BEFORE YOU START:
PLEASE NOTE THESE IMPORTANT ITEMS

USING #2 PENCIL, MAKE SURE THAT BOTH YOUR NAME, UW AND SCHOOL OF MEDICINE TEST ID (SPECIAL CODES) NUMBERS ARE CODED ON THE ANSWER SHEET AND WRITTEN ON ALL SHORT-ANSWER PAGES
NOW - BEFORE YOU BEGIN.

PAGES WITHOUT STUDENT NAME AND NUMBERS MAY NOT BE RECORDED.

THIS EXAMINATION IS TIME LIMITED – 4 HOURS MAXIMUM
ANSWER SHEETS TURNED IN LATE WILL NOT BE GRADED.

THIS EXAMINATION (300 POINTS TOTAL) CONTAINS
139 MULTIPLE CHOICE QUESTIONS
(1 THROUGH 93 and X01 THROUGH X36)
AND 6 SHORT ANSWER QUESTIONS ON A TOTAL OF xx PAGES
MAKE SURE ALL PAGES ARE PRESENT.

PUT ANSWERS ON ANSWER SHEET USING #2 PENCIL
BE SURE TO TURN IN ANSWER SHEET AND THE SHORT ANSWER PAGE

Some useful formulae:

natural logarithm of 2 = 0.693
F = AUCoral/AUCIV
CL = K_{elim} \times V_d
K_{elim} = 0.693/half life
half life = 0.693 \times V_d/CL
CL = 0.693 \times V_d/half life
C_{SS} = dosing rate \times F/CL
V_d = dose/conc

Some commonly encountered abbreviations
ACE angiotensin converting enzyme
BID (twice daily) B P blood pressure
BPM beats per minute CHF congestive heart failure
COPD chronic obstructive pulmonary disease FEV_1 forced expired volume in 1 sec
GERD gastroesophageal reflux disease HR heart rate
HT hypertension HS (at bedtime)
IM intramuscular, intramuscularly IV intravenous, intravenously
PRN (as needed) QD (daily)
QID (four times daily) RR respiratory rate
SubQ subcutaneous, subcutaneously SOB shortness of breath
TID (three times daily)
I. SELECT ONE BEST (3 points each). Each numbered item or incomplete statement in this section is followed by answers or completions of the statement. For items 1 through 57 select the ONE lettered answer or statement that is BEST.

1. A 62 year old male has had 3 days of increasing dyspnea and now orthopnea. He has a history of type II diabetes mellitus and hypertension. He reports to the emergency department with an irregular pulse (120/min), BP 170/105, respiratory rate of 34. The diagnosis is acute congestive heart failure, so he is placed in a semi-recumbent position. In addition to oxygen, nitroglycerin and morphine which of the following drugs should be given for his initial stabilization in the emergency department, prior to admission?

A) dopamine and furosemide  
B) digoxin and verapamil  
C) digitoxin and triamterene  
D) enalapril and losartan  
E) epinephrine and phentolamine

2. A 22 year old college student with a history of moderately persistent asthma presents to the emergency department with dyspnea. She is diaphoretic, anxious and using all accessory muscles to breath. Vital signs are: pulse 130, BP 150/100, RR 35, T 37.8 C, O2 saturation on room air is 94%. The diagnosis is acute asthma. In addition to oxygen and magnesium each of the following agents may be appropriate in the initial management of this patient EXCEPT:

A) disodium cromoglycate  
B) epinephrine  
C) ipratropium bromide  
D) prednisone  
E) terbutaline

3. A 65 year old male with long-standing, steroid-dependent asthma is to be treated for moderate hypertension. In creating an individualized step-care treatment plan, which of the following kinds of drugs is not appropriate in this patient?

A) ACE inhibitor  
B) adrenergic neuron blocker  
C) beta-blocker  
D) calcium channel blocker  
E) centrally acting sympatholytic

4. Each of the following diuretic drug-mechanism pairs is correct EXCEPT:

A) triamterene - inhibitor of carbonic anhydrase  

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*Final Examination*  
*December 11, 2003*  
*Page 2*
5. Which of the following mechanisms of drug interaction would be least likely to result in chronically increased actions of the object drug?

A) Altered drug absorption
B) Altered drug metabolism
C) Altered plasma protein binding
D) Altered renal excretion
E) Pharmacodynamic addition

6. In the treatment of asthma, which of the following agents acts as an antagonist of leukotriene receptors?

A) beclomethasone monopropionate (from dipropionate)
B) disodium cromoglycate
C) ipratropium
D) zafirlukast
E) zileuton

7. Which of the following drug metabolizing enzymes is considered to be the least inducible?

A) CYP2C9
B) CYP2C19
C) CYP2D6
D) CYP2E1
E) CYP 3A4

8. Each of the following beta receptor agonist compounds is considered to be a reliever in the treatment of asthma EXCEPT:

A) albuterol
B) epinephrine
C) isoproteronol
D) salmeterol
E) terbutaline
9. The diverse pharmacological actions of theophylline include each of the following EXCEPT:

A) agonism of adenosine receptors
B) cardiac stimulation
C) CNS stimulation
D) diuresis
E) inhibition of cyclic nucleotide phosphodiesterase

10. A 55 year old male appears in the emergency department after breaking a bone. He is a little confused mentally. His wife reports that the bone break occurred with no obvious trauma, but that he has recently experienced significant weight gain. Physical exam indicates moderate hypertension. About a year ago he was prescribed and has been using an inhaled drug for the treatment of late onset asthma. Which of the following drugs is most likely to account for this patient’s condition:

A) beclomethasone dipropionate
B) ipratropium
C) salmeterol
D) theophylline
E) zafirlukast

11. A 14 year old female patient reports to the emergency department in status asthmaticus. Which of the following drug agents would be most appropriately administered first?

A) albuterol
B) disodium cromoglycate
C) ipratropium
D) salmeterol
E) zileuton

12. In the development of new anticholinergic agents to treat asthma, in addition to a long half life and low or zero intrinsic activity which of the following set of properties would be most desirable?

A) high affinity for muscarinic M1 receptors, high affinity for muscarinic M2 receptors
B) high affinity for muscarinic M2 receptors, low affinity for muscarinic M3 receptors
C) high affinity for muscarinic M3 receptors, high affinity for muscarinic M2 receptors
D) high affinity for muscarinic M2 receptors, low affinity for muscarinic M3 receptors
E) high affinity for muscarinic M3 receptors, low affinity for muscarinic M2 receptors

13. A patient who has been chronically treated with theophylline for the treatment of asthma reports to the emergency department with nausea, vomiting and dysphoria. The lab report indicates a level of theophylline that is three times the normal therapeutic level. The patient, who was symptom
free until yesterday, has been treated with an antibiotic drug for the last week. Each of the following antibiotic drugs could be expected to account for impaired metabolism of theophylline EXCEPT:

A) ciprofloxacin
B) erythromycin
C) ketoconazole
D) rifampin
E) none of the above (i.e., all of the above inhibit the metabolism of theophylline)

14. A 48 year old male with hyperlipidemia has been treated with simvastatin for the past year. Control of lipid levels has been less than anticipated. Thus, it was recommended that an agent that reduces the substrate pool for cholesterol synthesis be added to the patient’s regimen. Which of the following agents would be most appropriate?

A) atorvastatin
B) cholesterol
C) cholestyramine
D) gemfibrozil
E) niacin

15. Each of the following membrane transport systems requires ATP as a direct energy source EXCEPT:

A) Na/K pump of the plasma membrane kidney cells
B) H/K pump of gastric mucosal cells
C) P-glycoprotein of intestinal cells
D) Na/Ca exchanger of the plasma membrane of cardiac muscle cells
E) Ca pump of sarcoplasmic reticulum of skeletal muscle cells

16. Each of the following is a general property of most calcium channel blockers EXCEPT:

A) low bioavailability
B) rapid absorption
C) excreted unchanged in the urine
D) largely bound to plasma proteins
E) high lipid solubility

17. A 50 year old female is brought to the emergency department by a fire department aid team. She is in apparent delerium and has apparently recently vomited. When some communication is established the patient is found to have blurred vision and a terrific headache. An attending
physician offers the opinion that the patient is suffering from cinchonism. Assuming that the attending physician is correct, which of the following agents is most likely responsible?

A) bretylium  
B) cocaine  
C) propranolol  
D) quinidine  
E) verapamil

18. The characteristic common to drugs that are metabolized by the liver CYP enzyme systems is:

A) a weakly basic nitrogen group 2 carbons from an aromatic ring  
B) a weakly acidic carboxyl group attached to an aromatic ring  
C) lipophilicity  
D) hydrophilicity  
E) molecular weight > 2000

19. Phase II biotransformation reactions include conjugation with of any of the following EXCEPT:

A) acetate  
B) creatinine  
C) glucuronic acid  
D) glutathione  
E) sulfate

20. The CYP enzyme involved in drug metabolism that is most likely to display polymorphism:

A) CYP1A2  
B) CYP2C9  
C) CYP2D6  
D) CYP2E1  
E) CYP3A4

21. An enzyme that limits the absorption of many drugs without metabolizing them:

A) creatinine kinase  
B) CYP3A4  
C) P-glycoprotein  
D) glucuronyl transferase  
E) H/K pump ATPase
22. Drug synergism is also known as:
   A) desensitization
   B) tolerance
   C) potentiation
   D) chelation
   E) physiological antagonism

23. According to the DSM IV, a ‘maladaptive pattern of substance use manifested by recurrent and significant adverse consequences related to repeated use of substances’ is:
   A) addiction
   B) tolerance
   C) physical dependence
   D) substance abuse
   E) psychological dependence

24. d-Tubocurarine:
   A) does not act synergistically with general anesthetics
   B) does not cause histamine release
   C) does not cause fasciculations prior to paralysis
   D) does not cause paralysis that can be reversed with an acetylcholinesterase inhibitor
   E) all of the above

25. Indicated in the treatment of organophosphate poisoning:
   A) albuterol
   B) atropine
   C) edrophonium
   D) labetalol
   E) succinylcholine

26. Causes reflex bradycardia following systemic administration:
   A) dopamine
   B) isoproterenol
   C) methacholine
   D) phentolamine
   E) phenylephrine

27. The most common presynaptic autoreceptor on adrenergic nerve terminals:
A) alpha1-adrenergic receptor
B) alpha2-adrenergic receptor XXXX
C) beta1-adrenergic receptor
D) beta2-adrenergic receptor
E) beta3-adrenergic receptor

28. 6-hydroxydopamine:
A) is a covalent antagonist at dopamine receptors in the kidney
B) blocks the reuptake of catecholamines into the nerve terminal
C) is a dopamine receptor agonist
D) causes the destruction of sympathetic nerve terminals XX
E) inhibits the activity of dopamine-beta-hydroxylase

29. Cevimeline is:
A) a selective agonist at the M1 muscarinic receptor
B) a selective antagonist at the M2 muscarinic receptor
C) indicated in the treatment of COPD
D) indicated in the treatment of dry mouth in patients with Sjögren’s syndrome XX
E) indicated in the treatment of tachycardia in patients with hyperthyroidism

30. Acts in the central nervous system to decrease sympathetic outflow:
A) alpha-methyl tyrosine (metyrosine)
B) clonidine XX
C) guanethidine
D) phentolamine
E) ritodrine

31. Administration of mecamylamine into an otherwise healthy subject should produce all of the following EXCEPT:
A) cycloplegia
B) miosis XX
C) postural hypotension
D) tachycardia
E) urinary retention

32. Acts on the central nervous system following systemic administration:
A) acetylcholine
B) epinephrine  
C) guanethidine  
D) propranolol XXXX  
E) d-tubocurarine  

33. Indicated in an emergency situation for the treatment of hypertension:
A) carbachol  
B) dobutamine  
C) fenoldopam XX  
D) norepinephrine  
E) phenylephrine  

34. An inhibitor of microtubule depolymerization that has significant activity against several cancers including ovarian cancer:
C  
A) cisplatin  
B) bleomycin  
C) paclitaxel (Taxol)  
D) methotrexate  
E) 5-fluorouracil  

35. Leucovorin rescue refers to:
C  
A) using a non cell cycle specific drug to induce cell division in slowly dividing tumors  
B) the addition of a leukocyte colony-stimulating factor to a cancer treatment to stimulate the bone marrow  
C) administration of a folate derivative to overcome high dose methotrexate  
D) the effect of interferon on the immune system  
E) insertion of Navy Seals into Saddam Hospital to extract Pvt. Jessica Lynch  

36. A drug that disrupts cell wall synthesis as its primary site of action:
A  
A) pyrazinamide  
B) amikacin  
C) trimethoprim  
D) chloramphenicol  
E) flucytosine  

37. Which of the following would be cell cycle specific and most active in the S (DNA synthesis) phase?
D
A) cyclophosphamide
B) taxol
C) cisplatin
D) methotrexate
E) L-asparaginase

38. Oral administration would be expected to give no significant therapeutic benefits for:
   C
   A) vancomycin
   B) zidovudine (AZT)
   C) interferon
   D) dicloxacillin
   E) gentamicin

39. You are treating a patient with a serious bacterial infection who is also immunocompromised. Assuming that this particular infectious agent is sensitive to all of the antibiotics listed below, choose one that is most likely to be bactericidal based on its mechanism of action and therefore preferred for this patient.
   D
   A) chloramphenicol
   B) trimethoprim
   C) doxycycline
   D) amikacin
   E) sulfisoxazole

40. The antifungal drug, ketoconazole, kills sensitive fungi by:
   C
   A) forming pores in the membrane
   B) blocking DNA synthesis
   C) inhibiting the P450 enzymes involved in ergosterol synthesis
   D) causing a reversible inhibition of RNA synthesis
   E) preventing assembly of the cell wall

41. Sulfisoxazole:
   E
   A) is a competitive inhibitor of dihydrofolate reductase (DHFR)
   B) can be synergistic when given with methotrexate
   C) is not well absorbed orally
   D) acts by inhibiting ribonucleotide reductase
   E) may cause hemolytic anemia in sensitive patients
42. The toxic effects of bleomycin:
   E
   A) are particularly evident in lungs and skin due to reduced hydrolase activity
   B) result in chronic pulmonary fibrosis
   C) can be increased in tissues that have been irradiated
   D) require the generation of free radicals
   E) all of the above

43. Each of the following drug-toxic effect combinations is correct EXCEPT:
   C
   A) gentamicin--nephrotoxicity
   B) bleomycin--pulmonary fibrosis
   C) cyclophosphamide--extravasation injury
   D) vincristine--peripheral neuropathy
   E) doxorubicin--cardiomyopathy

44. Which of the following toxicities should you be especially watchful for after clindamycin administration?
   E
   A) kidney failure due to crystallization
   B) allergic skin reactions
   C) kernicterus (deposition of bilirubin in basal ganglia)
   D) hemolytic anemia
   E) superinfection

45. Which of the following ß-lactam antibiotics is resistant to ß-lactamase cleavage?
   C
   A) penicillin G
   B) ticarcillin
   C) dicloxacillin
   D) ampicillin
   E) none of the above

46. The mechanism of selective toxicity of amphotericin B is due to:
   B
   A) preferential inhibition of fungal protein synthesis
   B) a greater affinity for ergosterol than cholesterol in membranes
   C) the inability of human cells to metabolically activate the drug
   D) selective degradation of the drug in mammalian membranes
   E) none of the above
47. A patient is being discussed who has begun to have difficulties hearing his television and complains of dizziness when trying to walk. Which of the following drugs would you consider the most likely to cause these symptoms?

B
A) fluconazole
B) tobramycin
C) sulfisoxazole
D) isoniazid
E) methotrexate

48. You have just seen your first patient with tuberculosis and your attending asks you to describe the important aspects of isoniazid therapy. Which of the following statements would you omit?

D
A) isoniazid acts by inhibiting fatty acid synthetase II and the synthesis of mycolic acid
B) the drug is orally active and distributes broadly
C) neurotoxicity can be controlled by administering supplemental vitamin B6 (pyridoxine)
D) the half-life of active drug is determined by renal excretion
E) resistance is an increasing problem and one form of resistance deletes a catalase type gene required for drug activation

49. Zidovudine (AZT) is useful in the treatment of AIDS because it:

B
A) stimulates the production of interferon
B) inhibits viral reverse transcriptase
C) interferes with viral thymidine kinase
D) inhibits thymidylate synthetase
E) binds to viral DNA and forms free radicals

50. In cells pretreated with interferon, an infecting virus:

B
A) can not penetrate protected cells
B) results in RNA degradation and inhibition of protein synthesis
C) is degraded by secreted proteases
D) becomes mutated during replication
E) attaches to the cell surface and is attacked by a complement mediated immune response

51. This drug inhibits the synthesis of precursors required for DNA synthesis:

D
A) cyclophosphamide
B) allopurinol
C) vincristine
D) hydroxyurea
E) actinomycin-D

52. Foscarnet is active against both CMV and HSV infections and can be useful when treating virus that have become resistant to other first line drugs. What is the basis for selective toxicity of foscarnet?

E
A) foscarnet has a high affinity for viral reverse transcriptase but not other polymerases
B) foscarnet is selectively activated in virally infected cells by thymidine kinase
C) the induction of interferon in virally infected cells makes them sensitive to activation of 2,5 A synthetase by foscarnet
D) foscarnet inhibits the specific aspartate protease required for processing of the viral coat proteins
E) foscarnet preferentially binds the pyrophosphate site on viral polymerase compared to human DNA polymerase

53. A 65-year-old male with atrial fibrillation is being treated with digoxin (0.5 mg daily, PO [a fairly high dose]) to control ventricular rate. The patient is, nevertheless, experiencing some mild edema and the attending physician wishes to add a diuretic agent. Which of the following possible agents would be the least likely to promote digoxin toxicity in this patient?

A) acetazolamide
B) furosemide
C) hydrochlorothiazide
D) spironolactone
E) triamterene XXX

54. Which of the following is the most likely mechanism of the therapeutic effect of nitroglycerin in patients with stable angina?

A) activation of endothelial muscarinic receptors causing release of NO
B) acutely decreased demand for oxygen by the heart XXX
C) acutely increased coronary blood flow
D) blockade of vascular smooth muscle alpha receptors
E) prevention of coronary artery spasm

55. Low potential for abuse. Use may lead to limited physical dependence or psychological dependence. Prescriptions may be oral or written. Up to 5 renewals are permitted in 6 months. The controlled substance classification that best fits this description is:

A) I
B) II
C) III
D) IV XXX
E) V
56. A 65 y/o female patient was diagnosed with hypertension a month ago. At that time BP was 160/97 with HR of 72 and she was given ‘some blood pressure pills’. Currently, BP is 131/75 with HR of 72, but she recently reported to the Emergency Department with dyspnea and wheezing. Which of the following drugs did the patient most likely take?

A) diltiazem
B) metoprolol
C) nifedipine
D) propranolol
E) verapamil

57. Stimulation of efferent vagal fibers to the heart would be expected to cause:

A) increased duration of atrial action potential
B) decreased conduction velocity through the AV node
C) decreased maximal diastolic potential (more negative) in SA node
D) decreased spontaneous heart rate
E) decreased resting potential in atrial muscle fibers
II. A, B, BOTH, NEITHER (2 points each).
For items 58 through 75 select:

A) if A is correct
B) if B is correct
C) if BOTH A AND B are correct
D) if NEITHER A NOR B is correct

58. The mechanism of bleomycin action involves:
C
A) binding to DNA
B) formation of free radicals
C) both
D) neither

59. Distribution of the drug into the central nervous system following oral administration is sufficient to reach therapeutic concentrations:
A
A) acyclovir
B) ketoconazole
C) both
D) neither

60. Cross-linking of DNA is the mechanism of action for:
B
A) etoposide
B) mechlorethamine
C) both
D) neither

61. Patients suffering from renal dysfunction are likely to require a lower maintenance dose of:
C
A) flucytosine
B) tobramycin
C) both
D) neither

62. The anti-inflammatory actions of glucocorticoids:
A
A) depend on redistribution of neutrophils away from sites of inflammatory activity
B) depend on lysis of T and B cells in the immune system
63. The liganded estrogen receptor may signal through a variety of pathways including:
C) both
A) non-nuclear events that lead to activation of src kinase and the map-kinase pathways
B) direct binding to estrogen receptor response elements in the DNA activating gene transcription
C) both
D) neither

64. Associated with torsade de pointes in overdosage:
A) amiodarone
B) quinidine
C) both
D) neither

65. Class III antiarrhythmic agent:
A) amiodarone
B) bretylium
C) both
D) neither

66. Causes release of catecholamines from the adrenal medulla:
A) amphetamine
B) ephedrine
C) both
D) neither

67. Indicated in the treatment of chronic obstructive pulmonary disease:
A) prazosin
B) propranolol
C) both
D) neither

68. Indicated in the treatment of benign prostatic hyperplasia:
A) metoprolol  
B) prazosin XX  
C) both  
D) neither

69. Causes increased cAMP in the heart:

A) beta-adrenergic receptors XX  
B) muscarinic acetylcholine receptors  
C) both  
D) neither

70. Labetalol is an antagonist at:

A) alpha1-adrenergic receptors  
B) beta1-adrenergic receptors  
C) both XX  
D) neither

71. Indicated in the treatment of glaucoma:

A) echothiophate  
B) timolol  
C) both XX  
D) neither

72. Causes decreased production of aqueous humor:

A) pilocarpine  
B) timolol XXXX  
C) both  
D) neither

73. Indicated for the diagnosis of impaired autonomic reflexes:

A) edrophonium  
B) phenylephrine XX  
C) both  
D) neither

74. Contraindicated in a patient with asthma:
A) methacholine 
B) propranolol 
C) both XX 
D) neither

75. Causes both mydriasis and cycloplegia:

A) ephedrine 
B) phenylephrine 
C) both 
D) neither XX
III. GREATER THAN–LESS THAN (1 point each)
For items 76 through 93 select:

A) if A is GREATER THAN B
B) if B is GREATER THAN A
C) if BOTH A and B are EQUAL or NEARLY EQUAL

76. Rate of kidney elimination of a water soluble weak base, pKa 6.4, when the pH of the urine is:
A) 5.4   xx
B) 7.4

77. Usefulness in the treatment of asthma:
A) first generation antihistamines
B) second generation antihistamines   xx

78. Number of approved clinical indications:
A) fexofenadine
B) promethazine            xxx

79. Intrinsic activity observable upon interaction with its receptor:
A) agonist        xxx
B) antagonist

80. Potency of an antagonist of histamine:
A) with pA2 = 6
B) with pA2 = 9       xxx

81. Duration of action of:
A) digoxin
B) digitoxin         xxx

82. Left ventricular end-diastolic pressure in a patient with congestive heart failure:
83. Cardiac output in a patient with congestive heart failure:
A) before treatment xxx
B) after successful treatment with digoxin

84. Heart rate in a patient with congestive heart failure:
A) before treatment xxx
B) after successful treatment with digoxin

85. Blood pressure in a patient with congestive heart failure:
A) before treatment
B) after successful treatment with digoxin CC

86. Vascular resistance in a patient with congestive heart failure:
A) before treatment xxx
B) after successful treatment with digoxin

87. AV nodal refactory period in a patient with congestive heart failure:
A) before treatment
B) after successful treatment with digoxin xxx

88. Spare receptors available in a particular system for:
A) a partial agonist
B) a full agonist xxx

89. Parasympathetic innervation of the:
A) sino-atrial node xx
B) ventricles

90. Cardioselectivity of:
A) esmolol       xx
B) propranolol

91. Duration of action of:
A) esmolol
B) propranolol       xx

92. Duration of action of:
A) edrophonium
B) neostigmine       xx

93. Duration of action of:
A) acetylcholine
B) carbachol       xx

NOTE: ANSWERS FOR THE REMAINING MULTIPLE CHOICE ITEMS (X01 THROUGH X36) MUST BE FILLED IN ON THE ‘BACK’ OF THE ANSWER SHEET
IV. AUTONOMIC CHECKERBOARD (4 POINTS EACH)

DIRECTIONS: (Items X01-X06) Please refer to the chart on the next page (you may wish to remove the next page for ease of comparison). Assume that each VERTICAL COLUMN represents a different animal which was pretreated with one or more drugs before the test drug sequence. Assume the pretreatment drugs are used in doses at least adequate to elicit their most characteristic pharmacological effects and that all pretreatment drugs act throughout the experiment. Assume further that test drugs are short-acting. The chart indicates the acute qualitative change (increase ⇑, decrease ⇓, no change ⇒, respectively) in TOTAL PERIPHERAL RESISTANCE after intravenous injection of each test drug. With careful attention to the key, you should choose the MINIMUM number of pretreatment drugs which would be required to account for and still be compatible with the observed results. SELECT:

A) atropine
B) diphenhydramine
C) guanethidine
D) mecamylamine
E) nadolol
F) phenolamine
G) ranitidine
H) atropine and phenoxybenzamine
I) atropine and propranolol
J) phenolamine and reserpine
K) atropine, phenolamine and propranolol
L) cocaine mecamylamine and scopolamine
M) atropine mecamylamine, prazosin and reserpine
N) bretylium, mecamylamine, scopolamine and timolol
O) diphenhydramine, labetalol, ranitidine and scopolamine
P) ipratropium, nadolol, prazosin and reserpine

FOR EACH ITEM, FILL IN ONLY ONE CIRCLE ON YOUR ANSWER SHEETS.

X01. Animal I was pretreated with: xxB guanethidine
X02. Animal II was pretreated with: xxG atropine & propranolol
X03. Animal III was pretreated with: xxH phenolamine & reserpine
X04. Animal IV was pretreated with: xxC mecamylamine
X05. Animal V was pretreated with: xx diphenhydramine, labetalol, ranitidine & scop
X06. Animal VI was pretreated with: xxK cocaine, mecamylamine & scop
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Where:
- ACh = acetylcholine
- AMP = amphetamine
- DMPP = dimethylphenylpiperazinium
- EPI = epinephrine
- HIST = histamine
- ISO = isoproterenol
- MCN = McN-A343
- OXO = oxotremorine
- PHEN = phenylephrine

Suggestion: remove this page for easy comparison.
V. Matching. Below is a list of drugs or phrases arranged. For items X07-X27 choose the corresponding letter which BEST matches or completes the description. Use each item once and only once (one point each).

A) atorvastatin
B) enalapril
C) lansoprazole
D) losartan
E) mnemonic description of cholinergic agonist overdosage
F) mnemonic description of anticholinergic overdosage
G) methylatropine
H) object drug
I) precipitant drug
J) pharmacodynamics
K) pharmacokinetics
L) ouabain
M) torsemide
N) triamterene
O) placebo
P) prednisone
Q) promethazine
R) propranolol
S) rifampin
T spironolactone
U) zileuton

X07. antagonist of aldosterone receptors T
X08. antagonist of H1 receptors Q
X09. antagonist of leukotriene receptors D
X10. anti-inflammatory steroid P
X11. class II antiarrhythmic R
X12. hot as a stove, red as a beet, dry as a bone, mad as a hatter F
X13. inducer of CYP 3A4 S
X14. inhibitor of angiotensin converting enzyme B
X15. inhibitor of HMG Co-A reductase A
X16. inhibitor of renal Na-K-2Cl symport M
X17. inhibitor of Na/K pump ATPase L
X18. inhibitor of proton/potassium pump C
X19. inhibitor of renal epithelial Na channels N
X20. inhibitor of 5-lipoxygenase U
X21. in amiodarone inhibition of P-glycoprotein mediated transport of digoxin in the gut, digoxin is the H
X22. in erythromycin inhibition of theophylline metabolism, erythromycin is the I
X23. quaternary ammonium antagonist of muscarinic receptors G
X24. salivation, lacrimation, urination, defecation, sweating E
X25. substance or procedure without specific activity for the condition being treated O
X26. systematic study of the effects of drugs on living systems K
X27. systematic study of the effects of living systems on drugs J
VI. MATCHING (2 points each) For items X28 through X36 AND SA1 AND SA2 please see the ‘Table of Pharmacokinetic Values (F03)’ on the next page (we suggest you remove that page for ease of consulting the data). For items X28 through X36 choose the one best answer (letter A through U) from the first column of the Table of Pharmacokinetic Values. Each ‘drug’ may be chosen once, more than once, or not at all.

X28. Based on ‘effective’ total plasma concentration, and ignoring other pharmacokinetic parameters, which drug appears to be the most potent on a weight basis? O

X29. Which drug has the shortest half-life? G

X30. Following time for distribution, which drug is present in the greatest total amount in the body of a patient when present at, the effective (i.e., therapeutic) concentration? S

X31. Based on ‘effective’ total plasma concentration, and ignoring plasma protein binding, which drug appears to be the least potent on a weight basis? N

X32. Of the drugs in this table for which appropriate information is available, which appears to have the smallest ‘therapeutic window’? F

X33. If dosing were begun at a constant rate, which drug would it require the longest time to achieve a steady state plasma concentration? E

X34. Which drug appears to have the largest first pass effect? G

X35. Which drug would be least ionized (i.e., have the smallest percentage of its molecules in an ionized state) at a plasma pH of 7.4? K

X36. Which drug would be most highly ionized (i.e., have the greatest percentage of its molecules in an ionized state) at a stomach pH of 2.4? M

X36. Based on ‘toxic’ plasma concentration, and ignoring plasma protein binding, which drug appears to be the most potent for toxicity on a weight basis? O
VII. SHORT ANSWER QUESTIONS (5 points each)

Based on the information available from the Table of Pharmacokinetic Values (F02) (previous page) answer items SA1 and SA2 in the spaces provided. Show your calculations.

Please clearly write your answers in the spaces below. (Note: answers that are not sufficiently legible to be deciphered will be assumed to be incorrect!)

SA1. What is the theoretical loading dose of drug D to be given intravenously in an 80 kg person to obtain the 'effective concentration'?

SA2. A 100 kg patient is to be given drug C by mouth (PO, BID). What is the calculated daily dosage to achieve an ‘effective’ average steady state plasma concentration of drug C in this patient? How should the dosage be given (once daily, BID, etc.)?
Short Answer/Essay Question (10 points):

Please clearly write your answer in the space below. You may use the back of this page in the unlikely event that you need more space.(Note: answers that are not sufficiently legible to be deciphered will be assumed to be incorrect!)

SA3. What is the change in heart rate that occurs after IV administration of norepinephrine (2 points)? Describe the pharmacological/physiological basis for this change (5 points).

SA4. List two pretreatment drugs with different mechanisms or sites of action which are not adrenergic receptor antagonists which would prevent this change in heart rate following subsequent administration of norepinephrine) Explain why each of these drugs would produce this effect (5 points).
Short Answer/Essay Question (5 points each):

Please clearly write your answer in the space below. You may use the back of this page in the unlikely event that you need more space. (Note: answers that are not sufficiently legible to be deciphered will be assumed to be incorrect!)

SA5. Glucocorticoids have strong anti-inflammatory actions and can be used chronically to block inflammation in autoimmune disease or inhibit rejection in transplant patients. However, the chronic systemic use of glucocorticoids for this purpose is also associated with physiological effects that become increasingly debilitating to the patient with long term treatment. Choose what you consider the 5 most serious of these toxicities and briefly describe the physiological basis for it.

1. thin skin, bruising due to inhibition of fibroblast proliferation
2. inappropriate fat redistribution due to stimulation of lipolysis and increased release of insulin
3. fractures due to stimulation of bone resorption (osteoporosis)
4. blindness due to cataract formation
5. severe muscle weakness due to increased release of amino acids and breakdown of proteins in muscle
6. hyperglycemia due to stimulated gluconeogenesis in the liver
7. mood changes due to CNS effects of glucocorticoids
8. increased susceptibility to infection due to anti-inflammatory actions
9. growth retardation especially in children

SA6. As part of your ISMS project you are experimenting with the treatment of mice injected with $10^{10}$ leukemia cells. You begin treatment right after injecting the leukemic cells and you treat every 3 weeks. Using a combination of ara-C and 5-fluorouracil you determine that your log kill is 5. Assuming that the leukemia cells regrow by 1 log per week, what is the minimum number of treatments you need to theoretically cure your mouse patient?

This is the end of the exam. Good luck. Have a great vacation!