PHARMACOLOGY

PreTest®
Self-Assessment
and Review

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Fourth Edition

Pharmacology:

PreTest® Self-Assessment and Review

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Pharmacology

NOTICE

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The editors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide drug dosage schedules that are complete and in accord with the standards accepted at the time of publication. However, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in these schedules is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

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Introduction

Pharmacology: PreTest® Self-Assessment and Review has been designed to provide medical students, as well as physicians, with a comprehensive and convenient instrument for self-assessment and review. The 500 questions provided have been designed to parallel the format and degree of difficulty of the questions contained in Part I of the National Board of Medical Examiners examinations, the Federation Licensing Examination (FLEX), and the Foreign Medical Graduate Examination in the Medical Sciences (FMGEMS). The drugs mentioned in these questions are those recognized by the authors as being particularly pertinent to basic pharmacology.

Each question in the book is accompanied by an answer, a paragraph explanation, and a specific page reference to either a current journal article, a textbook, or both. A bibliography, listing all the sources used in the book, follows the last chapter.

Perhaps the most effective way to use this book is to allow yourself one minute to answer each question in a given chapter; as you proceed, indicate your answer beside each question. By following this suggestion, you will be approximating the time limits imposed by the board examinations previously mentioned.

When you finish answering the questions in a chapter, you should then spend as much time as you need verifying your answers and carefully reading the explanations. Although you should pay special attention to the explanations for the questions you answered incorrectly, you should read **every** explanation. The contributors of this book have designed the explanations to reinforce and supplement the information tested by the questions. If, after reading the explanations for a given chapter, you feel you need still more information about the material covered, you should consult and study the references indicated.

This book meets the criteria established by the AMA's Department of Continuing Medical Education for up to 22 hours of credit in category 5D for the Physician's Recognition Award. It should provide an experience that is instructive as well as evaluative; we also hope that you enjoy it. We would be very happy to receive your comments.

Contents

General Principles

DIRECTIONS: Each question below contains five suggested answers. Choose the **one best** response to each question.

1. On the assumption that passive transport of the nonionized forms of the following drugs determines the rate of their absorption, which of the following drugs will be best absorbed in the small intestine?

(A) Acetylsalicylic acid (pK_a = 3.0)
(B) Ethacrynic acid (pK_a = 3.5)
(C) Sulfamethoxazole (pK_a = 5.6)
(D) Secobarbital (pK_a = 7.8)
(E) Theophylline (pK_a = 8.8)

2. If 91 percent of quinine, a weak base, is ionized in the blood, the pK_a of the drug is approximately

(A) 2.6
(B) 4.7
(C) 6.4
(D) 8.4
(E) 9.3

3. Drugs may be released slowly from various drug reservoirs over long periods of time. The body reservoir that holds the largest amount of the barbiturate thiopental is

(A) fat
(B) lung
(C) liver
(D) muscle
(E) serum albumin

4. Drug accumulation will occur after repeated injections if a drug is

(A) not metabolized by the liver
(B) administered intravenously
(C) administered at the $t_{1/2}$ of the drug
(D) distributed quickly into the extracellular space
(E) significantly protein-bound in the plasma

5. The route of excretion for drugs or their metabolic derivatives that is quantitatively the LEAST significant is which of the following?

(A) Biliary tract
(B) Kidneys
(C) Lungs
(D) Feces
(E) Milk

6. Oxidizable drugs form a complex with and are oxidized by which of the following iron-containing pigments in the microsomal fraction of liver?

(A) Cytochrome *a*
(B) Cytochrome *b*
(C) Cytochrome *c*
(D) Cytochrome c_1
(E) Cytochrome P-450

7. The following values were obtained for a patient: 24-hour urine volume = 720 ml; concentration of creatinine in 24-hr urine specimen = 0.6 mg/ml; and concentration of creatinine in plasma = 6.0 mg/100 ml. The patient's creatinine clearance (C_{Cr}) is

(A) 5 ml/min
(B) 10 ml/min
(C) 20 ml/min
(D) 60 ml/min
(E) 120 ml/min

8. The following pharmacokinetic data were obtained from a 70-kg patient treated with theophylline: plasma concentration = 10 μg/ml immediately after a dose of 5 mg/kg IV; plasma protein binding = 56%; biological $t_{1/2}$ = 8 hr. The total body clearance of theophylline in this patient was

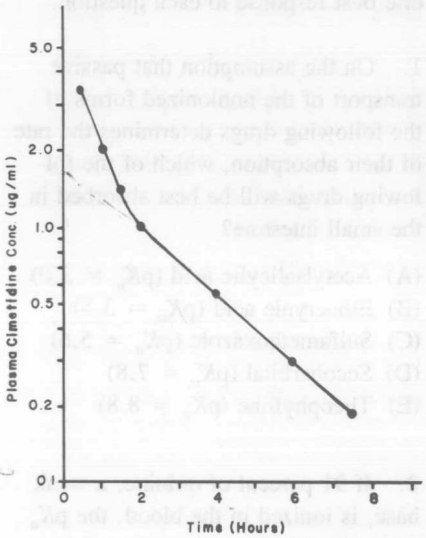
(A) 1.3 liters/hr
(B) 3 liters/hr
(C) 35 liters/hr
(D) 43 liters/hr
(E) 212 liters/hr

9. In the presence of impaired renal function, the time interval between maintenance doses needs to be lengthened for all the following antibiotics EXCEPT

(A) erythromycin
(B) streptomycin
(C) sulfisoxazole
(D) chlortetracycline
(E) ethambutol

Questions 10-13

Cimetidine (Tagamet) 200 mg was administered intravenously to a 70-kg man with peptic ulcer disease. The plasma concentrations of the drug were determined at various times after injection, as shown in the figure below.



10. The elimination half-life ($t_{1/2}$) of cimetidine (Tagamet) in this patient is

(A) 0.4 hr
(B) 0.8 hr
(C) 1.5 hr
(D) 2.3 hr
(E) 4.0 hr

11. The elimination rate constant (k_e) of cimetidine (Tagamet) in this patient is

(A) 0.1 hr^{-1}
(B) 0.2 hr^{-1}
(C) 0.3 hr^{-1}
(D) 0.4 hr^{-1}
(E) 0.5 hr^{-1}

12. The apparent volume of distribution of cimetidine (Tagamet) in this individual is

(A) 1.6 liters
(B) 39 liters
(C) 59 liters
(D) 111 liters
(E) 200 liters

13. The total body clearance of the drug is

(A) 33.5 liters/hr
(B) 48.0 liters/hr
(C) 60.0 liters/hr
(D) 255.0 liters/hr
(E) 370.5 liters/hr

14. If a drug has an elimination half-time ($t_{1/2}$) of 25 hr and 10 mg is administered intravenously every 12 hr, the expected average total body store of drug would be how many times greater than the 10 mg dose?

(A) 1.5
(B) 3.0
(C) 4.5
(D) 6.0
(E) 12.0

15. It was determined that 95 percent of an oral 80-mg dose of verapamil was absorbed in a 70-kg test subject. However, because of extensive biotransformation during its first pass through the portal circulation, the bioavailability of verapamil was only 25 percent. Assuming a liver blood flow of 1500 ml/min, the hepatic clearance of verapamil in this situation was

(A) 60 ml/min
(B) 375 ml/min
(C) 740 ml/min
(D) 1110 ml/min
(E) 1425 ml/min

16. Phase 2 clinical studies of a drug are for the purpose of

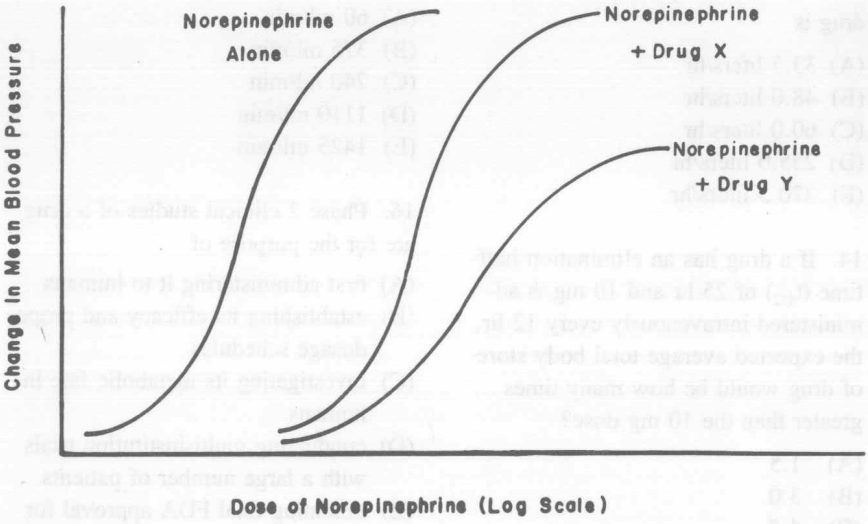
(A) first administering it to humans
(B) establishing its efficacy and proper dosage schedules
(C) investigating its metabolic fate in humans
(D) conducting multi-institution trials with a large number of patients
(E) obtaining final FDA approval for marketing

17. An enteric-coated dosage form can be used to avoid all the following problems possible from oral drug administration EXCEPT

(A) irritation to the gastric mucosa with nausea and vomiting
(B) destruction of the drug by gastric acid or digestive enzymes
(C) unpleasant taste of the drug
(D) formation of nonabsorbable drug-food complexes
(E) variability in absorption caused by fluctuations in gastric emptying time

18. The figure below shows the change in mean blood pressure as a result of increasing doses of norepinephrine and the antagonism of this response by drugs X and Y. Using the information provided in the diagram, which statement is correct?

(A) Drug X is a more potent antagonist than drug Y
(B) Drug X is a more effective antagonist than drug Y
(C) Drug Y shows the characteristics of competitive antagonism
(D) Drug Y shows the characteristics of noncompetitive antagonism
(E) None of the above



19. The pharmacokinetic value that most reliably reflects the amount of drug reaching the target tissue after oral administration is the

(A) peak blood concentration
(B) time to peak blood concentration
(C) product of the volume of distribution and the first-order rate constant
(D) volume of distribution
(E) area under the blood concentration-time curve

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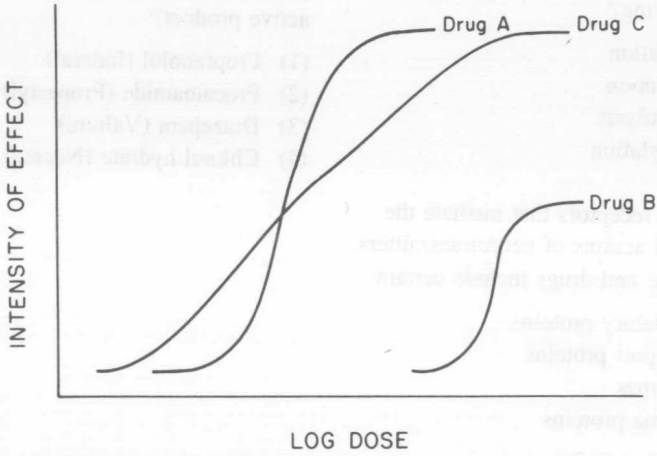
DIRECTIONS: Each question below contains four suggested answers of which **one** or **more** is correct. Choose the answer:

A	if	**1, 2, and 3**	are correct
B	if	**1 and 3**	are correct
C	if	**2 and 4**	are correct
D	if	**4**	is correct
E	if	**1, 2, 3, and 4**	are correct

20. From the graph below, correct statements include that



(1) Drug A is more potent than Drug B
(2) Drug A is less effective than Drug C
(3) Drug B is less effective than Drug C
(4) Drug A is more selective than Drug B

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21. Agents that appear to act via cellular receptors include

(1) mannitol
(2) halothane (Fluothane)
(3) ethylenediaminetetraacetic acid (EDTA)
(4) cimetidine (Tagamet)

22. Monitoring the blood levels of a drug is particularly important if the

(1) interpatient variability is considerable
(2) therapeutic index of the drug is low
(3) biological effect is difficult to monitor
(4) drug has a short duration of action

SUMMARY OF DIRECTIONS

A	B	C	D	E
1, 2, 3 only	1, 3 only	2, 4 only	4 only	All are correct

23. Biotransformation reactions classified as nonsynthetic include which of the following?

(1) Oxidation
(2) Reduction
(3) Hydrolysis
(4) Acetylation

24. True receptors that mediate the biological actions of neurotransmitters, hormones, and drugs include certain

(1) regulatory proteins
(2) transport proteins
(3) enzymes
(4) plasma proteins

25. Some drugs are transported across lipoid membranes by facilitated diffusion. This is a process that

(1) is carrier-mediated
(2) can be saturated
(3) is selective for certain compounds
(4) requires energy to function

26. Which of the following can be biotransformed to a pharmacologically active product?

(1) Propranolol (Inderal)
(2) Procainamide (Pronestyl)
(3) Diazepam (Valium)
(4) Chloral hydrate (Noctec)

DIRECTIONS: The groups of questions below consist of lettered choices followed by several numbered items. For each numbered item select the **one** lettered choice with which it is **most** closely associated. Each lettered choice may be used once, more than once, or not at all.

Questions 27-29

For each description of a drug reponse that follows, choose the term with which it is most likely to be associated.

(A) Supersensitivity
(B) Tachyphylaxis
(C) Tolerance
(D) Hyposensitivity
(E) Anaphylaxis

27. Immunologically mediated drug reaction observed soon after drug administration

28. A rapid reduction in the effect of a given dose of a drug after only one or two doses

29. Hyperreactivity to a drug seen as a result of denervation

Questions 30-32

For each description that follows, select the transmembranal transport mechanism it best defines.

(A) Filtration
(B) Simple diffusion
(C) Facilitated diffusion
(D) Active transport
(E) Endocytosis

30. Lipid-soluble drugs cross the membrane at a rate proportional to the concentration gradient across the membrane and the lipid:water partition coefficient of the drug

31. Bulk flow of water through membrane pores, resulting from osmotic differences across the membrane, transports drug molecules that fit through the membrane pores

32. Cell membranes engulf droplets of solutions that are released inside the cell

Questions 33-35

For each type of incompatibility described below, select the pair of substances that illustrates it.

(A) Tetracycline and milk
(B) Phenobarbital (Luminal) and secobarbital (Seconal)
(C) Isoproterenol (Isuprel) and propranolol (Inderal)
(D) Soap and benzalkonium chloride (Ionil)
(E) Doxycycline (Vibramycin) and chlortetracycline (Aureomycin)

33. Therapeutic incompatibility

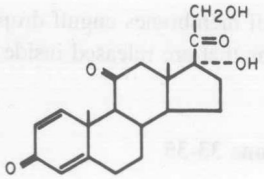
34. Physical incompatibility

35. Chemical incompatibility

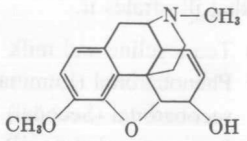
Questions 36-39

Many families of drugs consist of members that vary only with respect to substituents on a common ring structure. For each type of pharmacologic effect that follows, select the ring structure with which it is most likely to be associated.

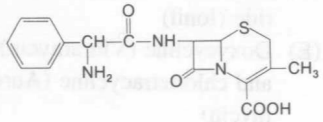
(A)



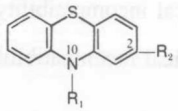
(B)



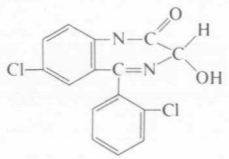
(C)



(D)



(E)



36. Analgesic

37. Antipsychotic

38. Antimicrobial

39. Anti-inflammatory

Questions 40-44

For each description that follows, choose the drug with which it is most likely to be associated.

(A) Chloramphenicol
(B) Doxycycline
(C) Erythromycin
(D) Methenamine mandelate
(E) Penicillin G

40. This drug, which normally is excreted as glucuronide by the kidneys, reaches toxic levels in newborn infants deficient in glucuronyl transferase

41. This drug becomes concentrated in the liver and is excreted in an active form in the bile

42. Can inhibit hepatic microsomal enzymes and increase the half-times and toxicity of other drugs metabolized by this system

43. Usually prepared as a potassium salt, it may contribute to a potassium imbalance in the presence of renal failure

44. Although systemically nontoxic, this drug is contraindicated in the presence of moderate to severe renal failure because it potentiates uremic acidosis

General Principles

Answers

1. The answer is E. *(Gilman, ed 6. p 4.)* The neutral nonionized form of a drug passes through a cellular membrane more easily than the ionized form because it is more lipid soluble. Thus, the rate of passive transport varies with the proportion of the drug that is nonionized. When the pH of a drug's environment is equal to its pK_a, the drug is half-dissociated. At an alkaline intestinal pH of about 8, of the drugs listed in the question, theophylline has the greatest percentage of its molecules in the nonionized form. The pH in the gastrointestinal tract is the major factor in absorption of many drugs. Weak acids (e.g., salicylates, barbiturates) are more readily absorbed from the stomach than from the other regions of the alimentary canal because these weak acids are mostly nonionized in the acidic environment of the stomach. The higher the value of the pK_a, the less ionized these acidic substances are in the stomach.

2. The answer is D. *(DiPalma, ed 2. p 21.)* The pH of the blood is approximately 7.35. The Henderson-Hasselbalch equation defines the pK_a and can be expressed as

$$pK_a = pH + \log \frac{\text{(percent of weak base ionized)}}{\text{(percent of weak base not ionized)}}$$

$$pK_a = 7.35 + \log \frac{(91)}{(9)}$$

$$pK_a = 7.35 + 1.0048$$

$$pK_a = 8.35$$

The transfer of drugs across membranes is dependent upon the pH of the internal environment and upon the pK_a of the drug. As the degree of ionization increases for a basic drug, the larger the value of the pK_a and the less the drug is permeable in membranes.

3. The answer is A. *(DiPalma, ed 2. p 27.)* Body fat may contain up to 70 percent of an administered dose of lipid-soluble thiopental 3 hours after injection. Other drugs may tend to accumulate in muscle or liver. For example, the concentration of the antimalarial drug quinacrine can be one thousand times greater in liver than in plasma. Serum albumin binds many drugs, some to appreciable degrees, thus reducing the free fraction that is pharmacologically effective. Plasma-bound drugs are readily released as the effective components are consumed by biotrans-

formation or excretion. Drugs are usually released much more slowly from fat because fat has a relatively limited blood supply.

4. The answer is C. *(Gilman, ed 6. pp 21-23.)* The elimination of most drugs from the body can be described as a first-order process. Thus a constant fraction of the drug present at a given moment is removed per unit time. Almost 94 percent of a drug is eliminated by four half-times ($t_{1/2}$), and, consequently, administration of drug after this time does not result in significant drug accumulation. In contrast, if the drug is administered at intervals shorter than the time necessary for its complete elimination, the drug will accumulate in the body regardless of route of administration, distribution, or metabolic fate.

5. The answer is E. *(Gilman, ed 6. pp 20-21.)* The amounts of drugs excreted in milk are small compared with those excreted by other routes; but drugs in milk may have significant, undesired pharmacologic effects on breast-fed infants. The principal route of excretion of the products of a given drug varies with the drug. Some drugs are predominantly excreted by the kidneys, whereas others leave the body in the bile and feces. Inhalation anesthetic agents are eliminated by the lungs. The path of excretion may affect the clinical choice of a drug, as is the case with renal failure or hepatic insufficiency.

6. The answer is E. *(DiPalma, ed 2. p 39.)* The smooth-surfaced endoplasmic reticulum of liver cells contains enzymes that oxidize some drugs and is found in the microsomal fraction of liver homogenates. Microsomal enzymes contain glucuronide transferases, oxidases, and some reductases and hydrolases. Cytochrome P-450 complexes with the drug to be oxidized (usually a lipophilic drug) and, with molecular oxygen and reduced cytochrome *c* reductase, oxidizes numerous functional groups. Oxidative reactions include: *N*- and *O*-dealkylation; aliphatic and aromatic hydroxylation; *N*-oxidation and *N*-hydroxylation; sulfoxide formation; deamination; and desulfuration. Cytochrome P-450 was so named because it absorbs light at 450 nm when complexed to carbon monoxide.

7. The answer is A. *(Curry, ed 3. pp 210-212.)* Creatinine clearance (C_{Cr}) is expressed in units of ml/min and is calculated according to the formula

$$C_{Cr} = \frac{(U_{Cr})\,(V)}{P_{Cr}}$$

where U_{Cr} represents the urinary concentration of creatinine in units of mg/ml, V represents the urine flow rate in units of ml/min, and P_{Cr} represents the plasma concentration of creatinine in mg/ml. After converting, where necessary, the data given in the question into appropriate units, the values for the terms of the formula are: U_{Cr}, 0.6 mg/ml (normal: 0.67 to 1.7); V, 0.5 ml/min (normal: 0.42 to 0.83);

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