1. Synaptic transmission at adrenergic synapses is terminated by

A. Acetylcholinesterase
B. Acetyl Coenzyme A
C. COMT
D. Choline acetyltransferase
E. Transmitter reuptake

2. Reserpine is a drug that decreases adrenergic transmission by interfering with storage of neurotransmitter in synaptic vesicles. This drug would likely produce all of the following EXCEPT:

A. Increased bronchial constriction
B. Increased GI motility
C. Reduced blood pressure
D. Pupil dilation
E. Reduced heart rate

3. Acetylcholine rapidly and transiently opens a ligand-gated sodium ion channel when it binds to the:

A. Alpha receptor
B. Beta receptor
C. Muscarinic receptor
D. Nicotinic receptor
E. Presynaptic autoreceptor

4. Dopamine beta hydroxylase is localized to the

A. Liver
B. Mitochondria
C. Synaptic cleft
D. Effector cell
E. Synaptic vesicle
5. Which of the following clinical scenarios describes a drug undergoing instantaneous absorption and first-order elimination?

A. A drug administered as an intravenous bolus, and eliminated at a rate proportional to plasma drug concentration.
B. A drug administered as an intravenous bolus, and eliminated at a constant rate.
C. A drug administered as a constant intravenous infusion, and eliminated at a rate proportional to plasma drug concentration.
D. A drug administered as an oral tablet, and eliminated at a rate proportional to plasma drug concentration.
E. A drug administered as an oral tablet, and eliminated at a constant rate.

6. Which of the following statements about drug binding to plasma proteins is TRUE?

A. Most clinical tests of plasma drug levels actually measure the concentration of free drug in the plasma.
B. The fraction of drug that is free (unbound) in the plasma would be greater than normal in a patient with hepatic cirrhosis.
C. Plasma lipoproteins preferentially bind drugs that are weak acids.
D. Alpha-1 acid glycoprotein preferentially binds drugs that are weak acids.
E. Serum albumin preferentially binds drugs that are weak bases.

7. Which of the following statements about the blood-brain barrier is FALSE?

A. Most lipid-soluble drugs cross the blood-brain barrier through facilitated diffusion.
B. P-glycoprotein on vascular endothelial cells is involved in the active transport of drugs away from the central nervous system.
C. There are relatively few fenestrations between vascular endothelial cells.
D. There are ample tight junctions between vascular endothelial cells.
E. Many water-soluble drugs cannot significantly permeate the blood-brain barrier.

8. Factors most likely to directly alter a drug's metabolic rate include all of the following EXCEPT?

A. Age
B. Gender
C. Weight
D. Genetic makeup
E. Altered blood flow
9. Patients using certain antibiotics, such as rifampicin that induces CYP3A, and who also are taking oral contraceptives should be warned that:

A. The use of the oral contraceptive will inhibit the effectiveness of rifampicin.
B. The use of the oral contraceptive will enhance the effectiveness of rifampicin.
C. The use of rifampicin will inhibit the effectiveness of the oral contraceptive.
D. The use of rifampicin will enhance the effectiveness of the oral contraceptive.
E. The coadministration of the rifampicin and oral contraceptive may lead to nausea and vomiting.

10. In a patient that presents a polymorphism in CYP2D6 that results in deletion of this gene, administration of tricyclic antidepressants will most likely result in:

A. Decreased plasma levels of the tricyclic antidepressant.
B. Increased cardiotoxicity of the tricyclic antidepressant.
C. Increased oxidation of the tricyclic antidepressant.
D. Increased clearance of the tricyclic antidepressant.
E. An increase in the dose to achieve effectiveness of the antidepressant.

11. Which of the following reactions would be LEAST likely to occur in infants due to their lack of bacterial flora in the GI?

A. Reduction
B. Oxidation
C. Hydrolysis
D. Conjugation
E. Dehalogenation

12. Which of the following statements is TRUE?

A. The functional groups on an agonist that determine the affinity for receptors are the same as those which determine intrinsic activity.
B. Competitive antagonists decrease the dissociation constants of agonists which act at the same receptor.
C. Phosphorylation of the receptor decreases the ability of the receptor to interact with G-proteins.
D. The nonlinear relationship between receptor occupancy and response occurs when there are large numbers of receptors expressed on the cell surface.
E. There is an inverse relationship between the affinity of a drug for its receptor and its intrinsic activity at that same receptor.
13. This drug can block vagally-mediated bronchial secretions, gastric acid secretion or bradycardia, but is unlikely to produce CNS effects, like hallucinations or delirium, in an overdose.
   A. Atropine
   B. Glycopyrrolate
   C. Physostigmine
   D. Pilocarpine
   E. Scopolamine

14. Which of the following receptor classes has a single membrane spanning region and may require homodimerization (joining of two receptors into a single functional unit) for full activity?
   A. G-protein coupled receptors
   B. Ligand-gated ion channels
   C. Kinase (growth factor) receptors
   D. Steroid receptors

15. This ocular drug is contraindicated in patients with narrow-angle (angle closure) glaucoma because it can block drainage of aqueous humor.
   A. Apracionidine
   B. Carbachol
   C. Etothiopate
   D. Timolol
   E. Tropicamide

16. Which one of the following incorrectly matches the cholinergic agent with its potential symptoms or toxic effects in an overdose?
   A. Atropine: hyperthermia, hallucinations and tachycardia
   B. Hexamethonium: mydriasis, tachycardia and hypotension
   C. Isoflurophate (DFP): miosis, bronchoconstriction, convulsions, respiratory collapse
   D. Neostigmine: muscle fasciculations, diarrhea, restlessnes, confusion and convulsions
   E. Nicotine: CNS stimulation followed by CNS depression, muscle fasciculations followed by muscle weakness, and release of epinephrine from the adrenal medulla
17. Which one of the following **incorrectly** matches the cholinergic agent with its potential therapeutic effect(s)?

A. Atropine: initial treatment for poisoning by organophosphate insecticides
B. Bethanechol: increase tone and activity of GI tract in patients with paralytic ileus
C. Neostigmine: symptomatic treatment of myasthenia gravis
D. Pilocarpine: reduce intraocular pressure, especially in acute glaucoma attack
E. Succinylcholine: long term, reversible muscle paralysis.

18. This neuromuscular blocker has a very rapid onset of action, but may cause hyperkalemia or postoperative muscle pain.

A. Atracurium
B. Mivacurium
C. Rocuronium
D. Succinylcholine
E. **α-Tubocurarine**

19. Which of the following pharmacological effects would be expected after systemic administration of bethanechol, as well as after systemic administration of physostigmine (each given independently)?

A. Convulsions and CNS effects
B. Diarrhea
C. Muscle fasciculations
D. Mydriasis
E. **Tachycardia**

20. Which of the following ocular drugs is useful in the long-term treatment of glaucoma because it inhibits formation of aqueous humor without affecting accommodation?

A. Cyclopentolate
B. Ecatiophate
C. Pilocarpine
D. Timolol
E. Tropicamide
21. Which of the following statements regarding therapy of COPD is TRUE?

A. Pharmacotherapy for COPD is generally more effective than drug treatment of asthma.
B. Albuterol has limited usefulness in COPD because it will not alter vagally-mediated bronchoconstriction.
C. Orally administered corticosteroids, like prednisone, are useful in treating COPD because they reduce chronic pulmonary inflammation with minimal side-effects.
D. Ipratropium bromide is useful in treating COPD because it will stabilize mast cells and inhibit infiltration of eosinophils into the lungs.
E. Theophylline is useful in COPD as an orally active bronchodilator which can also increase work of the diaphragm.

22. Which one of the following antiasthma drugs is NOT correctly paired with its side-effect?

A. Albuterol : tremors and tachycardia
B. Beclomethasone (inhaled) : adrenal suppression, weight gain, psychological disturbances
C. Fluticasone (inhaled) : oral candidiasis (thrush)
D. Ipratropium bromide : dry mouth and bradycardia
E. Theophylline: tremors, seizures, tachycardia

For questions 23-25, MATCH the one best receptor subtype to the numbered statements below. An answer may be used one, more than once, or not at all.

A. M1 muscarinic receptor
B. M2 muscarinic receptor
C. M5 muscarinic receptor
D. Ncns nicotinic receptor
E. Nnmt nicotinic receptor

23. This cholinergic receptor subtype would be the best target for a novel agonist drug with selective activity in the brain to treat cognitive disorders, such as Alzheimer's disease.

24. This cholinergic receptor subtype is arranged as a pentamer with 4 subunits, including 2 α’s and 3 β’s, and is NOT directly affected by α-bungarotoxin.

25. Activation of this cholinergic receptor at synaptic terminals will reduce intracellular calcium levels and inhibit acetylcholine release.
For questions 26-30 MATCH the ONE best drug to the mechanism described in the numbered statements below. An answer may be used one, more than once, or not at all.

A. Albuterol  
B. Beclomethasone  
C. Cromolyn sodium  
D. Epinephrine  
E. Ipratropium bromide  
F. Nedocromil  
G. Salmeterol  
H. Theophylline  
I. Zafirlukast  
J. Zileuton

26. Therapeutic effects in asthma are due, in part, to increased synthesis of beta-2 receptors in pulmonary smooth muscle.

27. Useful in asthma prophylaxis, especially nocturnal asthma, because of its prolonged bronchodilating effects and minimal systemic absorption after inhalation.

28. Selectively blocks leukotriene receptors thus reducing leukotriene-mediated bronchoconstriction and pulmonary inflammation in asthmatic patients.

29. Drug of choice for symptoms of anaphylaxis due to its bronchodilating and vasoconstrictive properties.

30. Exerts antiinflammatory effects, in part, by stimulating production of lipocortin, which inhibits phospholipase A2.

For questions 31-34, MATCH the ONE best word with the description below. An answer may be used once, more than once or not at all.

A. Alcohol dehydrogenase  
B. Aldehyde dehydrogenase  
C. Cytochrome P4503A  
D. Cytochrome P4502D6  
E. Glutathione S-transferase  
F. Sulfate Conjugation  
G. UDP glucuronyl transferase

31. Is inhibited by disulfiram

32. A phase II enzyme located in the smooth endoplasmic reticulum.

33. Participates in the highest percentage of phase II metabolism reactions.

34. Genetic polymorphisms in this enzyme lead to a wide disparity in patient response to a number of cardiovascular and antidepressant drugs.
For questions 35-38, MATCH the ONE best answer to the description. An answer may be used once, more than once, or not at all.

A. Buccal administration  
B. Intramuscular injection  
C. Intravenous injection  
D. Oral administration  
E. Rectal suppository  
F. Subcutaneous injection  
G. Sublingual administration  
H. Targeted drug delivery  
I. Transdermal administration

35. The route of administration that would cause the greatest problem with bioavailability when used with a drug sensitive to the first-pass effect.

36. The parenteral route of administration whose usefulness is most restricted by the limited number of drugs that can be absorbed through this route.

37. The route of administration most likely to ensure complete bioavailability of an administered drug.

38. This route of administration is used to deliver scopolamine in low doses over a prolonged time to treat motion sickness.

For questions 39-43, MATCH the ONE best drug to the numbered statements below. An answer may be used once, more than once, or not at all.

A. Atracurium  
B. Bethanechol  
C. Curare (d-tubocurarine)  
D. Neostigmine  
E. Nicotine  
F. Physostigmine  
G. Pilocarpine  
H. Scopolamine  
I. Succinycholine  
J. Trimethaphan

39. This drug is useful to immediately lower blood pressure by rapidly inhibiting sympathetic tone to peripheral blood vessels.

40. Effects of this drug include initial stimulation and subsequent inhibition (desensitization) of ligand-gated ion channels in the brain and peripheral nervous system.

41. This drug will directly stimulate cholinergic receptors in the GI or urinary tract, but NOT cholinergic receptors in skeletal muscle or autonomic ganglia.

42. This drug produces a reversible muscle paralysis without causing initial hypotension.

43. This drug can directly stimulate release of histamine from mast cells.
44. You wish to administer an intramuscular injection of a narcotic analgesic to one of your patients to relieve pain. However, this drug undergoes first-order elimination by the kidneys, and the patient has significantly decreased renal function. Which of the following statements about the pharmacokinetics of this drug would be FALSE, if the patient were to be injected with a standard dose of the drug?

A. The total drug exposure (represented by the area under the curve) would be increased, relative to a patient with normal renal function.
B. The peak plasma drug concentration would be increased, relative to a normal patient.
C. The time to reach the peak plasma drug concentration would be shorter, relative to a normal patient.
D. The elimination rate constant would be decreased, relative to a normal patient.

45. A child is brought into an emergency room after swallowing a large number of aspirin tablets, and is demonstrating symptoms of salicylate toxicity. Given that the salicylates (which includes aspirin) are weak acids, which of the following statements best describes how ion trapping could be used to accelerate renal elimination of the drug?

A. Sodium bicarbonate should be administered to increase the concentration of neutral drug in the urine.
B. Sodium bicarbonate should be administered to increase the concentration of charged drug in the urine.
C. Ammonium chloride should be administered to increase the concentration of neutral drug in the urine.
D. Ammonium chloride should be administered to increase the concentration of charged drug in the urine.

46. Diazepam is a drug used to treat anxiety disorders and has a half-time of elimination of 43 hours. If a patient took a single dose of diazepam that achieved a peak plasma concentration of 400 ng/ml, calculate what the plasma concentration should be 24 hours later. Select the range of values that best describes the correct answer. The following equations may or may not be useful.

\[ C = C_o * e^{(k_e * t)} \]
\[ X = X_o - V_{max} * t \]

A. > 350 ng/ml
B. 300-350 ng/ml
C. 250-200 ng/ml
D. 200-250 ng/ml
E. <200 ng/ml
47. Dopamine is a drug that can be administered through intravenous infusion at a high rate to support blood pressure during shock (20 micrograms/kg/min) or at a lower rate to support cardiac output and renal perfusion in congestive heart failure patients (5 micrograms/kg/min). Use the following data about dopamine to calculate the expected plasma drug concentration that would be reached when dopamine was infused at 5 micrograms/kg/min. Select the range of values that best describes the correct answer.

Dopamine $k_e = 0.35 \text{ min}^{-1}$
Dopamine $V_d = 2000 \text{ ml/kg}$
Patient weight: 70 kg
1 microgram = 1,000 nanogram (Ng)

A. $< 5 \text{ ng/ml}$
B. 5.0-10.0 ng/ml
C. 10.0-20.0 ng/ml
D. 20.0-100 ng/ml
E. $>100 \text{ ng/ml}$

48. Oxycodone is a narcotic analgesic that has a normal therapeutic concentration of 10 ng/ml. Oxycontin® is a controlled release oral tablet of oxycodone, that has sometimes been crushed by drug abusers and injected intravenously. Calculate the plasma drug concentration of oxycodone that would be reached if a person weighing 70 kg were to inject the contents of an 80 mg Oxycontin® tablet as an intravenous bolus. The volume of distribution of oxycodone is 2000 ml/kg. Select the range of values that best describes the correct answer.

A. 0-100 ng/ml
B. 100-200 ng/ml
C. 200-300 ng/ml
D. 300-500 ng/ml
E. $> 500 \text{ ng/ml}$

59. A drug is being administered as an intravenous bolus every six hours. The $k_e$ of the drug is 0.231 hr$^{-1}$. Assume that enough injections have been carried out that the peak and trough plasma drug concentrations have reached their plateau values. How large is the trough plasma drug concentration relative to the peak concentration? Select the range of values that best describes the correct answer.

A. 0-20%
B. 20-40%
C. 40-60%
D. 60-80%
E. 80-100%
For questions 50-51, consider the following data: Isoproterenol is a full agonist with intrinsic activity of 1.0 and a dissociation constant of 90 nM at the beta_1-adrenergic receptors in the heart. In a hypothetical heart preparation, there are 10 billion receptors. In this system only 5 billion receptors need to be activated to achieve a maximal response.

50. Of the numbers provided, which is the lowest concentration of isoproterenol that will produce a maximal increase in the force of contraction in this preparation?

A. 0.45 nM  
B. 0.9 nM  
C. 4.5 nM  
D. 9.0 nM  
E. 45nM  
F. 90 nM  
G. 450 nM  
H. 900 nM  
I. Cannot be determined with the information provided.

51. Increasing amounts of isoproterenol are given and the effect on heart rate determined and a dose-response curve is prepared. Which of the following will be the ED_{50} for isoproterenol?

A. 0.45 nM  
B. 0.9 nM  
C. 4.5 nM  
D. 9.0 nM  
E. 45nM  
F. 90 nM  
G. 450 nM  
H. 900 nM  
I. Cannot be determined with the information provided.
In this preparation the interaction of isoproterenol with other drugs are studied and the following dose-response curves generated. These are listed above. MATCH the correct dose-response curve to the drugs mostly likely to produce the illustrated effect.

52. The dose-response curve for isoproterenol in the absence and presence of propranolol, the latter having a dissociation constant of 40 nM and given at 400 nM.

53. The dose-response curve for isoproterenol in the absence and presence of atenolol, the latter having a dissociation constant of 30 nM and given at 0.3 nM.

54. The dose-responses curve for isoproterenol in the absence and in the presence of an irreversible beta, receptor antagonist given under conditions to inactivate at least 7 billion beta, receptors (assume there are 10 billion receptors in the preparation).
For questions 55-68, MATCH the mechanism of action and therapeutic use in the numbered statements to the choices below. An answer may be used once, more than once or not at all.

**Mechanism or Site of Action**
A. The alpha₁-adrenergic receptor  
B. DA₂ receptors of sympathetic nerve terminals  
C. The beta₁-adrenergic receptor of the heart  
D. Presynaptic alpha₂-adrenergic receptors  
E. The DA₁ receptor of vascular smooth muscle  
F. The alpha₂-adrenergic receptor in the nucleus tractus solitarius  
G. The beta₂-adrenergic receptor of smooth muscle  
H. Promotes the release of neurotransmitters from presynaptic nerve terminals

**Therapeutic Use**
A. Hypertension  
B. Ischemic heart disease  
C. Benign prostatic hypertrophy  
D. Asthma  
E. Orally for the treatment of congestive heart failure  
F. Hyperactivity in Children  
G. Cardiogenic shock  
H. Symptomatic relief of nasal stuffiness

From the above choices fill in the blanks in the following statements:

55-56. Propranolol acts at ___________ to decrease the oxygen consumption of the heart and this action makes the drug effective in treating ___________.

57-58. Albuterol acts at ___________ which makes the drug useful in the treatment of ___________.

59-60. Prazosin acts at the ___________ of vascular smooth muscle and this action makes the drug useful in treating ___________.

61-62. Phenylephrine acts at ___________ for the ___________.

63-64. Clonidine acts at ___________ and this makes the drug useful in the treatment of ___________.

65-66. Methylphenidate acts by ___________ and this makes the drug useful in treating ___________.

67-68. Dobutamine acts at the ___________ to increase the force of myocardial contraction and this action makes the drug useful in treating ___________.
For questions 69-71, consider the following data: An unknown drug is administered and the effect on a series of cardiovascular parameters is recorded and presented below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prior to unknown administration</th>
<th>2 minutes after unknown administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>90</td>
<td>162</td>
</tr>
<tr>
<td>Contractile force (grams developed tension)</td>
<td>153</td>
<td>435</td>
</tr>
<tr>
<td>Total peripheral vascular resistance (relative units)</td>
<td>1.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mm Hg)</td>
<td>85</td>
<td>97</td>
</tr>
</tbody>
</table>

69. Which of the following is most likely the unknown?

   A. Tamsulosin  
   B. Isoproterenol  
   C. Phentylephrine  
   D. Phenoxycabamine  
   E. Norepinephrine  
   F. A high dose of epinephrine

70. Which of the following could block ALL of the effects of the unknown?

   A. Clonidine  
   B. Prazosin  
   C. Methylphenidate  
   D. Propranolol  
   E. Reserpine  
   F. Clonidine  
   G. Tamsulosin  
   H. Guanethidine

71. Which of the following could **selectively** block effects of the unknown on heart rate and contractile force?

   A. Clonidine  
   B. Prazosin  
   C. Methylphenidate  
   D. Atenolol  
   E. Reserpine  
   F. Clonidine  
   G. Albuterol  
   H. Terbutaline
For questions 72-73, consider the following case: Peter Piper, a 37-year old farmer from Pulaski, was the victim of botulinum toxin poisoning after eating a peck of home-canned pickled peppers prepared by his wife, Priscilla.

72. Which of the following signs or symptoms would be LEAST likely in Mr. Piper?

A. Constipation  
B. Difficulty swallowing  
C. Delirium and hallucinations  
D. Muscle weakness and fatigue  
E. Mydriasis and blurred vision

73. This poisoning could have been prevented or reversed by

A. Heating the peppers thoroughly before ingestion  
B. Immediate administration of pralidoxime (2-PAM)  
C. Pretreatment with atropine before ingestion of the peppers  
D. Treatment with atropine after ingestion of the peppers  
E. Treatment with neostigmine after ingestion of the peppers

For questions 74-75, consider the following case: Fred F, a 38 year old caveman, was out at dawn hunting dinosaur eggs for his family's breakfast when he heard the roar of a nearby sabertooth tiger also looking for a morning meal. In a panic, Fred ran several miles before slipping on some pebbles and rubble, and falling down a slope onto solid bedrock. He escaped by swimming across a small stream.

74. Which of the following autonomic nervous system responses activated during his escape would be mediated via the postganglionic transmitter acetylcholine?

A. Mydriasis  
B. Production of thick, ropy saliva  
C. Profuse, generalized sweating  
D. Release of epinephrine from the adrenal medulla  
E. Vasodilation of blood vessels in large muscles

75. Although Fred F suffered numerous small cuts and scrapes in his fall, he did not sustain significant blood loss. This was most likely due to autonomic nervous system effects on blood vessels in the skin mediated by what neurotransmitter?

A. Acetylcholine  
B. Dopamine  
C. Epinephrine  
D. Nicotine  
E. Norepinephrine
For questions 76-79, identify the key enzymes and substances involved in cholinergic signal transduction from the letters (A-I) in the following figure:

76. A form of phospholipase C that is directly activated by Gq.
77. A so-called "second messenger" that directly releases Ca^{++} from internal stores.
78. An M2 muscarinic receptor subtype.
79. A G-protein that responds to cholinergic receptor activation by inhibiting adenylyl cyclase.
80. Which ONE of the sites from the figure above is incorrectly matched with a competitive antagonist of the principal receptors located at that site?

A. Site A (in heart) : trimethaphan
B. Site B (in heart) : atropine
C. Site C (in heart) : propranolol
D. Site D (in adrenals): trimethaphan
E. Site E : succinylcholine

81. Tyrosine hydroxylase is the rate-limiting step in synthesis of the major transmitter released at which site?

A. Site A
B. Site B
C. Site C
D. Site D
E. Site E

82. Actions of the neurotransmitter released at site B are terminated by which one of the following enzymes or processes?

A. acetylcholinesterase (AChE)
B. choline acetyltransferase (ChAT)
C. high-affinity reuptake
D. monoamine oxidase (MAO)
E. pseudo- or plasma cholinesterase