vein thrombosis (DVT).

63. C. Rationale: Digoxin immune antigen binding fragments (FAB) is an antidote for digoxin toxicity, which can be life-threatening.

64. E. Rationale: Patients with low body weight, severe renal insufficiency, and pregnant females with a mechanical prosthetic heart valve should have the enoxaparin dose adjusted.

65. A. Rationale: Digoxin is a cardiac glycoside that has inotropic and antiarrhythmic effects. Digoxin is used in the treatment of CHF and arrhythmias.

66. E. Rationale: Lovenox (enoxaparin) is a LMWH indicated for prevention of deep vein thrombosis. Dosing options for DVT prophylaxis include 30 mg every 12 hours subcutaneously or 40 mg qd subcutaneously.

67. B. Rationale: Numerous drugs and drug classes including cephalosporins (e.g., cefotetan), sulfonamides, salicylates, and tricyclic antidepressants can increase INR in patients taking warfarin, which can lead to bleeding. The dose of warfarin may have to be reduced in order to minimize this side effect. Monitor INR and advise patients to report any signs of bruising or bleeding.

68. A. Rationale: Atenolol and other beta blockers may increase the risk of developing diabetes mellitus, or it can

enhance or prolong hypoglycemia. It can mask the signs of hypoglycemia including tachycardia, tremor, and palpitations.

69. B. Rationale: Furosemide (Lasix®) is a loop diuretic that acts at the thick ascending loop of Henle and can be used in the management of ascites. Furosemide can cause tinnitus, hyperuricemia, and hypocalcemia.

70. B. Rationale: Spironolactone (Aldactone®), a potassium-sparing diuretic, inhibits aldosterone at the distal tubule, which increases excretion of sodium and water and decreases excretion of potassium. Patients should be advised to avoid overconsumption of potassium rich foods (e.g., bananas, citrus fruits, and tomatoes), potassium supplements, and potassium containing salt substitutes when taking spironolactone. Spironolactone has several adverse endocrine (e.g., gynecomastia, menstrual irregularities), and metabolic (e.g., hyperkalemia, hyponatremia and metabolic acidosis) effects.

71. A. Rationale: Diazoxide (Proglycem®), an antihypertensive and antihypoglycemic, has a similar structure to thiazide diuretics.

72. C. Rationale: The ACE inhibitor, enalapril (Vasotec®), is used for the treatment of hypertension. Enalapril adverse effects include hypotension, agranulocytosis, acute renal failure, alopecia, and abnormal taste.

73. E. Rationale: Cardiac glycosides' adverse effects can result in anorexia, vomiting, AV block, confusion, and yellow-green halos in the vision.

74. E. Rationale: Beta-adrenergic agents block beta receptors in the cardiac, bronchial, and vascular muscles. Beta-blockers can have adverse effects that include hypotension, CHF, increased airway resistance, and bradycardia.

75. D. Rationale: Warfarin inhibits vitamin K epoxide reductase, which prevents carboxylation of vitamin K dependent clotting factors II, VII, IX, and X. Monitor INR and patients closely for bleeding due to warfarin's ability to cause hemorrhaging. Hematuria is the most common sign of warfarin toxicity.

76. D. Rationale: Digitoxin has decreased polarity and is more extensively cleared by the liver than digoxin. Digitoxin also has higher oral availability, more plasma protein binding and a longer half-life and than digoxin. It may take 1 month for digitoxin versus 1 week for digoxin to achieve steady-state.

77. C. Rationale: Ototoxicity is a complication of furosemide therapy. It may cause excess fluid loss and electrolyte imbalances and patients should be monitored for hyponatremia, hypokalemia, hypocalcemia, hypochloremia, and hypomagnesemia.

78. B. Rationale: Warfarin is an anticoagulant that acts by inhibiting the hepatic synthesis of vitamin K-dependent

clotting factors II, VII, IX, and X. Adding Vitamin K to the diet should be avoided. Examples of foods high in vitamin K include leafy green vegetables and vegetable oils.

79. B. Rationale: Cardiac glycosides are used to treat CHF, atrial fibrillation, atrial flutter, and paroxysmal atrial tachycardia. Cardiac glycosides are contraindicated in patients with ventricular tachycardia (if not caused by heart failure) and ventricular fibrillation.

80. A. Rationale: Midamor® (amiloride) is safe to use in a hypokalemic patient. Midamor® is a potassium-sparing diuretic inhibits sodium reabsorption and potassium excretion which can cause increased potassium levels in the body. Symptoms of hyperkalemia include bradycardia, muscular weakness, paresthesia, and fatigue.

81. E. Rationale: Amiodarone (Coradarone®, Pacerone®) and digoxin should not be taken together due to the potential for digoxin toxicity. Digoxin toxicity can cause premature ventricular contraction (PVC), second degree AV block, third degree AV block, and atrioventricular junctional escape beats.

82. B. Rationale: Clonidine (Catapres®), a centrally acting alpha-2 adrenergic agonist, decreases peripheral vascular resistance and sympathetic outflow. Clonidine is used in the treatment of hypertension.

83. B. Rationale: Clonidine is an antihypertensive agent that is a direct-acting alpha-2 adrenergic agonist.

84. B. Rationale: Furosemide (Lasix®), a loop diuretic, treats edema through its excretion of water and electrolytes by inhibiting sodium and chloride reabsorption in the kidney. Adverse effects of furosemide include vertigo, pancreatitis, orthostatic hypotension, and agranulocytosis. Furosemide can be administered IV, IM, and orally.

85. E. Rationale: Heparin binds to antithrombin-III (AT-III), which inactivates factors Xa, IIa, IXa, and XIIa. Factor Xa is much more sensitive to heparin than other serine proteases. Due to heparin's high risk of bleeding and high patient variability in response to heparin therapy, aPTT (activated partial thromboplastin time) is used to monitor heparin's effect and to make dosage adjustments. Heparin also causes priapism and upon discontinuance of heparin rebound hypertension can occur.

86. E. Rationale: Angiotensin II receptor blockers (ARBs) lower blood pressure by inhibiting the pressor effects of the renin-angiotensin system through blocking angiotensin II binding to receptors in various tissues such as vascular smooth muscles and the adrenal gland. Cozaar® (losartan), Diovan® (valsartan) and Avapro® (irbesartan) are angiotensin II receptor blockers.

87. B. Rationale: Statins and fibrates are antilipemic drugs that can cause the adverse effect myositis. Advise patients to report any symptoms of muscle pain or weakness especially when accompanied by fever or malaise. Colestipol (Colestid®) is an anion exchange resin antilipemic agent which does not cause myositis.

88. A. Rationale: Disopyramide (Norpace®) is a class IA antiarrhythmic with strong anticholinergic effects. Patients taking disopyramide may experience common anticholinergic side effects such as dry mouth, blurry vision, constipation, and urinary retention.

89. A. Rationale: One of quinidine's serious adverse effects is torsades de pointes. Torsades de pointes is a polymorphic ventricular tachycardia that can occur in patients taking drugs that prolong QT interval such as quinidine or sotalol. Central nervous system (CNS) symptoms can manifest in patients with torades de pointes.

90. A. Rationale: Verapamil (Isoptin, Verelan, Calan, Covera-HS), a calcium channel blocker, acts on the atrioventricular node to delay calcium channel depolarization. Verapamil anti-arrhythmic pharmacological effects are used in the management of supraventricular tachyarrhythmias, atrial flutter, atria fibrillation, and paroxysmal supraventricular tachycardia (PSVT).

91. B. Rationale: Bretylium is a class III antiarrhythmic used for the treatment of ventricular fibrillation and ventricular tachycardia. It is available as an IM or IV injection. Bretylium can cause hypotension and bradycardia.

92. D. Rationale: Pulmonary fibrosis, hyperthyroidism, optic neuropathy, and elevated liver function tests are all adverse effects associated with amiodarone. Amiodarone (Cordarone®) can be given as once daily dosing.

93. A. Rationale: Common side effects of hydralazine (Apresoline®) are reflex tachycardia and headache. Headaches will usually subside after the first initial occurrence 2-4 hours after the first dose. Although not as common, hydralazine can also cause orthostatic hypotension, edema, and angina adverse cardiovascular effects.

94. D. Rationale: Nitroprusside causes serious toxic effects, which include cyanide toxicity, thiocyanate toxicity, methemoglobinemia, acidosis, and increased intracranial pressure. Thiocyanate toxicity can produce CNS effects, seizures, and muscle spasms.

95. D. Rationale: Penbutolol (Levitol®) is a non-selective beta-blocker due to its effects on both beta-1 and beta-2 receptors. Bronchospasm, cardiac decompensation, and bradycardia can occur with penbutolol use.

96. E. Rationale: Ramipril (Altace®) is an ACE inhibitor. These types of drugs may cause dry cough, hyperkalemia, skin rash, proteinuria, and angioedema.

97. D. Rationale: Methyldopa's (Aldomet®) adverse effects include fever, postural hypotension, and hemolytic anemia. A positive Coombs test indicates a diagnosis of hemolytic anemia.

98. A. Rationale: Pindolol (Visken®) has intrinsic sympathomimetic activity and is considered a partial agonist.

99. C. Rationale: Labetalol (Normodyne®, Trandate®) is an alpha adrenergic receptor blocker and a reversible beta-blocker. Labetalol is indicated for the treatment of hypertension and pheochromocytoma.

100. D. Rationale: Esmolol (Brevibloc®) has a half-life of 10 minutes and has the shortest duration of action. Esmolol is used for the management of supraventricular tachycardia.

101. B. Rationale: Nadolol (Corgard®), a non selective beta-blocker, has a half-life of 14-24 hours and has a prolonged duration of action. Nadolol is used in the treatment of hypertension, arrhythmias, and the prophylactic management of angina.

102. E. Rationale: Bisoprolol (Zebeta®) has the most cardioselective effects out of the five mentioned agents. Bisoprolol is a selective beta-1 blocker used in the management of hypertension.

103. C. Rationale: Clopidigrel (Plavix®) is an antiplatelet agent that acts through inhibition of adenosine diphosphate (ADP) binding to its platelet receptor and the consequent activation of glycoprotein IIb/IIIa complex. It rarely causes thrombocytopenia, but may cause bleeding at a similar risk to aspirin.

104. A. Rationale: Aspirin's antiplatelet effects are due to its ability to prevent the formation of thromboxane A2 through blocking prostaglandin synthetase.

105. C. Rationale: Normal serum concentration of potassium is 3.5-5 mEq/L. Potassium is an important electrolyte in the regulation of muscle and nervous tissue excitability.

106. A. Rationale: Hypertensive crisis is when systemic blood pressure is over 240/130 mm Hg without symptoms or elevated blood pressure with headache, heart failure, or chest pain. Intravenous nitroprusside is the drug of choice in hypertensive crisis because it can be titrated rapidly and safely. Esmolol and hydralazine may also be used in patients with severe hypertension.

107. C. Rationale: Unstable angina is a type of chest pain that occurs when the heart does not get enough oxygen. Taking nitroglycerin may not help.

108. B. Rationale: Lovastatin is a member of the statin family of drugs that target HMG-CoA reductase, the rate-limiting enzyme of the mevalonate pathway of cholesterol synthesis.

109. D. Rationale: Calcium channel blockers inhibit myocardial and smooth muscle by blocking calcium influx at cellular membranes, which results in decreased myocardial contractility and vasodilation. Consequently, myocardial oxygen consumption is decreased.

110. B. Rationale: Minoxidil is a vasodilator that is used for severe and drug-resistant hypertension. It produces

a vasodilatory effect on arterial smooth muscles, causing a reduction in blood pressure in peripheral resistance.

111. E. Rationale: Captopril is an ACE inhibitor. ACE inhibitors are commonly associated with a dry cough.

112. E. Rationale: Thiazide diuretics induce excretion of sodium, chloride and water due to its inhibition of tubular sodium transport. Thiazide diuretics can cause fluid and electrolyte imbalances such as hyponatremia, hypochloremia, hypercalcemia and most commonly hypokalemia. Orthostatic hypotension, photosensitivity and anorexia can also occur with thiazide diuretic use.

113. B. Rationale: ACE inhibitors block the conversion of angiotensin I to angiotensin II and the metabolism of angiotensin-(1-7). They reduce angiotensin II concentrations and increase rennin concentrations.

114. A. Rationale: Amiodarone is a class III antiarrhythmic agent indicated for the treatment of refractory life-threatening ventricular arrhythmias.

115. D. Rationale: Familial hypercholesterolemia is a genetic disorder that is characterized by the accumulation of low-density lipoproteins (LDL) transporting cholesterol in the blood. LDL receptor defects cause impaired uptake of the lipoprotein resulting in enhanced intracellular biosynthesis of the lipid.

116. B. Rationale: Carvedilol (Coreg®) is a combined alpha- and nonselective beta-blocker that antagonizes both alpha- and beta-receptors.

117. A. Rationale: Fenofibrate (Tricor®) is indicated as an adjunctive therapy to diet for the treatment of hyperlipidemia, mixed dyslipidemia, and hypertriglyceridemia. It decreases hepatic production of apolipoprotein CIII via activation of peroxisome proliferator activator receptors (PPARS) and induces lipoprotein lipase.

118. E. Rationale: The goal of treatment in patients with congestive heart failure is to increase strength and efficiency of contraction of the heart muscle, treat complications of arrhythmias, and reduce abnormal water and sodium retention. Digitalis (digoxin), diuretics (hydrochlorothiazide), and vasodilators (hydralazine) are used to treat patients with heart failure.

119. D. Rationale: The combined use of HMG-CoA reductase inhibitors such as simvastatin with fibrates like gemfibrozil may increase the risk of developing myopathy and rhabdomyolysis.

120. A. Rationale: A chest x-ray may be performed initially to determine if there is fluid around the lungs.

121. A. Rationale: Angiotensin-converting enzyme (ACE) inhibitors such as enalapril have been shown to reduce mortality rates in patients with heart failure. Beta-blockers have also been shown to reduce mortality rates.

122. A. Rationale: Saline nasal spray can help reduce symptoms of nasal congestion without adversely affecting blood pressure or thyroid function like other cough and cold medications such as pseudoephedrine, chlorpheniramine, and phenylephrine.

123. B. Rationale: Trimethoprim-sulfamethoxazole (Bactrim®, Septra®) may increase the INR in patients who are taking warfarin. Patients should be monitored for bleeding.

124. D. Rationale: Stop warfarin therapy, give oral vitamin K, and monitor INR levels frequently when INR levels are greater than 9.

125. B. Rationale: Warfarin inhibits vitamin K epoxide reductase, which prevents carboxylation of vitamin K dependent factors II, VII, IX, and X. Warfarin has an onset of action of ½ to 3 days and a duration of action of 2-5 days. Warfarin is highly bound to plasma protein and is primarily metabolized by CYP 1A2 and CYP 2C9.

126. E. Rationale: Disopyramide, procainamide, and quinidine are class IA antiarrhythmics that block sodium channels and therefore slow conduction and increase refractory period. Class IA antiarrhythmic agents produce the following pharmacodynamic effects: prolong P-R and Q-T intervals, reduce Purkinje fiber automaticity, and decrease the rate of rise and amplitude of phase 0 depolarization.

127. E. Rationale: Class IB antiarrhythmic drugs shorten action potential and phase 3 repolarization. Lidocaine, mexiletine, tocainide, and phenytoin are class IB antiarrhythmics.

128. B. Rationale: Tocainide (Tonocard®) is a class IB antiarrhythmic that shortens the refractory period of the AV node. Tocainide's actions are similar to lidocaine; however, its cardiac effects are not as strong as lidocaine.

129. D. Rationale: Pneumonitis is a serious life-threatening pulmonary side effect of amiodarone. Photosensitivity and pseudocyanosis are adverse skin reactions caused by amiodarone therapy.

130. E. Rationale: Class IC antiarrhythmics cause phase 0 depolarization depression and inhibition of sodium transport during phase 0 depolarization. Flecainide (Tambocor®) and propafenone (Rythmol®) are class IC antiarrhythmics.

131. A. Rationale: The antiarrhythmic drug disopyramide can cause serious adverse cardiovascular effects such as heart block, arrhythmias, and heart failure. Common side effects of disopyramide include blurry vision and dry eyes.

132. A. Rationale: Beta-blockers (e.g., propranolol) are class II antiarrhythmic agents. Class I antiarrhythmic (e.g., lidocaine, procainamide, quinidine) drugs block sodium channels, decrease excitability, and slow conduction velocity. Phenytoin is an anticonvulsant that may be used

in the treatment of ventricular arrhythmias if first-line agents fail.

133. B. Rationale: Quinidine at therapeutic doses increases QRS and QT intervals, which can be assessed on the ECG to determine the drug's efficacy and/or toxicity. Quinidine, a class IA antiarrhythmic, depresses myocardial contractility, prolongs the refractory period, and increases action potential.

134. A. Rationale: Quinidine is a class IA antiarrhythmic indicated for the treatment of premature ventricular arrhythmias (PVCs). Some common side effects of quinidine are headache, tinnitus, and nausea. Torsades de pointes is a serious cardiovascular adverse effect of quinidine.

135. C. Rationale: Procainamide, quinidine, and disopyramide are class IA antiarrhythmics whose primary mechanism of action is blocking sodium channel. Their cardiac effects are to prolong action potential and increase ventricular refractory period. Quinidine is indicated for the treatment of premature ventricular arrhythmias (PVCs).

136. A. Rationale: Quinidine is a class IA antiarrhythmic that causes decreased conduction velocity, anticholinergic activity and prolonged ventricular refractory period. Quinidine is indicated for the treatment of premature ventricular arrhythmias (PVCs). Quinidine has negative inotropic effects.

137. B. Rationale: Quinidine, a class IA antiarrhythmic, depresses myocardial contractility, prolongs the refractory period and increases action potential. Quinidine toxicity can produce ventricular arrhythmias, extrasystoles, heart block, heart failure, coma, and generalized seizures. Quinidine should be used in patients with complete heart block.

138. C. Rationale: Procainamide decreases ectopic myocardial automaticity, myocardial excitability and conduction velocity. Its other pharmacodynamic effects include anticholinergic activity and depressing myocardial contractility. Procainamide, a class IA antiarrhythmic, is indicated for the treatment of PVCs, ventricular tachycardia, atrial fibrillation, atrial flutter and paroxysmal atrial tachycardia.

139. C. Rationale: Beta agonists can cause desensitization of receptors with prolonged use. Beta adrenergic receptors may decrease due to down-regulation, sequestration and phosphorylation.

140. C. Rationale: Lidocaine toxicity can cause seizures, respiratory depression and hypotension.

141. E. Rationale: Bretylium is a class III antiarrhythmic used for the treatment of ventricular fibrillation and ventricular tachycardia. Propafenone and flecainide are class IC antiarrhythmics with a strong affinity and slow dissociation from sodium channels. Quinidine is a class IA antiarrhythmic indicated for the treatment of premature ventricular arrhythmias (PVC's).

142. B. Rationale: Lidocaine, a class IB antiarrhythmic, has rapid association and dissociation from sodium channels. Lidocaine suppresses automaticity, shortens action potential and shortens refractory period. Lidocaine is used in the treatment of ventricular arrhythmias that does not response to defibrillation or epinephrine.

143. D. Rationale: Adenosine is the drug of choice in treating supraventricular tachycardia. Adenosine inhibits reentry and slows conduction in the AV node.

144. C. Rationale: Bretylium is a class III antiarrhythmic used for the treatment of ventricular fibrillation and ventricular tachycardia. Bretylium prolongs refractory period and widens action potential duration. Additionally, bretylium causes an initial release of norepinephrine, resulting in transient hypertension followed by hypotension.

145. A. Rationale: Although not fully understood, the iodine content in amiodarone may contribute to hypothyroidism or hyperthyroidism. Amiodarone can interfere with thyroid hormone and thyroid functions. Thyroid function should be monitored in patients taking amiodarone.

146. A. Rationale: The pharmacokinetic profile of amiodarone is as follows: highly protein bound in circulation, has a large volume of distribution, metabolized in the liver, and a slow, variable absorption. Its onset of action can vary from a couple days to a couple months. Amiodarone is a very effective antiarrhythmic however its adverse effects limit its use.

147. B. Rationale: Lidocaine, a class IB antiarrhythmic, has rapid association and dissociation from sodium channels. Lidocaine suppresses automaticity, shortens action potential and shortens refractory period. Lidocaine is used in the treatment of ventricular arrhythmias.

148. E. Rationale: Flecainide, a class IC antiarrhythmic, with a strong affinity and slow dissociation from sodium channels. Flecainide slows phase 0 depolarization and suppresses automaticity. Flecainide is used in the treatment of ventricular arrhythmias and premature ventricular contraction (PVC).

149. A. Rationale: Propafenone (Rythmol®) is a class IC antiarrhythmic that blocks sodium channel, slows action potential, exerts weak beta-blocking activity and increased QRS duration.

150. C. Rationale: Sotalol (Betapace) blocks potassium channels which prolongs repolarization and increases effective refractory period. Bradycardia is a side effect of sotalol.

151. B. Rationale: The nonselective beta-blocker propranolol has quinidine-like effects on cellular membranes at blood concentrations greater than its beta-blocking activity. This effect does not appear to have significant clinical importance.

152. C. Rationale: Acebutolol, metoprolol, esmolol, and atenolol are examples of cardioselective beta-1 antagonists. Acebutolol is only available as a capsule and has intrinsic sympathomimetic activity (ISA). Beta-blockers with ISA display a lessened effect on cardiac output and cardiac rate.

153. D. Rationale: Sotalol blocks potassium channels, which prolongs repolarization and increases effective refractory period. Sotalol is used to treat life-threatening ventricular arrhythmias.

154. A. Rationale: Acebutolol, metoprolol, esmolol, and atenolol are examples of selective B-1 antagonists. Esmolol is only administered intravenously and has a short elimination half-life. Dosing of esmolol has to be titrated in a step-wise manner with a loading dose given prior to maintenance infusion.

155. B. Rationale: Nifedipine (Adalat®, Procardia®), verapamil (Isoptin®, Verelan®, Calan®, Covera-HS®) and diltiazem are calcium channel blockers. Verapamil and diltiazem, class IV antiarrhythmics, slow conduction and prolong refractory period through inhibiting calcium influx at the AV node. Nifedipine does not exhibit substantial activity on the SA and AV nodes compared to verapamil and diltiazem.

156. C. Rationale: Diazoxide (Proglycem®), an antihypertensive and antihypoglycemic, has a similar structure to thiazide diuretics.

157. A. Rationale: Thiazide diuretics (e.g., chlorothiazide) can cause hyperuricemia and gout. Thiazide diuretics should be avoided or used cautiously in patients with a history of gout or high uric acid blood levels.

158. E. Rationale: Reserpine is a rauwolfia alkaloid that deplete catecholamine and serotonin in several organs. Diarrhea, bradycardia, and depression can occur with reserpine use. The depression may last several months after the drug has been discontinued and reserpine use is contraindicated in patients with depression.

159. C. Rationale: Propranolol is a beta-blocker that is used to treat tachycardia and can cause bradycardia as an adverse effect.

160. E. Rationale: Methyldopa's adverse effects include drowsiness, fever, postural hypotension, nephrotic syndrome, and hemolytic anemia. A positive coombs test indicates a diagnosis of hemolytic anemia. Methyldopa can have adverse effects on the liver and is contraindicated in patients with liver disease.

161. C. Rationale: Hydralazine (Apresoline®) lowers blood pressure by vasodilating vascular smooth muscle primarily on arterioles with less effect on venules and veins. Hydralazine can cause several side effects including neutropenia, leukopenia, orthostatic hypotension, and tachycardia.

162. B. Rationale: Methyldopa (Aldomet®) is a centrally acting antiadrenergic used for the treatment of hypertension. Methyldopa can cause side effects such as somnolence, weakness, and dizziness.

163. E. Rationale: The antihypertensive agents guanethidine, methyldopa, and clonidine can cause salt and water retention. Edema and weight gain can result from sodium and water retention.

164. A. Rationale: Clonidine, a centrally acting alpha-adrenergic agonist, decreases peripheral vascular resistance and sympathetic outflow. Clonidine's adverse effects include rebound hypertension, lethargy, dry mouth, and dizziness.

165. D. Rationale: Propranolol is a beta-blocker whose pharmacodynamic effects cause decreased heart rate (negative chronotropy), myocardial oxygen consumption, myocardial contraction (negative inotropic effects), and renin release. These effects contribute to propranolol's antihypertensive, antianginal, and antiarrhythmic actions. An adverse side effect of propranolol is bronchoconstriction.

166. A. Rationale: Hydralazine lowers blood pressure by vasodilating vascular smooth muscle, primarily on arterioles with less effect on venules and veins. Hydralazine can cause increased cardiac output, stroke volume, and tachycardia, which may be a result of a reflex response to decreased peripheral resistance.

167. C. Rationale: Trimethaphan, an antihypertensive, lowers sympathetic tone of the vasculature and causes vasodilation.

168. D. Rationale: Thiazide diuretics are recommended as the preferred initial choice for treatment of hypertension due to their ability to prevent cardiovascular complications. Thiazides are also generally well tolerated and relatively inexpensive.

169. D. Rationale: Minoxidil and hydralazine lower blood pressure by vasodilating vascular smooth muscle, primarily on arterioles with less effect on venules and veins. Prazosin is an alpha-blocker that causes dilation on both arterial and venous smooth muscle.

170. E. Rationale: The onset of action of intravenous nitroprusside can range from 60-120 seconds.

171. B. Rationale: Methyldopa is contraindicated in hepatic disease and liver function tests should be monitored.

172. D. Rationale: Hydralazine, a peripheral vasodilator, is contraindicated in patients with coronary artery disease and mitral valve rheumatic heart disease.

173. E. Rationale: A serious adverse effect of rauwolfia alkaloids (e.g., reserpine) is depression that could result in suicide. The depression may last several months after the drug has been discontinued.

174. E. Rationale: The rauwolfia alkaloid, reserpine and guanethidine, deplete catecholamines which may cause a decrease tissue concentration of norepinephrine. Reserpine and guanethidine are used in the treatment of hypertension.

175. C. Rationale: Propranolol is contraindicated in certain conditions such as asthma, bradycardia, heart block, and heart failure.

176. E. Rationale: Guanethidine inhibits norepinephrine (NE) release, depletes NE, and decreases vasoconstriction, which leads to reduced blood pressure. Guanethidine adverse effects include constipation, diarrhea, bradycardia, retrograde ejaculation, and orthostatic hypotension.

177. C. Rationale: The beta-blocker propranolol can be used for migraine prophylaxis. Propranolol is contraindicated in asthma, bradycardia, heart block, and heart failure.

178. C. Rationale: Hydralazine's antihypertensive effects are due to its vasodilating actions on vascular smooth muscle. A patient may experience headache as a side effect.

179. D. Rationale: Clonidine should not be discontinued abruptly and taper drug gradually to prevent rebound hypertension. Clonidine can be given 4-6 hours before a scheduled operation.

180. D. Rationale: Tricyclic antidepressants (TCAs) block the uptake of guanethidine at the adrenergic neuron. TCAs antagonize alpha-2 receptors, which interferes with clonidine's alpha-2 agonist effects to decrease blood pressure. The concurrent use of clonidine or guanethidine with TCAs may result in decreased drug efficacy.

181. E. Rationale: Hydralazine and diazoxide can cause several side effects including tachycardia. Hydralazine lowers blood pressure by vasodilating vascular smooth muscle primarily on arterioles with less effect on venules and veins. Diazoxide is a peripheral vasodilator used for the management of hypertensive crisis and hypoglycemia. Clonidine, an alpha adrenergic agonist, is an antihypertensive agent that can cause bradycardia as an adverse effect.

182. A. Rationale: Nitroprusside is an arterial and venous dilator given via IV infusion for the treatment of hypertensive emergencies and acute heart failure. Nitroprusside causes serious adverse effects such as toxicity from the metabolite thiocyanate.

183. A. Rationale: Ethacrynic acid is a loop diuretic that promote the excretion of water and electrolytes by inhibiting sodium and chloride reabsorption in the kidney. Metabolic alkalosis, hyperuricemia, and potassium loss are side effects of ethacrynic acid use.

184. B. Rationale: Spironolactone, a synthetic steroid, is a mineralocorticoid (aldosterone) antagonist. Spironolactone

is used in the treatment of precocious puberty, detection of hyperaldosteronism, and hirsutism. Spironolactone is also a potassium sparing diuretic and antihypertensive agent.

185. B. Rationale: Spironolactone, a potassium-sparing diuretic, inhibits aldosterone effects at the distal tubule, which increases excretion of sodium and water and decreases excretion of potassium.

186. A. Rationale: Triamterene (Dyrenium) is a potassium-sparing diuretic that inhibits sodium reabsorption and potassium excretion in the distal renal tubules. Ethacrynic acid and furosemide are loop diuretics that treat edema through its excretion of water and electrolytes by inhibiting sodium and chloride reabsorption at the ascending loop of Henle. Hydrochlorothiazide and chlorothiazide are thiazide diuretics that induce excretion of sodium, chloride, and water due to its inhibition of tubular sodium transport in the cortical diluting portion of the kidney.

187. E. Rationale: Thiazide diuretics (e.g., chlorothiazide) are used in the management of hypertension and edema. The loop diuretics and thiazide diuretics can cause metabolic alkalosis resulting from hypokalemia and hyponatremia. Patients with potassium and chloride depletion due to vomiting, diarrhea, gastrointestinal drainage, excessive sweating, paracentesis, or renal diseases are more susceptible to metabolic alkalosis.

188. D. Rationale: Thiazide diuretics induce excretion of sodium, chloride, and water due to its inhibition of tubular sodium transport. Thiazide use would result in decreased urine output of calcium. Thiazide diuretics can cause fluid and electrolyte imbalances such as hyperuricemia, hyperglycemia, hyponatremia, hypochloremia, hypercalcemia, and most commonly hypokalemia.

189. A. Rationale: Furosemide is a loop diuretic that promote the excretion of water and electrolytes by inhibiting sodium and chloride reabsorption in the kidney. Furosemide's antihypertensive effects are due to its ability to increase glomerular filtration rate (GFR), cause renal and peripheral vasodilation, and decrease peripheral vascular resistance.

190. C. Rationale: Thiazide diuretics can cause laboratory disturbances such as hyperuricemia, hyperglycemia, and hyponatremia. Hypokalemia commonly occurs in patients taking thiazide diuretics.

191. E. Rationale: Thiazide diuretics cause numerous hematological (e.g., thrombocytopenia), dermatological (e.g., photosensitivity), and gastrointestinal (e.g., jaundice) adverse effects.

192. A. Rationale: Triamterene is a potassium-sparing diuretic that can cause hyperkalemia. Patients should be advised to avoid potassium supplements, potassium containing salt substitutes, and overconsumption of

potassium rich foods (e.g., bananas, citrus fruits, tomatoes).

193. D. Rationale: Thiazide diuretics induce excretion of sodium, chloride, and water due to its inhibition of tubular sodium transport. Thiazides also exhibit antihypertensive effects, which may be due to their ability to cause vasodilation of the arterioles and to lower total peripheral resistance.

194. B. Rationale: Saluresis is defined as sodium in the urine. Diuretics induce excretion of sodium, other electrolytes, and water at different sites in the nephron. Diuretics are commonly used in the treatment of edema and hypertension.

195. E. Rationale: Spironolactone is a potassium-sparing diuretic and aldosterone receptor antagonist. Spironolactone has several endocrine adverse effects, which include gynecomastia, erectile dysfunction, and menstrual abnormalities. Spironolactone's metabolic adverse effects are hyperkalemia, hyponatremia, and metabolic acidosis.

196. E. Rationale: Ethacrynic acid is a loop diuretic that promotes the excretion of water and electrolytes by inhibiting sodium and chloride reabsorption in the kidney. Alkalosis, hyperuricemia, and potassium loss are side effects of ethacrynic acid use.

197. A. Rationale: Triamterene is a potassium sparing diuretic that causes hyperkalemia. Patients should be advised to avoid potassium supplements, potassium containing salt substitutes, and overconsumption of potassium rich foods (e.g., bananas, citrus fruits, tomatoes).

198. D. Rationale: Loop diuretics cause fluid and electrolyte imbalances. Ethacrynic acid and furosemide can cause metabolic alkalosis resulting from hypokalemia and hypochloremia. Patients with potassium and chloride depletion due to vomiting, diarrhea, GI drainage, excessive sweating, paracentesis, or renal diseases are more susceptible to metabolic alkalosis.

199. C. Rationale: Triamterene is a potassium-sparing diuretic that can cause hyperkalemia. Patients should be advised to avoid potassium supplements, potassium containing salt substitutes, and overconsumption of potassium rich foods (e.g., bananas, citrus fruits, tomatoes).

200. B. Rationale: Spironolactone is contraindicated in patients with renal insufficiency, anuria, and hyperkalemia. Use with caution in patients with impaired renal function, electrolyte and fluid imbalances, and hepatic disease.

201. D. Rationale: Captopril is an ACE inhibitor used in the treatment of hypertension. Captopril's adverse effects include angioedema, which can be life-threatening. Rash and cough are common side effects of captopril use.

202. C. Rationale: Acetazolamide's diuretic effects are due to its ability to inhibit carbonic anhydrase, which leads to lower hydrogen in the kidneys and increased excretion of electrolytes and water.

203. A. Rationale: The primary mechanism of action of diuretics for the treatment of edema is excretion of sodium.

204. B. Rationale: Spironolactone, a synthetic steroid, is a mineralocorticoid (aldosterone) antagonist and a potassium sparing diuretic and antihypertensive agent. Spironolactone has several endocrine adverse effects, which include gynecomastia, erectile dysfunction, and menstrual abnormalities. Spironolactone's metabolic adverse effects are hyperkalemia, hyponatremia, and metabolic acidosis.

205. E. Rationale: Triamterene and amiloride are potassium-sparing diuretics that can cause hyperkalemia. Patients should be advised to avoid potassium supplements, potassium containing salt substitutes, and overconsumption of potassium rich foods (e.g., bananas, citrus fruits, tomatoes).

206. E. Rationale: The loop diuretics (e.g., bumetanide and furosemide) and thiazide diuretics (e.g., hydrochlorothiazide) can cause metabolic alkalosis resulting from hypokalemia and hypochloremia. Patients with potassium and chloride depletion due to vomiting, diarrhea, GI drainage, excessive sweating, paracentesis, or renal diseases are more susceptible to metabolic alkalosis. Potassium chloride supplementation has been used to prevent hypokalemic and hypochloremic alkalosis.

207. D. Rationale: Potassium supplementation should be avoided in patients taking spironolactone since excess potassium intake may cause hyperkalemia.

208. B. Rationale: Spironolactone, a potassium-sparing diuretic, inhibits aldosterone at the distal tubule, which increases excretion of sodium and water and decreases excretion of potassium. Patients should be advised to avoid overconsumption of potassium rich foods (e.g., bananas, citrus fruits, tomatoes), potassium supplements, and potassium containing salt substitutes when taking spironolactone.

209. B. Rationale: Mannitol elevates osmotic pressure of the glomerular filtrate and inhibits reabsorption of electrolytes and water in the proximal tubule.

210. C. Rationale: Potassium-sparing diuretics (e.g., spironolactone, triamterene) are contraindicated in hyperkalemic patients. Patients taking potassium-sparing diuretics should be advised to avoid potassium supplements, potassium containing salt substitutes, and overconsumption of potassium rich foods (e.g., bananas, citrus fruits, tomatoes).

211. B. Rationale: Dobutamine is a selective beta-1 stimulator that causes a positive inotropic effect.

Amphetamine, dopamine, and ephedrine are mixed/indirect adrenergic agents.

212. A. Rationale: Ganglionic blockers are not selective in blocking parasympathetic or sympathetic ganglia at nicotinic receptors. Tachycardia, hypotension, decreased cardiac output, and arteriolar vasodilation can occur with ganglion-blocking agents. These drugs are not used often as drug therapy in clinical use today due to their adverse effects and non-selective actions.

213. D. Rationale: The dose of digoxin should be adjusted in patients with renal impairment.

214. C. Rationale: Gemfibrozil is a fibric acid derivative that lowers triglycerides levels by increasing catabolism of VLDL. Bile acid sequestrants (e.g., colesipol, cholestyramine) and Statins (e.g., lovastatin) do not lower triglycerides as effectively as fibrates. Fibrates can cause a 20%-50% reduction in triglyceride levels

215. A. Rationale: Clofibrate (Atromid-S®) is a fibric acid derivative that lowers triglycerides levels by increasing catabolism of very-low-density lipoprotein (VLDL) and it inhibits the synthesis of cholesterol. Adverse effects of clofibrate include musculoskeletal (myalgia, arthralgia), gastrointestinal (abdominal pain, vomiting, nausea), and hepatic (gallstones, hepatomegaly) reactions.

216. E. Rationale: Clofibrate is a fibric acid derivative that lowers triglycerides levels by decreasing VLDL and it inhibits the synthesis of cholesterol. Statins such as atorvastatin and lovastatin decrease LDL and increase HDL. Neomycin, an aminoglycoside antibiotic, can lower LDL cholesterol as a final option after conventional treatments fail.

217. B. Rationale: An HMG CoA reductase inhibitor combined with a bile acid sequestrant (e.g., cholestyramine) or niacin is used in the treatment of hypercholesterolemia.

218. C. Rationale: Lovastatin (Mevacor®) exerts its antihyperlipidemic effects through inhibiting HMG CoA reductase. HMG CoA reductase inhibitors are widely referred to as statin medications and decrease LDL and triglycerides while increasing HDL.

219. A. Rationale: Taking aspirin 30 minutes before niacin may reduce its side effect of flushing. Flushing is a reddening of the skin which usually occurs on the face and neck.

220. E. Rationale: Niacin is an antilipemic agent that may cause flushing. Taking aspirin 30 minutes before niacin may reduce its side effect of flushing.

221. B. Rationale: Spironolactone, a synthetic steroid, is a mineralcorticoid (aldosterone) antagonist and a potassium sparing diuretic and antihypertensive agent. Spironolactone has several endocrine adverse effects, which include gynecomastia, erectile dysfunction, and menstrual abnormalities. Spironolactone's metabolic

adverse effects are hyperkalemia, hyponatremia, and metabolic acidosis.

222. D. Rationale: Potassium-sparing diuretics (e.g., amiloride and triameterene) inhibit aldosterone at the distal tubule, which increases excretion of sodium and water and decreases excretion of potassium. Patients should be advised to avoid overconsumption of potassium rich foods (e.g., bananas, citrus fruits, tomatoes), potassium supplements, and potassium containing salt substitutes.

223. E. Rationale: The loop diuretics (e.g., furosemide and bumetanide) and thiazide diuretics (e.g., hydrochlorothiazide) can cause metabolic alkalosis. Potassium-sparing diuretics can cause metabolic acidosis.

224. E. Rationale: Beta-blockers with cardioselective beta-1 activity will have fewer effects on beta-2 receptors in the lungs and less effect on peripheral vasoconstriction. Acebutolol, metoprolol, esmolol, and atenolol are examples of selective beta-1 antagonists. Timolol is a non-selective beta-blocker that is used for the treatment of glaucoma due to its ability to decrease intraocular pressure.

225. D. Rationale: Clonidine and reserpine do not cause reflex tachycardia. Due to reflex tachycardia and several other serious cardiovascular adverse effects associated with minoxidil therapy, patients should be closely monitored. Beta-blockers can be administered to prevent tachycardia.

226. D. Rationale: Lipid soluble drugs can cross the blood brain barrier more easily than hydrophilic drugs. Atenolol and nadolol are hydrophilic beta-blockers and are more likely to produce CNS effects.

227. A. Rationale: Guanethidine and guanadrel are adrenergic neuron blockers that cause antihypertensive effects through peripheral inhibition of NE. Guanabenz and methyldopa are centrally antihypertensives and clonidine is a centrally acting alpha-adrenergic agonist.

228. D. Rationale: Guanethidine adverse effects include diarrhea, bradycardia, and orthostatic hypotension. Patients should be advised to report persistent diarrhea to their prescriber and to avoid activities that can potentiate orthostatic hypotension.

229. D. Rationale: Common cardiovascular side effects of hydralazine are reflex tachycardia and palpitations. Although not as common, hydralazine can also cause orthostatic hypotension, edema, and angina adverse cardiovascular effects.

230. B. Rationale: Dyazide is the combination of two diuretics—the thiazide diuretic hydrochlorothiazide and the potassium-sparing diuretic triamterene.

231. D. Rationale: Epinephrine's cardiac stimulation effects are due to its action on beta-1 receptors in the heart, and its vasodilation effects are due to its action on

beta-2 receptors. Epinephrine's bronchodilation effect is due to its ability to stimulate beta-2 receptors in the bronchial smooth muscle.

232. A. Rationale: Captopril (Capoten®), an ACE inhibitor, should be used with caution in patients with bilateral renal artery stenosis. Captopril increases the risk of reducing renal perfusion and therefore renal function should be closely monitored for the first few weeks of therapy.

233. B. Rationale: Systolic blood pressure in the range of 120-139 mm Hg and diastolic blood pressure in the range of 80-89 mm Hg is classified as high normal blood pressure or "prehypertension."

234. A. Rationale: Due to heparin's high risk of bleeding and high patient variability in response to heparin therapy, activated partial thromboplastin time (aPTT) is used to monitor heparin's effect and to make dosage adjustments. The earliest time the blood sample should be drawn and measured is around 6 hours after the bolus dose.

235. B. Rationale: Methyldopa is drug of choice for treatment of hypertension during pregnancy due to a more favorable safety profile.

236. B. Rationale: Bumex® (bumetanide) and Demadex® (toresemide) are loop diuretics.

237. A. Rationale: An intact tablet may appear in the stool and patients should be counseled that this is normal and the medication was absorbed.

238. E. Rationale: Nifedipine is a calcium channel blocker used for the treatment of angina and hypertension. Nifedipine has several adverse effects, which include peripheral edema, palpitations, dizziness, and nausea.

239. E. Rationale: Common side effects of ACE inhibitors are dry-hacking cough, hypotension, and neutropenia. Patients should not take potassium-containing salt substitutes with ACE inhibitors due to the potential for hyperkalemia.

240. A. Rationale: Calcium channel blockers like Verelan® (verapamil) should be avoided in patients with CHF. Calcium channel blockers can worsen heart failure. Diuretics, vasodilators (e.g., ACE inhibitors), beta-blockers, and inotropic agents (e.g., digoxin) are commonly used in CHF.

241. E. Rationale: Ticlopidine (Ticlid®), an antithrombotic, exhibits antiplatelet action and is used in the management of stroke. Dipyridimole is a coronary vasodilator and a platelet aggregation inhibitor that can be combined with warfarin or aspirin in treating various thromboembolic disorders. Acetylsalicylic acid (aspirin) antiplatelet effects are due to its ability to by preventing the formation of thromboxane A₂ through blocking prostaglandin synthetase.

242. E. Rationale: Digitalis toxicity can cause hypokalemia, hypercalcemia, and hypomagnesemia. Electrolytes should be monitored in patients receiving digitalis therapy.

243. A. Rationale: Clonidine, a centrally acting alpha-adrenergic agonist, decreases peripheral vascular resistance and sympathetic outflow. Clonidine's adverse effects include rebound hypertension, lethargy, dry mouth, and dizziness.

244. A. Rationale: Certain drugs produce a pharmacological effect by acting as an agonist or antagonist to adrenergic receptors (alpha-1, alpha-2, beta-1, beta-2). Methoxamine and phenylephrine are alpha-1 selective agonists. Stimulation of alpha-1 receptors can result in vasoconstriction, increased blood pressure, and increased peripheral resistance.

245. B. Rationale: Verapamil, a calcium channel blocker, acts on the atrioventricular node to delay calcium channel depolarization. Verapamil is used in the management of supraventricular tachyarrhythmias, atrial flutter, atrial fibrillation, and PSVT.

246. A. Rationale: The class III antiarrhythmic, bretylium, is effective in the acute management of ventricular tachycardia, including ventricular fibrillation. Bretylium prolongs refractory period and widens action potential duration. Additionally, bretylium causes an initial release of norepinephrine, resulting in transient hypertension followed by hypotension.

247. E. Rationale: The vasodilator, hydralazine, can cause reflex tachycardia, headache, and postural hypotension.

248. C. Rationale: Nitroprusside causes serious toxic effects, which include cyanide toxicity, thiocyanate toxicity, hypotension, and increased intracranial pressure. Thiocyanate toxicity can produce CNS effects, seizures, and muscle spasms.

249. C. Rationale: In the presence of acidosis, acetazolamide may cross the blood-brain barrier, which could ultimately result in CNS damage and death.

250. C. Rationale: Acetazolamide's diuretic effects are due to its ability to inhibit carbonic anhydrase, which leads to lower hydrogen in the kidneys and increased excretion of bicarbonate, potassium, sodium, and water.

251. B. Rationale: Mannitol, an osmotic diuretic, improves water flow into extracellular fluid through elevating plasma osmolality, which causes reduction in intracranial or intraocular pressure.

252. E. Rationale: Digitoxin also has higher oral availability, more plasma protein binding, and a longer half-life than digoxin. Digitoxin has a half-life of 7 days versus 40 hours for digoxin. It may take 1 month for digitoxin versus 1 week for digoxin to achieve steady-state.

253. A. Rationale: Catapres® (clonidine), a centrally acting alpha-2 adrenergic agonist, is used in the treatment of hypertension. Clonidine can cause depression and it is recommended to monitor for signs of depression.

CHAPTER 11

1. C. Rationale: Triamcinolone is also a medium potency topical steroid that would be replaced by the preferred formulary agent mometasone. Desonide is a lower-medium potency agent and clobetasol is a superpotent topical steroid.

2. D. Rationale: Dexamethasone is an antiinflammatory and immunosuppressant agent used in the treatment of several conditions such as adrenal insufficiency, dermatitis, asthma, and Addison's disease. An adverse effect of glucocorticoid treatment is osteoporosis.

3. A. Rationale: Topical treatments including metronidazole and azelaic acid are first line therapy for mild rosacea.

4. A. Rationale: Plaque psoriasis is a skin disease that is characterized by thick red lesions with silvery scales. Smoking, stress, cold climates, and certain drugs (e.g., beta-blockers) are risk factors for psoriasis.

5. A. Rationale: Topical corticosteroids such as hydrocortisone are commonly prescribed for the treatment of mild localized psoriasis. Other drugs such as topical calcipotriene, coal tar products, tazarotene, and anthralin are also utilized as first-line treatment options.

6. C. Rationale: Methotrexate is an antimetabolite that inhibits mitosis and DNA synthesis; however, its action in psoriasis is most likely due to its ability to affect the activated APC-T cell complex found in psoriatic lesions.

7. B. Rationale: High potency steroids such as clobetasol 0.05% are used as second-line treatment for patients that have developed thick chronic plaques that did respond to lower potency topical steroids.

8. E. Rationale: Topical corticosteroids such as hydrocortisone are commonly prescribed for the treatment of mild localized psoriasis. Side effects of topical corticosteroid treatment include pruritus, erythema, folliculitis, and hypertrichosis.

9. E. Rationale: Methotrexate is an antineoplastic and immunosuppressant agent that is used for a variety of conditions including lymphoma, rheumatoid arthritis, Crohn's disease, esophageal cancer, and choriocarcinoma.

CHAPTER 12

1. A. Rationale: Lipohypertrophy in patients with diabetes is due to repeated injections at the same site. The lipogenic effect of insulin can cause hypertrophy of subcutaneous fat at the local injection site. Lipohypertrophy can be prevented by rotating the injection site.

2. E. Rationale: Insulin is a peptide hormone composed of amino acids that is synthesized and secreted in pancreatic beta cells. It suppresses hepatic gluconeogenesis and promotes glucose uptake and utilization. Cells cannot utilize glucose without insulin.

3. A. Rationale: All of these insulins are available in products synthesized via recombinant DNA technology. However, human insulin lispro is an insulin analog.

4. C. Rationale: Glucocorticoids can be classified based on their duration of actions. Betamethasone and dexamethasone are long-acting agents with a duration of action from 1-3 days whereas hydrocortisone is a short-acting glucocorticoid with a duration of action ranging from 8-12 hours.

5. D. Rationale: Diabetic patients have an increased risk of developing ulcers or amputations based on male gender, diabetes onset > 10 years, poorly managed glucose, and co-morbidities (e.g., renal, retinal, cardiovascular, foot). Foot conditions that increase the likelihood of amputations include peripheral neuropathy, peripheral vascular disease, erythema, body deformity, and hemorrhage under a callus. Preventative measures can be implemented to reduce ulcers and amputations.

6. D. Rationale: Thyroid storm is a condition of excess thyroid hormone. It is a rare and potentially fatal complication of hyperthyroidism. Propylthiouracil may be given to block thyroid hormone production. Hydrocortisone may be given to counter relative adrenal insufficiency.

7. A. Rationale: Thiazolidinediones are contraindicated in patients with active liver disease and elevated liver enzymes. Thiazolidinediones require periodic monitoring of liver function. If patients have symptoms of dark urine, nausea, vomiting, anorexia, abdominal pain, or fatigue, it may be an indication of liver problems.

8. A. Rationale: Renal function should be assessed through monitoring serum creatinine and BUN. There is an increased risk of hyperkalemia in diabetes patients, which requires potassium monitoring. Other electrolytes like sodium can be monitored as well.

9. C. Rationale: Elevated AST and ALT indicate hepatic disease or damage. Acarbose, an alpha-glucosidase inhibitor antidiabetic agent, can cause elevated serum aminotransferase levels. Serum aminotransferase should be monitored periodically in patients.

10. E. Rationale: Androgens (e.g., testosterone) are hormones that promote normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. Adverse effects include priapism, jaundice, gynecomastia, and acne.

11. E. Rationale: Sulfonylureas' antidiabetic effects are through the stimulation of the pancreatic release of

insulin. Sulfonylureas adverse effects include jaundice, photosensitivity and nausea.

12. E. Rationale: Insulin is a peptide hormone composed of amino acids that is synthesized and secreted in pancreatic beta cells. It suppresses hepatic gluconeogenesis and promotes glucose uptake and utilization. Cells cannot utilize glucose without insulin.

13. E. Rationale: Cholinesterase inhibitor overdose can precipitate a cholinergic crisis that manifests as sweating, weakness, fasciculations, salivation, seizures, and respiratory depression. Myasthenia gravis is a chronic autoimmune disorder that causes weakness of the skeletal muscles. Myasthenia gravis can present as the following symptoms: drooping of the eyelids, blurry vision, double vision, impaired speech, and muscle weakness.

14. E. Rationale: Secretion of antidiuretic hormone (SIADH) may be caused by various conditions or drugs. Psychotropic drugs including antipsychotics and selective serotonin reuptake inhibitors (SSRIs) have been associated with SIADH. Ecstasy or MDMA is an amphetamine that has been linked to SIADH, although the mechanism is not well understood. Cases of vincristine-induced SIADH have also been well documented.

15. B. Rationale: Tolazamide, chlorpropamide, and tolbutamide are examples of first generation sulfonylureas. The second generation sulfonylureas (e.g., glipizide) have fewer side effects and are more potent agents. Sulfonylureas should not be used in pregnant women due to the risk of severe hypoglycemia in neonates.

16. A. Rationale: Glyburide is a sulfonylurea antidiabetic drug that stimulates insulin release from the pancreas to lower blood glucose. The initial dose of glyburide is 2.5-5mg PO daily with breakfast and the maintenance dose is 1.25-20mg PO qd in divided doses or as a single dose.

17. D. Rationale: Chlorpropamide is a sulfonylurea antidiabetic drug. The concomitant use of alcohol and chlorpropamide can stimulate a disulfiram-like reaction. Symptoms of a disulfiram reaction include headache, tachycardia, nausea and vomiting, perspiration, cardiovascular problems, delirium, seizures, and, occasionally, death.

18. C. Rationale: Somatostatin inhibits the releases of insulin whereas secretin, gastrin, and cholecystokinin are enteric hormones that can increase insulin activity after glucose consumption.

19. A. Rationale: The sulfonylurea, glipizide, exerts its antidiabetic effect primarily through stimulating the release of insulin from the beta cells of the pancreas. Metformin is a biguanide that decreases glucose production in the liver and Acarbose is an alpha-glucosidase inhibitor that decreases oral glucose absorption.

20. E. Rationale: There are various oral medications used to treat type 2 diabetes. These drugs may reduce insulin resistance, stimulate endogenous insulin secretion or insulin itself, or delay the absorption of carbohydrate from the gastrointestinal tract.

21. E. Rationale: Rosiglitazone and metformin are active ingredients in Avandamet®.

22. A. Rationale: Serum transaminase enzyme levels (e.g., AST) should be monitored since Precose® (acarbose) may elevate liver enzymes when given at doses of 75-100 mg 3 times per day.

23. A. Rationale: Glyset® (miglitol) inhibits glycoside hydrolase enzymes called alpha-glucosidases.

24. C. Rationale: Beta-blockers (e.g., propranolol) are used to treat hyperthyroid symptoms (e.g., anxiety, rapid heart rate). Methimazole (thyroid hormone antagonist), Propylthiouracil (thyroid hormone antagonist), and Lugol's solution (iodine solution) are used to manage hyperthyroidism. Bromocriptine is indicated for the treatment of Parkinson's disease.

25. B. Rationale: A potential side effect of biosynthetic growth hormone is the ability to develop antibodies. Serum levels can be monitored for antibody formation of growth hormone use.

26. E. Rationale: Insulin is primarily metabolized in the liver by the enzyme glutathione insulin transhydrogenase and almost completely reabsorbed in the renal tubules. Insulin has a half life of less than 10 minutes. Furthermore, insulins can be categorized based on their various pharmacokinetic profiles in reference to onset, peak, and duration.

27. E. Rationale: GIP, secretin, gastrin, and cholecystokinin are enteric hormones that can increase insulin activity after glucose consumption.

28. A. Rationale: Insulin has several effects on the adipose tissues, liver, and muscle. Insulin inhibits intracellular lipase, inhibits glycogenolysis, and increases glycogen synthesis.

29. D. Rationale: Pharmacokinetic profiles of insulins can vary in each patient. Insulin ultralente can have an onset of action of 6-8 hours, minimal peak activity, and duration of action up to 36 hours.

30. C. Rationale: Chlorpropamide is a sulfonylurea antidiabetic drug. The concomitant use of alcohol and chlorpropamide can stimulate a disulfiram-like reaction. Chlorpropamide adverse effects include hypoglycemia, SIADH, and rash.

31. E. Rationale: Sulfonylureas' antidiabetic effects are primarily through the stimulation of pancreatic release of insulin. With prolonged use, sulfonylureas can exert antidiabetic effects in the peripheral tissues and liver and by increasing insulin-receptor binding. Sulfonylureas

increase peripheral tissue insulin sensitivity and decrease hepatic gluconeogenesis.

32. B. Rationale: Chlorpropamide can cause the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Geriatric patients are at increased risk of this adverse effect. SIADH symptoms of water intoxication manifest as mental confusion, nausea, anorexia, dizziness and mental depression, decreased serum sodium concentration, increased urinary and decreased serum osmolality. Restriction of water intake (e.g., 800 mL daily) and discontinuing chlorpropamide are used to manage SIADH.

33. E. Rationale: Sulfonylureas are classified as first and second generation agents based on differences in duration of action, dosing, and side effects profile. Second generation sulfonylurea antidiabetic agents have fewer side effects, are more potent, and have a lipophilic side chain compared to first generation sulfonylureas.

34. A. Rationale: Sulfonylureas' antidiabetic effects are primarily through stimulating the release of insulin from the beta cells of the pancreas. With prolonged use, sulfonylureas can exert antidiabetic effects in the peripheral tissues and liver by increasing insulin-receptor binding. Sulfonylureas increase peripheral tissue insulin sensitivity and decrease hepatic gluconeogenesis.

35. E. Rationale: Insulin Lispro is a rapid-acting insulin with a quick onset of action (10-15 minutes). Regular insulin is a short-acting insulin with an onset of action of 30 minutes to 1 hour. Insulin glargine is a long-acting insulin with an onset of action of 1.5-2 hours.

36. E. Rationale: Insulin has several effects on the adipose tissues, liver, and muscle. Insulin inhibits intracellular lipase, inhibits glycogenolysis, increases triglyceride synthesis, and increases glycogen synthesis.

37. D. Rationale: NPH insulin is an intermediate-acting insulin. The pharmacokinetic profile of initial onset at 10-15 min, a peak at 2-4 hrs, and a duration of 3-5 hrs resembles rapid-acting agents such as insulin lispro and insulin aspart.

38. E. Rationale: Methimazole is an antithyroid agent used in the treatment of hyperthyroidism. Methimazole commonly causes adverse dermatological side effects like pruritis, rash, urticaria, and hair loss. Methimazole can also cause hematological adverse effects like agranulocytosis.

39. C. Rationale: The usual maintenance dose of glyburide is in the range of 1.25 to 20 mg daily.

40. B. Rationale: Chlorpropamide is a sulfonylurea antidiabetic drug. The concomitant use of alcohol and chlorpropamide can stimulate a disulfiram-like reaction. Symptoms of a disulfiram reaction include headache, tachycardia, nausea and vomiting, perspiration, cardiovascular problems, delirium, seizures, and the possibility of death.

41. D. Rationale: The 50 gram glucose tolerance test is used to determine if a pregnant women has gestational diabetes. Low-risk patients may not need screening and are identified as normal body weight, less than 25 years old, no history of abnormal glucose metabolism, no past history of poor obstetrical outcome, no family history of DM, and are not members of high-risk ethnic groups (Hispanic, Native American, African-American, or Pacific islanders).

42. D. Rationale: Cerebral edema can be fatal and it occurs most commonly in children and patients in their twenties. Mannitol is used for the treatment of cerebral edema due to its ability to elevate plasma osmolality and to reduce intracranial pressure.

43. C. Rationale: The normal blood glucose value for a fasting patient is between 80 to 120 mg/dl.

44. C. Rationale: Type 2 diabetes mellitus is a metabolic disorder that manifests as elevated blood glucose levels due to insulin resistance and insulin deficiency. There are several risk factors for type 2 diabetes mellitus that include poor diet, family history, sedentary lifestyle, age over 45, and impaired glucose tolerance.

45. B. Rationale: Patients with type 2 diabetes mellitus are started on metformin and diet therapy. Metformin at a dose of 500 mg bid with morning and evening meals can be given initially. Dose should be titrated to the goal maximum dose of 2500 mg/day.

46. E. Rationale: Metformin is a biguanide antidiabetic agent that primarily acts through decreasing hepatic glucose production by decreasing gluconeogenesis. Adverse effects include diarrhea, lactic acidosis, and megaloblastic anemia.

47. E. Rationale: Glipizide is a sulfonylurea antidiabetic agent with a mechanism of action that enhances insulin release, enhances peripheral insulin sensitivity, and inhibits hepatic glucose production. Common adverse effects are hypoglycemia and weight gain.

48. A. Rationale: Pioglitazone is a thiazolidinedione antidiabetic that does not require renal dosage adjustment. Adverse effects include upper respiratory infection, anemia, sinusitis, and edema when used in combination of insulin.

49. A. Rationale: Pioglitazone is a thiazolidinedione antidiabetic agent that is highly protein bound and is predominately excreted in the bile and eliminated in the feces. Adverse effects include upper respiratory infection, anemia, sinusitis, and edema when used in combination with insulin.

50. C. Rationale: Hemoglobin A1c represents the average blood glucose for 3 months. This test helps determine glycemic control. An HbA1c of 6% or less is normal. If it is above 7%, the patient's diabetes is not well controlled, since the optimum goal is a level as close to 7% as possible.

51. E. Rationale: Diabinese® (chlorpropamide) is a sulfonylurea used for type 2 diabetes. Diabinese® has noticeably more side effects due to its prolonged duration of action. It has an increased risk of hypoglycemia and disulfiram-like reactions.

52. D. Rationale: Avandia® (rosiglitazone) improves insulin sensitivity but not secretion, and inhibits hepatic glucose production.

53. E. Rationale: Humalog® is insulin Lispro with a rapid onset of action. It should be administered subcutaneously and within 15 minutes of a meal.

54. C. Rationale: Lactic acidosis is a rare but serious side effect of Glucophage® (metformin).

55. A. Rationale: Lantus® (insulin glargine) is a long-acting basal insulin.

CHAPTER 13

1. E. Rationale: Lansoprazole is a proton pump inhibitor used for the treatment of ulcers and gastroesophageal reflux disease (GERD).

2. D. Rationale: All of the above, Fibercon® (calcium polycarbophil) is useful in the management of constipation by adding fiber; it can be useful for certain types of non-infectious diarrhea, such as irritable bowel syndrome (IBS). Because the drug contains calcium, it can bind to tetracyclines and render them non-effective; doses should be separated by at least 2 hours from one another.

3. B. Rationale: Famotidine is a H₂ receptor blocker used for the treatment of ulcers, GERD, and heartburn.

4. E. Rationale: Cimetidine is a H₂ receptor antagonist used for the treatment of gastric and duodenal ulcers, GERD, and heartburn. Cimetidine can have adverse effects on the liver including jaundice, hepatitis, and increased liver function tests (LFTs). Cimetidine can also cause several other side effects including dizziness, confusion, diarrhea, gynecomastia, and increased prolactin levels.

5. E. Rationale: Histamine receptors are found in several organ systems in the body. H₁ is located in the smooth muscles, endothelium, and brain. H₂ is located in the gastric mucosa, cardiac muscle, mast cells, and the brain; H₃ receptors are distributed throughout the central nervous system (CNS). Histamine can cause capillary dilation, increased blood pressure (or sometimes decreased blood pressure), gastric hypersecretion, vascular permeability. However, it causes INCREASED airway mucous, so answer E is the exception and the answer to the question.

6. B. Rationale: Bisacodyl (Dulcolax®) is a stimulant laxative that produces colonic mucosal irritation and fluid secretion. Dulcolax® is minimally absorbed with an oral onset of action of 6–10 hours. Normal adult doses are 10–15 mg PO, but it can be dosed up to 30 mg PO per day when used before gastrointestinal procedures for bowel

evacuation. Ingestion orally with milk may cause irritation and vomiting, so oral bisacodyl should not be administered with milk.

7. D. Rationale: Aspirin and ethanol can breakdown the gastrointestinal (GI) mucosal barrier. Enteric-coated tablets are available to minimize GI upset. Enteric-coated medications are formulated to allow release of the medication in the small intestine and bypass the stomach. Caffeine has not been noted to cause breakdown of the GI mucosal barrier.

8. D. Rationale: Cholinergic inhibitors, such as atropine, hyoscyamine, and belladonna alkaloids, decrease gastric motility, gastric secretions, and pancreatic secretions.

9. B. Rationale: Liver damage is usually assessed by clinical symptoms (e.g., jaundice) and hepatic changes, along with increased liver function tests (LFTs). Increased blood urea nitrogen (BUN) and serum creatinine are often used to assess renal function.

10. C. Rationale: Amitiza® (lubiprostone) is a prostaglandin E-1 derivative that is a chloride channel activator indicated for chronic idiopathic constipation and the treatment of irritable bowel syndrome with constipation.

11. E. Rationale: Sulfasalazine is a prodrug that is converted into two metabolites in the colon that are responsible for sulfasalazine's pharmacological effects. The metabolites (active moieties) are mesalamine (exerts antiinflammatory effects) and sulfapyridine (exerts antibacterial effects).

12. A. Rationale: Anzemet® (dolasetron) is a 5-HT₃ (serotonin) antagonist that treats nausea and vomiting.

13. B. Rationale: Metoclopramide's antiemesis effects are due to its ability to inhibit dopamine receptors in the chemoreceptor trigger zone in the brain. However, in patients with poor gastric motility (e.g., diabetic gastroparesis) or with reflux (GERD), metoclopramide is also used as a prokinetic agent that increases gastric emptying (decreases gastric emptying time).

14. E. Rationale: Cimetidine (Tagamet®) and nizatidine (Axid®) are both H₂ receptor antagonists used for the treatment of ulcers, GERD, and heartburn.

15. B. Rationale: Ranitidine is a H₂ receptor blocker (histamine antagonist) used for the treatment of peptic ulcers, GERD, and heartburn.

16. C. Rationale: Of the listed drugs, only diphenhydramine is available over the counter; the rest are prescription-only for nausea and/or motion sickness.

17. E. Rationale: Antacids act by increasing gastric pH. The increase in pH inhibits the proteolytic action of pepsin. The increased pH also increases lower esophageal sphincter pressure, which helps relieve reflux into the esophagus. Some antacids are constipating (e.g.,

aluminum hydroxide) and some may cause laxation (e.g., magnesium containing antacids).

18. C. Rationale: Concomitant use of aluminum, calcium, or magnesium antacids and tetracycline can cause tetracycline to be poorly absorbed. These agents should not be taken together.

19. E. Rationale: The sodium, magnesium, and phosphate content of antacids are of particular concern to patients with ascites, congestive heart failure, and renal insufficiency. Decompensation of the disease or electrolyte imbalances may occur in these patients if there is a poor choice in antacid selection.

20. A. Rationale: Omeprazole is a proton pump inhibitor (PPI). The PPIs are H⁺/K⁺ ATPase pump inhibitors in the gastric parietal cell. PPI are used in the treatment of ulcers and GERD.

21. B. Rationale: A bowel movement can be produced by laxatives that differ based on mechanism of action. Types of laxatives are bulk-forming, hyperosmotic, lubricant, saline, stimulant laxatives, and stool softeners. Castor oil is a stimulant that increases peristaltic activity. Mineral oil lubricates the stool. Methycellulose adds fiber and bulk. Sodium citrate and sodium bicarbonate are alkalinizing agents and antacids; they are not laxatives.

22. B. Rationale: The antacid aluminum hydroxide has minimal systemic absorption, but absorption may be of concern in patients with renal insufficiency. Sodium bicarbonate and calcium carbonate are absorbed systemically.

23. E. Rationale: Lactulose reduces fecal pH through its acidification in the colon by bacteria. Lactulose reduces serum ammonia levels by increasing the conversion of ammonia to ammonium, which is excreted in the stool; part of this action may be due to the increased bacterial assimilation of ammonia. As lactulose is degraded in the colon, it produces an osmotic effect that decreases constipation and increases stool frequency. Lactulose's side effects include diarrhea, abdominal cramps, belching, and flatulence.

24. C. Rationale: Cimetidine has no known clinically significant drug interactions with digoxin. Cimetidine decreases the CYP 450 metabolism of several drugs including, but not limited to, warfarin, phenytoin, quinidine, and isoniazid. This may result in increased drug levels in the body and the potential for toxicity. A dosage reduction may be necessary.

25. C. Rationale: Many prostaglandin E drugs may cause diarrhea. The ability to resolve constipation is used therapeutically (i.e., Amitiza, prostaglandin E1 derivative) or is a common side effect (e.g., Prostin-E2 suppository, prostaglandin E2).

26. B. Rationale: Concomitant use of aluminum antacids and tetracycline can cause the tetracycline to be poorly absorbed. These agents should not be taken together.

27. E. Rationale: Several drug classes including prostaglandins (e.g., misoprostol), Proton Pump Inhibitors (PPIs) (e.g., lansoprazole), and H₂ antagonists (e.g., famotidine) are used to treat peptic ulcer disease. Antacids can provide symptomatic relief while ulcers heal. Peptic ulcers that are infected with *H. pylori* can be treated with up to three antibiotics. Prior to the advent of the formerly listed therapies, muscarinic antagonists were used to reduce acid secretion and provide symptomatic relief; however, while some muscarinic antagonists (e.g., hyoscyamine) are still labeled for such adjunctive use, they are not employed commonly today since more effective ulcer treatments are available.

28. B. Rationale: Emollient laxatives (e.g., docusate) are also called stool softeners. They can take up to 3 days to generate a bowel movement.

29. C. Rationale: Ranitidine is a H₂ receptor blocker used for the treatment of peptic ulcers, GERD, and heartburn.

30. A. Of the choices listed, only amitriptyline is not used for GERD or esophagitis related to reflux. In fact, amitriptyline is one drug that can relax the lower esophageal sphincter and contribute to reflux symptoms; other problems include epigastric distress and constipation. Other common medications that worsen GERD by relaxing the lower esophageal sphincter include calcium channel blockers. All the other choices presented are labeled to be used in GERD and esophagitis related to reflux.

31. E. Rationale: Spastic colitis, dehydration, intestinal obstruction, diarrhea, and hypokalemia are all potential adverse effects of chronic laxative use. Patients should be counseled on dietary sources of fiber.

32. B. Rationale: Saline laxatives (e.g., magnesium citrate) increase intestinal volume through the hyperosmotic effect of ions in the small intestine, which leads to increased intestinal motility.

33. D. Rationale: Laxatives are used to eliminate certain poisons (e.g., drug overdose) from the body, alleviate constipation and straining in various disease states such as cardiovascular disease, and to reduce intraluminal and rectosigmoid pressure in diverticulitis.

34. D. Rationale: Laxatives differ based on mechanism of action. Types of laxatives are bulk-forming (increase stool bulk), hyperosmotic, lubricant (lubricate the stool), saline, stimulant laxatives (increase peristalsis), and emollient (soften the stool).

35. D. Rationale: Metoclopramide's mechanism of action is complex; it may cause extrapyramidal side effects and actions include inhibition of peripheral muscarinic synapses.

36. D. Rationale: Sucralfate, a pepsin inhibitor, forms an adherent and protective coating (barrier) against pepsin, gastric acid, and bile salts when the drug attaches to proteins on the surface of the ulcer. A common side effect of sucralfate is constipation.

37. A. Rationale: Sodium phosphate is a saline cathartic that can be administered as a solution (Fleet Phospho-Soda®) or as an enema (Fleet Enema®). Sodium bicarbonate is an alkalinizing agent used primarily in the treatment of metabolic acidosis, and has been used as an antacid. Methylcellulose is a bulk-forming laxative.

38. A. Rationale: Gastroesophageal reflux disease is primarily caused when the lower esophageal sphincter relaxes, which allows acidic stomach contents to reflux into the esophagus, causing irritation. Symptoms of GERD include heartburn, regurgitation, chest pain, dysphagia, and sore throat.

39. E. Rationale: Complications of GERD include asthma, laryngitis, Barrett esophagus, and peptic strictures or subglottic stenosis. Complications are largely prevented with effective treatments, including use of PPIs or H₂ blockers.

40. B. Rationale: Cimetidine is a H₂ blocker used for the treatment of GERD. Bethanechol is used for urinary retention, and dextromethorphan is a cough suppressant.

41. B. Rationale: Cimetidine's common adverse effects include headache, diarrhea, confusion, and dizziness.

42. E. Rationale: There are several lifestyle modifications that can be implemented for the management of GERD. Counsel patient to elevate the head during sleep, do not eat within 30 minutes before lying down, avoid any foods that aggravate symptoms, and avoid smoking.

43. B. Rationale: Cimetidine at a dose of 400 mg qid or 800 mg bid can be used to relieve GERD. Patients can take before meals and at bedtime.

44. E. Rationale: Cimetidine decreases the liver CYP 450-mediated metabolism of several medications including lidocaine and warfarin, which can lead to toxic effects. In combination with cyclosporine, cimetidine may increase the risk of cyclosporine-induced nephrotoxicity and may decrease cyclosporine metabolism. Patients taking these medications in combination with cimetidine should be monitored closely. Cimetidine can also inhibit the renal cationic tubular secretion of dofetilide and cause dofetilide toxicity; cimetidine is contraindicated for use with dofetilide.

45. D. Rationale: Peptic ulcers occur when the digestive juices that help food digest damage the walls of the stomach or duodenum. The most common cause is the infection with a bacterium called *Helicobacter pylori* (*H. pylori*). Another cause is the long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen. Spicy foods do not cause ulcers, but can aggravate them and make them worse.

46. B. Rationale: The most common symptoms of GERD are heartburn, regurgitation, hypersalivation, and belching.

CHAPTER 14

1. B. Rationale: Akathisia is characterized by a feeling of "inner restlessness." Akathisia is a common adverse effect with antipsychotic drugs.

2. E. Rationale: Alzheimer disease can be diagnosed based on the exclusion of other causes of dementia plus a review of history of memory loss and other cognitive impairments. Cholinesterase inhibitors such as donepezil (Aricept®), rivastigmine (Exelon®), and galantamine (Reminyl®) may improve cognitive function by increasing acetylcholine in the brain. Psychotropic medications may be used to treat secondary symptoms of Alzheimer disease such as agitation.

3. D. Rationale: With increased age, the pharmacokinetic profiles of certain drugs change. The hepatic clearance of theophylline, meperidine, barbiturates, quinidine, certain benzodiazepines (e.g., alprazolam), and several other drugs are affected in geriatric patients.

4. E. Rationale: Levodopa can cause hypotension and orthostatic effects including orthostatic hypotension. Gastrointestinal effects including nausea, vomiting, duodenal ulcer, and coffee-ground emesis has occurred during levodopa therapy. It may also cause or exacerbate dyskinesias.

5. D. Rationale: Benztropine and trihexyphenidyl block cholinergic receptors and are used in the treatment of Parkinson disease. Tolcapone is a catechol-o-methyl transferase (COMT) inhibitor used for the treatment of Parkinson disease.

6. A. Rationale: Levodopa is extensively metabolized before reaching the blood-brain barrier and requires higher doses when administered as monotherapy. A dopa decarboxylase inhibitor (e.g., carbidopa) is often administered with levodopa to increase the penetration of levodopa into the brain and to reduce the dosage requirements of levodopa when administered as monotherapy. Levodopa can produce serious cardiovascular adverse effect such as tachycardia, ventricular extrasystoles, and atrial fibrillation.

7. E. Rationale: Parkinson disease is a neurological disorder caused by the loss of dopaminergic neurons. A component of Parkinson disease drug therapy is targeted at restoring the dopamine/acetylcholine balance. Selegiline, bromocriptine, and levodopa treat Parkinson disease by increasing dopamine in the brain.

8. C. Rationale: Nervousness is a symptom of thyrotoxicosis. Decreased appetite, drooping eyelids, mental slowness, and lethargy are indicators of hypothyroidism.

9. A. Rationale: Cholinesterase inhibitors increase the amount of acetylcholine in the body. Cholinesterase inhibitors are used in the treatment of glaucoma, myasthenia gravis, Alzheimer disease, and dementia.

10. D. Rationale: Beta blockers (e.g., timolol), cholinesterase inhibitors (e.g., physostigmine), cholinergic agonists (pilocarpine), and the adrenergic agonist (epinephrine) are used in the treatment of glaucoma. Atropine is an anticholinergic agent that is not useful in the treatment of glaucoma.

11. A. Rationale: Alfuzosin relieves benign prostatic hypertrophy (BPH) symptoms through alpha-1 adrenergic blockage in the lower urinary tract. The symptoms include frequency, urgency, hesitancy, and improvement in urinary flow rate.

12. B. Rationale: In general, doses of levodopa should not exceed 8 g per day, when given as monotherapy.

13. E. Rationale: Carbidopa is given with levodopa to reduce peripheral conversion and peripheral adverse effect of levodopa. If carbidopa is given in a separate dosage form, the dose of levodopa can be decreased by 75%.

14. A. Rationale: Patients should stop taking monoamine oxidase (MAO) inhibitors 2–4 weeks before initiating levodopa therapy. The concomitant use of levodopa and MAO inhibitors can cause hypertensive crisis.

15. E. Rationale: Levodopa increases dopamine in the brain by stimulating dopaminergic receptors in the basal ganglia for the treatment of Parkinson disease. Adverse effects include gastric upset, suicidal tendencies, and involuntary movements.

16. D. Rationale: All of the above are not true. Amantadine is antiviral agent with dopaminergic properties. Amantadine has numerous adverse effects and contraindications. Amantadine should be used with caution in patients with seizures, hepatic disease, renal impairment, and heart failure.

17. D. Rationale: Serum albumin, body water, and lean body mass are examples of variables that decline with increased age. These variables can affect the pharmacokinetic profile of drugs.

18. D. Rationale: Tranylcypromine (Parnate®) is a MAO inhibitor used for depression. Pergolide (Permax®) and bromocriptine (Parlodel®) are dopamine receptor agonists.

19. Answer: B Rationale: The use of benzodiazepines, particularly long-term, is a risk factor for increased cognitive decline in the elderly.

20. B. Rationale: The primary defect in Parkinson's disease is a loss of dopaminergic neurons in the substantia nigra. Conventional therapy focuses on increasing the production and utilization of dopamine.

21. D. Rationale: The most common community acquired infection that results in hospitalization in the elderly patient is pneumonia.

22. C. Rationale: Carbonic anhydrase inhibitors inhibit hydrogen ion excretion in the renal tubule. They also decrease aqueous humor secretion, which results in lower intraocular pressure and can be used for the treatment of glaucoma. Carbonic anhydrase inhibitors are excreted in the urine unchanged and can lead to CNS side effects such as ataxia, asthenia, confusion, fatigue.

23. D. Rationale: Pilocarpine is a cholinergic agonist that causes miosis. Pilocarpine can be used to treat chronic simple glaucoma; however, it is contraindicated in patients with acute inflammation of the anterior chamber and certain types of secondary glaucoma. Ciliary spasms, blurred vision, retinal detachment, and changes in field vision are adverse effects of pilocarpine use.

24. C. Rationale: Phenylephrine is an alpha-adrenergic agonist that increases blood pressure, increases total peripheral resistance, activates the pupillary dilator muscle to cause contraction and causes vasoconstriction. Phenylephrine is used in therapy for several conditions including hypotension, tachycardia and glaucoma. IV phenylephrine has an immediate onset of action.

25. B. Rationale: Physostigmine is an antimuscarinic agent that prevents acetylcholine degradation through inhibiting acetylcholinesterase. Physostigmine is contraindicated in several conditions as cardiovascular disease. Ophthalmic physostigmine has a quick onset of 10-30 minutes and a duration of 12-48 hours.

26. E. Rationale: Physostigmine is an antimuscarinic agent that prevents acetylcholine degradation through inhibiting acetylcholinesterase. Physostigmine is contraindicated in patient with diabetes, GI obstruction, asthma, urinary obstruction, vagotonia, cardiovascular disease, and gangrene.

27. C. Rationale: Urinary incontinence is the lack of ability to control urination. Urinary incontinence is more common in women than in men and increases with age.

28. C. Rationale: Alzheimer disease is a progressive, degenerative disease of the brain that results in impaired memory, thinking, and behavior.

29. D. Rationale: Dementia may be caused by head trauma, vitamin B12 deficiency, hypothyroidism, depression, encephalitis, Huntington's disease, and various other conditions.

30. C. Rationale: Excessive drinking over a period of years may lead to alcohol dementia.

31. E. Rationale: Due to decreased renal function that may occur in geriatric patients, certain antimicrobial therapy (e.g., aminoglycosides) may need dosage adjustment. Geriatric patients are more susceptible to respiratory depression, a serious adverse effect of opioid analgesics therapy. The half-life of sedative hypnotics such as benzodiazepines and barbiturates can increase with older age.

32. D. Rationale: Metaproterenol is a beta-2 agonist used in the treatment of asthma. Amphetamine is an indirect acting sympathomimetic agent that is used as a CNS stimulant for the treatment of ADHD. Phenylephrine is a direct acting sympathomimetic drug that binds primarily to alpha-1 receptors and are useful in the treatment of supraventricular tachycardia.

33. D. Rationale: Betaxolol is a selective for beta-1 adrenoreceptors. Timolol is non-selective for beta-1 and beta-2 adrenoreceptors.

34. E. Rationale: Parkinson's disease is a degenerative disorder that impairs motor skills and speech. It is a chronic and progressive disorder that is characterized by muscle rigidity and tremor.

35. A. Rationale: Alpha-1 receptors are presynaptic and alpha-2 receptors are postsynaptic. Cholinergic agonists have both indirect and direct effects on nicotinic and muscarinic receptors. Atropine is an antimuscarinic agent that does not block nicotinic receptors and therefore does not have activity at the autonomic ganglia or skeletal muscular junction. Most of the ganglion blockers (except mecamylamine) do not cross the blood brain barrier and do not cause CNS effects.

36. A. Rationale: Physostigmine and neostigmine are antimuscarinic agents that prevent acetylcholine degradation through inhibiting acetylcholinesterase. Physostigmine is a tertiary amine, and neostigmine is a carbamate ester. Physostigmine is used for the treatment of anticholinergic toxicity caused by drugs and plants. Neostigmine does not cause CNS symptoms; however, physostigmine causes severe adverse CNS effects.

37. E. Rationale: The major risk factors for primary open angle glaucoma include advanced age, elevated intraocular pressure, African-American race, and family history.

38. E. Rationale: Cholinergic synapses are located in the sympathetic ganglion cells, motor end plates, autonomic effector sites, and the adrenal medulla. Drugs that exert pharmacological activity on these receptors can be broadly classified as cholinergic agonists and anticholinergic agents.

39. A. Rationale: Alpha agonists are used for the treatment of supraventricular tachycardia, nasal decongestion, and hypertension. Phenylephrine, methoxamine, and clonidine are examples of alpha agonists. Alpha agonists can produce hyperglycemia, arteriolar constriction, and iris radial muscle contraction.

40. C. Rationale: Diphenhydramine has anesthetic, antitussive, sedative, antiemetic, antivertigo, antidyskinetic, and antihistamine effects. Diphenhydramine is used for the treatment of Parkinson's disease, allergies, rhinitis, motion sickness, cough, insomnia, and sedation. Diphenhydramine is the active ingredient in several OTC products such as Benadryl®, Sominex®, Nytol®, and Compoz®.

41. C. Rationale: Donepezil is an acetylcholinesterase inhibitor that increases acetylcholine leading to improved cognitive function in Alzheimer's disease patients.

42. A. Rationale: Primary open-angle glaucoma occurs more frequently in African Americans over 40 years and is the leading cause of blindness in African Americans. Open-angle glaucoma is treated with topical medications that increase the aqueous outflow and decrease intraocular pressure.

43. A. Rationale: Physical findings that indicate glaucoma are optic nerve cupping, asymmetric cup in one eye, disc ratio abnormalities, and visual fields disturbances.

44. D. Rationale: Instill 1 drop of 2% pilocarpine solution every 5 minutes in the eye for 3 to 6 doses then 1 drop every 1-3 hours until the IOP is controlled.

45. E. Rationale: Acute-angle glaucoma indicates a rise in IOP due to the obstruction of aqueous humor flow. Asian and Eskimo race, female gender, and age over 40 years, especially the elderly, are risk factors for angle-closure glaucoma.

46. C. Rationale: Sweating, which can lead to dehydration, may occur with pilocarpine use. Lid edema is a common side effect of apraclonidine. Timolol may decrease blood pressure.

47. A. Rationale: Entacapone treats Parkinson's disease through inhibition of catechol-O-methyltransferase (COMT).

48. B. Rationale: Pilocarpine and bethanechol are direct acting cholinergic agonists. Pilocarpine is used in the treatment of glaucoma, whereas bethanechol is used for the treatment of urinary retention.

49. C. Rationale: Cholinesterase inhibitors increase the amount of acetylcholine in the body. Cholinesterase inhibitors cause bronchoconstriction, urinary urgency, peristaltic activity, miosis, and an increase in bronchiolar and lacrimal secretions.

50. C. Rationale: Osteoarthritis is the most common joint disease in the elderly and the leading cause of disability in persons over 65 years.

CHAPTER 15

1. D. Rationale: Management of human immunodeficiency virus (HIV) and concurrent tuberculosis (TB) can be complex due to the large number of medications used to treat both conditions and the potential drug-drug interactions. Hepatitis is a severe adverse effect of anti-TB therapy and requires close monitoring of symptoms and measurement of serum aspartate aminotransferase (AST) and bilirubin levels. Liver function tests (LFTs) should be initially performed at 2, 4, and 6 weeks.

2. D. Rationale: Nevaripine and Efavirenz are examples of non-nucleoside reverse transcriptase inhibitors for the

treatment of HIV. Ganciclovir is antiviral agent used for the treatment of cytomegalovirus, which is a comorbidity of HIV.

3. B. Rationale: The patient has recurrent genital herpes. The most appropriate regimen is to treat her current outbreak with Valtrex® (valacyclovir) 500 mg PO twice daily for 3 days. This patient should then be considered for suppressive treatment, given the frequent outbreaks.

4. E. Rationale: The RPR (rapid plasma regain) and FTA (Fluorescent Treponemal Antibody) - ABS (Absorption) positive results confirm that the patient has syphilis. Benzathine penicillin G 2.4 mcg IM for one dose is the treatment for syphilis of less than 1-year duration. A penicillin skin test should be performed to determine if the patient has a true allergy to penicillin.

5. D. Rationale: Ritonavir (Norvir®), saquinavir (Invirase®, Fortovase®) and indinavir (Crixivan®) are examples of protease inhibitors that are used in the treatment of HIV. Several drug classes should not be prescribed concomitantly with protease inhibitors due to their ability to inhibit CYP P450 oxidations. Antihistamines (e.g., terfenadine), benzodiazepines (e.g., triazolam), antiarrhythmics (e.g., quinidine), and several other drugs are contraindicated with protease inhibitor treatment.

6. B. Rationale: Common side effects of indinavir (Crixivan®) include nausea, abdominal/flank pain, headache, diarrhea, weakness, and vomiting. Indinavir may also cause kidney stones and symptoms related to diabetes (increased thirst, increased urination, weight loss, fatigue).

CHAPTER 16

1. B. Rationale: Depending on the cause of the acidosis, treatment with bicarbonate is controversial. The alkalinizing agent sodium bicarbonate is most often used in the treatment of severe metabolic acidosis (pH < 7.2). Bicarbonate will dissociate and produce a higher ratio of bicarbonate to hydrogen ions.

2. B. Rationale: Acute glomerulonephritis is a group of renal disorders that manifest as damage and inflammation of the glomeruli due to immunological triggers. Maintenance of fluid balance and correction of electrolyte abnormalities is important. Antihypertensives are given to control blood pressure. Protein intake may be limited to reduce kidney damage. Treatment of associated high cholesterol would be a secondary treatment.

3. A. Rationale: Vasopressin is an antidiuretic hormone that induces the water permeability in the renal convoluted tubule, which results in decreased urinary flow.

4. D. Rationale: Erythropoietin agents (e.g., Epogen) are used in the treatment of anemia secondary to renal failure. Erythropoietin therapy is used when the hematocrit levels are low, which is generally < 30%. The increased hematocrit from 22% to a stable hematocrit level of 30% would result in continuation of the same dose

of erythropoietin. NOTE: A caveat here is that if there was a rapid rise in either hematocrit or hemoglobin in any 2-week period, the epoetin dose would need adjustment downward by ~ 25% to maintain appropriate responses.

5. D. Rationale: The normal sodium range is 135-146 mEq/L. Maintaining normal sodium levels is important in the regulation of serum osmolality, achieving acid/base and fluid balance, and controlling important bodily functions.

6. E. Rationale: In chronic kidney failure, a urinalysis may show excessive protein. Abnormal urinalysis may occur 6 months to 10 years even before symptoms are present.

7. B. Rationale: Acetazolamide (Diamox®) acts on the proximal tubule through inhibition of carbonic anhydrase. Furosemide (Lasix®) is a loop diuretic that acts at the loop of Henle. Hydrochlorothiazide (HCTZ®) is a thiazide diuretic that acts on the distal convoluted tubule. Spironolactone (Aldactone®) antagonizes aldosterone at the collecting duct. Triamterene (Dyrenium®) also acts at the collecting duct but by blocking sodium channels.

8. D. Rationale: There are two possible causes of hyponatremia in this patient—cirrhosis or syndrome of inappropriate antidiuretic hormone secretion (SIADH) in small cell lung cancer (SCLC). In cirrhosis, the effective circulating volume is reduced due to venodilation and sodium retention will occur. However, in SIADH, there would be no increase in sodium. The urine sodium value can be helpful, since urine sodium is elevated in SIADH. Urine sodium is usually low in patients with cirrhosis.

9. A. Rationale: To calculate anion gap, use one of the following equations:

$$\text{Anion gap} = [\text{Na}^+] - [\text{Cl}^-] - [\text{HCO}_3^-]$$

or alternative formula:

$$\text{AG} = [\text{Na}^+] + [\text{K}^+] - [\text{Cl}^-] - [\text{HCO}_3^-].$$

For this patient, the anion gap is elevated (25 mEq/L), which indicates metabolic acidosis. The bicarbonate level is normal because the vomiting has concurrently induced metabolic alkalosis.

10. B. Rationale: The patient has achieved the appropriate hemoglobin and hematocrit target and is asymptomatic at the current dose. The patient will continue to need epoetin treatment to maintain this goal, as long as both hemoglobin and hematocrit values remain at appropriate levels.

11. B. Rationale: The alkalinizing agent sodium bicarbonate is used in the treatment of metabolic acidosis. Bicarbonate will dissociate and produce a higher ratio of bicarbonate to hydrogen ions.

CHAPTER 17

1. E. Rationale: The MOPP regimen consists of mustargen (Mechlorethamine®), vincristine (Oncovin®), procarbazine, and prednisone. Dacarbazine is not a drug used in the regimen.

2. C. Rationale: Vincristine is an antineoplastic agent that can be administered IV. A medication given intrathecally would be injected into the cerebral spinal fluid around the brain and spinal cord. Intrathecal vincristine would be FATAL.

3. A. Rationale: Alkylating drugs are cytotoxic through the alkylation of DNA and are used in the treatment of cancer. Etoposide is an antineoplastic agent that may exert its cytotoxic effects through inhibiting DNA synthesis.

4. B. Rationale: Tamoxifen is a nonsteroidal antiestrogen antineoplastic agent. Tamoxifen's side effects include leucopenia, rash, flushing, and peripheral edema.

5. D. Rationale: Doxorubicin is an antineoplastic antibiotic in which the mechanism of action is not known. Its proposed pharmacological effects are through the intercalation into DNA pairs, inhibiting protein synthesis, and iron chelation.

6. A. Rationale: Based on the low laboratory Hgb, Hct, MCV, and MCH values, the patient appears to have iron deficiency anemia. Iron supplementation is the most appropriate initial therapy in the treatment of iron deficiency anemia.

7. A. Rationale: Vinca alkaloids like vinblastine are antineoplastic agents whose cytotoxic effects are through the depolymerization of microtubules.

8. E. Rationale: The antineoplastic agent, Irinotecan®, is a type I DNA topoisomerase inhibitor used for the treatment of colon cancer. Adverse effects include diarrhea and weight loss.

9. C. Rationale: Nilutamide is an antiandrogen used for metastatic prostate cancer in combination with surgical castration. It is only available for oral use. Nilutamide may elevate liver enzymes and should not be used in patients with severe hepatic impairment. Nilutamide may make it harder for the patient's eyes to adjust from light to dark so the patient should be advised to wear sunglasses or tinted lenses.

10. A. Rationale: 5-Fluorouracil is an antimetabolite used for the treatment of colorectal carcinoma and can be administered parenterally and topically. 5-Fluorouracil competes for the enzyme, thymidylate synthase, for the inhibition of DNA synthesis. Adverse effects include diarrhea, dermatitis, anorexia, and alopecia. It is not associated with constipation.

11. E. Rationale: Anticancer agents including the alkylating drugs, which can produce acute and delayed toxic effects. Most alkylating drugs (e.g., carmustine, cisplatin) are associated with nausea and vomiting. Cyclophosphamide's acute toxic effects are nausea and vomiting, and its delayed toxic effects include alopecia and hemorrhagic cystitis.

12. A. Rationale: Doxorubicin is an antineoplastic antibiotic used for the treatment of cancer. Doxorubicin's

adverse effects include myelosuppression, cardiac diseases, and GI toxicity.

13. E. Rationale: Allopurinol® reduces the metabolism of oral mercaptopurine via inhibition of xanthine oxidase. A dosage reduction of mercaptopurine is required to prevent adverse effects.

14. E. Rationale: Alkylating drugs are cytotoxic through the alkylation of DNA and are used in the treatment of cancer. Busulfan, carmustine, and cyclophosphamide are examples of alkylating agents.

15. A. Rationale: Cyclophosphamide is an alkylating agent used in the treatment of cancer, nephrotic syndrome, and rheumatoid arthritis. Cyclophosphamide can cause serious adverse effects such as leukocytosis and hemorrhagic cystitis.

16. C. Rationale: ABVD is the chemotherapy acronym for Adriamycin, Bleomycin, Vinblastine, and Dacarbazine. The MOPP regimen consists of mustargen, vincristine (Oncovin), procarbazine, and prednisone. ABVD and MOPP are two regimens used for the treatment of Hodgkin's disease. Prostate cancer can be treated with FL, which is flutamide and leuprolide.

17. B. Rationale: Cyclosporine is an immunosuppressant agent that is used for the prophylaxis of organ rejection. Cyclosporine can cause hepatotoxicity and nephrotoxicity.

18. C. Rationale: Cyclosporine is an immunosuppressant agent that is used for the prophylaxis of organ rejection.

19. E. Rationale: Cisplatin is an alkylating agent used for the treatment of cancer. Cisplatin can cause nephrotoxicity, ototoxicity, and electrolyte imbalances.

20. E. Rationale: Cancer is treated with a combination of chemotherapeutic agents due to the different mechanisms of action, toxicity profiles, and mechanisms of tumor resistance. The advantages include efficacy against a wide range of tumors and to prevent resistance. Cancer drug treatment protocols can be identified by acronyms (e.g., MOPP)

21. A. Rationale: Doxorubicin is an antineoplastic antibiotic used for the treatment of cancer. Doxorubicin's adverse effects include myelosuppression, heart failure, and GI toxicity.

22. E. Rationale: 17-Alpha alkylated androgens are primarily synthetic or anabolic agents that result in hepatic side effects. The patient can develop hepatic adenocarcinoma, peliosis hepatitis, elevated hepatic transaminases, and cholestatic hepatitis.

23. E. Rationale: Androgens (e.g., testosterone) are steroid hormones that are useful in several treatments including androgen replacement therapy. Androgens are also used to palliate breast cancer and treat hereditary angioneurotic edema, hypogonadism, and promote erythropoiesis.

24. D. Rationale: Several anticancer agents can produce delayed toxic effects. Carmustine causes leukopenia and thrombocytopenia and cisplatin produces renal dysfunction and acoustic nerve dysfunction. Cyclophosphamide has several delayed toxic effects including alopecia and hemorrhagic cystitis.

25. E. Rationale: Anti-androgen treatment can be used in patients who secrete high levels of androgens (e.g., testosterone). Anti-androgens can be used in the treatment of prostate cancer, pattern baldness, BPH, and hirsutism in women.

26. E. Rationale: Aminoglutethimide inhibits cholesterol conversion to pregnenolone, which blocks steroid production. Aminoglutethimide is used in combination with other agents in the treatment of breast cancer and Cushing's syndrome.

27. E. Rationale: Interferon is produced in response to viral infections. Interferon's ability to enhance the expression of major histocompatibility complex (MHC) can result in antiviral effects such as the elimination of infected hepatocytes in the treatment of hepatitis. Interferons are antioncogenic and antiviral agents used in the treatment of several types of cancers, hepatitis, and multiple sclerosis.

28. E. Rationale: Interleukins are immunomodulating agents that are part of the class of proteins called cytokines. Interleukin-1 enhances endothelial adhesion factor expression and act to reset the hypothalamic thermoregulatory center.

29. B. Rationale: Interleukins are immunomodulating agents that are part of the class of proteins called cytokines. Interleukin-4 causes B cell proliferation and activates Type 2 T helper cells and cytotoxic T lymphocytes.

30. E. Rationale: Several anticancer agents can produce delayed toxic effects. Carmustine causes leukopenia and thrombocytopenia and cisplatin produces renal dysfunction and acoustic nerve dysfunction. Cyclophosphamide has several delayed toxic effects including alopecia.

31. A. Rationale: Natural Killer cells causes lysis of tumor cells and can be activated by cytokines such as interferon-alpha and interferon-beta. Natural Killer cells is a line of defense against viruses and has a role in tumor rejection.

32. C. Rationale: The complement pathway is activated when the skin, which is the first barrier of protection, is compromised. C3b is an opsonin that helps phagocytes digest bacteria. C3a and C5b attract phagocytes for bacterial lysis.

33. B. Rationale: The IgG antibody is one out of five classes of antibodies and it is primarily found in the blood and lymph. IgG antibodies can cross the placenta to provide immunity during pregnancy. Hemolytic disease of

the newborn is caused by anti-Rh IgG antibodies that attack red blood cells in an Rh-positive fetus.

34. D. Rationale: Antigen presenting cells (e.g., macrophages, B lymphocytes, dendritic cells) are a part of the innate immune response system. Antigen presenting cells activate cytotoxic T cells and internalize antigens from the extracellular space. Antigen presenting cells provide peptides from digested antigens to T helper cells through MHC II bound surface proteins.

35. B. Rationale: Alkylating drugs are cytotoxic through the alkylation of DNA and are used in the treatment of cancer. Leukeran® (chlorambucil) is an example of an alkylating agent.

36. A. Rationale: Tamoxifen is a nonsteroidal antiestrogen antineoplastic agent. Tamoxifen is indicated for the treatment of breast cancer in postmenopausal women with positive lymph nodes.

37. C. Rationale: Vincristine is an antineoplastic agent that can only be administered IV since it is irritating when given by other routes of administration. Intrathecal administration of vincristine can be fatal and requires specific instructions on the label that states: "Fatal if given intrathecally. For intravenous use only."

38. B. Rationale: Doxorubicin is an antineoplastic antibiotic used for the treatment of cancer. Adverse effects include cardiac depression, heart failure, irreversible cardiomyopathy, and arrhythmias.

39. A. Rationale: Paclitaxel is an antimicrotubule antineoplastic agent. Adverse effects include peripheral neuropathy, which may necessitate a dose reduction. Counsel patients to report symptoms such as burning, tingling, or numbness in the extremities, which are signs of peripheral neuropathy.

40. E. Rationale: ABVD is the chemotherapy acronym for Adriamycin, Bleomycin, Vinblastine, and Dacarbazine. ABVD is used for the treatment of Hodgkin's disease.

41. A. Rationale: Bleomycin is an antibiotic antineoplastic agent. Bleomycin's respiratory adverse effects include pulmonary fibrosis and pneumonitis.

42. A. Rationale: Anzemet® (dolasetron) is a serotonin antagonist used for the prevention of nausea and vomiting in cancer patients.

43. E. Rationale: Mitotic inhibitors disrupt mitotic spindle activity, which causes cytotoxic effects. Oncovin® (vincristine), Taxotere® (docetaxel), and Taxol® (paclitaxel).

44. B. Rationale: Topotecan (Hycamtin®) is an antineoplastic agent used in the treatment of metastatic carcinoma if chemotherapy failed. Topotecan has severe hematological adverse reactions and requires consistent monitoring of blood cells.

CHAPTER 18

1. D. Rationale: Dexamethasone is an antiinflammatory and immunosuppressant agent used in the treatment of several conditions such as adrenal insufficiency, dermatitis, asthma, and Addison's disease. An adverse effect of glucocorticoid treatment is osteoporosis.

2. B. Rationale: Codeine is a narcotic analgesic used in the treatment of mild to moderate pain. Codeine is metabolized in the liver by the enzyme glutathione transferase and is demethylated to morphine, the active metabolite.

3. B. Rationale: Nitrous oxide has the fastest onset of action due to its low blood solubility, which is shown by the anesthetic/partition coefficient 0.47. An anesthetic/partition coefficient indicates the ability of the inhaled anesthetic to diffuse from the lungs to the arterial blood. The more quickly the drug reaches the blood, the faster the anesthetic will enter into the brain for rapid anesthesia.

4. B. Rationale: Nitrous oxide does not affect uterine smooth muscle in contrast to halogenated hydrocarbon anesthetics that relax uterine muscles.

5. C. Rationale: The minimum alveolar anesthetic concentration (MAC) is the concentration in which 50% of patients are immobilized when exposed to a harmful stimulus. Methoxyflurane has a low MAC value of 0.16%, which makes it the agent with the highest potency.

6. B. Rationale: The minimum alveolar anesthetic concentration (MAC) is the concentration in which 50% of patients are immobilized when exposed to a harmful stimulus. Nitrous oxide has a high MAC value of 105%, which makes it the agent with the lowest potency.

7. A. Rationale: Acetaminophen, an analgesic, inhibits prostaglandin synthesis and has a duration of 3-4 hours. Acetaminophen has antipyretic and analgesic effects but does not relieve inflammation. Acetaminophen can cause hematological adverse effects and should be used with caution in patients with hepatic disease.

8. C. Rationale: Aspirin, a salicylate, is a non narcotic analgesic with antipyretic, anti-inflammatory, and antiplatelet effects. Aspirin has an onset of action of 5-30 minutes, peak concentrations range from 15 minutes to 8 hours, and a duration of analgesic action of 1-4 hours. Aspirin is hydrolyzed in the bloodstream and excreted in the urine. Aspirin does not cause hypertension.

9. E. Rationale: Acetaminophen is a non narcotic analgesic, antipyretic that can cause adverse reactions such as skin rash and hepatotoxicity with overdose. Acetaminophen is safe to use in children with influenza infection.

10. A. Rationale: Salicylates are contraindicated in children with symptoms that resemble the flu (e.g., fever, dry cough, fatigue, and muscle aches) due to the potential

to develop Reye's syndrome. Reye's syndrome is a life-threatening illness that affects many organs of the body including the brain.

11. E. Rationale: Injection of a local anesthetic into a circulatory vessel may cause circulatory collapse, myocardial depression, respiratory depression, and seizures. Local anesthetics are prone to cause side effects when the drug is administered mistakenly by the intravascular route, high dosages, excessive rates of injection, slow metabolism, or injection into highly vascular tissue.

12. D. Rationale: Opioids are narcotic analgesic that are used to manage pain, diarrhea, suppress cough, and for premedication before anesthesia. NSAIDs and steroids are used to relieve inflammation.

13. B. Rationale: Meperidine is an opioid analgesic that is metabolized in the liver to the toxic metabolite normeperidine. Meperidine can cause CNS adverse effects secondary to normeperidine accumulation, hypotension, and urinary retention. Meperidine crosses the placenta.

14. A. Rationale: Succinylcholine, a neuromuscular blocking agent, produces depolarization at the motor end-plate similar to the actions of acetylcholine. Succinylcholine is used to induce skeletal muscle relaxation, as an adjunct to general anesthesia, intubation, and ventilation.

15. A. Rationale: Toradol® (ketorolac), an NSAID, is indicated for the short-term management of pain. Toradol's mechanism of action is similar to other NSAIDs, which is the inhibition of the synthesis of prostaglandins.

16. E. Rationale: Toradol® is available as a tablet (orally), ophthalmic solution (topically), or injectable (IV or IM). Dosage adjustment is required for the oral and parenteral formulations in patients with low body weight, renal impairment, and over 65 years.

17. D. Rationale: Toradol® (ketorolac), an NSAID, is indicated for the short-term management of pain. Toradol's adverse effects include headache, pruritis, abdominal pain, hypertension, and edema.

18. E. Rationale: Toradol® should be used very cautiously in patients taking warfarin and salicylates due to the potential in toxicity of warfarin or salicylates. Patients should be counseled on the adverse GI effects associated with alcohol and Toradol use and advised to avoid alcohol. Concomitant use of NSAIDs and Toradol is contraindicated due to the potential for synergistic adverse effects.

19. E. Rationale: Naproxen, an NSAID, is used for the treatment of several conditions including gout, dysmenorrhea, and mild to moderate pain. Naproxen is available as a tablet or oral suspension. Naproxen's adverse effects include edema, ulcers, GI upset, rash, and neutropenia. Bioavailability is roughly 95%.

20. E. Rationale: Glucocorticoids can be classified based on their duration of actions. Betamethasone and dexamethasone are long-acting agents with a duration of action from 1-3 days, whereas hydrocortisone is a short-acting glucocorticoid with a duration of action ranging from 8-12 hours. Prednisolone and methylprednisolone are intermediate-acting with 18-36 hour duration of action.

21. D. Rationale: Ketamine is an IV or IM anesthetic with a duration of action of 5-10 minutes (IV) and 12-25 minutes (IM). Ketamine's adverse cardiovascular effects include hypertension, arrhythmias, tachycardia, hypotension, and bradycardia.

22. B. Rationale: Corticosteroids can be administered by several different routes including intra-articularly. Aspirin can be taken by mouth or as rectal suppositories. Ibuprofen, penicillamine, and auranofin are taken by mouth.

23. C. Rationale: Ibuprofen and other NSAIDs can cause CNS side effects such as headache, dizziness, and drowsiness.

24. C. Rationale: Indomethacin can cause severe CNS effects such as seizures, psychic disturbances, and peripheral neuropathy.

25. A. Rationale: Aspirin can cause severe gastrointestinal adverse effects including bleeding and dyspepsia. Enteric-coated tablets are available to minimize GI upset. Enteric-coated medications are formulated to allow release of the medication in the small intestine and bypass the stomach.

26. E. Rationale: The concomitant use of aspirin and methotrexate can result in increased levels of methotrexate in the body. Salicylates may inhibit the renal excretion of methotrexate and displace of methotrexate from protein binding sites.

27. A. Rationale: Ibuprofen is an NSAID derived from phenylpropionic acid and is primarily available orally however a parenteral form exists. Ibuprofen is used in the treatment of arthritis (e.g., rheumatoid, juvenile), gout, and mild to moderate pain. Ibuprofen has analgesic, antiinflammatory, and antipyretic properties.

28. D. Rationale: Enflurane has adverse CNS effects at high doses, which can cause seizure activity.

29. C. Rationale: Opioids are narcotic analgesic used in the management of pain. A serious side effect of opioid use is respiratory depression.

30. D. Rationale: Opioids are narcotic analgesic used in the management of pain. Opioids (e.g., propoxyphene, oxycodone) are associated with dependence, tolerance, and the potential for addiction. Opioids can cause constipation, to which a patient does not develop tolerance. Opioids can cause serious adverse effects with overdose such as coma, pinpoint pupils, CNS depression, and respiratory depression.

31. B. Rationale: Meperidine is an opioid analgesic that is metabolized in the liver to the toxic metabolite normeperidine. Meperidine can cause CNS adverse effects secondary to normeperidine accumulation and should be used with caution in patients at greater risk for toxicity such as those with renal and hepatic impairments. Geriatric patients are at increased risk of normeperidine accumulation and CNS toxicity since meperidine is eliminated in this population at a slower rate.

32. C. Rationale: Methoxyflurane is associated with nephrotoxicity. Nephrotoxicity occurs because of the by-product of inorganic fluoride, which results after methoxyflurane metabolism.

33. D. Rationale: Salicylates and NSAIDs can cause gastric mucosal damage, which may be a result of COX-1 inhibition of prostaglandin synthesis. They increase hydrogen ion permeability of the gastric mucosa, which leads to cellular damage.

34. A. Rationale: Naloxone is an opioid antagonist used for the reversal of opioid adverse effects, including respiratory depression, caused by natural, synthetic, and certain opiate partial agonists (e.g., pentazocine).

35. D. Rationale: Salicylates can cause gastric mucosal damage, which may be a result of COX-1 inhibition of prostaglandins synthesis. Salicylates increase hydrogen ion permeability of the gastric mucosa, which leads to cellular damage. To prevent GI effects, salicylates can be taken immediately after meals or with food, antacids, or a large quantity of water or milk. Salicylates are also available as enteric-coated tablets, which are formulated to allow release of the medication in the small intestine and bypass the stomach.

36. B. Rationale: Morphine is an opioid agonist used in treatment of severe pain. Morphine has several adverse effects including increased biliary tract pressure and the potential for urine retention.

37. D. Rationale: NSAIDs (e.g., ibuprofen and naproxen) and salicylates (e.g., aspirin) may cause nephropathy. NSAIDs can cause several renal adverse effects with use such as azotemia, cystitis, hematuria, decreased creatinine clearance, elevated serum creatinine concentrations, and increased BUN. The mechanism of action for these renal effects is not fully understood; however, it may be due to inhibition of renal prostaglandin synthesis, which can result in renal ischemia or the drug, and its metabolites may have a toxic effect on the cells.

38. B. Rationale: The daily dose of APAP should not exceed 4 g/day. APAP toxicity can occur with chronic use, large doses, or with one toxic dose. APAP toxicity can be managed with the antidote acetylcysteine and activated charcoal may also be used if administered early. Acetaminophen toxicity can cause several adverse effects in the body including the heart, brain, and liver. It is the most common cause of hepatic failure.

39. D. Rationale: Respiratory depression is a common side effect of opioid therapy. Complications such as atelectasis (lung collapse) can occur especially in patients with preexisting pulmonary disorders.

40. D. Rationale: Opioids are narcotic analgesic used in the management of pain. Opioids can cause serious adverse effects with overdose such as coma, pinpoint pupils, CNS depression, and respiratory depression. Immediate clinical focus should be on restoring adequate respiration.

41. D. Rationale: Opioids stimulate vasopressin (ADH), which may cause water intoxication in postoperative patients. Opioids may suppress thyrotropin secretion, which can result in lower levels of thyroid hormone. Other endocrine adverse effects include decreased LH release, decreased libido, and hyperglycemia.

42. A. Rationale: Duration of action for the opioid agonists are as follows: meperidine (2-4 hours), methadone (4-6 hours), morphine (3-7 hours), hydromorphone (4-6 hours), and codeine (4-6 hours).

43. E. Rationale: Buprenorphine, Butorphanol, Pentazocine are opioid receptor agonist-antagonists. Naloxone is an opioid antagonist used for the reversal of opioid adverse effects, including respiratory depression, caused by natural, synthetic, and certain opiate partial agonists (e.g., pentazocine).

44. D. Rationale: Aspirin, a salicylate, is a non narcotic analgesic with antipyretic, antiinflammatory, and antiplatelet effects. Aspirin's analgesic effect is partly attributed to the inhibition of cyclooxygenase, which decreases prostaglandin synthesis. High dose aspirin can lower serum urate and is metabolized by both first and zero order kinetics

45. A. Rationale: The duration of action of subcutaneous administration for the opioid agonists are as follows: meperidine (2-4 hours), methadone (4-6 hours), morphine (3-7 hours), hydromorphone (4-6 hours), and codeine (4-6 hours).

46. B. Rationale: Butorphanol is a mixed opiate agonist-antagonist and may induce withdrawal in patients dependent on opioids. Methadone is used to prevent abstinence withdrawal syndrome in heroin addicted patients in the inpatient setting. Meperidine is not used to prevent abstinence withdrawal.

47. A. Rationale: Salicylates have been used to treat gout due to their uricosuric activity. However, salicylates may cause uric acid retention, antagonize the effects of other uricosuric drugs, and are usually contraindicated in patients with gout.

48. B. Rationale: Pentazocine is a partial opioid agonist that can produce dysphoria at doses of 60–90 mg due to its activity at σ -receptors. The opioid antagonist naloxone can reverse this effect.

49. E. Rationale: Opioid agonists (e.g., morphine) can produce miosis through effects on the oculomotor nerve. Tolerance to miosis does not occur and therefore has been used to diagnosis opioid toxicity.

50. C. Rationale: Aspirin, a salicylate, is a non narcotic analgesic with antipyretic, antiinflammatory and antiplatelet effects. Aspirin's analgesic effect is partly attributed to the inhibition cyclooxygenase, which decreases prostaglandin synthesis.

51. E. Rationale: Salicylate intoxication can occur with salicylate overdose. Acute toxicity has occurred with doses 150–500 mg/kg and higher (life-threatening toxicity > 500mg/kg) while chronic toxicity has been associated with doses of 100 mg/kg daily for 2 days or longer. Acid-base disturbances, electrolyte imbalances, and fever can manifest.

52. A. Rationale: Hepatic necrosis is a life-threatening serious adverse effect of acetaminophen overdose. The maximum recommended daily dose of APAP is 4 g/day.

53. A. Rationale: Opioid agonists (e.g., morphine) can cause adverse effects such as miosis, respiratory depression, postural hypotension, and behavioral changes. Constipation is a common side effect of opioid therapy. Patients do not develop tolerance to constipation; however, they can increase dietary fiber or take a stool softener with opioid therapy.

54. D. Rationale: Indomethacin, an NSAID, is used to treat bursitis and rheumatoid arthritis at a dose of 25-50 mg PO, 2 to 3 times per day. Adverse GI effects are indigestion, anorexia, nausea, diarrhea, ulcers, constipation, and GI bleeding. Indomethacin is absorbed from the GI tract, undergoes liver metabolism, and is excreted in the urine and feces.

55. D. Rationale: Tizanidine (Zanaflex®) is a centrally acting skeletal muscle relaxant and alpha-2 adrenergic agonist. It is primarily metabolized by the CYP 1A2 isozyme.

56. A. Rationale: Aspirin should be stopped 7 days before an elective surgery (e.g., dental surgery) associated with a high risk of bleeding or serious adverse events.

57. A. Rationale: Etomidate, a parenteral IV sedative-hypnotic, is indicated for the induction and maintenance of general anesthesia. Etomidate has a rapid onset of action and can cause involuntary muscle movements.

58. E. Rationale: Fentanyl is an opioid analgesic available as a transdermal patch, transmucosal lozenge, and parenteral formulation. Fentanyl is used in surgery due to analgesic effect, but requires patient to be on mechanical ventilation. Fentanyl is used as an adjunct in anesthesia.

59. E. Rationale: Ketamine is classified as an NMDA antagonist. It is used for the induction or maintenance of general anesthesia. Ketamine may cause hallucinations during recovery.

60. D. Rationale: Duration of analgesic action for the opioid agonists are as follows: meperidine (2-4 hours), methadone (4-6 hours), morphine (3-7 hours), and hydromorphone (4-6 hours).

61. D. Rationale: Aspirin, a salicylate, is a non narcotic analgesic with antipyretic, antiinflammatory, and antiplatelet effects. Aspirin inhibits cyclooxygenase and prostaglandin synthesis. Tranexamic acid is an antifibrolentic, whereas dipyridamole and ticlopidine are platelet aggregation inhibitors.

62. A. Rationale: The Pain Ladder, a widely accepted 3-step approach to implementing the three categories of pain medication, was developed by the World Health Organization (WHO).

63. E. Rationale: Halothane carries a high risk for hepatitis, jaundice, and liver necrosis. Certain individuals may be prone to hepatotoxicity with halothane use based on a defect in their hepatic cells.

64. A. Rationale: Etomidate, a parenteral IV sedative-hypnotic, is indicated for the induction and maintenance of general anesthesia. Etomidate has minimal effects on the cardiovascular and respiratory system but it can cause dose dependent CNS depressant effects.

65. B. Rationale: Ketamine is an IV/IM dissociative anesthetic used for the induction of general anesthesia. Ketamine can cause arrhythmias, hypertension, and tachycardia.

66. B. Rationale: Propofol is a local anesthetic used for induction and maintenance of anesthesia. Hypotension is a common cardiovascular side effect; however, hypertension and bradycardia can occur as well. Half-life correlates with duration of CNS depression (i.e., dose dependent). Propofol is highly lipophilic and provides a rapid recovery from anesthesia.

67. B. Rationale: Ketamine is an IV/IM dissociative anesthetic used for the induction of general anesthesia. Ketamine can cause respiratory depression and apnea. Ketamine is a strong analgesic and can cause adverse CNS effects such as hallucinations during recovery.

68. A. Rationale: Etomidate, a parenteral IV sedative-hypnotic, is indicated for the induction and maintenance of general anesthesia. Etomidate does not exert analgesic effects.

69. D. Rationale: Midazolam is a benzodiazepine indicated for the management of sedation and anesthesia. Midazolam can be used off label for the treatment of seizures.

70. A. Rationale: Bupivacaine is a local anesthetic with a long duration of action, therefore repeated doses are generally not needed. Duration of action can last up to 9 hours depending on dose.

71. B. Rationale: The visual analog scale (VSA) is a tool used to help a person rate the intensity or severity of certain sensations and feelings, such as pain.

72. C. Rationale: Neuropathic pain is classified as pain resulting from damage of the sensory transmission pathways in the peripheral or central nervous system.

73. D. Rationale: The corticosteroid dexamethasone can be used in the treatment of adrenal insufficiency, cerebral edema, and inflammation. Wilson's disease is an elevated level of copper in the liver, brain, eyes, and other vital organs and is treated with penicillamine.

74. E. Rationale: Corticosteroids are potent antiinflammatory medications used in the treatment of a wide range of disease state including asthma, allergic conditions, rheumatic disorders, and adrenal insufficiency. Corticosteroids can produce numerous adverse musculoskeletal (osteonecrosis), endocrine (hyperglycemia), and ocular (cataract) effects.

75. C. Rationale: Methadone (Dolophine) has NMDA (N-methyl-D-aspartate) antagonistic properties. It is free of active metabolites. Methadone has an unpredictable and long half-life.

76. E. Rationale: A prodrug metabolizes to an active agent in order to produce a pharmacological effect in the body. Nabumatone transforms to the active metabolite 6MNA. Sulindac transforms to two metabolites; however, only the sulfide metabolite exerts pharmacological activity.

77. B. Rationale: The ceiling effect of a drug refers to the dose beyond which there is no additional analgesic effect. Higher doses do not provide any additional pain relief but will increase the likelihood of side effects.

78. E. Rationale: Corticosteroids are potent antiinflammatory medications used in a wide range of disease state including asthma, allergic conditions, rheumatic disorders, and adrenal insufficiency. Corticosteroids can produce numerous dermatological adverse effects such as hirsutism, acne, ecchymosis, and striae.

79. E. Rationale: Hydrocortisone is a glucocorticoid antiinflammatory medication. Hydrocortisone is administered topically or systemically. Hydrocortisone (systemic) has a half life elimination of 8-12 hours, is metabolized in the liver, and is predominately excreted in the feces.

80. E. Rationale: Various drugs may be used for the treatment of opioid-induced nausea and vomiting including droperidol (Inapsine®), prochlorperazine (Compazine®), promethazine (Phenergan®), metoclopramide (Reglan®), and granisetron (Kytril®).

81. E. Rationale: Constipation, nausea or vomiting, pruritus or urticaria, mental confusion, and sedation are common side effects of opioids.

82. E. Rationale: Morphine, fentanyl, meperidine, hydromorphone, sufentanil, and methadone are drugs used for chronic spinal delivery.

CHAPTER 19

1. E. Rationale: Benzodiazepines influence various neurotransmitters, including gamma-Aminobutyric acid (GABA). The primary mechanism for benzodiazepines is enhancing GABA receptor function.

2. E. Rationale: Schizophrenia is a psychiatric disorder that is characterized by positive (e.g., delusions) and negative (e.g., flat affect, alogia, social withdrawal) symptoms. Family history, environmental, and developmental factors are risk factors for developing schizophrenia. Schizophrenia can be managed with antipsychotic medications and nonpharmacological therapies such as psychosocial treatments.

3. A. Rationale: Delusion is an incorrect belief that is continued despite adequate evidence to the contrary. A delusion is a positive schizophrenic symptom.

4. C. Rationale: Antipsychotic medications reduce the levels of dopamine in the central nervous system (CNS). Although there are several dopaminergic receptors, specifically blocking the dopamine receptor D2 provides the most significant antipsychotic effect. Atypical antipsychotic agents inhibit both serotonin and dopamine.

5. D. Rationale: Tardive dyskinesia is recognized by choreoathetotic movements and the inability to perform voluntary movements. The prolonged use of antipsychotic medications can cause tardive dyskinesia due to their dopamine antagonist effects.

6. A. Rationale: The antipsychotic chlorpromazine (Thorazine®) can exhibit extrapyramidal side effects such as tremor, akathisia, and tardive dyskinesia. Diphenhydramine (Benadryl®) can be used to treat extrapyramidal effects and is used in Parkinson disease to manage tremors.

7. B. Rationale: The antipsychotic fluphenazine (Prolixin®) can exhibit extrapyramidal side effects such as tremor, dystonia, akathisia, and tardive dyskinesia. Diphenhydramine (Benadryl®) can be used to treat extrapyramidal effects like acute dystonia.

8. D. Rationale: Anticonvulsant, carbamazepine (Tegretol®), can be used as a second line agent if the patient is unresponsive to lithium. Selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine and carbamazepine) are given if depression occurs. Amantadine (Symmetrel®) is used for the treatment of Parkinson's disease. Atypical antipsychotics would be used instead of chlorpromazine, which is an older antipsychotic.

9. C. Rationale: Schizophrenia is a psychiatric disorder that is characterized by positive (e.g., delusions) and

negative (e.g., flat affect, alogia, social withdrawal) symptoms. Schizophrenia can be managed with antipsychotic medications and nonpharmacological therapies such as psychosocial treatments. Examples of psychosocial treatments are family interventions, social skills training, employment programs, and group therapy.

10. E. Rationale: Neuroleptic malignant syndrome (NMS) is a rare, but life-threatening reaction that is characterized by fever, muscular rigidity, altered mental status, and autonomic dysfunction.

11. E. Rationale: Imipramine (Tofranil®) is a tricyclic antidepressant agent. Norepinephrine, epinephrine, dopamine, and serotonin are neurotransmitters that are produced in the body.

12. E. Rationale: Neuroleptic malignant syndrome (NMS) may be caused by potent neuroleptics (haloperidol, fluphenazine), as well as other agents including prochlorperazine (Compazine®), promethazine (Phenergan®), clozapine (Clozaril®), risperidone (Risperdal®), metoclopramide (Reglan®), amoxapine (Ascendin®), and lithium.

13. A. Rationale: Increased fluid intake, osmotic diuretics, and caffeine decrease lithium concentrations. Nonsteroidal antiinflammatory drugs (NSAIDs) reduce lithium excretion and lead to elevated lithium serum concentrations.

14. E. Rationale: Monoamine oxidase (MAO) inhibitors (e.g., isocarboxazid) are used in the treatment of depression. Patients taking MAO inhibitors should avoid food high in tyramine or tryptophan to avoid hypertensive crisis. There are several foods that patients should be instructed to avoid including aged cheese and red wine.

15. C. Rationale: Monoamine oxidase (MAO) inhibitors (e.g., isocarboxazid) are used in the treatment of depression. Patients taking MAO inhibitors should avoid food high in tyramine or tryptophan to avoid hypertensive crisis. There are several foods that patients should be instructed to avoid including aged cheese and red wine.

16. A. Rationale: Selective serotonin reuptake inhibitors (SSRIs) antidepressants (e.g., sertraline) are first-line treatment for major depressive disorder. Nortriptyline (Pamelor®, Aventyl®; a tricyclic antidepressant) and phenelzine (Nardil®; MAO inhibitor) are not used as frequently due to their adverse effects and drug interactions. Mirtazapine (Remeron®) is a tetracyclic used for the treatment of depression. Gabapentin (Neurontin®) is an anticonvulsant that is used for the treatment of epilepsy and neuropathic pain.

17. C. Rationale: Atypical antipsychotics such as risperidone (Risperdal®), is the most appropriate therapy due to the potential for less extrapyramidal side effects compared to first generation antipsychotics (e.g., thiothixene, chlorpromazine). Clozapine (Clozaril®) is an atypical antipsychotic; however, it is associated with hematological adverse effects that require close and

continual monitoring. Lithium (Eskalith®, Lithobid®) is a first-line agent in the treatment of bipolar disorder.

18. A. Rationale: Trazodone (Desyrel®) is a serotonin and norepinephrine reuptake inhibitor in the CNS. Adverse effects include memory impairment, menstrual irregularities, and akathisia.

19. C. Rationale: Imipramine (Tofranil®) is a tricyclic antidepressant agent that inhibits the reuptake of serotonin and norepinephrine. Imipramine is used in the treatment of childhood enuresis.

20. A. Rationale: Buspirone (Buspar®) is an anxiolytic without anticonvulsant or hypnotic effects. MAO inhibitors (e.g., phenelzine and tranylcypromine), trazodone, and tricyclic antidepressants (e.g., imipramine) are used in the treatment of depression.

21. E. Rationale: Benzodiazepines are used as anticonvulsants, preanesthetics, and anxiolytics and during acute alcohol withdrawal. Benzodiazepines can cause CNS adverse effects such as dementia.

22. E. Rationale: Aripiprazole (Abilify®) is an atypical antipsychotic used for the treatment of schizophrenia.

23. B. Rationale: Geodon® (ziprasidone) is an atypical antipsychotic used for the treatment of schizophrenia. Ziprasidone's adverse effects include abnormal vision, akathisia, weight gain, somnolence, and postural hypotension.

24. B. Rationale: Aripiprazole (Abilify®) is an atypical antipsychotic used for the treatment of schizophrenia and bipolar disorder and as an adjunct treatment for major depression.

25. B. Rationale: Olanzapine (Zyprexa®) has a high risk of causing weight gain. Aripiprazole (Abilify®) has a low risk of weight gain. Risperidone (Risperdal®) and quetiapine (Seroquel®) has a moderate risk.

26. D. Rationale: Haloperidol (Haldol®) is a first-generation antipsychotic. Impaired liver function and jaundice are side effects of haloperidol.

27. C. Rationale: Selective serotonin reuptake inhibitors (SSRIs) antidepressants (e.g., sertraline) are first-line treatment for major depressive disorder. SSRI and several other antidepressant classes produce changes in sleep architecture by suppressing rapid eye movement (REM) sleep.

28. B. Rationale: Patients with a history of hypersensitivity to tricyclic antidepressants should not be given carbamazepine. Tricyclic antidepressants (TCAs) and carbamazepine (Tegretol®) have similar chemical structures.

29. A. Rationale: The concomitant use of sibutramine and lithium can increase the levels of serotonin, which can precipitate the life-threatening condition serotonin

syndrome. A patient with serotonin syndrome may experience excitement, loss of consciousness, confusion, agitation, hyperthermia, diaphoresis, emesis, and tachycardia.

30. D. Rationale: Tricyclic antidepressants (TCAs) have similar therapeutic efficacy; therefore clinicians can prescribe an agent based on side effect and pharmacokinetic profiles.

31. B. Rationale: Lithium (Eskalith®, Lithobid®) is a first-line agent for the treatment of bipolar disorder. Hand tremor frequently occurs at the start of lithium therapy; however, it subsides with continued use. Hand tremor may become worse if the patient develops anxiety, thyrotoxicosis, or ingests caffeine.

32. A. Rationale: Catapres® (clonidine), an alpha-2 agonist, can cause depression as an adverse effect.

33. B. Rationale: Monoamine oxidase (MAO) inhibitors (e.g., isocarboxazid) are used in the treatment of depression. Patients taking MAO inhibitors should avoid food high in tyramine or tryptophan to avoid hypertensive crisis. There are several foods that patients should be instructed to avoid including aged cheese and red wine.

34. C. Rationale: Lithium levels of 1–1.2 mEq/L are within therapeutic range during acute episodes. Lithium levels should never be higher than 1.5 mEq/L during the acute treatment phase.

35. A. Rationale: Chlorpromazine (Thorazine®) is an antipsychotic that blocks dopamine in the CNS. Chlorpromazine has an onset of action between 30 minutes to 1 hour.

36. C. Rationale: Alprazolam (Xanax®) has an active metabolite: 3-hydroxy-alprazolam. Lorazepam (Ativan®), triazolam (Halcion®), and clonazepam (Klonopin®) do not have active metabolites.

37. C. Rationale: Negative symptoms of schizophrenia include apathy, lack of emotion, and poor or nonexistent social function. Delusions, hallucinations, and racing thoughts are positive symptoms of schizophrenia.

38. C. Rationale: Risperidone (Risperdal®) has not been associated with urinary retention. Common side effects are weight gain, sedation, sexual dysfunction, tremor, muscle pain and stiffness, and anxiety.

39. A. Rationale: The appropriate therapeutic range for lithium is 0.4–0.6 mEq/L.

40. E. Rationale: Antipsychotic agents are typically used in the treatment of schizophrenia and manic episodes of bipolar disorder. They may also be used for Tourette syndrome, Asperger's syndrome, and uncontrollable hiccups.

41. E. Rationale: Norepinephrine, 5-hydroxytryptamine, gamma-Aminobutyric acid (GABA), and dopamine are

common neurotransmitters within the CNS. Many drugs' pharmacological action can either increase or decrease these neurotransmitters, which can lead to therapeutic effects for treatment and adverse effects.

42. D. Rationale: Inhibitory neurotransmitters cause hyperpolarization, which is a result of an increase in chloride ion permeability. Excitatory neurotransmitters cause an excitatory postsynaptic potential, which is a result of sodium and potassium permeability.

43. B. Rationale: Tricyclic antidepressants (TCAs) antidepressants like amitriptyline (Elavil®) can cause anticholinergic side effects such as dry mouth, constipation, and urinary retention. Bupropion (Wellbutrin®, Wellbutrin XL®) is an antidepressant and smoking cessation aid that weakly inhibits reuptake of dopamine, norepinephrine, and serotonin without anticholinergic actions. Sertraline is an SSRI antidepressant that does not exhibit anticholinergic activity.

44. B. Rationale: Tricyclic antidepressants (TCAs) can cause anticholinergic side effects such as dry mouth, constipation, and urinary retention. TCAs also have adverse cardiovascular effects, orthostatic hypotension, and sedation.

45. C. Rationale: A significant and life-threatening side effect of clozapine (Clozaril®) is agranulocytosis that requires weekly monitoring. Clozapine has to be closely monitored through programs such as the Clozaril National Registry. Clozapine and other antipsychotics can cause anticholinergic side effects such as dry mouth and constipation.

46. B. Rationale: Bupropion (Wellbutrin®, Wellbutrin XL®) is an antidepressant and smoking cessation aid that weakly inhibits reuptake of dopamine, norepinephrine, and serotonin. Bupropion has the ability to lower seizure threshold and precipitate seizures. The risk of seizure may be decreased with lower dosages.

47. C. Rationale: Linezolid (Zyvox®) is an antibiotic and weak inhibitor of monoamine oxidase. The concomitant use of linezolid and SSRIs can precipitate serotonin syndrome. Serotonin syndrome can cause irritability, altered consciousness, nausea, confusion, anxiety, myoclonus, coma, and death.

48. A. Rationale: Tardive dyskinesia is recognized by choreoathetotic movements and the inability to perform voluntary movements. The prolonged use of antipsychotic medications can cause tardive dyskinesia due to their dopamine antagonist effects. Tardive dyskinesia can be irreversible and may be dependent on drug dosage and duration.

49. D. Rationale: Elevated sodium ingestion can increase renal clearance of lithium while decreased sodium intake can decrease lithium renal clearance. Counsel patients to avoid significant changes in salt intake. Clinicians should closely monitor sodium and lithium levels during lithium therapy.

50. E. Rationale: Lithium (Eskalith®, Lithobid®) overdose can result in edema, tremor, polyuria, visual disturbances, arrhythmias, and several other serious adverse effects. Overdose can be managed by hemodialysis, which can remove circulating lithium, and activated charcoal, which can prevent absorption.

51. A. Rationale: Phenothiazine antipsychotics like chlorpromazine (Thorazine®) can cause cholestatic jaundice, which can develop a couple of weeks after the start of therapy. Monitor bilirubin levels during the first month of therapy. Jaundice has improved in some patients upon discontinuation of phenothiazines.

52. D. Rationale: A common CNS effect of haloperidol is extrapyramidal reactions, which can develop at the initiation of therapy. Often times, extrapyramidal effects are dose-related and can improve with reducing drug dosage or discontinuing therapy, if the effects are persistent. Anticholinergic drugs (e.g., benztropine) for the treatment of Parkinson's disease may be an option to alleviate extrapyramidal reactions.

53. B. Rationale: Lithium (Eskalith®, Lithobid®) is used for the treatment of bipolar disorder and is associated with numerous adverse effects (e.g., hypothyroidism, sedation, tremor, and polyuria).

54. C. Rationale: Although many gastrointestinal side effects like nausea and vomiting commonly occur at the beginning of therapy, these effects usually subside with prolonged treatment. Gastrointestinal adverse events may be a result of elevated serum lithium levels can be minimized by taking lithium with food, dividing dosage, or using an extended-release formulation.

55. C. Rationale: Tricyclic antidepressants (TCAs) (e.g., amitriptyline, clomipramine) inhibit reuptake of serotonin and norepinephrine. Different drugs within the class of TCAs will inhibit serotonin or norepinephrine to varying degrees of selectivity. The SSRI antidepressant, paroxetine, inhibits the reuptake of serotonin.

56. E. Rationale: Chlorpromazine (Thorazine®) exerts alpha adrenergic blockade, which can lead to hypotension. The use of support stockings, an increase in dietary salt intake, use of fludrocortisone (Florinef®), and the administration of norepinephrine or phenylephrine for severe cases are used to manage hypotension as a result of antipsychotic therapy. Epinephrine is not a treatment option since phenothiazines can block epinephrine's vasopressor activity and cause more pronounced hypotension.

57. C. Rationale: The TCAs, amitriptyline (Elavil®) and doxepin (Sinequan®), can cause sedation and anticholinergic side effects such as dry mouth, constipation, and urinary retention. The antidepressant trazodone (Desyrel®) is a serotonin and norepinephrine reuptake inhibitor that has sedative properties but does not have anticholinergic effects.

58. B. Rationale: The antidepressant trazodone is a serotonin and norepinephrine reuptake inhibitor with

sedative properties. Trazodone (Desyrel®) has less anticholinergic properties compared to the TCAs. The TCAs, nortriptyline (Pamelor®, Aventyl®), and doxepin (Sinequan®) can cause sedation and anticholinergic side effects such as dry mouth, constipation, and urinary retention.

59. C. Rationale: TCAs (e.g., nortriptyline, doxepin) inhibit reuptake of serotonin and norepinephrine. The antidepressant trazodone (Desyrel®) is a serotonin and norepinephrine reuptake inhibitor. Sertraline (Zoloft®) is a selective serotonin reuptake inhibitor (SSRI) antidepressant.

60. A. Rationale: Extrapyramidal side effects can be caused by dopamine deficiency in the basal ganglia. Antipsychotics, especially first-generation, can cause extrapyramidal side effects. Examples of extrapyramidal effects are tardive dyskinesia and tardive dystonia.

61. C. Rationale: Cyclic antidepressants are used in the treatment of major depression, chronic pain, obsessive-compulsive disorder (OCD), and anorexia. Cyclic antidepressants can cause seizures.

62. E. Rationale: Dopamine excess and dopamine hypersensitivity causes schizophrenia. Antipsychotic medications reduce the levels of dopamine in the central nervous system (CNS).

63. A. Rationale: Monoamine oxidase (MAO) inhibitors (e.g., phenelzine) inhibit monoamine metabolism and are used in the treatment of depression. Patients taking MAO inhibitors should avoid food high in tyramine (e.g., red wine, aged cheese) to avoid hypertensive crisis.

64. E. Rationale: Antipsychotic medications reduce the levels of dopamine in the central nervous system. Antipsychotic medications can cause many adverse effects including mydriasis, orthostatic hypotension, jaundice, and gynecomastia. Thyroid function is not affected.

65. C. Rationale: Monoamine oxidase (MAO) inhibitors inhibit monoamine metabolism and are used in the treatment of depression. Patients taking MAO inhibitors should avoid food high in tyramine or tryptophan to avoid hypertensive crisis. MOA inhibitors can cause orthostatic hypotension and precipitate seizures (decreased seizure threshold).

66. A. Rationale: Fluoxetine (Prozac®, Sarafem®) is a selective serotonin reuptake inhibitors (SSRIs) antidepressant that selectively blocks serotonin uptake. Fluoxetine is indicated for the treatment of depression and has also been used in the management of anxiety, obesity and bipolar disorder.

67. B. Rationale: Lorazepam (Ativan®) is a benzodiazepine whose primary mechanism is enhancing GABA receptor function. Lorazepam undergoes hepatic metabolism to inactive metabolites.

68. E. Rationale: Tricyclic antidepressants (TCAs) can take up to 4 weeks to produce a maximum antidepressant effect after initiation of treatment. The patient should be advised to continue the current treatment and that it may take a few weeks to see improvements.

69. A. Rationale: Antipsychotic medications block dopamine receptors, which accounts for its extrapyramidal side effects including akathisia, dystonia, and Parkinson syndrome.

70. A. Rationale: Tardive dyskinesia is recognized by choreoathetotic movements and the inability to perform voluntary movements. The prolonged use of antipsychotic medications can cause tardive dyskinesia due to their dopamine antagonist effects. Tardive dyskinesia can be irreversible and may be dependent on drug dosage and duration.

71. A. Rationale: Haloperidol (Haldol®) is a first generation antipsychotic that exerts its pharmacological effects by blocking dopamine receptors.

72. A. Rationale: Antipsychotic medications, especially chlorpromazine (Thorazine®) and thioridazine (Mellaril®), can cause anticholinergic side effects such as constipation, dry mouth, urinary retention, and blurred vision. Patients frequently become tolerant to anticholinergic adverse effects.

73. C. Rationale: Fluphenazine enanthate and fluphenazine decanoate are the depot injection formulations. Depot injections are an option for patients with a preference for parenteral therapy and non-compliant patients.

74. B. Rationale: The SSRI, fluoxetine (Prozac®, Sarafem®), is FDA approved for the treatment of depression. Fluoxetine has been used off-label for the treatment of anxiety, obesity, and bipolar disorder.

75. B. Rationale: Rauwolfia alkaloids (e.g., reserpine) along with MAO inhibitors use can result in excitement and hypertension. Avoid administering these medications concomitantly.

76. A. Rationale: Primary prevention of TD involves using the lowest dose possible over the shortest period of time. If TD occurs, a primary strategy is to discontinue or decrease the neuroleptic dose to see if the condition improves. Often though, some symptoms remain and TD can be difficult to treat with medications (e.g., Antiparkinsonian medications).

77. B. Rationale: Phenothiazines (e.g., chlorpromazine) are typical antipsychotics that can be used as an antiemetic agent. Phenothiazines can cause adverse anticholinergic and extrapyramidal effects.

78. C. Rationale: Neuroleptic malignant syndrome is a result of antipsychotic use and can present as catatonia, hyperpyrexia, and autonomic dysfunction. Neuroleptic malignant syndrome may be caused by the prolonged blocking of dopamine receptors.

79. D. Rationale: Phenothiazines can cause pigment deposition on the anterior lens and posterior cornea in patients taking for chronic therapy at high doses. Other ocular adverse effects can occur such as visual impairment, star-shaped opacities, epithelial keratopathy, lacrimation, and pigmentary retinopathy. Exposure to light may be another risk factor at developing ocular adverse effects and it may be necessary to discontinue drug or reduce dosage.

80. B. Rationale: Phenothiazines (e.g., thioridazine) are typical antipsychotics that can be used as an antiemetic agent. Phenothiazines can cause orthostatic hypotension, hyperprolactinemia, anticholinergic, and extrapyramidal adverse effects.

81. A. Rationale: The concomitant use of certain benzodiazepines and cimetidine (Tagamet®) may result in the inhibition of benzodiazepine metabolism. This drug interaction may result in increased benzodiazepine effects and necessitate a lowered dose of the benzodiazepine.

82. D. Rationale: Antipsychotic medications can cause numerous side effects as a result of their activity in the autonomic, CNS, endocrine systems, and cardiovascular systems. Antipsychotic can cause adverse endocrine, behavioral, cardiac, neurological, and anticholinergic adverse reactions.

83. C. Rationale: Tricyclic antidepressants (TCAs) can cause seizures (e.g., decrease seizure threshold). TCAs should be used cautiously in patients with epilepsy.

84. B. Rationale: Antipsychotic medications block dopamine receptors in contrast to dopamine agonists, which are used to treat Parkinson's disease. Antipsychotics can cause extrapyramidal side effects such as Parkinsonian signs and symptoms. Antipsychotics should not be used in Parkinson's disease.

85. C. Rationale: Phenothiazines (e.g., chlorpromazine) are typical antipsychotics that can be used as an antiemetic agent. Chlorpromazine's mechanism of action is the blocking of dopamine receptors.

86. B. Rationale: Maprotiline (Deprilept®, Ludiomil®, Psymion®) is a tetracyclic antidepressant, closely related pharmacologically to the TCAs with the exception of its ability to inhibit serotonin reuptake. Tranylcypromine (Parnate®) and phenelzine (Nardil®) are MAO inhibitors.

87. A. Rationale: Monoamine oxidase (MAO) inhibitors inhibit monoamine metabolism and are used in the treatment of depression. Patients taking MAO inhibitors should avoid food high in tyramine or tryptophan to avoid hypertensive crisis.

88. D. Rationale: The primary mechanism for benzodiazepines is enhancing GABA receptor function. Benzodiazepines' adverse effects include paradoxical stimulation, dependence, withdrawal, hypotension, and respiratory depression.

89. E. Rationale: Lorazepam (Ativan®), a benzodiazepine anxiolytic, can cause adverse CNS effects such as anterograde amnesia, sedation, syncope, and confusion. High doses of triazolam (Halcion®) are associated with an increased risk of developing anterograde amnesia.

90. B. Rationale: The TCAs, imipramine (Tofranil®) and amitriptyline (Elavil®), are metabolized in the liver to desipramine and nortriptyline, respectively. The SSRI, fluoxetine (Prozac®, Sarafem®), is metabolized several metabolites including norfluoxetine.

91. C. Rationale: Polyuria and polydipsia occurs frequently in patients taking lithium and can continue in a smaller percentage of patients for up to 2 years of therapy. Discontinuation of lithium, dosage reduction of lithium, or treatment with diuretics can be used to manage polyuria. Infrequently irreversible diabetes insipidus can develop; however, polyuria is generally reversible within the first year of discontinuing the drug.

92. A. Rationale: Phenothiazines (e.g., chlorpromazine) are typical antipsychotics that can be used as an antiemetic agent. Phenothiazines can cause adverse endocrine effects such as hyperprolactinemia and decrease adrenocorticotropin, gonadotropin, vasopressin estrogen, and progesterin levels.

93. D. Rationale: Phenothiazine antipsychotics can cause cholestasis, which can develop a couple of weeks after the start of therapy.

94. D. Rationale: Ephedrine and amphetamine, indirect acting sympathomimetics, precipitate the release of catecholamine stores, which are increased with MAOIs (e.g., phenelzine) use. The concomitant use of ephedrine or amphetamine with an MAOI can result in increased sympathomimetic effects such as hypertensive crisis, toxic neurological effects, and the possibility of death.

95. B. Rationale: Haloperidol (Haldol®) is a first generation antipsychotic that exerts its pharmacological effects by blocking dopamine receptors. Haloperidol decanoate are given to patients who will need therapy for an extended period of time. It is administered once every month.

CHAPTER 20

1. E. Rationale: Beta-agonists (Albuterol®) can be used in the treatment of asthma based on their bronchial relaxation. Isoproterenol and epinephrine stimulate beta-2 receptors and can have a therapeutic effect in the treatment of asthma.

2. B. Rationale: Allergic rhinitis is quite prevalent among younger children but decreases with age; therefore is lower in the elderly population. Allergic rhinitis affects 40% of children, and it is more common in boys than girls. Several factors such as maternal smoking, allergens, and environmental triggers are associated with the development of allergic rhinitis.

3. B. Rationale: Ipratropium (Atrovent®) is an anticholinergic bronchodilator used for the treatment of bronchospasm in chronic obstructive pulmonary disease (COPD), bronchitis, and emphysema.

4. B. Rationale: Nizatidine (Axid®) is not an H₂ blocker but is an H₂ blocker used for the treatment of gastroesophageal reflux disease (GERD) and ulcers.

5. B. Rationale: Theophylline has to be dosed carefully due to its narrow therapeutic range. Theophylline dosing is affected by several factors including smoking, concomitant drug therapy, cardiac decompensation, cor pulmonale, and hepatic failure. It is not affected by renal impairment.

6. D. Rationale: Cimetidine (Tagamet®) decreases theophylline clearance, which can result in elevated theophylline blood levels. Due to theophylline's narrow therapeutic index, toxicity can occur. Concomitant administration of cimetidine and theophylline should be avoided.

7. B. Rationale: Tiotropium (Spiriva®) is a long-acting bronchodilator that acts as a muscarinic antagonist. Although tiotropium is dispensed as capsules, they should not be taken orally. The medication should be put into an inhalation device.

8. D. Rationale: Allegra® (fexofenadine) is a non-sedating H₁ receptor blocker used in the treatment of allergic rhinitis. Allegra has an onset of action of 60 minutes.

9. A. Rationale: Atropine is an anticholinergic agent that affects several organ systems, which can lead to both therapeutic and toxic effects in the body. Atropine can cause adverse GI tract (constipation, dry mouth), eye (mydriasis), and cardiovascular system (increased pulse) effects. Photophobia can also occur and patient should be advised to wear dark glasses in bright light to minimize this reaction.

10. E. Rationale: Cimetidine and ciprofloxacin inhibit the metabolism of theophylline, which can result in elevated theophylline blood levels. Due to theophylline's narrow therapeutic index, toxicity can occur. Management may involve discontinuing or switching cimetidine or ciprofloxacin to another agent, and/or reducing the theophylline dose.

11. B. Rationale: Epinephrine is a direct acting adrenergic agonist. Epinephrine is a preferred agent for the treatment of anaphylaxis. Anaphylaxis can manifest as urticaria, pruritus, and angioedema.

12. B. Rationale: Activated charcoal increases theophylline clearance and is used to manage theophylline overdose.

13. C. Rationale: Ipratropium is an anticholinergic agent that is used in the treatment of asthma and COPD. Inhaled ipratropium pharmacological effects are limited to the specific site and not systemic side effects are minimal.

14. A. Rationale: Albuterol® is a selective beta-2 agonist used as a bronchodilator for the treatment of asthma. Atropine and Ipratropium are anticholinergic drugs, Cimetidine is a H₂ antagonist and epinephrine is an alpha and beta agonist.

15. D. Rationale: Ipratropium (Atrovent®) is an anticholinergic bronchodilator used for the treatment of bronchospasm in chronic obstructive pulmonary disease (COPD), bronchitis, and emphysema. Ipratropium is available as a nasal spray for the management of rhinorrhea.

16. B. Rationale: Levalbuterol (Xopenex®) is a beta-2 agonist used to prevent and treat bronchospasm. Levalbuterol can be administered through a nebulizer or as an inhaler.

17. B. Rationale: Due to its narrow therapeutic index, the theophylline content is an important factor in selecting the appropriate theophylline medication.

18. D. Rationale: Selective beta-2 agonists and supplemental oxygen are used as initial treatments to manage acute exacerbations in the emergency room. Systemic oral corticosteroids and inhaled anticholinergic bronchodilators have been used as second-line therapies.

19. C. Rationale: Asthma can manifest as shortness of breath, wheezing, dyspnea, chest tightening, and cough. Maintenance of normal daily activity, prevention of acute exacerbations, and prevention of chronic symptoms can be managed by utilizing anti-asthmatic medications. Anti-asthmatic medications are divided into several drug classes including beta-2 agonists, corticosteroids, anticholinergics, leukotriene inhibitors, methylxanthines, and cromolyn, which have varied adverse effect profiles to consider when initiating treatment.

20. C. Rationale: Bethanechol (Urecholine®) is a cholinergic agonist that acts primarily on muscarinic receptors. Bethanechol is used for the treatment of bladder retention due to its ability to cause the bladder to contract and increase urination. Albuterol (Proventil®), metaproterenol (Alupent®) and terbutaline (Brethine®) affect beta-adrenergic receptors such as beta-2 receptors that relax bronchial smooth muscles for the treatment of bronchospasm.

21. D. Rationale: Beta-agonists can be used in the treatment of asthma (albuterol), congestive heart failure (dopamine), and as cardiac stimulants (isoproterenol). Beta-agonists' pharmacological effects include tachycardia, bronchial relaxation, increased myocardial contractility, and vasodilation.

22. C. Rationale: Phenylephrine is an alpha agonist used for the treatment of hypotension and shock.

23. D. Rationale: Isoproterenol (Isuprel®) is a beta-1 and beta-2 agonist used as a cardiac stimulant and bronchodilator. Isoproterenol causes decreased peripheral resistance and increased heart rate. Isoproterenol's cardiovascular effects include elevating myocardial oxygen consumption and magnifying ischemic symptoms.

24. D. Rationale: Theophylline toxicity can generally occur when blood levels are over 20 mcg/mL. Theophylline has a narrow therapeutic index and toxicity can manifest as several symptoms including seizure, tremor, vomiting, tachyarrhythmia, delirium, severe dehydration, albuminuria, and hyperthermia.

25. E. Rationale: Theophylline antagonizes adenosine, inhibits phosphodiesterase, which subsequently increases intracellular cAMP and is involved in the translocation of calcium. Theophylline has a broad range of pharmacodynamic activity due to its mechanism of actions involving cAMP and calcium.

26. E. Rationale: Diphenhydramine is an antihistamine used in the treatment of rhinitis and allergy symptoms. Diphenhydramine toxicity can cause drowsiness (common), hallucinations, blurred vision, dry mouth, and sinus tachycardia.

27. A. Rationale: Norepinephrine is a direct-acting adrenergic agonist. Norepinephrine does not have a strong effect on beta receptors and would exhibit the smallest bronchodilatory effect.

28. E. Rationale: Theophylline has a narrow therapeutic index and toxicity can manifest as several symptoms including seizure, tremor, vomiting, tachyarrhythmia, delirium, severe dehydration, and agitation.

29. C. Rationale: Theophylline antagonizes adenosine and inhibits phosphodiesterase, which subsequently elevates cAMP. Theophylline is a bronchodilator used in the treatment of asthma.

30. A. Rationale: Ipratropium is an anticholinergic bronchodilator used for the treatment of bronchospasm in COPD, bronchitis, and emphysema.

31. B. Rationale: Beta-2 agonists cause bronchodilation and are used for the treatment of asthma. Side effects of beta-2 bronchodilators are tremors, headache, insomnia, nervousness, and tachycardia.

32. C. Rationale: Isoproterenol is a synthetic beta-1 and beta-2 agonist used as a cardiac stimulant and bronchodilator.

33. A. Rationale: Cromolyn is a mast cell stabilizer used as an adjunct and prophylactic agent for the treatment of asthma.

34. C. Rationale: Theophylline toxicity can occur when blood levels are over 20 mcg/mL. Theophylline has a narrow therapeutic index and toxicity can manifest as several symptoms including seizure, tremor, vomiting, tachyarrhythmia, delirium, severe dehydration, albuminuria, and hyperthermia.

35. B. Rationale: Atropine, an antimuscarinic, is a potent bronchodilator. Atropine is used for the short-term prevention of bronchospasm.

CHAPTER 21

1. A. Rationale: Allopurinol is used to treat hyperuricemia (excessive uric acid). Paroxetine is a selective serotonin reuptake inhibitor (SSRI) drug used for the treatment of depression. Nizatidine is an H₂ antagonist used for the treatment of peptic ulcer disease (PUD) and gastroesophageal reflux disease (GERD).

2. A. Rationale: Colchicine toxicity can result in adverse gastrointestinal complaints including abdominal pain, nausea, vomiting, and severe bloody diarrhea.

3. E. Rationale: Auranofin (Ridaura[®]) is an oral gold compound.

4. E. Rationale: Pharmacists should instruct patients to take penicillamine on an empty stomach: 1 hour before meals, 2 hours after meals, and at least 1 hour without taking any other food, milk, supplement, vitamins, antacids, or other medications.

5. B. Rationale: Concomitant use of allopurinol and mercaptopurine may increase the risk of mercaptopurine toxicity, likely due to inhibition of first-pass oxidative metabolism of mercaptopurine by xanthine oxidase. If concomitant therapy is necessary, reduce the dose of mercaptopurine to one third or one fourth the usual dose.

6. C. Rationale: The uricosuric drugs, probenecid and sulfinpyrazone, increase the excretion of uric acid by inhibiting its reabsorption in the kidneys.

7. C. Rationale: NSAIDs (e.g., indomethacin), corticosteroids, and colchicine are first-line therapy in the treatment of acute gout attacks. Allopurinol is an urate lowering medication used in the treatment of chronic gout.

8. A. Rationale: Rheumatoid arthritis (RA) is a chronic disease that is usually initially diagnosed in people between the ages of 40 and 60. RA is more common in women than men. Although the exact cause is unknown, there may be a genetic component. Smoking appears to increase the risk of RA.

9. A. Rationale: Although colchicine's exact mechanism of action is unknown, its interference with leukocyte functions plays a role in its antigout activity.

10. E. Rationale: Osteoarthritis is a common joint disorder that involves three tissues—bone, articular cartilage, and the synovium. All of these tissues undergo alterations in response to mechanical stress.

CHAPTER 22

1. E. Rationale: Anticonvulsant medications are used in the treatment of epilepsy and neuropathic pain. Anticonvulsant therapy can cause gastric upset and changes in appetite, body weight, and cognition.

2. E. Rationale: Anticonvulsant medications are used in the treatment of epilepsy. Anticonvulsant therapy can

cause teratogenicity (e.g., fetal hydantoin syndrome), withdrawal effects if the drug is not tapered, and CNS depressant effects with overdose.

3. C. Rationale: Gingival hyperplasia is an adverse effect of phenytoin (Dilantin®) that occurs frequently in children. Gingival hyperplasia can result in surgery and patients should be advised to maintain good oral hygiene and gum massage.

4. B. Rationale: Ethosuximide (Zarontin®) is the most appropriate anticonvulsant for initial management of absence seizures. Ethosuximide can be used in adults and children over the age of 3 years.

5. B. Rationale: Dilantin® (phenytoin) is a hydantoin derivative anticonvulsant used in the management of tonic-clonic seizures, status epilepticus, complex partial seizures, and nonepileptic seizures. Phenytoin's adverse effects include hypertrichosis, hypotension, cardiac arrhythmia, lupus erythematosus, and megaloblastic anemia.

6. A. Rationale: Dilantin® (phenytoin) is a hydantoin derivative anticonvulsant used in the management of tonic-clonic seizures, status epilepticus, complex partial seizures, and nonepileptic seizures. Dilantin® is not used in absence seizures.

7. E. Rationale: Anticonvulsant medications are used in the treatment of epilepsy and neuropathic pain. Anticonvulsant therapy can cause headache, dizziness, gastric upset, and changes in appetite, body weight, and cognition.

8. C. Rationale: Valproic acid is 80%-95% protein bound, which is concentration dependent. Older age, renal and hepatic impairment, or concomitant use with protein bound drugs can decrease valproic acid's protein binding.

9. E. Rationale: Temporal lobe epilepsy (TLE) is a condition characterized by recurrent unprovoked seizures originating from the medial or lateral temporal lobe. Drugs commonly used for TLE include phenytoin, carbamazepine, valproate, and phenobarbital.

10. B. Rationale: Any level between 7.5–20 mcg/mL is within the serum phenytoin therapeutic range.

11. E. Rationale: Gabapentin (Neurontin®) is an anticonvulsant used in the treatment of seizures and neuropathic pain. Common side effects of gabapentin therapy are fatigue, somnolence, and dizziness.

12. E. Rationale: Carbamazepine (Tegretol®) is an anticonvulsant used in the management of partial seizures, generalized tonic-clonic seizures, and mixed seizure patterns. Significant improvement has been shown with carbamazepine in patients with complex partial seizures.

13. E. Rationale: Acutely injecting moderate to large amounts of alcohol can increase the level of phenytoin in

the blood. Chronic alcohol injection can increase phenytoin metabolism. Phenytoin may lower blood levels of oral contraceptives. Valproate is metabolized by conjugation, beta-oxidation, and cytochrome P-450 oxidation (CYP 2C9, CYP 2C19, and CYP 2A6) and also acts as an inhibitor of a variety of hepatic enzymes including glucuronyltransferase, epoxide hydrolase, and the CYP 2C enzymes. Valproate can increase phenobarbital levels by inhibition of phenobarbital metabolism.

14. E. Rationale: Carbamazepine's dose related side effects include nausea, ataxia, diplopia, and headache.

15. E. Rationale: Carbamazepine (Tegretol®) is an anticonvulsant used in the management of complex partial seizures, generalized tonic-clonic (grand mal) seizures, and mixed seizure patterns. Carbamazepine can be used in other conditions such as bipolar disorder prophylaxis, acute mania, and trigeminal neuralgia.

16. C. Rationale: Ethosuximide (Zarontin®) works by inhibiting the influx of calcium ions when they travel through T-type calcium channels.

17. B. Rationale: Phenytoin can increase levels of gamma-glutamyl transpeptidase (GGT) concentrations, which could be an indicator of phenytoin toxicity. Elevated GGT may indicate hepatotoxicity.

18. A. Rationale: Seizures are classified into two groups—partial and generalized. Drug therapy is selected based on seizure type since anticonvulsant medications are not useful in all seizures. Tonic-clonic (grand mal) is a generalized seizure, while complex partial is a partial seizure.

19. A. Rationale: A patient that presents with acute barbiturate overdose is initially managed with maintenance of airway. Additional therapies include oxygen, assisted respiration, and activate charcoal when administered immediately.

20. B. Rationale: Simple partial seizures are partial seizures in which consciousness is not impaired. Any cortical region may be affected, but the most common sites are frontal and temporal lobes. Most simple partial seizures only last between 20 and 60 seconds.

21. E. Rationale: Phenytoin and primidone are preferred agents in treatment of complex partial seizures, and carbamazepine is an alternative treatment option.

22. D. Rationale: Valproate sodium can be used alone or in combination with other agents, such as ethosuximide, for the management of petit mal seizures. Petit mal seizures (absence seizures) manifest as a brief loss of consciousness.

23. A. Rationale: Phenytoin increased hepatic degradation of prednisone. Prednisone will have reduced pharmacologic effects, which can increase asthma symptoms.

24. D. Rationale: Fast drug absorption is essential when treating status epilepticus, and typically drugs need to

be administered intravenously. Diazepam (Valium®), Diastat®) may be given intravenously or rectally, and is often a first agent used. IV valproate is also used for status epilepticus.

25. A. Rationale: Facial changes in coarsening, enlargement of the lips and nose, hirsutism, acne, and pigmentation may occur from chronic phenytoin (Dilantin®) therapy.

26. E. Rationale: Clonazepam (Klonopin®) may be used for partial and generalized seizures (including absence and myoclonus). It may also be used for Lenno-Gastaut syndrome, neonatal seizures, infantile spasms, and status epilepticus.

27. E. Rationale: Primidone and carbamazepine undergoes liver metabolism to the metabolite and phenylethylmalondiamide (PEMA) and carbamazepine-10, 11-epoxide (CBZ-E), respectively.

28. C. Rationale: Valproate sodium (Depakote®) can be used alone or in combination with other agents, such as ethosuximide (Zarontin®), for the management of petit mal seizures. Petit mal seizures (absence seizures) manifest as a brief loss of consciousness.

29. A. Rationale: Although rare, phenytoin can cause lymphadenopathy, hepatosplenomegaly, leucopenia, and megaloblastic anemia.

30. B. Rationale: Ethosuximide is the most appropriate anticonvulsant for initial management of absence (petit mal) seizures.

31. E. Rationale: The barbiturates, phenobarbital (Luminal®) and mephobarbital (Mebaral®), are used for the management of seizures due to their ability to enhance the effects of GABA. Benzodiazepines (e.g., diazepam) influence various neurotransmitters including GABA and can be useful in the management of epilepsy.

CHAPTER 23

1. E. Rationale: Osteoporosis is a complex disorder that involves various pathogenic factors. Osteoclasts degrade bone by attaching to bone surface and secreting enzymes and acids into the surface. Cytokines, including interleukin-1 and interleukin-6, increase osteoclastic activity. The loss of estrogen accelerates bone loss.

2. D. Rationale: The mini pill is a progestin-only contraception that works by reducing the volume of cervical mucus and increasing its viscosity, which prevents sperm from passing through the cervical canal and endometrial cavity. Changes in menstrual bleeding pattern including irregular bleeding or spotting may occur.

3. E. Rationale: Hormone replacement therapy may cause breast pain, nausea, bloating, and fluid retention. It may also increase the risk of blood clots, gallbladder disease, and endometrial, breast, and ovarian cancers.

4. B. Rationale: Liothyronine (Cytomel®) is a thyroid medication that does not contain a steroidal nucleus. Norethindrone (a progestin), ethinyl estradiol (an estrogen) and fluoxymesterone (an androgen) are steroid sex hormones. Prednisolone (Prelone®) is a corticosteroid used for the treatment severe inflammation.

5. B. Rationale: Misoprostol (Cytotec®) is a prostaglandin analog that inhibits gastric secretion and gastrointestinal mucosal protective effects and increases uterine contractions. Misoprostol is used for the treatment of ulcers, medical abortion, and the induction of labor.

6. A. Rationale: Misoprostol (Cytotec®) is contraindicated in pregnant and breast-feeding women. Misoprostol should only be prescribed to women of childbearing years that are at high risk for nonsteroidal antiinflammatory drug (NSAID)-induced ulcers, and patients should be counseled on the risk of miscarriage.

7. E. Rationale: Testosterone therapy can be used for the treatment of several indications including palliation of metastatic breast cancer, male hypogonadism, and constitutional pubertal delay. Testosterone is the primary endogenous androgen steroid hormone used as replacement therapy.

8. C. Rationale: Elevated levels of thyroid hormone can result in the life-threatening condition, thyroid storm. The antithyroid medication, propylthiouracil (PTU), is a drug of choice in the treatment of thyroid storm. Lithium (Eskalith®, Lithobid®) is used for the treatment of bipolar disorder.

9. A. Rationale: Jolivet® is an oral contraceptive that contains only a progestin (norethindrone).

10. E. Rationale: History of deep vein thrombosis (DVT), breast carcinoma, abnormal genital bleeding, and ischemic heart disease are contraindicated in oral contraceptive use. Oral contraception should be used with caution or avoided in patients with certain conditions including migraines, liver disease, asthma, hypertension, and optic neuritis.

11. C. Rationale: Somatostatin is a growth hormone-inhibiting hormone (GHIH) and exists in many parts of the body such as the pancreas and CNS. Octreotide is a somatostatin analog, which is used in various conditions including the treatment of acromegaly.

12. A. Rationale: Weight gain is not a usual symptom of hyperthyroidism. Typically, weight loss is seen even though there is an increase in appetite. Other symptoms include tachycardia, arrhythmia, palpitations, nervousness, tremor, sweating, changes in menstrual patterns, increased sensitivity to heat, changes in bowel patterns, and enlarged thyroid gland (goiter).

13. E. Rationale: Synthetic progestins have similar pharmacological effects as progesterone such as elevating body temperature at ovulation, inhibiting endocervical secretion forming, and eliciting inherent estrogenic activity.

14. D. Rationale: The mini-pill only contains progesterin (e.g., norethindrone or norgestrel) and acts primarily via thickening of cervical mucus and preventing ovulation.

15. E. Rationale: Gonadotropin-releasing hormone (GnRH) regulates the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary. Gonadotropin-releasing hormone analog therapy can be used in the treatment of several conditions including central precocious puberty, endometriosis, female infertility, and prostatic cancer.

16. B. Rationale: Tamoxifen (Nolvadex®) is both an estrogen antagonist and estrogen agonist used for the treatment of cancer.

17. B. Rationale: Gonadotropin-releasing hormone (GnRH) regulates the secretion FSH and LH from the pituitary. Gonadotropin-releasing hormone analog therapy can be used in the treatment of several condition including central precocious puberty, endometriosis, female infertility, and prostatic cancer.

18. E. Rationale: Tamoxifen (Nolvadex®) is both an estrogen antagonist and estrogen agonist used for the treatment of cancer. Tamoxifen's antiestrogenic effects are on estrogen receptors in breast tissue and the CNS.

19. B. Rationale: Estrogen (e.g., ethynodiol diacetate) and progesterin (e.g., norgestrel, levonorgestrel) are used in combination as oral contraception. Mifepristone is antiestrogen used for medical abortion.

20. D. Rationale: Vivelle-Dot® and Alora® are estrogen patches used to reduce symptoms of menopause. Vivelle-Dot® and Alora® are applied twice weekly. Menostar® should only be applied once a week.

21. D. Rationale: Oral contraceptives are associated with several side effects including hepatic adenoma, cholelithiasis, and weight gain. Oral contraceptives have serious cardiovascular adverse effects such as thromboembolism, thrombophlebitis, and hypertension.

22. E. Rationale: Gonadotropin-releasing hormones (GnRH) analogs regulate the secretion FSH and LH from the pituitary. GnRH analogs are used in the treatment of prostate cancer, female infertility, and endometriosis. Adverse effects include multiple births, ovarian enlargement, male gynecomastia, menopausal symptoms (hot flashes), and amenorrhea.

23. E. Rationale: The mini-pill only contains a progesterin (e.g., norethindrone, norgestrel) and acts primarily via thickening of cervical mucus and decreasing ovulation. The limitations of the mini-pill are that it is less effective than combined oral contraceptives and commonly causes breakthrough bleeding. Ovulation does not occur when taken correctly every day.

CHAPTER 24

1. C. Rationale: Mast cells play a key role in immediate allergic reactions and inflammation. They are capable of producing a number of inflammatory mediators including histamine, prostaglandins, and cytokines. Basophils are important in type I hypersensitivity reactions as well. Erythrocytes, or red blood cells, transport oxygen and carbon dioxide between the lungs and all the tissues of the body.

2. D. Rationale: The normal range for a WBC (white blood cell) count varies slightly between laboratories but is typically between 4300-10800 cells per cubic millimeter.

3. B. Rationale: Cytotoxic T cells are a subgroup of T lymphocytes that destroy specific target cells. They are not involved in antibody mediated response like plasma cells, T helper cells or B lymphocytes. *Plasma cells* actively produce antibodies against certain pathogens.

4. A. Rationale: Plasma cells produce antibodies against certain pathogens. B cells are produced in the bone marrow and become plasma cells. T cells are involved in cellular immunity, which is mediated by thymus-derived lymphocytes.

5. E. Rationale: Elevated white blood cells or leukocytosis may be caused by viral or bacterial infection, stress, medications (e.g., corticosteroids, certain antibiotics, and antiseizure drugs), chronic bone marrow diseases, acute or chronic leukemia, and tissue damage (e.g., burns).

6. B. Rationale: CD-8 receptors are expressed on 30% of T cells. CD8+ cells recognize cell bound antigens in association with Class I MHC antigens.

7. E. Rationale: Measles, mumps, and the oral polio vaccines (no longer routinely administered in United States) are live vaccines. Injectable polio vaccine is inactivated.

8. A. Rationale: There have been reported cases of intussusception, a type of bowel obstruction, with the use of the vaccines against rotavirus. Certain congenital GI malformations may increase the risk of this effect, and the vaccines are contraindicated in such infants.

9. C. Rationale: MMRII and Menomune need to be reconstituted before administration. Pneumovax 23 does not require dilution or reconstitution.

10. E. Rationale: Rotavirus, DTaP, Hib, and pneumococcal vaccines should not be administered to children younger than 6 weeks of age because of other components.

11. A. Rationale: A quadrivalent vaccine by definition would contain 4 types of antigens. The quadrivalent HPV vaccine contains virus like particles that resemble HPV virions of HPV Types 6, 11, 16, and 18.

CHAPTER 25

1. C. Rationale: Sirolimus and cyclosporine are immunosuppressant agents. However, demeclocycline is a tetracycline antibiotic.

2. E. Rationale: Nephrotoxicity, hyperlipidemia, hypertension, gingival hyperplasia, as well as diabetes mellitus, neurotoxicity, alopecia, hyperkalemia, hypomagnesemia, and hemolytic uremia syndrome are all adverse effects associated with cyclosporine.

3. C. Rationale: Cyclosporine has a narrow therapeutic window range that is not absolutely defined. It inhibits T cell proliferation. However, Sandimmune®, Neoral®, and Gengraf® are NOT bioequivalent and should not be used interchangeably.

4. C. Rationale: Although not structurally similar, tacrolimus and cyclosporine share biologic characteristics and both target calcineurin. However, cyclosporine binds to a family of cyclophilins whereas tacrolimus binds to FK506-binding proteins or FKBP.

5. C. Rationale: Thymoglobulin® is better tolerated than ATGAM® and has predictable suppression of T cells; however the incidences of CMV infections are comparable to that of ATGAM®.

6. E. Rationale: Azathioprine (Imuran®) is used for all of the above—as adjunct therapy in renal transplant patients, for rheumatoid arthritis, and for inflammatory bowel disease (non-FDA approved use).

7. E. Rationale: Weight gain, cataracts, osteoporosis, growth retardation, as well as numerous other side effects, are associated with methylprednisolone (and all glucocorticoid) use.

8. E. Rationale: Tacrolimus (Prograf®) is highly lipophilic and undergoes extensive tissue distribution. It is metabolized by the CYP 3A4 hepatic enzyme system. The trough levels of tacrolimus should be monitored and range between 5-20 ng/mL.

9. E. Rationale: All of the following are true about the mechanism of action of mycophenolate mofetil. It inhibits purine synthesis, inhibits synthesis and proliferation of T and B lymphocytes, and blocks activity of inosine monophosphate dehydrogenase (IMPDH). It has minimal effect on cytokine production.

10. A. Rationale: Cyclosporine, as well as other immunosuppressants, may cause hypertension. Indapamide, a diuretic, and prazosin, an alpha blocker, are antihypertensive agents and may lower blood pressure.

CHAPTER 26

1. D. Rationale: Oral ferrous iron salts such as ferrous sulfate, ferrous gluconate, and ferrous fumarate are cost-effective and clinically efficacious first line drugs for the treatment of iron deficiency anemia. Parenteral iron

should be reserved for treatment failure with oral iron or for anemia that is not adequately controlled.

2. A. Rationale: OTC Minoxidil® is available as solution and foam. Tablets are prescription only and not available OTC. A gel is not available.

3. A. Rationale: Clotrimazole comes in many dosage forms due to the nature and where fungal infections tend to occur. Clotrimazole also comes in combination with other medications.

4. A. Rationale: Any systemically-absorbed clotrimazole is primarily excreted in the feces as metabolites. Pharmacodynamic/kinetic data shows very minimal levels are absorbed systemically after topical application. The time to peak serum concentration of an oral troche is roughly 3 hours if the troche is allowed to dissolve in the mouth for 30 min.

5. B. Rationale: Oxymetazoline nasal spray should be discontinued after 3 days due to risk of rebound congestion and exacerbation of nasal symptoms.

CHAPTER 27 RATIONALES

1. E. Rationale: H₂ antagonists (e.g., ranitidine), regular human insulin, and heparin may be added to parenteral nutrition solutions.

2. A. Rationale: Peripheral parenteral nutrition (PPN) is used when central line access is not available. PPN should only be used short-term and may be infused through a small vein. PPN solutions MUST be isotonic to prevent damage to veins.

3. E. Rationale: Fatty liver, hyperglycemia, and pneumothorax are all potential complications of the administration of parenteral nutrition solutions.

4. E. Rationale: When a patient is receiving TPN, there is risk of various complications including electrolyte imbalances. Patients receiving TPN with kidney disease or acute renal failure may develop hypermagnesemia, hypocalcemia, hyperphosphatemia, and hyperkalemia.

5. A. Rationale: PPN (Peripheral Parenteral Nutrition) refers to solutions supplied via a peripheral vein.

6. C. Rationale: Each gram of dextrose supplies approximately 3.4 kcal of energy to a patient. Because 1 liter of dextrose 10% solution contains 100 g of dextrose, the administration of 1 liter will supply the patient with approximately 340 kcal.

7. B. Rationale: Each gram of protein supplies about 4 kcal, each gram of carbohydrate supplies about 3.4 kcal, and each gram of fat supplies about 9 kcal.

12 gram • 4 kcal	= 48
24 gram • 3.4 kcal	= 81.6
0 gram • 9 kcal	= 54
	= 183.6

8. A. Rationale: The caloric density of proteins is 4 kcal/g.

9. E. Rationale: Liposyn II is given to prevent fatty acid deficiencies and contains 5% safflower oil, 5% soybean oil, and up to 1.2% egg phospholipids. In a 10% solution, each mL provides 1.1 kcal. The emulsion appears cloudy, like a milky appearance, and will impart a cloudiness to most items with which it is physically mixed.

10. A. Rationale: Egg phospholipids are found in Liposyn® and are used as emulsifying agents. Patients with severe allergies to eggs should not be given Liposyn®.

CHAPTER 28

1. B. Rationale: Steady state of a drug is defined as the rate of drug entering the body equals the rate of elimination. It generally takes between 4.5-6 half-lives of a drug to achieve steady state.

2. C. Rationale:

$$\begin{aligned} t_{1/2} &= \frac{0.693 \cdot V_d}{Cl} \\ &= \frac{0.693 \cdot 310}{72} \\ &= 3 \text{ hours} \end{aligned}$$

3. D. Rationale: A patient with renal failure has all of these issues, which can cause altered drug absorption and bioavailability.

4. D. Rationale: The first pass effect refers to the hepatic metabolism of oral drugs prior to reaching systemic circulation. Choice A refers to diffusion. Choice B refers to dispersion. Choice C refers to clearance. Choice E refers to absorption.

5. B. Rationale: The serum level does have to be adjusted when albumin is reduced because phenytoin is a highly protein bound drug that would yield a higher free fraction of phenytoin in the low albumin state.

6. A. Rationale: Cytochrome P450 enzymes exert their enzymatic effects through oxidation reactions. Methylation is simply the adding of a methyl (CH₃) and occurs in hundreds of reactions throughout the body. Conjugation enzymes are used in phase II metabolism. Acetylation is the adding of an acetyl-group and is used in industry in the manufacturing of aspirin.

7. A. Rationale: Drug metabolism is a primary mechanism for elimination of many drugs from the body. However, some drugs are eliminated unchanged.

8. B. Rationale: Since the pH of the solution is below the pK_a of amphetamine the molecule will be protonated and thus acidified. At 1 increment of pH below the pK_a, the molecule will be 90% ionized, at 2 increments of pH below the pK_a, the molecule will be 99% ionized. Further acidification of the urine will further ionize the molecule, thus enhancing renal clearance. This leads us to choice B, 98.44% and acidified.

9. C. Rationale: In a patient currently not experiencing renal failure the corrected phenytoin equation is measured phenytoin level/[albumin × 0.2 + 0.1]. Using the patient-specific information from the question gives us an answer of 10.56 mcg/mL. Given the average therapeutic phenytoin levels of 10-20 mcg/mL, this patient does not require a loading dose unless warranted by continued seizure activity.

10. B. Rationale: The formula for volume of distribution is the total amount of drug in the body divided by the drug plasma concentration. So, 300 mg/4.6 mg/L = 65.2 L.

11. A. Rationale:

$$CrCl = [(140 - \text{age}) \times IBW] / (Scr \times 72) \quad (\times 0.85 \text{ for females})$$

$$PT IBW = 81 \text{ kg}$$

Note: if the ABW (actual body weight) is less than the IBW use the actual body weight for calculating the CRCL.

Patient is close to IBW.

$$\begin{aligned} CrCl &= [(140 - 58) \cdot 81 \text{ kg}] / (2.0 \text{ mg/dL} \cdot 72) \\ &= 49.2 \text{ mg/dL} \end{aligned}$$

12. A. Rationale: A drug-drug interaction is the effect of concomitant use of two separate drugs within the body. Monitoring for drug interactions is important especially with the introduction of several new drugs each year. Drug interactions can be serious and pharmacists should identify and manage potential interactions in all patients.

13. B. Rationale: Any level between 7.5–20 mcg/mL is within the serum phenytoin therapeutic range at steady-state.

14. C. Rationale: Lithium levels of 1–1.2 mEq/L are within therapeutic range during acute episodes. Lithium levels should never be higher than 1.5 mEq/L during the acute treatment phase.

15. A. Rationale: Chlorpromazine is an antipsychotic that blocks dopamine in the central nervous system (CNS). Oral chlorpromazine has an onset of action between 30 minutes to 1 hour and thus would provide clinical activity quicker than the other choices.

16. B. Rationale: Drugs such as aspirin undergo zero order kinetics in which the drug is metabolized at a constant rate over time. In first order kinetics, drug metabolism is directly proportional to drug concentration. $V = V_{max}[C]/K_m$ is the first order kinetics equation.

17. E. Rationale: Digoxin, acetaminophen, morphine, and diazepam undergo phase II glucuronidation reaction. Dopamine and other catecholamines undergo phase II methylation reactions.

18. A. Rationale: Time required for half of the drug to be eliminated from the body is the drug's half life. Dosage adjustments may be required if the half-life of a drug is changed.

19. E. Rationale: Bioavailability is the fraction of drug that reaches systemic circulation unchanged and can be

affected by several factors including first pass metabolism and drug solubility. First pass metabolism occurs when an oral medication is absorbed across the GI tract and then metabolized by the liver before it enters systemic circulation. The drug's solubility is determined by its hydrophilic or lipophilic properties that affects drug absorption. Generic medications to an innovator brand product are to produce similar bioavailability.

20. E. Rationale: Phase I reactions introduce small chemical changes to make a compound more hydrophilic. Phase I reactions involve oxidation, reduction, and hydrolysis.

21. B. Rationale: Phase I reactions (e.g., hydroxylation) introduces or unmasks a hydroxyl or other hydrophilic functional group. Phase I reactions can occur as oxidations, reductions, and hydrolyses. Phase II reactions (sulfation, conjugation, glucuronidation) are reactions that further increase a compounds solubility for elimination.

22. A. Rationale: The transdermal route is applied directly to skin and generally has limited first pass effect and an extended duration of action. Sustained release or extended release medications are frequently delivered via the transdermal route. An example is the fentanyl transdermal patch, which is indicated for every 72 hour dosing.

23. E. Rationale: After an oral medication is absorbed across the GI tract, the liver metabolizes the drug before it enters systemic circulation, which is defined as hepatic first pass metabolism. The SC, IM, and IV routes would avoid first pass metabolism.

24. D. Rationale: Cimetidine decreases theophylline clearance, which can result in elevated theophylline blood levels. Due to theophylline's narrow therapeutic index, toxicity can occur. Concomitant administration of cimetidine and theophylline should be avoided.

25. E. Rationale: Examples of cytochrome P-450 3A4 (CYP 3A4) substrates are verapamil, quinidine, and estrogens. These medications will have enhanced metabolism when taken with CYP 3A4 inducers (e.g., rifampin).

26. E. Rationale: Digoxin, acetaminophen, morphine, and diazepam undergo phase II glucuronidation reaction. Dopamine and other catecholamines undergo phase II methylation reactions.

27. B. Rationale: Intramuscular (IM) preparations are administered into the muscle and can be painful. IM drugs can provide a sustained dose if administered as a depot preparation (e.g., haloperidol decanoate).

28. A. Rationale: The rate of drug metabolism and drug concentration is directly proportional in first order kinetics. Doubling the rate of administration of a first-order elimination drug will double the steady state plasma concentration.

29. B. Rationale: Bioavailability is the fraction of drug that reaches systemic circulation unchanged. A drug injected directly into the vein would have achieved 100% bioavailability.

30. A. Rationale: Half-life is the time required for the total body amount of drug to be decreased by 50%, and it can be used to estimate time required to reach steady state concentration. Dosage adjustments may be required if the half-life of a drug is changed.

31. E. Rationale: Phase II reactions convert drug metabolites to more polar conjugates. *O*-methylation, *N*-acetylation, and glucuronidation are types of phase II reactions. Hydrolysis is a phase I reaction.

32. A. Rationale: Rifampin is an inducer of CYP 3A4 substrates. CYP 3A4 substrates like verapamil, quinidine, and estrogens will have enhanced metabolism when taken with rifampin.

33. E. Rationale: Rectal, sublingual, and intramuscular administrations all avoid the first pass effect. The first pass effect plays its biggest role when drugs are taken orally.

34. A. Rationale: Phenobarbital is an inducer of cytochrome P-450 2C9 (CYP 2C9) substrates. CYP 2C9 substrates like phenytoin will have enhanced metabolism when taken with Phenobarbital.

35. C. Rationale: Drug elimination via hemodialysis depends on molecular size of the drug, protein binding, and volume of distribution. Drugs with molecular weight less than 500 Dalton (Da) normally pass through the dialysis filter easily if they are not protein bound.

36. D. Rationale: Half-life is the time required for the total body amount of drug to be decreased by 50%, and it can be used to estimate time required to reach steady state concentration. Facts pertaining to linear pharmacokinetics and half-life include: a) If total body clearance is doubled, elimination half-life is decreased; b) if volume of distribution is doubled, elimination half-life is increased; and c) if total body clearance and volume of distribution are both decreased to the same degree, there will be no effect on elimination half-life.

37. C. Rationale: While not always practical, the best way to minimize adverse drug events in patients with impaired renal function is to minimize the number of medications given.

38. E. Rationale: Cimetidine and quonolones inhibit the metabolism of theophylline, which can result in elevated theophylline blood levels. Due to theophylline's narrow therapeutic index, toxicity can occur. Management of this drug interaction may involve discontinuing or switching cimetidine and ciprofloxacin, and/or reducing the theophylline dose.

39. B. Rationale: Of the choices given, only warfarin does not affect theophylline clearance. Ciprofloxacin and

erythromycin can decrease the clearance of theophylline, which could lead to toxicity.

40. B. Rationale: Theophylline has to be dosed carefully due to its narrow therapeutic range. Theophylline dosing is affected by several factors including smoking, concomitant drug therapy, cardiac decompensation, cor pulmonale, and hepatic failure.

41. B. Rationale: Activated charcoal increase theophylline clearance and are used to manage theophylline overdose.

42. E. Rationale: Digitoxin also has higher oral availability, more plasma protein binding, and a longer half-life than digoxin. Digitoxin has a half-life of 7 days versus 40 hours for digoxin. It may take 1 month for digitoxin versus 1 week for digoxin to achieve steady-state.

43. C. Rationale:

$Co = \text{Dose} / Vd$

$Co = 500\text{mg} / (50\text{kg} \times 2\text{L/kg})$

$500\text{ mg} / 100\text{ L}$ or 5 mg/L

Convert mg/L to mcg/ml, so the answer is 5mcg/ml.

44. B. Rationale: Imitrex (sumatriptan) undergoes incomplete absorption and presystemic metabolism, which accounts for the low oral bioavailability. Sumatriptan has a high bioavailability of 97% when administered subcutaneously.

45. C. Rationale: The amount of the drug dose and the volume of distribution affect initial drug concentration.

CHAPTER 29

1. B. Rationale: In poor metabolizers of codeine, the codeine is not converted to active pharmacologic form, and the patient is likely to notice the medication as ineffective.

2. B. Rationale: The drug targets the HER2/neu oncogene in order to produce effect.

3. B. Rationale: Patients with the HLA-B*5701 allele are at greatly increased risk of serious hypersensitivity reactions to abacavir, which can be fatal. Labeling advises against starting abacavir in patients positive for this marker.

4. A. Rationale: Patients with reduced activity of either CYP 2C9 or VKORC1 may need a lower warfarin dose or take longer to achieve target maintenance dosing due to slower metabolism; such patients may be at increased risk of bleeding. CYP 3A4 and CYP 2D6 do not contribute to the metabolism of warfarin.

CHAPTER 30

1. A. Rationale: Sodium bicarbonate is first-line treatment of QRS complex prolongation caused by tricyclic antidepressant overdose.

2. E. Rationale: Amyl nitrite, sodium thiosulfate, and hydroxocobalamin are all used in the treatment of cyanide toxicity. Amyl nitrite is useful as a temporary therapy in the absence of IV access. Sodium thiosulfate regenerates sulfur-dependent rhodanese activity and is administered with or after hydroxocobalamin.

3. E. Rationale: Treatment of acetaminophen toxicity includes N-acetylcysteine. Early administration of NAC (i.e., within 8 hours of ingestion) will help protect the liver.

4. C. Rationale: The patient should be educated that ipecac should not be used for home management of poisoning. Local poison control centers have experts that are available 24 hours a day, 7 days a week to provide instructions if someone has been poisoned.

5. E. Rationale: Tachycardia, dry mucus membranes, urinary retention, as well as altered mental status, flushed skin, mydriasis, fever, and hypertension are all signs of anticholinergic toxicity.

6. C. Rationale: Sodium bicarbonate is used for the treatment of aspirin toxicity. Alkalinization of the urine promotes excretion of salicylates.

7. D. Rationale: Atropine is not used in ethylene glycol toxicity. Fomepizole is an inhibitor of alcohol dehydrogenase. Ethanol (EtOH) is used when fomepizole is not available. Pyridoxine and thiamine are cofactors in ethylene glycol metabolism. Pyridoxine enhances metabolism of glyoxylate to glycine; thiamine catalyzes metabolism of glyoxylate from glycolic acid.

8. B. Rationale: Naloxone is an opioid antagonist used to reverse respiratory depression in patients with opioid overdose.

9. D. Rationale: Flumazenil is an antidote for benzodiazepine overdose. It acts as a competitive antagonist at the central benzodiazepine receptor.

10. B. Rationale: Digibind dose (in vials)
 $= (\text{digoxin concentration [ng/mL]})(\text{body weight [kg]})/100$
 $= (4.1\text{ ng/mL} \times 80\text{kg})/100$
 $= 3.3\text{ vials (round to 4 vials)}$

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