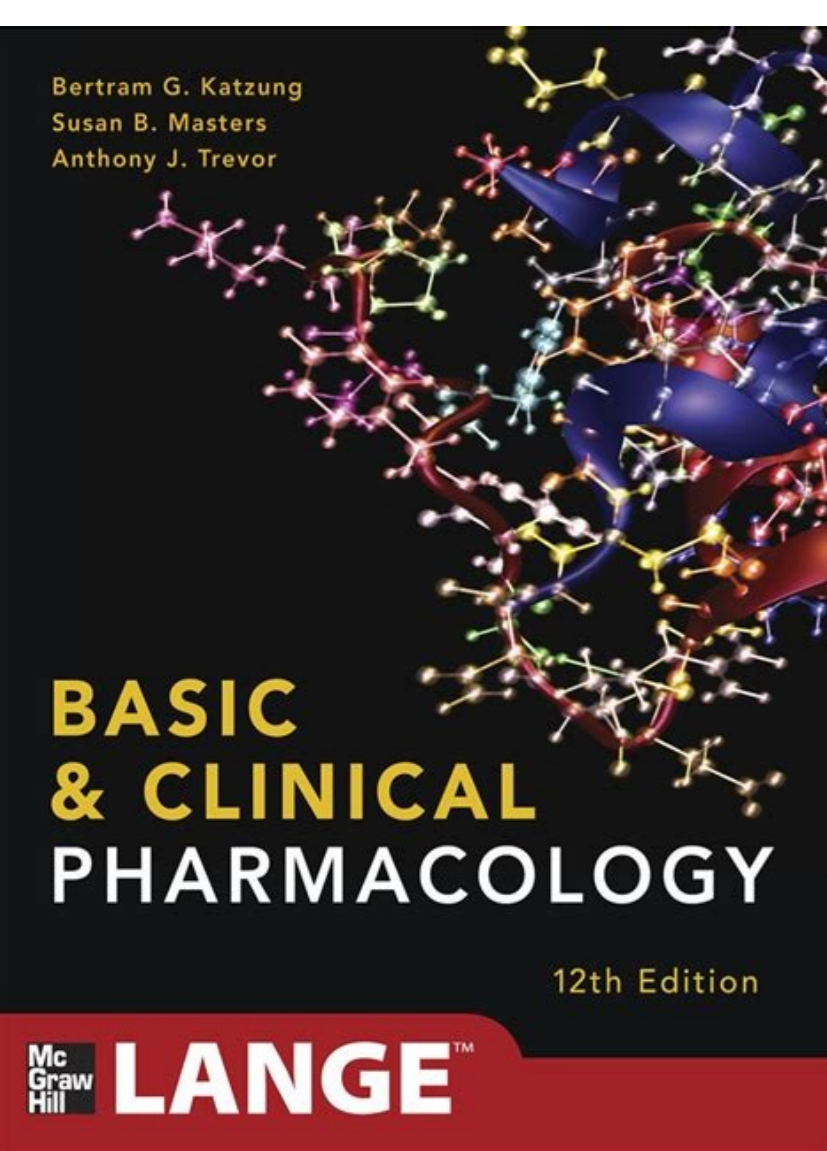


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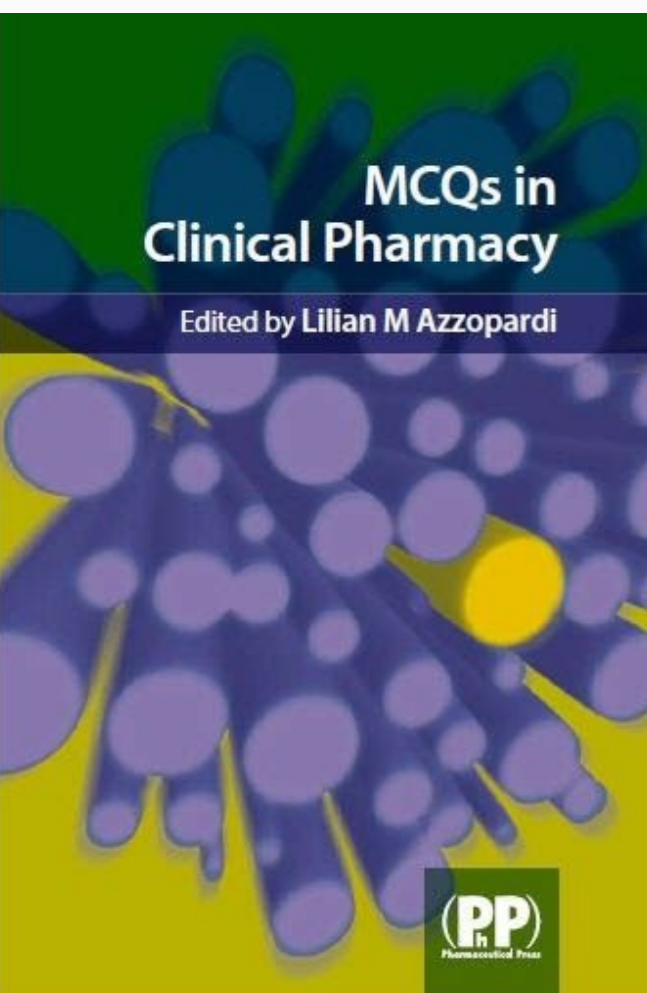
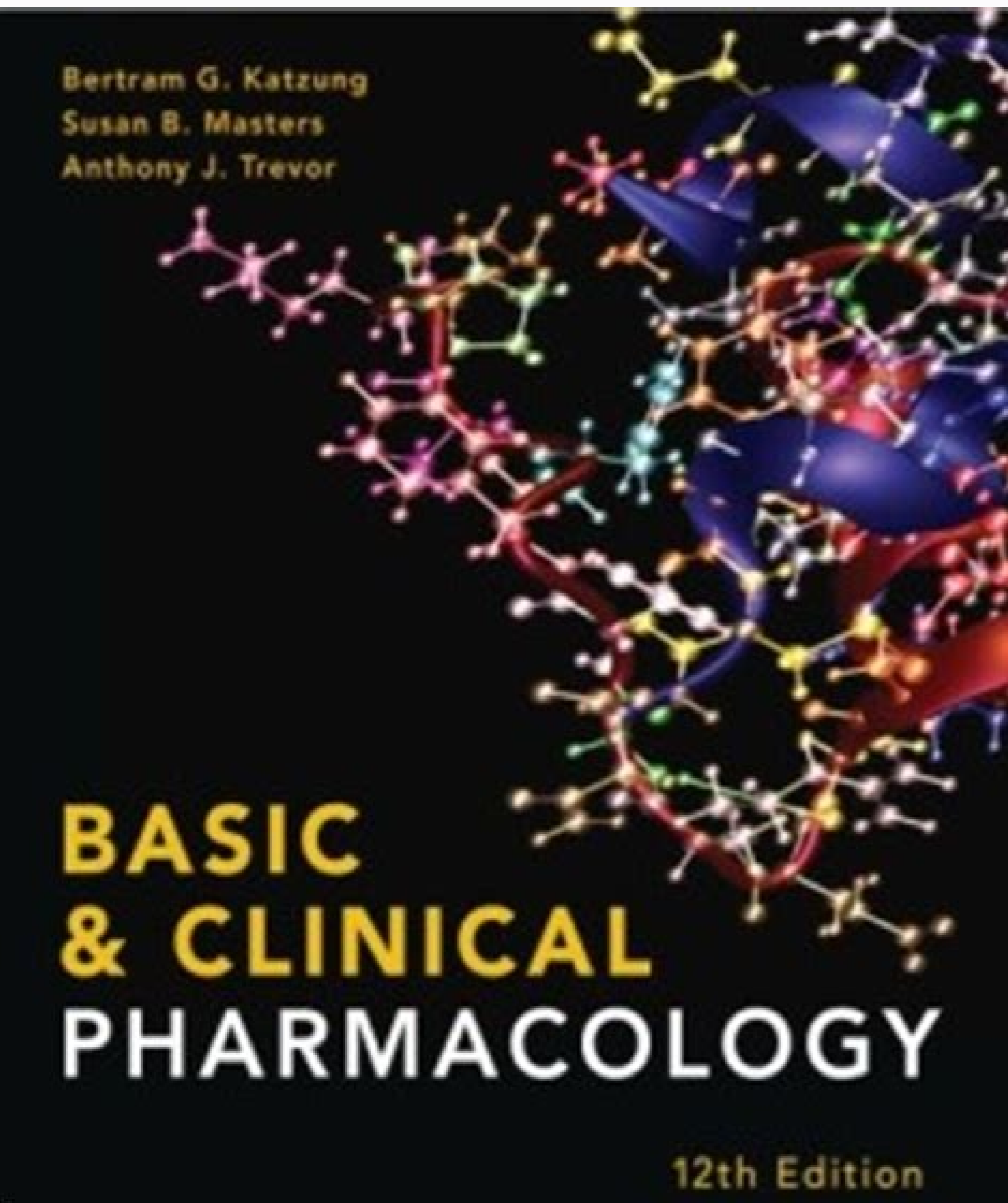


General rules of chemotherapy

•Aggressive high-dose chemotherapy

- Dose-** limiting is toxicity towards normal cells
- Cyclic regimens** - repeated administrations with appropriate intervals for regeneration of normal cells (e.g., bone marrow cells)
- Supportive therapy** - to reduce toxicity
 - hematotoxicity – bone marrow transplantation, hematopoietic growth factors
 - Specific antagonists: antifolate (methotrexate) – folate (leucovorin)
 - MESNA - donor of –SH groups, decreased urotoxicity of cyclophosphamide. Detoxifying agent.
 - dexrazoxane: chelates iron, reduced anthracycline cardiotoxicity
 - amifostine: reduces hematotoxicity, ototoxicity and neurotoxicity of alkylating agents

10



Use the following terms to answer the questions. A. 1.5 Drugs showing zero-order kinetics of elimination. B. Are more common than those showing first-order kinetics. C. Decrease in concentration exponentially with time. D. Have a half-life independent of dose. D. Show a plot of drug concentration versus time that is linear. E. Show a constant fraction of the drug eliminated per unit of time. | P a g e ¶ General Pharmacology MCQs 1.6 A drug, given as a 100-mg single dose, results in a peak plasma concentration of 20 µg/mL. The apparent volume of distribution is assumed to be equal to the actual volume of distribution (assume a rapid distribution and negligible elimination prior to measuring the peak plasma level). A. 0.5 L B. 1 L C. 2 L D. 5 L E. 10 L 1.7 A drug with a half-life of 12 hours is administered by continuous IV infusion. How long will it take for the drug to reach ninety percent of its final steady-state level? A. 18 hours. B. 24 hours. C. 30 hours. D. 40 hours. E. 90 hours. 1.8 Which of the following results in a doubling of the steady-state concentration of a drug? A. Doubling the rate of infusion. B. Maintaining the rate of infusion but doubling the loading dose. C. Doubling the rate of infusion and doubling the concentration of the infused drug. D. Tripling the rate of infusion. E. Quadrupling the rate of infusion. Pharmacodynamics 2.1 Which of the following statements is correct? A. If 10 mg of Drug A produces the same response as 100 mg of Drug B, Drug A is more efficacious than Drug B. B. The greater the efficacy, the greater the potency of a drug. C. In selecting a drug, potency is usually more important than efficacy. D. A competitive antagonist increases the ED50. E. Variation in response to a drug among different individuals is most likely to occur with a drug showing a large therapeutic index. 2.2 Variation in the sensitivity of a population of individuals to increasing doses of a drug is best determined by which of the following? A. Efficacy. B. Potency. C. Therapeutic index. D. Graded dose-response curve. E. Quantal dose-response curve. 2.3 Which of the following statements most accurately describes a system having spare receptors? A. The number of spare receptors determines the maximum effect. B. Spare receptors are sequestered in the cytosol. C. A single drug-receptor interaction results in many cellular response elements being activated. D. Spare receptors are active even in the absence of agonist. E. Agonist affinity for spare receptors is less than their affinity for nonspare receptors. | P a g e ¶ General Pharmacology MCQs Katzung's Questions (60 MCQ) : 1. A 3-year-old child is brought to the emergency department having just ingested a large over-dose of promethazine, an antihistaminic drug. Promethazine is a weak base with a pKa of 9.1. It is capable of entering most tissues, including the brain. On physical examination, the heart rate is 100/min, blood pressure 110/60 mm Hg, and respiratory rate 20/min. In this case of promethazine overdose: A. Urinary excretion would be accelerated by administration of NH4Cl B. Urinary excretion would be accelerated by giving NaHCO3 C. More of the drug would be ionized at blood pH than at stomach pH D. Absorption of the drug would be faster from the stomach than from the small intestine E. Hemodialysis is the only effective therapy 2. All of the following are general mechanisms of drug permeation EXCEPT A. Aqueous diffusion B. Aqueous hydrolysis C. Lipid diffusion D. Endocytosis E. Special carrier transport 3. Which one of the following processes is best suited for permeation of very large protein molecules into cells ? A. Aqueous diffusion B. Aqueous hydrolysis C. Lipid diffusion D. Endocytosis E. Special carrier transport 4. A patient with a history of episodic attacks of coughing, wheezing, and shortness of breath is being evaluated in the asthma clinic. Several drug treatments with different routes of administration are under consideration. Which of the following statements about routes of administration is MOST correct? A. Blood levels often rise more slowly after intramuscular injection than after oral dosing B. The "first-pass" effect is the result of metabolism of a drug after administration and before it enters the systemic circulation C. Administration of antiasthmatic drugs by inhaled aerosol is usually associated with more adverse effects than is administration of these drugs by mouth D. Bioavailability of most drugs is greater with rectal (suppository) administration than with sublingual administration. E. Administration of a drug by transdermal patch is often faster but is associated with more first-pass metabolism than oral administration 5. Aspirin is a weak organic acid with a pKa of 3.5. What percentage of a given dose will be in the lipid-soluble form in the duodenum at a pH of 4.5? A. About 1% B. About 10% C. About 50% D. About 90% E. About 99% | P a g e ¶ General Pharmacology MCQs 6. If the plasma concentration of a drug declines with "first-order kinetics," this means that A. There is only one metabolic path for drug disposition B. The half-life is the same regardless of the plasma concentration C. The drug is largely metabolized in the liver after oral administration and has low bioavailability D. The rate of elimination is proportional to the rate of administration at all times E. The drug is not distributed outside the vascular system 7. Regarding termination of drug action , A. Drugs must be excreted from the body to terminate their action B. Metabolism of drugs always increases their water solubility C. Metabolism of drugs always abolishes their pharmacologic activity D. Hepatic metabolism and renal excretion are the two most important mechanisms involved E. Distribution of a drug out of the bloodstream terminates the drug's effects 8. Distribution of drugs to specific tissues A. Is independent of blood flow to the organ B. Is independent of the solubility of the drug in that tissue C. Depends on the unbound drug concentration gradient between blood and the tissue D. Is increased for drugs that are strongly bound to plasma proteins E. Has no effect on the half-life of the drug 9. Timolol is being considered for the treatment of glaucoma in a 58-year-old patient. Except for elevated intraocular pressure, the patient's history and physical exam are unremarkable. Timolol is a weak base of pKa 9.2 . Which of the following statements is FALSE ? A. After parental administration, the concentration of timolol in the aqueous humor (pH 7.8) will be lower than the concentration in the duodenum (pH 5.5) B. When administered as eye drops, the rate of absorption into the eye will be slower if the drops are alkaline (pH 8.0) than if they are acidic (pH 5.0) C. Excretion in the urine will be slower if urine pH is alkaline (pH 8.0) than if the urine pH is acidic (pH 5.8) D. The proportion of timolol in the protonated form will be approximately 10% at pH 8.2 E. The proportion of timolol in the more lipid soluble form will be approximately 10% at pH 10.2 10. For which of the following drugs will excretion be most significantly accelerated by acidification of the urine ? A. Weak acid with pK of 5.5 B. Weak base with pK of 3.5 C. Weak acid with pK of 7.5 D. Weak base with pK of 6.5 | P a g e ¶ General Pharmacology MCQs 11. A physical process by which a weak acid becomes less water-soluble and more lipid-soluble at low pH is : A. Distribution B. Elimination C. First-pass effect D. Permeation E. Protonation 12. The set of properties that characterize the effect of a drug on the body is called : A. distribution B. permeation C. pharmacodynamics D. pharmacokinetics E. protonation 13. The set of properties that characterize the effect of the body on a drug is called : A. absorption B. distribution C. elimination D. first-order kinetics E. pharmacokinetics 14. The most general term for the process by which the amount of active drug in the body is reduced after absorption into the systemic circulation : A. distribution B. elimination C. excretion D. first-order elimination E. metabolism 15. The process by which the amount of drug in the body is reduced after administration but before entering the systemic circulation : A. excretion B. first-order elimination C. first-pass effect D. metabolism E. pharmacokinetics 16. The kinetics that is characteristic of the elimination of ethanol and high doses of phenytoin and aspirin are called : A. distribution B. excretion C. first-pass effect D. first-order elimination E. zero-order elimination | P a g e ¶ General Pharmacology MCQs 17. A 55-year-old woman with heart failure is to be treated with a diuretic drug. Drugs X and Y have the same mechanism of diuretic action. Drug X in a dose of 5 mg produces the same magnitude of diuresis as 500 mg of drug Y. This suggests that A. Drug Y is less efficacious than drug X B. Drug X is about 100 times more potent than drug Y C. Toxicity of drug X is less than that of drug Y D. Drug X is a safer drug than drug Y E. Drug X will have a shorter duration of action than drug Y because less of drug X is present for a given effect 18. Dose-response curves are used for drug evaluation in the animal laboratory and in the clinic. Quantal dose-response curves are A. Used for determining the therapeutic index of a drug B. Used for determining the maximal efficacy of a drug C. more precisely quantitated than ordinary graded dose-response curves D. Obtainable from the study of intact subjects but not from isolated tissue preparations E. Used to determine the statistical variation (standard deviation) of the maximal response to the drug 19. The results shown in the graph below were obtained in a comparison of positive inotropic agents. Which of the following statements is MOST correct ? A. B. C. D. E. Drug A is most effective Drug B is least potent Drug C is most potent Drug B is more potent than drug C and more effective than drug A Drug A is more potent than drug B and more effective than drug C 20. In the absence of other drugs, pindolol causes an increase in heart rate by activating beta adrenoreceptors. In the presence of highly effective beta stimulants, however, pindolol causes a dose-dependent, reversible decrease in heart rate. Therefore, pindolol should be classified as A. An irreversible antagonist B. A physiologic antagonist C. A chemical antagonist D. A partial agonist E. A spare receptor agonist | P a g e ¶ General Pharmacology MCQs 25. Which of the following terms best describes a drug that blocks the action of epinephrine at its receptors by occupying those receptors without activating them? A. Pharmacologic antagonist B. Partial agonist C. Physiologic antagonist D. Chemical antagonist E. Noncompetitive antagonist 26. Which of the following provides information about the variation in sensitivity to the drug within the population studied ? A. Maximal efficacy B. Therapeutic index C. Drug potency D. Graded dose-response curve E. Quantal dose-response curve 27. Which of the following most accurately describes the transmembrane signaling process involved in steroid hormone action ? A. Action on a membrane-spanning tyrosine kinase B. Activation of a G protein, which activates or inhibits adenylyl cyclase C. Diffusion into the cytoplasm and binding to an intracellular receptor D. Diffusion of "STAT" molecules across the membrane E. Opening of transmembrane ion channels 28. Which of the following provides information about the largest response a drug can produce, regardless of dose ? A. Drug potency B. Maximal efficacy C. Mechanism of receptor action D. Therapeutic index E. Therapeutic window 29. Verapamil and phenytoin are both eliminated from the body by metabolism in the liver. Verapamil has a clearance of 1.5 L/min, approximately equal to liver blood flow, whereas phenytoin has a clearance of 0.1 L/min. When these compounds are administered along with rifampin, a drug that increases hepatic drug-metabolizing enzymes, which of the following is most likely? A. The clearance of both verapamil and phenytoin will be increased B. The clearance of both verapamil and phenytoin will be decreased C. The clearance of verapamil will be unchanged, whereas the clearance of phenytoin will be increased D. The clearance of phenytoin will be unchanged, whereas the clearance of verapamil will be increased E. The clearance of both drugs will be unchanged | P a g e ¶ General Pharmacology MCQs Each of the curves in the graph below may be considered a concentration effect curve or a concentration-binding curve. For each numbered item, select the ONE lettered option that is most closely associated with it. 30. Describes the percentage binding of a full agonist to its receptors as the concentration of a partial agonist is increased from low to very high levels A. curve 1 B. curve 2 C. curve 3 D. curve 4 E. curve 5 31. Describes the percentage effect when a full agonist is present throughout the experiment, and the concentration of a partial agonist is increased from low to very high levels A. curve 1 B. curve 2 C. curve 3 D. curve 4 E. curve 5 32. Describes the percentage binding of the partial agonist whose effect is shown by curve 4, if the system has many spare receptors A. curve 1 B. curve 2 C. curve 3 D. curve 4 E. curve 5 33. A city clinic is considering the substitution of generic drugs in order to save money. The clinical pharmacologist is asked to advise on the bioavailability of the generic products. She informs the head of the clinic that the bioavailability of drugs is : A. Established by FDA regulation 100% for preparations for intramuscular injection B. 100% for oral preparations that are not metabolized in the liver C. Calculated from the peak concentration of drug divided by the dose administered D. Important because bioavailability determines what fraction of the administered dose reaches the systemic circulation E. Equal to 1 (100%) only for drugs administered by any parenteral route | P a g e ¶ General Pharmacology MCQs 34. You have diagnosed asthma in a 19-year-old patient with recurrent, episodic attacks of bronchospasm with wheezing. You are concerned about drug interactions caused by changes in drug metabolism in this patient. Drug metabolism usually results in a product that is A. More likely to distribute intracellularly B. Less lipid-soluble than the original drug C. More likely to be reabsorbed by kidney tubules D. More lipid-soluble than the original drug E. More likely to produce adverse effects 35. If therapy with multiple drugs causes induction of drug metabolism in your asthma patient, it will A. Result in increased smooth endoplasmic reticulum B. Result in increased rough endoplasmic reticulum C. Result in decreased enzymes in the soluble cytoplasmic fraction D. Require 3-4 months to reach completion E. Be irreversible 36. A factor that is likely to increase the duration of action of a drug that is partially metabolized by CYP3A4 in the liver is A. Chronic administration of phenobarbital prior to and during therapy with the drug in question B. Chronic therapy with cimetidine prior to and during therapy with the drug in question C. Displacement from tissue binding sites by another drug D. Increased cardiac output E. Chronic administration of rifampin 37. Which of the following is a phase II drug-metabolizing reaction? A. Acetylation B. Deamination C. Hydrolysis D. Oxidation E. Reduction 38. Reports of cardiac arrhythmias caused by unusually high blood levels of two antihistamines (terfenadine and astemizole, led to their removal from the market. These effects were best explained by A. Concomitant treatment with phenobarbital B. Use of these drugs by smokers C. A genetic predisposition to metabolize succinylcholine slowly D. Treatment of these patients with ketoconazole, an antifungal agent 39. Which of the following drugs is associated with slower metabolism in Caucasians and African-Americans than in most Asians? A. Cimetidine B. Procaainamide C. Quinidine D. Rifampin E. Succinylcholine | P a g e ¶ General Pharmacology MCQs 40. Which of the following drugs may inhibit the hepatic microsomal P450 responsible for warfarin metabolism? A. Cimetidine B. Ethanol C. Phenobarbital D. Procaainamide E. Rifampin 41. Which of the following drugs is hydrolyzed by a plasma esterase that is abnormally low in activity in about one out of every 2500 humans? A. Cimetidine B. Ethanol C. Procaainamide D. Rifampin E. Succinylcholine 42. Chronic use of which of the following drugs may increase the toxicity of acetaminophen? A. Cimetidine B. Ethanol C. Ketoconazole D. Procaainamide E. Quinidine F. Ritonavir G. Succinylcholine H. Verapamil 43. Which of the following drugs has higher first-pass metabolism in men than in women ? A. Cimetidine B. Ethanol C. Ketoconazole D. Procaainamide E. Quinidine F. Ritonavir G. Succinylcholine H. Verapamil 44. Which of the following drugs is an established inhibitor of P-glycoprotein (P-gp) drug transporters ? A. Cimetidine B. Ethanol C. Ketoconazole D. Procaainamide E. Quinidine F. Ritonavir G. Succinylcholine H. Verapamil | P a g e ¶ General Pharmacology MCQs 45. Which of the following agents, when used in combination with other anti-HIV drugs permits dose reduction ? A. Cimetidine B. Ethanol C. Ketoconazole D. Procaainamide E. Quinidine F. Ritonavir G. Succinylcholine H. Verapamil Problem Solving Questions (Katzung) : Mr. Jones is admitted to General Hospital with pneumonia due to gram-negative bacteria. The antibiotic tobramycin is ordered. The CL and Vd of tobramycin in Mr. Jones are 80 mL/min and 40 L, respectively. 46. What maintenance dose should be administered intravenously every 6 hours to eventually obtain average steady-state plasma concentrations of 4 mg/L? A. 0.32 mg B. 19.2 mg C. 115 mg D. 160 mg E. 230 mg 47. If you wish to give Mr. Jones an IV loading dose to achieve the therapeutic plasma concentration of 4 mg/L rapidly, how much should be given? A. 0.1 mg B. 10 mg C. 115.2 mg D. 160 mg E. None of the above 48. Despite your careful adherence to basic pharmacokinetic principles, your patient on digoxin therapy has developed digitalis toxicity. The plasma digoxin level is 4 mg/mL. Renal function is normal, and the plasma 1/2 of digoxin in this patient is 1.6 days. How long should you withhold digoxin in order to reach a safer yet probably therapeutic level of 1 mg/mL? A. 1.6 days B. 2.4 days C. 3.2 days D. 4.8 days E. 6.4 days | P a g e ¶ General Pharmacology MCQs 49. A 60-year-old man enters the hospital with a myocardial infarction and a severe ventricular arrhythmia. The antiarrhythmic drug chosen has a narrow therapeutic window; the minimum toxic plasma concentration is 1.5 times the minimum therapeutic plasma concentration. The half-life is 6 hours. It is essential to maintain the plasma concentration above the minimum therapeutic level to prevent a possibly lethal arrhythmia. Of the following, the most appropriate dosing regimen would be A. Once a day B. Twice a day C. Three times a day D. Four times a day E. Constant IV infusion 50. A 50-year-old woman with metastatic breast cancer has elected to participate in the trial of a new chemotherapeutic agent. It is given by constant IV infusion of 8 mg/hour. Plasma concentrations (Cp) are measured with the results shown in the table. Time After Plasma Start of Concentration Infusion (mg/L) (hours) 1 0.8 2 1.3 4 2.0 8 3.0 10 3.6 16 3.7 20 3.84 25 3.95 30 4.0 40 4.0 From these data it may be concluded that A. Volume of distribution is 20 L B. Clearance is 2 L/h C. Elimination follows zero-order kinetics D. Half-life is 8 hours E. Doubling the rate of infusion would result in a plasma concentration of 16 mg/L at 40 hours 51. A nineteen-year-old woman is brought to the hospital with severe asthmatic wheezing. You decide to use IV theophylline for treatment. The pharmacokinetics of theophylline include the following average parameters: Vd 35 L; CL 48 mL/min; half-life 8 hours. If an IV infusion of theophylline is started at a rate of 0.48 mg/min, how long will it take to reach 93.75% of the final steady state concentration? A. Approximately 48 minutes B. Approximately 7.4 hours C. Approximately 8 hours D. Approximately 24 hours E. Approximately 32 hours | P a g e ¶ General Pharmacology MCQs 52. Your 74-year-old patient with a myocardial infarction has a severe cardiac arrhythmia. You have decided to give lidocaine to correct the arrhythmia. A continuous IV infusion of lidocaine, 1.92 mg/min, is started at 8 am. The average pharmacokinetic parameters of lidocaine are: Vd 77 L; CL 640 mL/min; half-life 1.4 hours. The expected steady-state plasma concentration is approximately A. 40 mg/L B. 3.0 mg/L C. 0.025 mg/L D. 7.2 mg/L E. 3.46 mg/L 53. Your patient has been receiving lidocaine for 8 hours and you decide to obtain a plasma concentration measurement. When the results come back, the plasma level is exactly twice of what you expected. The infusion rate should : A. be changed to 0.48 mg/min B. be changed to 0.96 mg/min C. be halted for 1.4 h and then restarted at 0.96 mg/min D. be halted for 1.4 h and then restarted at 1.92 mg/min E. not be changed but the plasma level should be measured again 54. A patient requires an infusion of procainamide. Its half-life is 2 hours. The infusion is begun at 9 AM. At 1 PM the same day a blood sample is taken; the drug concentration is found to be 3 mg/L. What is the probable steady-state drug concentration, eg, after 12 hours of infusion? A. 3 mg/L B. 4 mg/L C. 6 mg/L D. 9.9 mg/L E. 15 mg/L 55. A young man is brought to the emergency room in a deep coma. His friends state that he took a large dose of morphine 6 hours earlier. An immediate blood analysis shows a morphine blood level of 0.25 mg/L. Assuming that the pharmacokinetics of morphine in this patient are Vd 200 L and half-life is 3 hours, how much morphine did the patient inject 6 hours earlier ? A. 25 mg B. 50 mg C. 100 mg D. 200 mg E. not enough data to predict 56. A normal volunteer will receive a new drug in a phase I clinical trial. The clearance and volume of distribution of the drug in this subject are 1.386 L/h and 80 L, respectively. The half-life of the drug in this subject will be approximately: A. 83 hours B. 77 hours C. 58 hours D. 40 hours E. 0.02 hours | P a g e ¶ General Pharmacology MCQs 57. Gentamicin is often given in intermittent IV bolus doses of 100 mg three times a day to achieve target peak plasma concentration of about 5 mg/L. Gentamicin's clearance (normally 5.4 L/h/70kg) is almost entirely by glomerular filtration. Your patient, however, is found to have a creatinine clearance one-third of normal. Your initial dosage regimen for this patient would probably be: A. 20 mg three times a day B. 33 mg three times a day C. 72 mg three times a day D. 100 mg twice a day E. 150 mg twice a day A new drug was studied in 20 healthy volunteers to determine basic pharmacokinetic parameters. A dose of 100 mg was administered as an intravenous bolus to each volunteer and blood samples were analyzed at intervals as shown in the graph below. The average plasma concentrations at each time are shown by the solid circles at 10 and 30 minutes and at 1, 2, 3, 4, 6, and 8 hours after administration. 58. The elimination half-life of the new drug is approximately A. 1.5 hours B. 2 hours C. 4 hours D. 6 hours E. 8 hours 59. The volume of distribution of the new drug is approximately A. 0.05 L B. 0.1L C. 5 L D. 10 L E. 20 L 60. The clearance of the new drug is approximately A. 0.43 L/h B. 0.86 L/h C. 1.15L/h D. 2.3 L/h E. Too few data to answer | P a g e ¶

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