

Directions: Select the **SINGLE** best choice

THE FOLLOWING INFORMATION APPLIES TO THE NEXT THREE (3) QUESTIONS:

Your 75 kg patient has potentially life-threatening symptoms. You need to achieve a blood plasma concentration of 5 mg/L of a drug quickly to stabilize his condition. The drug is known to distribute rapidly in total body water (0.6 L/kg), and has an elimination half-life of 8 hours.

1. Which loading dose listed below will immediately establish a therapeutic level closest to your target concentration?

A. 80 mg
B. 200 μ g
C. 0.25 g
D. 0.75 g
E. 3 g

$$0.6 \times 75 = V_d = 45 \text{ L}$$

$$5 \frac{\text{mg}}{\text{L}} \times 45 \text{ L} = \underline{225 \text{ mg}}$$

2. After administering the loading dose, you immediately start an i.v. drip that will maintain the desired drug concentration. What is the closest rate of drug administration that will achieve this aim?

A. 12 mg/h
B. 20 mg/h
C. 75 mg/h
D. 110 mg/h
E. 200 mg/h

$$C_{ss} = \frac{DR}{CL} \Rightarrow DR = C_{ss} \times CL = 5 \frac{\text{mg}}{\text{L}} \times 3.90 \frac{\text{L}}{\text{h}} =$$

$$CL = \frac{0.693 V_d}{t_{1/2}} = \frac{0.693(45 \text{ L})}{8 \text{ h}} = 3.90$$

$$\underline{19.50}$$

3. After two days of drug administration you notice toxic side effects and decide to halve the dose. Approximately how long will it take to reach the new steady-state blood concentration of the drug?

A. 32 h
B. 20 h
C. 12 h
D. 3 h
E. 1 h

4. Which of the following agents is a selective D_1 (dopamine₁) receptor agonist that can be used to reduce severely elevated blood pressure and can improve renal blood flow in spite of the decreased arterial pressure, and thus maintain or increase urine output?
- A. phenylpropanolamine
 - B. metoprolol
 - C. fenoldopam
 - D. prazosin
 - E. dopamine
5. A 66 year old hypertensive man was recently diagnosed with benign prostatic hypertrophy (BPH). His urologist suggested that one drug could be used to treat both his hypertension and his BPH. The drug most likely to be used is a
- A. non-selective β_1 adrenergic receptor antagonist.
 - B. nicotinic (N_2) ganglionic receptor agonist.
 - C. muscarinic M_2 receptor agonist.
 - D. selective α_1 adrenergic receptor antagonist.
 - E. indirect acting sympathomimetic amine.
6. A 72 year-old man with hypertension and angina pectoris is treated with metoprolol. In this patient, metoprolol is exerting its therapeutic effects by each of the following mechanisms **EXCEPT**
- A. blockade of vascular adrenergic receptors.
 - B. reduction of the release of renin and lowering of plasma angiotensin II levels.
 - C. decreasing cardiac cAMP formation.
 - D. reducing myocardial contractility.
 - E. blocking β_1 adrenergic receptors with relative selectivity.
7. Which statement about neurotransmission in postganglionic sympathetic nerves is **TRUE**?
- A. The primary mechanism of the removal of norepinephrine released from nerves into the synaptic space is metabolism by monoamine oxidase.
 - B. The transport of norepinephrine into the synaptic vesicle is blocked by cocaine.
 - C. Activation of presynaptic α_2 receptors increases the amount of norepinephrine released with subsequent nerve impulses
 - D. Activation of α_1 adrenergic receptors results in the intracellular increase in cyclic AMP.
 - E. Indirect acting sympathomimetic amines, like amphetamine, are transported into the nerve terminal by the neuronal membrane transporter

8. Which of the following drugs binds to adrenergic receptors, contracts smooth muscle, and increases intracellular inositol-1,4,5-trisphosphate (IP₃)?
- A. albuterol
 - B. amphetamine
 - C. cyproheptadine
 - D. carbachol
 - E. phenylephrine
9. Administration of propranolol to a 46 year-old diabetic woman may cause each of the following **EXCEPT**
- A. block the tachycardic response to insulin-induced hypoglycemia.
 - B. slow the recovery of plasma glucose levels after insulin administration.
 - C. bradycardia.
 - D. decreased exercise performance.
 - E. skeletal muscle tremor.
10. A 54 year-old hypertensive patient who is being treated with prazosin reports dizziness immediately after getting out of bed in the morning. The most likely explanation of the dizziness is the ability of prazosin to
- A. inhibit sympathetic reflexes to the heart.
 - B. produce orthostatic hypertension.
 - C. block nicotinic ganglionic receptors.
 - D. prevent vasoconstriction subsequent to activation of baroreceptors.
 - E. cause renal vasodilation and diuresis.
11. Each of the following drugs is paired with a likely therapeutic use **EXCEPT**
- A. albuterol : bronchial asthma
 - B. phenylephrine : acute hypertensive crisis
 - C. phentolamine : erectile dysfunction
 - D. dobutamine : cardiogenic shock
 - E. pindolol : chronic hypertension
12. Which statement concerning lead intoxication is **TRUE**?
- A. Children are more sensitive than adults to overt encephalopathy.
 - B. Children are more sensitive than adults to peripheral neuropathy.
 - C. An increase in erythrocyte protoporphyrin in blood is an indication that blood lead has reached levels consistent with those of hemolytic anemia.
 - D. Bone lead cannot be mobilized with chelating agents.
- (NO fifth choice is offered for this question.)

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13. Which statement concerning carbon monoxide kinetics is **TRUE**?
- A. At 50% carboxyhemoglobin, the molecular ratio of carbon monoxide to hemoglobin is approximately 245.
 - B. At 50% carboxyhemoglobin, the ratio of the partial pressure of carbon monoxide to that of oxygen is 245.
 - C. At 50% carboxyhemoglobin, the hemoglobin-oxygen dissociation curve is to the left of that for hemolytic anemia, in which hemoglobin is one-half of normal.
 - D. The biological half-life of carboxyhemoglobin is independent of the PO_2 .
 - E. None of the above.
14. In organophosphate nerve agent intoxication, atropine is administered to
- A. re-activate the acetylcholinesterase.
 - B. interact directly with the nerve agent to prevent further inhibition of the acetylcholinesterase.
 - C. counteract the direct effect of the nerve agent on the muscarinic cholinergic receptor.
 - D. counteract the effect of the excessive levels of acetylcholine on the muscarinic cholinergic receptor.
 - E. potentiate the reactivation of acetylcholinesterase by 2-PAM.
15. The most important mechanistic difference between the nerve agent, soman, and other organophosphate anticholinesterase agents (sarin, tabun, VX) which affects the ability to provide antidotal therapy for soman intoxication is the
- A. rate of onset of signs and symptoms of nerve agent intoxication following aerosol exposure to a lethal concentration of soman.
 - B. direct interaction between atropine and soman.
 - C. direct interaction between pyridostigmine and soman.
 - D. rate of "ageing" of the soman-acetylcholinesterase bond.
 - E. ability of soman to activate acetylcholinesterase.
16. Pyridostigmine
- A. is a very effective antidote when administered orally, after exposure to a nerve agent, for the reversal of nerve agent intoxication.
 - B. is very effective in binding directly with the organophosphate nerve agents.
 - C. functions as an adjunct to atropine and must be administered before exposure to an organophosphate nerve agent.
 - D. prevents reactivation of acetylcholinesterase by 2-PAM.
 - E. counteracts the direct effect of the nerve agent on the muscarinic cholinergic receptor.

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17. A new antihistamine that it is metabolized by the cytochrome P450 system is being evaluated. The clearance of the drug is increased in tobacco smokers. Which of the following cytochrome P450 isoforms would you expect to be involved in the metabolism of the new drug?
- A. CYP2C19
 - B. CYP1A2
 - C. CYP3A
 - D. CYP2C9
 - E. CYP2D6
18. Which of the following reactions is **NOT** commonly used to metabolize drugs?
- A. O-dealkylation
 - B. hydroxylation
 - C. conjugation with glutathione
 - D. methylation
 - E. phosphorylation
19. You are asked to evaluate a liver transplant patient who is having difficulty maintaining therapeutic concentrations of cyclosporin A due to rapid metabolism of the drug via CYP3A. Which drug is a useful rapid metabolic inhibitor that might be added to the patient's medical regimen?
- A. codeine
 - B. ranitidine
 - C. omeprazole
 - D. disulfiram
 - E. ketoconazole
20. During a routine medical check-up, a 25 year-old female complains of fatigue and muscular weakness. You see that she has ptosis (one eyelid droops). An electromyographic test shows decremental response of skeletal muscle to stimulation of the nerve. To verify your diagnosis, what drug should you administer just prior to repeating the electromyograph?
- A. edrophonium
 - B. tubocurarine
 - C. succinylcholine
 - D. pyridostigmine
 - E. prednisone

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21. A 26 year-old man has a severe hypotensive episode during knee surgery. This episode might have been prevented if the anesthesiologist had induced muscle relaxation with
- A. physostigmine.
 - B. tubocurarine.
 - C. pyridostigmine.
 - D. succinylcholine.
 - E. pancuronium.
22. Compared with lidocaine and procaine, cocaine is the only one of the three that
- A. is metabolized by plasma cholinesterase.
 - B. blocks uptake of norepinephrine by adrenergic nerve terminals and increases blood pressure.
 - C. does not block pain nerve fibers.
 - D. can enter the CNS and cause seizures (convulsions).
 - E. is metabolized in the liver.
23. In the emergency room, a 22 year-old Army Ranger who requires sutures for a cut on his hand tells you that he is allergic to procaine. Before suturing, you should
- A. inject lidocaine at the site of the cut.
 - B. inject a solution of procaine that does not contain epinephrine.
 - C. have his plasma cholinesterase levels determined in the lab.
 - D. tell him to forego the local anesthetic and just bite on a bullet.
 - E. inject procaine, but be prepared to treat an anaphylactic reaction.
24. After the intravenous administration of thiopental, patients are rendered profoundly unconscious for 3-5 minutes. If no other drugs are given, a patient will quickly regain consciousness because
- A. ester hydrolysis causes rapid breakdown of thiopental in the plasma.
 - B. of the first pass metabolism of thiopental in the liver.
 - C. of the redistribution of thiopental to muscle and fat.
 - D. of the rapid binding of thiopental to plasma albumin.
 - E. thiopental has an ultra-short metabolic half-life
25. All of the following will increase the rate of onset of an inhalational anesthetic agent **EXCEPT**
- A. increasing pulmonary ventilation.
 - B. increasing pulmonary blood flow.
 - C. decreasing agent solubility.
 - D. increasing agent concentration in the inspired air.
 - E. choosing an agent with low tissue solubility.

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26. Which intravenous agent has been associated with hallucinations and occasionally prolongs recovery post-operatively?
- A. midazolam
 - B. sodium pentothal
 - C. propofol
 - D. etomidate
 - E. ketamine
27. Which statement concerning the minimum alveolar concentration (MAC) of an inhalational anesthetic agent is **FALSE**?
- A. It is defined as the steady state concentration of agent that renders 50% of patients immobile at surgical incision.
 - B. It is useful when estimating comparable doses of different inhalation anesthetic agents.
 - C. Giving other inhalational or intravenous anesthetics effectively decreases required MAC.
 - D. Several multiples of MAC can be used to rapidly achieve adequate brain levels of anesthetic.
 - E. It is used to estimate the agent's speed of onset (higher MAC, faster onset).
28. A clinical investigator plots a graph comparing the mean increases in blood pressure induced by acute administration of a range of doses of two novel agents in two groups of subjects. Which of the following statements best describes the most likely form of the relationship between drug dose and blood pressure response?
- A. A plot of the percentage of subjects who become hypertensive at each dose of drug will be linear for both drugs.
 - B. The concentrations of each drug which give 50% of the maximal increase in blood pressure for each drug will be identical.
 - C. The maximum response produced by the highest tested dose of each drug will be identical.
 - D. A linear relationship between mean response and administered dose will be observed for both drugs.
 - E. A sigmoid relationship between mean response and logarithm of administered dose will be observed for both drugs.
29. Which of the following statements referring to the binding of drugs to their specific receptors is **FALSE**?
- A. Agonists activate receptors because they bind with greater affinity than antagonists.
 - B. Agonist binding is usually reversible.
 - C. Agonists cannot activate receptors without binding to them.
 - D. Binding specificity often distinguishes between stereo-isomers of the same molecule.
 - E. Agonist binding can be affected by other ligands binding at allosteric sites.

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30. A competitive antagonist reduces the sensitivity of a tissue to the actions of an agonist
- A. by binding to the agonist before it can occupy the receptor.
 - B. because it occupies the site on the receptor at which an agonist must bind to induce a response.
 - C. by impairing the function of the effector system which the agonist-occupied receptor activates.
 - D. because it reduces the maximum response that an agonist can induce in the tissue.
 - E. because of all the above actions.
31. The dissociation constant (K_D) for the interaction of a ligand and its receptor is
- A. equal to the EC_{50} for the ligand.
 - B. equal to the concentration of ligand occupying 50% of receptors present.
 - C. determined only by the rate of association of the ligand and the receptor.
 - D. cannot be determined experimentally because the number of receptors present in a tissue is not usually known.
 - E. equal to the LD_{50} for the ligand.
32. Ionized and/or lipid-insoluble drugs
- A. may pass through the small aqueous channels or pores of cell membranes in many tissues.
 - B. generally do not gain entry to cells in the central nervous system.
 - C. cross biologic membranes less readily than non-ionized drugs.
 - D. all of the above
 - E. none of the above.
33. Consider the absorption from the stomach (pH approx. 1.5) to the plasma (pH approx. 7.5) of drug X (a weak acid, pK_a 4.5). Which of the following statements is most likely to be **CORRECT**? (Assume the pyloric sphincter remains closed; i.e., all absorption occurs from the stomach.)
- A. At equilibrium, the concentration of drug X remaining in the stomach will be 100-fold higher than its concentration in plasma.
 - B. At equilibrium, the concentration of drug X in the stomach will be similar to its concentration in plasma.
 - C. At equilibrium, the concentration of drug X remaining in the stomach will be less than 1% of its concentration in plasma.
 - D. Drug X will not be absorbed from the stomach.
 - E. None of the above.

FIVE CHOICE CLASSIFICATION

PHARMACOLOGY PHO2001
Wednesday, 27 January 1999
EXAMINATION #1 Page 9

Directions: For each numbered word or phrase, select the one LETTERED heading that is most closely related to it.

- A. acetylcholine
- B. atropine
- C. bethanechol
- D. succinylcholine
- E. tubocurarine

- 34. A muscarinic receptor agonist used to treat post-surgical abdominal distension.
- 35. A muscarinic receptor antagonist used as a pre-anesthetic medication to reduce respiratory tract secretions.
- 36. A depolarizing neuromuscular blocking agent used to relax muscles for intubation before surgery.

- A. atypical pseudocholinesterase
- B. defective ryanodine receptor gene
- C. polymorphism of CYP2D6
- D. defective erythrocyte glucose-6-phosphate dehydrogenase
- E. polymorphism of CYP2C19

- 37. Inheritance of this autosomal recessive trait has a relatively high incidence in Caucasians and may result in excessive action of β -adrenergic receptor antagonists, tricyclic antidepressants, and a number of other drugs.
- 38. Associated with hemolysis after treatment with analgesics, sulfonamides, or anti-malarial agents.

The cardiovascular effects of several novel chemical agents are being studied in an anesthetized dog preparation. Match the following potential **sites/mechanisms of action** (listed by **letter**) with the following **pharmacologic responses** (listed by **number**).

- A. blockade of histamine receptors in the peripheral blood vessels.
- B. blockade of α -adrenergic receptors in peripheral blood vessels
- C. blockade of muscarinic receptors in the peripheral blood vessels
- D. blockade of β -adrenergic receptors in peripheral blood vessels
- E. blockade of neuronal nicotinic (N_A) receptors in autonomic ganglia

- 39. Antagonism of the fall in blood pressure induced by acetylcholine but not by isoproterenol.
- 40. Antagonism of the increase in blood pressure induced by either nicotine or norepinephrine.

ANSWER SHEET

PHARMACOLOGY EXAM #1

January 27, 1999

- | | |
|-------|-------|
| 1. C | 21. E |
| 2. B | 22. B |
| 3. A | 23. A |
| 4. C | 24. C |
| 5. D | 25. B |
| 6. A | 26. E |
| 7. E | 27. E |
| 8. E | 28. E |
| 9. E | 29. A |
| 10. D | 30. B |
| 11. B | 31. B |
| 12. A | 32. D |
| 13. C | 33. C |
| 14. D | 34. C |
| 15. D | 35. B |
| 16. C | 36. D |
| 17. B | 37. C |
| 18. E | 38. D |
| 19. E | 39. C |
| 20. A | 40. B |