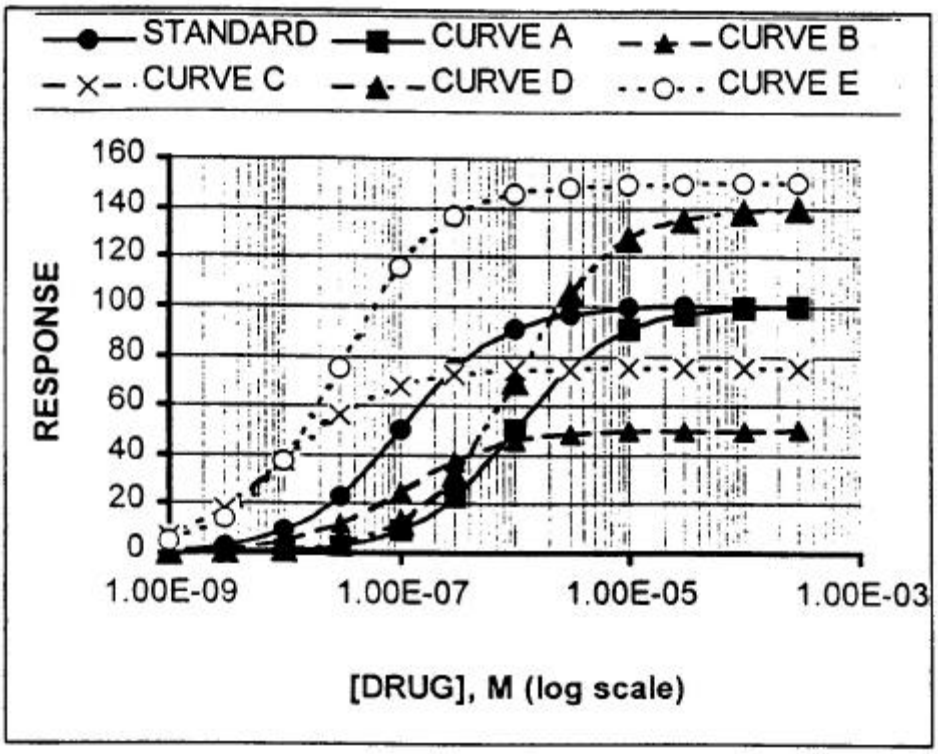
YR 2 PHARMACOLOGY UNIT EXAMINATION 1 -- February 24, 1999.

CHOOSE THE SINGLE BEST ANSWER FOR QUESTIONS 1 - 72.



In the above graph, the curve labeled STANDARD shows the log dose-response curve for a standard agonist. Use this graph for the next three questions.

1. Which of the curves shows the log dose-response curve expected when various concentrations of the standard agonist are tested in the presence of a fixed concentration of a noncompetitive antagonist?

   A. Curve A

   B. Curve B

   C. Curve C

   D. Curve D

   E. Curve E

2. Which of the curves shows the log dose-response curve expected when various concentrations of the standard agonist are tested in the presence of a fixed concentration of a competitive antagonist?

   A. Curve A

   B. Curve B

   C. Curve C

   D. Curve D

   E. Curve E

3. Which of the curves shows the log dose-response curve expected when various concentrations of a new agonist with greater potency and greater efficacy than the standard agonist are tested in the absence of the standard agonist?

   A. Curve A

   B. Curve B

   C. Curve C

   D. Curve D

   E. Curve E

4. The Area-Under-Curve (AUC) for the oral route of administration is a measure of:

   A. the time required to achieve peak plasma concentration.

   B. the amplitude between peak and trough plasma concentrations.

   C. the amount of the dose gaining access to the systemic circulation.

   D. the percentage of the dose that rapidly distributes from the circulation to tissue sites.

   E. the duration of the time that the plasma concentration is below the effective concentration.

5. Drug Q has an apparent volume of distribution (Vd) of 10 liters in a 70 kg patient. This suggests that the drug:

   A. is extensively bound to plasma proteins.

   B. distributes similarly throughout the body.

   C. is extensively accumulated or bound at sites outside the circulation.

   D. exhibits zero order elimination kinetics

   E. cannot gain access to the central nervous system.

6. A drug has a V_d of 50 L and a total systemic clearance rate of 5 L/hr, with 60% being eliminated by the liver and 40% eliminated by the kidney. The maintenance infusion rate for a normal patient is 10 mg/hr. Which of the following infusion rates should be used to maintain the same steady-state plasma concentration in a patient with 50% renal function?

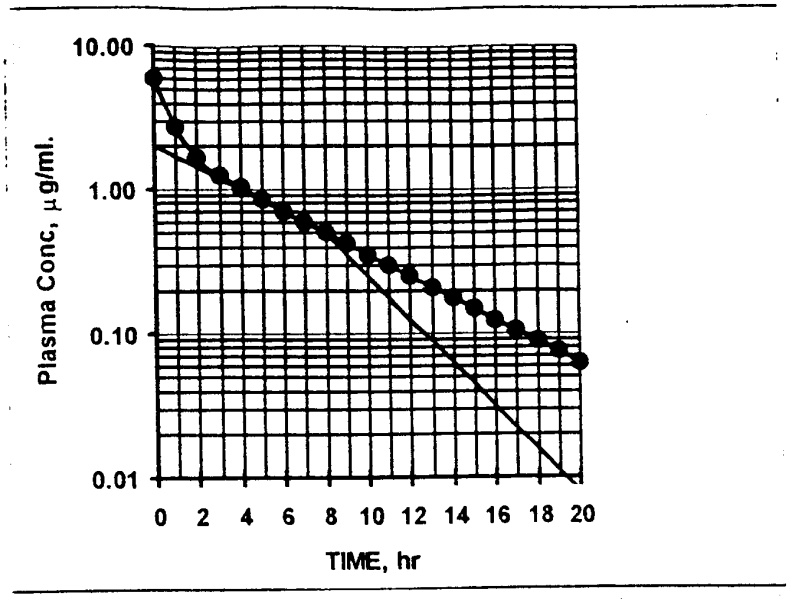
   A. 3 mg/hr

   B. 8 mg/hr

   C. 12 mg/hr

   D. 18 mg/hr

   E. 30 mg/hr



The filled circles in the above graph show the plasma concentrations in μg/ml of Drug Q as a function of time after intravenous injection of 200 mg of the drug. The solid line without filled circles shows the elimination data expected if sodium bicarbonate were administered starting at Hour 8. Use this graph for the next three questions.

7. The volume of distribution (Vd) for Drug Q is:

   A. 2 liter

   B. 7 liter

   C. 10 liter

   D. 50 liter

   E. 100 liter

8. The half-life for elimination of Drug Q in the absence of sodium bicarbonate administration is:

   A. 1 hr

   B. 2 hr

   C. 4 hr

   D. 8 hr

   E. 12 hr

9. The effect of sodium bicarbonate administration on the clearance kinetics indicates that the chemical nature of Drug Q is that of a:

A. strong organic acid

B. weak organic acid

C. nonelectrolyte

D. weak organic base

E. strong organic base

10. A patient taking drug Y develops toxicity. His physician decides to decrease his dosage of Y by one half and hospitalize the patient until his blood level reaches 94% of the new steady state level. If the $t_{1/2}$ for drug Y is 12 hrs, the patient's blood level is 10 mg/l and his excretion rate is 5 mg/hr, how long will this take?

A. 6 hr

B. 12 hr

C. 24 hr

D. 36 hr

E. 48 hr

11. The following are pharmacokinetic data for Drug X: Clearance, 20 L/hr in a 70 kg adult; Effective plasma concentration, 5 ng/ml; Oral availability (= 100 x fractional absorption), 50%. Calculate the oral maintenance dosing rate for Drug X in a 70 kg person.

A. 10 ug/hr

B. 200 ug/hr

C. 1 mg/hr

D. 4 mg/hr

E. 50 mg/hr

12. When a steady state concentration of drug is present in the systemic circulation and equilibration between the systemic circulation and tissue compartments has been achieved, which of these fluid compartments will have the largest total fluid:blood concentration ratio for the weak acid sulfadiazine (pKa = 6.5).

A. Alkalinized urine at pH 8.0

B. Acidified urine at pH 5.0

C. Bacterial abscess at pH 4.5

D. Jejunum-ileum contents at pH 7.6

E. Stomach contents at pH 2.0

13. The metabolic biotransformation of a drug generally results in:

A. the pharmacological inactivation of the drug

B. a decrease in the lipid solubility of the drug

C. an increase in the drug's half-life

D. an increase in the drug's lipid:water partition coefficient

E. a decrease in the body's ability to excrete the drug

14. Which of the following reactions would be typical of a Phase II enzyme?

A. Aromatic oxidation

B. S-dealkylation

C. Dehydrogenation

D. Glucuronidation

E. N-hydroxylation

15. Which of the following enzymes is considered a Phase I enzyme?

A. UDP-glucuronosyl transferase

B. Sulfotransferase

C. CYP2D6

D. N-acetyltransferase

E. Glutathione-S-transferase

16. Acetaminophen toxicity is generally only observed at high doses because of the following:

A. It is only a high doses that "first pass metabolism" of acetaminophen is overcome, thereby allowing the parent drug to enter the systemic circulation and cause toxicity.

B. The principal route of metabolism is via a phase II enzyme, i.e., sulfotransferase. It is only when this pathway is saturated that metabolism occurs via CYP2E1, resulting in the formation of a toxic metabolite.

C. High doses of acetaminophen are required to induce CYP2E1, resulting in the increased formation of toxic metabolites.

D. CYP1A1 is the principal enzyme responsible for acetaminophen metabolism, leading to inactivation of the compound. However, at high doses, high enough steady-state concentrations of the parent drug are obtained to allow metabolism by CYP3A4, resulting the formation of toxic metabolites.

E. It is only a high doses of acetaminophen that sufficient quantities of acetaminophen cross the blood-brain barrier, resulting in toxicity.

17. An individual who experiences a sulfonamide hypersensitivity reaction:

A. is likely a fast acetylator

B. forms glutathione conjugates effectively and rapidly.

C. is likely to have a unusually large amount of reactive hydroxylamine metabolites

D. is at little risk for a repeat hypersensitity reaction

E. should not be concerned about other family members having a similar problem

18. Poor debrisoquine metabolism is:

A. found in about 3% of Caucasians

B. inherited as an autosomal dominant trait

C. likely to be associated with poor metabolism of mephenytoin

D. determined by one of the genes from the Cytochrome P450 supergene family, in particular, Cytochrome P4502D6

E. more common than slowly acetylation.

19. Slow acetylation:

A. is only seen in about 5% of African Americans.

B. requires only one "slow" allele for N-acetyltransferase.

C. is associated with increased risk of poor efficacy during isoniazid treatment.

D. is associated with increased risk of toxicity during isoniazid treatment

E. is more common in individuals of Asian descent than European descent.

20. On a written prescription, the **Sigma** refers to:

A. the name of the medication and the dosage quantity

B. the directions to the pharmacist on how to compound the prescription

C. the signature of the physician

D. information about refills

E. directions to the patient on how to take the medication

21. Which of the following is **NOT** a good practice when writing a prescription:

A. write the prescription in pen

B. use the metric system for weights and measures

C. write out the word "units" rather than indicating as a "u"

D. write dosage units (e.g. 1 tablet) rather than exact dosage strengths (*e.g.*, 10 mg) when more than one strength of a drug is available.

E. review the order for accuracy and legibility immediately after writing

22. Which of the following is true regarding refills of controlled substance prescriptions in Schedules III-V?

A. they may not be refilled

B. they may be refilled as often as indicated by the prescriber

C. they may be refilled as authorized up to 6 times in 5 months

D. they may be refilled as authorized up to 5 times in 6 months

E. they may be refilled as authorized up to 12 months

23. Which of the following is **False** regarding Michigan regulations on writing/dispensing prescriptions?

A. There may be no more than two prescriptions written on any one prescription blank prescriptions.

B. Prescribers are not permitted to write a controlled substance on the same prescription blank.

C. Pre-printed prescriptions may only be used if all of the information printed on the prescription form applies to the patient.

D. Under no circumstances can CII prescriptions be dispensed in partial quantities.

E. If samples are dispensed by the physician they must include the name of the product, expiration date, and patient instructions in writing on the sampler or on a patient information sheet dispensed with the sample.

24. Onset of action of this agent is associated with muscle twitching over the upper thorax, limbs and neck.

A. Dantrolene

B. Scopolamine

C. Succinylcholine

D. Vecuronium

E. Pirenzepine

25. Which of the following agent covalently binds to acetylcholinesterase?

A. Edrophonium

B. Bethanachol

C. Atracurium

D. Parathion

E. Sucralfate

26. A patient undergoing a surgical procedure is given a competitive skeletal muscle blocking agent that has the added effect of increasing his heart rate. The most likely drug would have been:

A. Gallamine

B. Atropine

C. Tropicamide

D. Vecuronium

E. Chlorpheniramine

27. Botulinum toxin (Botox) affects skeletal muscle contractions primarily by:

A. blocking the release of calcium from the endoplasmic reticulum.

B. depressing the synthesis of acetylcholine by inhibiting CAT.

C. blocking the incorporation of finished acetylcholine into synaptic vesicles.

D. binding to the intracellular docking proteins.

E. acting at the presynaptic calcium channels to decrease conductance.

28. Which of the following agents is useful in slowing the rapid progression of Alzheimer s disease?

A. Tacrine

B. Scopolamine

C. Atracurium

D. Ondanesetron

E. Mecamylamine

29. All of the following are side effects associated with the chronic use of scopolamine for motion sickness **EXCEPT:**

A. constipation

B. dryness of the eyes

C. sedation

D. bradycardia

E. warm red skin

30. Diaphoresis can be best induced with:

A. chlorpheniramine

B. pilocarpine

C. dantrolene

D. vecuronium

E. castor oil

31. Narrow angle glaucoma symptoms can be precipitated by the topical ophthalmic use of which of the following agents?

A. neostigmine

B. carbamylcholine

C. isoflurophate

D. atropine

E. pilocarpine

32. Regeneration of the hydroxyl group of the acetylcholinesterase enzyme following malathion poisoning, can be accelerated with:

A. loratadine

B. atropine

C. sevin

D. pralidoxime

E. physostigmine

33. Which of the following agents when used topically is the most useful to produce cycloplegia

A. phenylephrine

B. physostigmine

C. tropicamide

D. ephedrine

E. propranolol

34. Dantrolene acts specifically by:

A. Blocking synthesis of acetylcholine at CAT

B. Blocking the active transport of choline into somatic nerves

C. Auto-feedback inhibition of acetylcholine release from somatic nerves

D. Reducing sarcoplasmic release of calcium

E. Producing a depolarizing blockade at motor end-plate nicotinic receptors

35. In the treatment of bronchial asthma a useful quaternary amine drug is:

A. Ipratropium

B. Neostigmine

C. Pralidoxime

D. Propranolol

E. Atenolol

36. Treatment of the muscarinic symptoms following toxic exposure to malathion is best treated with:

A. Physostigmine

B. Propantheline

C. Edrophonium

D. Pralidoxime

E. Atropine

37. Degradation by plasma pseudocholinesterase is the primary route of metabolism for:

A. Atropine

B. Edrophonium

C. Succinylcholine

D. Hexamethonium

E. Gallamine

38. Injection of alpha-methyl-p-tyrosine causes depletion of norepinephrine from sympathetic neurons by inhibiting:

A. Phenylethanolamine-n-methyl transferase

B. Dopamine-beta-hydroxylase

C. DOPA decarboxylase

D. Tyrosine hydroxylase

E. Catecholamine transporter

39. Norepinephrine is inactivated by reuptake into the sympathetic nerve terminals, uptake occurring via:

A. Postsynaptic alpha1-adrenergic receptors

B. Presynaptic alpha2-adrenergic receptors

C. Presynaptic muscarinic receptors

D. A specialized transport site (U_1 or NET) located on presynaptic nerve terminals

E. Monoamine oxidase

40. Reserpine causes depletion of dopamine in dopaminergic nerve terminals by:

A. Inhibiting vesicular enzyme dopamine-beta-hydroxylase

B. Inhibiting transport of dopamine into vesicles

C. Inhibiting reuptake of dopamine into dopaminergic nerve terminals

D. Causing degeneration of dopaminergic nerve terminals

E. Inhibiting D_2 receptors

41. An angina patient is placed on 200 mg of propranolol daily for one month. It is likely that the drug will produce:

A. An increase in the concentration of alpha-adrenergic receptors in the heart

B. A decrease in the concentration of alpha-adrenergic receptors in the heart

C. An increase in the concentration of beta-adrenergic receptors in the heart

D. A decrease in concentration of beta-adrenergic receptors in the heart

E. An increase in the concentration of muscarinic receptors in the heart

42. Which of the following drugs would be definitely <u>contraindicated</u> in a patient with hypertension due to a pheochromocytoma?

A. Clonidine

B. Phentolamine

C. Desipramine

D. Prazosin

E. Propranolol

43. The order of potency of norepinephrine (NE), epinephrine (EPI) isoproterenol (ISO) and phenylephrine (PE) in causing direct relaxation of bronchospasm is:

A. PE>ISO>EPI>NE

B. PE=NE>ISO>EPI

C. ISO=EPI>NE>PE

D. EPI>NE>PE>ISO

E. EPI>NE>ISO>PE

44. The order of potency of norepinephrine (NE), epinephrine (E) isoproterenol (ISO) and phenylephrine (PE) in causing vasoconstriction of resistance blood vessel of the skin is:

A. NE=EPI>PE>ISO

B. ISO>EPI NE>PE

C. PE>NE>EPI>ISO

D. NE>EPI>ISO>PE

E. ISO=NE>EPI>PE

45. Concerning phenoxybenzamine:

A. It is a reversible competitive antagonist for beta-adrenergic receptors

B. It is a irreversible noncompetitive antagonist for beta-adrenergic receptors

C. It is an irreversible antagonist for alpha1-and alpha2-adrenergic receptors

D. It is highly useful as a general antihypertensive drug

E. It is a quaternary amine used in treating bronchospasm

46. The following compounds are good substrates for monoamine oxidase **EXCEPT**:

A. Dopamine

B. Amphetamine

C. Norepinephrine

D. Tyramine

E. Epinephrine

47. All the following statements concerning **guanethidine** are correct **EXCEPT**:

A. One of its main side effects is orthostatic hypotension

B. It lowers blood pressure by inhibiting the stimulation of evoked-release of norepinephrine

C. Its antihypertensive action can be interfered with by concomitant administration of desipramine

D. It is particularly useful in the treatment of hypertension caused by pheochromocytoma

E. It does not cross the blood:brain barrier

48. Propranolol is a useful drug in the treatment of following conditions **EXCEPT**:

A. angina pectoris

B. some cardiac arrhythmias

C. some cases of essential hypertension

D. bronchial asthma

E. tachycardia of thyrotoxicosis

49. All the following statements concerning **clonidine** are correct **EXCEPT**:

A. its antihypertensive effect is primarily due to an action in the CNS

B. it has some ability to cause vasoconstriction

C. sudden withdrawal of the drug in a hypertensive patient may lead to a rebound in blood pressure to high levels

D. it must be accumulated by active transport to have its effects.

E. it is a selective inhibitor of presynaptic alpha2-adrenergic receptors.

50. All the following statements concerning EPINEPHRINE are correct **EXCEPT**:

A. it increases the rate of diastolic depolarization of sinus node pace-maker cells of the heart

B. it acts on beta2-adrenergic receptors of the cardiac muscle to produce inotropic and chronotropic effects

C. it increases the plasma level of glucose

D. it increases the cellular influx of Ca^{2+} occurring with each action potential in the heart

E. it increases lipolysis in adipose tissue

51. Agonist acting on alpha adrenergic receptors cause contraction of the smooth muscle of all the following organs or tissues EXCEPT:

A. blood vessels

B. intestine

C. radial muscle of the iris

D. splenic capsule

E. vas deferens

52. Mannitol:

A. Is distributed throughout the intracellular and extracellular spaces.

B. Causes increased intracranial pressure.

C. Increases extracellular volume.

D. Is an orally effective diuretic.

E. Is metabolized to glucuronic acid.

53. Acetazolamide:

A. Acidifies the urine.

B. Inhibits the Na/K/2Cl symporter.

C. Can increase intraocular pressure.

D. Increases the dissolution of kidney stones.

E. Is actively transported into the lumen of the proximal tubule.

54. Which of the following is NOT caused by hydrocholorothiazide?

A. Reduced lithium clearance.

B. Increased uric acid reabsorption.

C. Metabolic alkylosis.

D. Antagonism of the effects of antidiuretic hormone.

E. Increased cholesterol and LDLs.

55. Which of the following is affected by BOTH spironolactone and amiloride?

A. Carbonic anhydrase

B. The Na channel of the late distal tubule and collection duct

C. The Na/K ATPase

D. The Na/Cl symporter

E. The Na/K/2Cl symporter

56. Which of the following is affected by furosemide?

A. Carbonic anhydrase

B. The Na channel of the late distal tubule and collection duct

C. The Na/K ATPase

D. The Na/Cl symporter

E. The Na/K/2Cl symporter

57. Which of the following diuretics may impair insulin secretion?

A. Furosemide

B. Hydrochlorothiazide

C. Amiloride

D. Mannitol

E. Acetazolamide

58. Abrupt withdrawal of a glucocorticoid after a long course of therapy often results in:

A. Steroid psychosis

B. Adrenal insufficiency

C. Leukemia

D. Osteoporosis

E. Edema due to sodium retention

59. Glucocorticoids elevate blood uric acid due to lysis of circulating lymphocytes when used in

A. Acute leukemia

B. Addison's disease

C. Rheumatoid arthritis

D. Lupus erythmatosis

E. Allergy to sulfa drugs

60. The drug of choice in the treatment of Addison's disease is:

A. Dexamethasone

B. Prednisolone

C. Prednisone

D. Cortisol

E. Ketoconazole

61. Which of the following drugs irreversibly inhibits cyclo-oxygenase I?

A. Dexamethasone

B. Naproxen

C. Indomethacin

D. Aspirin

E. Celecoxib

62. Misoprostol is used to protect against which of the following effects of aspirin?

A. Decreased uric acid elimination

B. Gastric bleeding

C. Metabolic acidosis

D. Respiratory alkalosis

E. Respiratory depression

63. Acetaminophen has all of the following properties **EXCEPT**:

A. Hepatotoxic

B. Analgesic

C. Antipyretic

D. Anti-inflammatory

E. Low potential for gastric irritation

64. Which of the following drugs is a selective inhibitor of cyclo-oxygenase II?

A. Naproxen

B. Celecoxib

C. Ibuprofen

D. Indomethacin

E. Acetaminophen

65. Which of the following drugs is useful in the treatment of patent ductus arteriosus?

A. Sulfinpyrazone

B. Colchicine

C. Methotrexate

D. Indomethacin

E. Penicillamine

66. Which of the following is NOT sign of salicylate intoxication?

A. Hyperventilation

B. Ringing in the ears

C. Impaired hearing

D. Vertigo

E. Hypothermia

67. Probenecid and sulfinprazone are effective in gout because they:

A. Inhibit cyclo-oxygenase II

B. Inhibit the reabsorption of urate

C. Limit phagocyte mobility

D. Induce xanthine oxidase

E. Inhibit xanthine oxidase

68. Which of the following drugs is contraindicated in gout?

A. Acetaminophen

B. Mannitol

C. Colchicine

D. Aspirin

E. Phenylbutazone

69. Which of the following drugs would be the most appropriate choice for a patient with mild rheumatoid arthritis who could not take aspirin?

A. Indomethacin

B. Methotrexate

C. Ibuprofen

D. Chloroquine

E. Penicillamine

70. The antioxidant that has been demonstrated to be effective in cardioprotection studies is:

A. Vitamin A

B. beta-carotene

C. Vitamin C (ascorbic acid)

D. Vitamin D

E. Vitamin E (alpha-tocopherol)

71. All of the following are strategies that have been used for prevention of reperfusion injury **EXCEPT**:

A. Use of allopurinol to inhibit xanthine oxidase

B. Addition of superoxide dismutase and catalase when restoring blood flow

C. Addition of ferric iron when restoring blood flow

D. Use of 21-aminosteroids as radical traps

E. Use of N-acetylcysteine as a radical trap

72. The oxygen species that is most damaging to intracellular proteins, lipids and nucleic acids in oxidative stress conditions is:

A. O_2

B. OH^-

C. O_2^-

D. H_2O_2

E. OH