Several hospitals are participating in a study to test the efficacy of a newly developed drug prior to its release. This drug is designed to lower cholesterol levels. Of the one thousand patients that are involved in this study, half of the participants receive the drug and half receive a placebo. Neither the physicians in charge of the study nor the patients are permitted to know what the patients have received. Which of the following steps in the drug development process does this scenario most closely describe?

A. Investigational New Drug (IND) Application  
B. New Drug Application (NDA)  
C. Phase I  
D. Phase II  
E. Phase III  
F. Phase IV  

Explanation:  
The correct answer is E. Phase III trials consist of large, double-blind, controlled studies using patients for whom the drug is targeted. Typically, 500–5000 patients participate in the study, which is designed to determine whether the drug is more efficacious than placebo, and to compare it to older therapies. Drug toxicity is also monitored; infrequent toxicities have a greater likelihood of appearing in this phase (because of the greater number of subjects) than the previous two phases.  

In order for human testing to commence, an Investigational New Drug (IND) (choice A) Application must be submitted by the manufacturer to the Food and Drug Administration (FDA). This application includes chemical and manufacturing information about the drug, data from animal testing, and designs for clinical testing.  

The NDA (choice B), which contains the results of the clinical studies, must be submitted following human testing in order to gain approval for general marketing of a drug for prescription use.  

Phase I trials (choice C) are the first phase of clinical testing. Approximately 20–30 normal volunteers are used to determine the safety and pharmacokinetic properties of a new drug. Occasionally, patients are used in this phase (e.g., cancer patients who are tested with new chemotherapeutic agents).  

Phase II (choice D) tests a new drug on a small group of selected patients (100–300) with regard to therapeutic efficacy, dose range, kinetics, and metabolism.  

Phase IV (choice F) is the post-marketing surveillance phase. This phase is not regulated by the FDA, and essentially consists of physicians reporting toxic side effects to the FDA. This phase hopefully detects drugs with infrequent side effects that could not be determined with the limited number of subjects that are used in clinical testing. If it is determined that a drug does exhibit toxic side effects, and that its benefits do not outweigh its costs, the drug can be pulled from the market. (Incidentally, this is how the diet drug fenfluramine was removed from the market.)  

A 28-year-old man is placed on haloperidol after he is diagnosed with schizophrenia. A few days later his concerned mother brings him back to the psychiatrist because he is exhibiting strange movements. The physician observes movements that consist of sustained contractions and twisting motions of his limbs and trunk, with his eyes tonically deviated upward for several minutes. Which of the following adverse reactions is occurring in this patient?
A. Akathisia
B. Dystonia
C. Neuroleptic malignant syndrome
D. Parkinsonism
E. Tardive dyskinesia

Explanation:

The correct answer is B. This patient is exhibiting dystonia, an acute extrapyramidal side effect that can be a consequence of neuroleptic therapy. Acute dystonic reactions generally occur within the first few days of the initiation of neuroleptic therapy, tend to occur more frequently in children and young adults, and occur in males more often than females. The sustained eye deviation described in the question is a form of dystonia called an oculogyric crisis. These reactions are reversible with antihistamines (e.g., diphenhydramine), anticholinergic drugs (e.g., benztropine), or diazepam. All of the other answer choices can also be consequences of neuroleptic therapy.

Akathisia (choice A) is an extrapyramidal syndrome characterized by a feeling of restlessness, frequent, repetitive stereotyped movements and an inability to sit still for more than a short period of time. It usually occurs during the first few months of drug use.

Neuroleptic malignant syndrome (choice C) is a rare, but potentially fatal syndrome that usually occurs within 10 days of starting neuroleptic therapy. Clinical manifestations include fever, encephalopathy, muscle rigidity, dystonia, diaphoresis, tachycardia, and labile blood pressure.

Parkinsonism (choice D), as the name implies, is similar to Parkinson's disease: mask-like facies, drooling, tremors, pill-rolling motion, cogwheel rigidity, and shuffling gait all may be present. Parkinsonism can be produced by neuroleptic drugs, usually beginning about three weeks after the initiation of therapy.

Tardive dyskinesia (choice E) is an often irreversible syndrome characterized by involuntary, choreoathetoid movements in patients treated with antipsychotic medications. The frequency of tardive dyskinesia increases with age and with the length of therapy. This disorder would be unlikely to occur within a few days of the initiation of drug therapy.

A seasoned marathon runner drinks a cup of strong black coffee about an hour before his race to enhance his performance. By which of the following mechanisms does caffeine directly contribute to enhanced performance?

A. Allosteric activation of adenylyl cyclase
B. Allosteric activation of glycogen phosphorylase
C. Allosteric activation of hormone sensitive lipase
D. Inhibition of dephosphorylation of protein kinase A
E. Inhibition of phosphodiesterase
The correct answer is E. Caffeine inhibits phosphodiesterase and thereby prevents cAMP from being degraded. Consequently, cAMP continues to activate protein kinase A, which results in both glycogen and triglyceride breakdown.

Caffeine has no direct or indirect effect on adenylyl cyclase (choice A).

Caffeine does not directly interact with glycogen phosphorylase (choice B) or hormone-sensitive lipase (choice C) and cannot allosterically activate these enzymes. However, because cAMP is not degraded due to the action of caffeine on phosphodiesterase, the cAMP will continue to activate protein kinase A. In turn, activation of protein kinase A will lead to phosphorylation of glycogen phosphorylase and hormone-sensitive lipase, resulting in glycogen and triglyceride breakdown.

Protein kinase A is not phosphorylated under normal physiological circumstances, and therefore caffeine cannot inhibit its dephosphorylation (choice D).

A 64-year-old man presents to his doctor with aching, burning pain after meals. He had been self-medicating for several months with antacids, but he found this to be increasingly ineffective. His physician decides to take him off the antacids and instead places him on a combination of ranitidine and sucralfate. Why is this combination a bad idea?

A. Ranitidine increases the toxicity of sucralfate
B. Ranitidine inhibits the action of sucralfate
C. Sucralfate and ranitidine coprecipitate
D. Sucralfate increases the toxicity of ranitidine
E. Sucralfate inhibits the action of ranitidine

Explanation:

The correct answer is B. Sucralfate is a promising drug that is not presently in widespread use because it is incompatible with H2 antagonists such as cimetidine, ranitidine, famotidine and nizatidine. Sucralfate is aluminum sucrose sulfate, a sulfated disaccharide, which polymerizes and binds to ulcerated tissue. It forms a protective coating against acid, pepsin and bile, giving the tissue a chance to heal. Unfortunately, a low gastric pH is required for polymerization, meaning that sucralfate is incompatible with drugs that reduce gastric acidity, such as H2 blockers and antacids. The moral of the story is that you cannot assume that two medications that are individually helpful in a medical condition will be synergistic. Learning the mechanisms by which the drugs work will help you spot potential interactions and earn you points on the USMLE.

A 26-year-old woman is undergoing surgery and is anesthetized with an inhalant anesthetic. She is also given an IV dose of succinylcholine. Within minutes, she develops a heart rate of 124 and increasing core body temperature. What is the mechanism of action of the drug of choice for this patient's condition?

A. It interferes with the release of Ca2+ from the sarcoplasmic reticulum
B. It is a competitive antagonist of ACh at the motor end plate
C. It is a GABA receptor agonist that enhances inhibition of nerve impulses
D. It uncouples oxidative phosphorylation, thereby preventing heat formation

Explanation:

The correct answer is A. This is a three-step question. First you need to figure out the diagnosis, then you need to determine the drug of choice for this condition, and finally, you need to remember the mechanism of action of that drug. The clinical picture presented suggests malignant hyperthermia. The treatment for this condition (a USMLE favorite) is dantrolene. Dantrolene prevents the release of Ca²⁺ from the sarcoplasmic reticulum, thereby reducing skeletal muscle contractions. Side effects include muscle weakness and hepatotoxicity (if used chronically). Other uses include spasticity, multiple sclerosis, and cerebral palsy.

Nondepolarizing blockers competitively inhibit the activity of acetylcholine at the neuromuscular junction (choice B). Examples include curare, atracurium, and vecuronium.

Baclofen is a GABAB receptor agonist that is inhibitory at synapses in the spinal cord (choice C).

Uncouplers of oxidative phosphorylation (choice D) include dinitrophenol and thermogenin (found in brown fat mitochondria and acts to keep blood warm in a neonate).

A 12-year-old boy presents with complaints of chronic cough and inability to keep up with his schoolmates during physical education class. The patient's mother states that he has just recovered from his fourth bout of pneumonia in the past 5 months. On examination, digital clubbing, hyperresonance to percussion, and basilar crackles are noted. The boy's sweat chloride concentration is 87 mEq/L. Which of the following agents would most likely serve to alleviate his chronic signs and symptoms?

A. Dextromethorphan (PO)
B. Ipratropium (aerosolized)
C. N-acetylcysteine (aerosolized)
D. Pentamidine (aerosolized)
E. Vancomycin (IV)

Explanation:

The correct answer is C. The patient is presenting with signs and symptoms of cystic fibrosis (CF). CF is an autosomal recessive disorder of the exocrine glands. The pulmonary manifestations include acute and chronic bronchitis, bronchiectasis, chronic bouts of pneumonia, hemoptysis, and cor pulmonale, which can occur late in the disease. Other common findings include chronic cough, exercise intolerance, recurrent respiratory infections, digital clubbing, increased anteroposterior diameter, and basilar crackles. If the pilocarpine sweat test reveals sodium and chloride levels greater than 80 mEq/L, a diagnosis of CF can be made. The primary goals of treatment include thinning the mucus secretions, keeping the airways open, and treating recurrent infections. Thinning of mucus can be achieved with mucolytics such as N-acetylcysteine. N-Acetylcysteine (Mucomyst) splits the disulfide linkages between these mucoproteins, resulting in a decrease in mucous
viscosity. It is indicated as adjuvant therapy in the treatment of abnormal viscid or inspissated mucus secretions in CF, chronic lung disease, post-traumatic chest complications, and atelectasis secondary to mucus obstruction. Inhaled bronchodilators are used to open the airways. Furthermore, prednisone has been shown to increase pulmonary function and increase body weight. The definitive treatment is lung transplantation.

Dextromethorphan (choice A), a cough suppressant, is contraindicated in patients with CF since it will prevent the removal of mucus from the lungs.

Ipratropium (choice B) is an anticholinergic that will cause a drying and thickening of the mucus in this patient; therefore, it is contraindicated.

Pentamidine (aerosolized) (choice D) is an antiprotozoal agent primarily used in the treatment of Pneumocystis carinii pneumonia in HIV-infected patients.

Vancomycin (choice E) is an anti-infective agent used in the treatment of life-threatening, gram-positive infections.

A 54-year-old man with emphysema presents to his physician with a blood pressure of 157/101 mm Hg. Over the next several months the physician prescribes angiotensin converting enzyme inhibitors, diuretics, and calcium channel blockers, but the patient has to discontinue each agent because of undesirable side effects. The physician then decides to prescribe a beta antagonist. Which of the following beta antagonists would be most appropriate for this particular patient?

A. Metoprolol
B. Nadolol
C. Propranolol
D. Sotalol
E. Timolol

Explanation:

The correct answer is A. Patients with nonallergic bronchospastic conditions, such as emphysema and chronic bronchitis, are generally not prescribed beta-receptor blocking agents since these agents can cause bronchoconstriction by blocking beta-2 receptors. However, relatively low doses of selective beta-1 receptor antagonists, such as metoprolol and atenolol, are relatively well tolerated in patients with emphysema. As a precautionary measure, emphysema patients receiving beta-1-selective blocking agents should use a bronchodilator with beta-2-stimulating activity. All the other answer choices are nonselective beta receptor blocking agents and should not be used in the treatment of hypertension in patients with nonallergic bronchospasm since they are likely to exacerbate the signs and symptoms of the condition.

A 16-year-old boy presents to the emergency room after suffering a generalized tonic-clonic seizure. He is presently restless and irritable, and complains of nausea and headache. A careful history reveals that he had been experimenting with cocaine earlier that day. Physical examination is remarkable for a heart rate of 130 and blood pressure of 150/95. Which of the following mechanisms is most likely responsible for the cocaine-induced hypertension?
A. Blocking norepinephrine reuptake  

B. Directly stimulating alpha-1 receptors  

C. Directly stimulating beta-1 receptors  

D. Directly stimulating beta-2 receptors  

E. Inducing norepinephrine release  

F. Metabolism to a false neurotransmitter  

Explanation:  

The correct answer is A. Cocaine is a stimulant that causes hypertension and tachycardia by blocking norepinephrine uptake. This leads to an accumulation of norepinephrine in the synapse, causing greater stimulation of postsynaptic receptors. The receptors that mediate the systemic vasoconstriction are alpha-1 adrenergic receptors, and the receptors that mediate the increases in heart rate and inotropic state are beta-1 adrenergic receptors.  

Direct stimulation of alpha-1 receptors (choice B) would increase blood pressure, but this is not cocaine's mechanism of action.  

Direct stimulation of beta-1 receptors (choice C) could increase blood pressure by increasing inotropic state, but this is not cocaine's mechanism of action.  

Direct stimulation of beta-2 receptors (choice D) would cause vasodilation in the skeletal muscle vasculature, leading to a decrease in blood pressure.  

Induction of norepinephrine release (choice E) would increase blood pressure, but this is the mechanism of action of amphetamine, not cocaine.  

Cocaine is not metabolized to a false neurotransmitter (choice F).  

A 28-year-old female complains to her doctor that she is in danger of losing her job. She states that she is late to work almost everyday because, before she leaves for work, she must check all of the faucets to make sure the water is turned off. She also needs to repeatedly check to make sure that her stove is off. When she is finally ready to leave, she returns from her car several times to ensure that her doors and windows are locked. Which of the following drugs will her physician most likely prescribe?  

A. Buspirone  

B. Chlorpromazine  

C. Clomipramine  

D. Imipramine  

E. Phenelzine  

F. Zolpidem
Explanation:

The correct answer is C. This patient is suffering from obsessive-compulsive disorder. Clomipramine, a tricyclic antidepressant, and the selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, are effective in this disorder. None of the other answer choices listed constitute effective therapy for this disorder.

Buspirone (choice A) is a non-benzodiazepine anxiolytic that does not have marked sedative or euphoric effects. Unlike the benzodiazepines, buspirone is devoid of hypnotic, anticonvulsant, and muscle relaxant properties.

Chlorpromazine (choice B) is an antipsychotic (phenothiazine) drug.

Imipramine (choice D) is a tricyclic antidepressant.

Phenelzine (choice E) is a monoamine oxidase inhibitor type of antidepressant.

Zolpidem (choice F) is a non-benzodiazepine hypnotic agent.

A 67-year-old male presents to the emergency room with shaking chills and a fever of 101°F. Laboratory examination reveals a hematocrit of 23% and urine tests are positive for blood. The patient states that he is only taking one medication for his "irregular heartbeat." Which of the following drugs most likely caused the appearance of these signs and symptoms in this patient?

A. Digoxin  
B. Hydralazine  
C. Propranolol  
D. Quinidine  
E. Verapamil

Explanation:

The correct answer is D. Hemolytic anemia is a disorder in which red blood cell survival is decreased, either episodically or continuously. Although the bone marrow has the ability to increase erythroid production, this type of anemia is typically seen when the bone marrow is unable to compensate for the marked hemolysis of red blood cells. Since red blood cells typically survive for 120 days, the hematocrit will fall at a rate of 1% per day, in the absence of red blood cell production. The mechanism for the hemolytic anemia in this patient is related to the formation of an immune complex between a circulating red blood cell and quinidine, a medication used in the treatment of premature atrial, AV-junctional and ventricular contractions as well as various other arrhythmias. Since the immune complex is viewed as being foreign, the red blood cell in this complex is lysed by the complement system. The quinidine molecule then dissociates from the lysed red blood cell and binds to another red blood cell to repeat the process. This recycling of drug-antibody complex accounts for the dramatic decrease in the hematocrit.

Digoxin (choice A) is typically used to treat atrial fibrillation, atrial flutter and paroxysmal atrial tachycardia. Digoxin is not associated with the development of hemolytic anemia.
Hydralazine (choice B) is a vasodilator used in the treatment of essential hypertension. Although it is not associated with the development of hemolytic anemia, it has been known to cause a lupus-like syndrome.

Neither propranolol (choice C), a beta-blocker, nor verapamil (choice E), a calcium channel blocker, is associated with the development of hemolytic anemia.

A 74-year-old male has been unsuccessful in passing urine today, but was able to pass urine normally for the previous two days. Physical examination is remarkable for a blood pressure of 175/90 mm Hg. Laboratory examination reveals a serum creatinine of 4.5 and a blood urea nitrogen of 115 mg/dL. Urinalysis reveals a specific gravity of 1.01 mg/dL, and an occasional white blood cell per high-powered field. Which of the following could be used to ameliorate the patient's symptoms?

A. Benazepril  
B. Doxazosin  
C. Furosemide  
D. Hyoscyamine  
E. Phenazopyridine

Explanation:

The correct answer is B. Prostatic hypertrophy in elderly men is very common; therefore, it should be considered as a primary cause of renal insufficiency until proven otherwise. The patient's signs and symptoms are consistent with obstructive uropathy; there is a history of high urine output followed by periods of almost no urine output. This pattern of urine output leads to the accumulation of urine in the collecting system, which creates a high pressure system. This high pressure is then "transmitted" back to the kidney and results in renal insufficiency. Since the patient's obstructive uropathy is most likely caused by prostatic hypertrophy, doxazosin should be used to treat the cause of these signs and symptoms. Doxazosin is a peripherally acting alpha-1-adrenergic blocking agent indicated for the treatment of urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH). It is also indicated for the treatment of hypertension, especially in men with BPH. Therefore, the use of this agent will correct the obstructive uropathy and treat his hypertension.

Benazepril (choice A) is an ACE inhibitor used in the treatment of hypertension; however, it is known to cause azotemia and oliguria, especially in those with renal insufficiency. Therefore, this agent would be contraindicated.

Furosemide (choice C) is a "loop" diuretic used to increase urine output in patients without a urinary tract obstruction.

Hyoscyamine (choice D) is used in the treatment of gastrointestinal disorders caused by spasm and hypermotility. Since this agent is a potent anticholinergic, it would not be recommended in a patient with urinary obstruction. Remember, anticholinergic agents cause urinary retention.

Phenazopyridine (choice E) is a urinary tract analgesic used to decrease the dysuria associated with urinary tract infections. The use of this agent in patients with renal insufficiency is not recommended because phenazopyridine can accumulate, resulting in renal stones and transient renal failure.
An anticancer chemotherapeutic agent that acts by first-order kinetics would be expected to kill a

A. constant number of cancer cells  
B. constant proportion of cancer cells  
C. variable number of cells depending on the half-life of the drug  
D. variable number of cells depending on the proportion of cells in S phase  
E. variable proportion of cells depending on the number of cells in the G0 phase

Explanation:

The correct answer is B. First-order kinetics, when applied to the concept of cytotoxicity, means that the drug will kill a constant proportion of tumor cells (rather than a constant number, choice A). The log kill hypothesis refines this by stating that the magnitude of killing by a cytotoxic agent is a logarithmic function. Therefore, a drug producing a 3-log kill will reduce 1012 cells to 109, or will reduce 106 cells to 103 (three orders of magnitude in either case). This hypothesis accounts for the far better results observed with chemotherapy when the total tumor burden is low.

The half-life of the drug (choice C) does not determine the number of cells killed, assuming an adequate dose is given.

Choices D and E are both reflections of cell cycle specificity, the ability of a drug to specifically kill cells in a particular phase of the cell cycle (eg, S phase or G0 phase), and are unrelated to first-order kinetics.

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Q2

A pharmacologist is examining a new drug with potential sedative properties. He begins by analyzing the pharmacokinetic properties of the drug. Studies of the drug's rate of elimination yield the above data. Which of the following drugs has similar kinetics to the drug being studied?
A. Carbamazepine
B. Cimetidine
C. Ethanol
D. Ketoconazole
E. Phenobarbital

Explanation:
The correct answer is C. The graph presented is classic for zero-order elimination; the graph is a straight line using standard graphical coordinates. Note that the plasma concentration of the drug diminishes linearly with time. Zero-order elimination means that the rate of elimination is constant and is independent of the drug plasma concentration. Another way of saying this is that a constant amount of drug is cleared per unit time. There are very few drugs that exhibit zero-order elimination; examples include alcohol, phenytoin and aspirin (at high concentrations).

The vast majority of drugs exhibit first-order elimination kinetics. First-order elimination means that a constant fraction of the drug is cleared per unit time. Thus, elimination is proportional to the drug plasma concentration. This can be graphically depicted in several different ways. Using standard graphical coordinates, an exponential decrease in the concentration of the drug is seen. If a semi-logarithmic scale is used, the graph will appear as a straight line, similar to the graph in this question.

A 68-year-old male presents with complaints of chronic fatigue, exertional and nocturnal dyspnea, orthopnea, and a chronic nonproductive cough. On examination, respiratory wheezing and rhonchi are noted. Cardiac examination reveals a diminished first heart sound and an S3 gallop. The patient indicates that he was recently treated for hypertension and vasospastic angina. Based on his initial presentation, which of the following agents was most likely prescribed?

A. Amlodipine
B. Captopril
C. Furosemide
D. Hydralazine
E. Verapamil

Explanation:
The correct answer is E. The patient is presenting with classic signs and symptoms of congestive heart failure: chronic fatigue, exertional and nocturnal dyspnea, orthopnea, a chronic nonproductive cough, respiratory wheezing and rhonchi, as well as a diminished first heart sound and an S3 gallop. Verapamil is a calcium channel blocker used to treat both hypertension and vasospastic angina. However, it has a strong negative inotropic effect on the heart which can cause signs and symptoms of heart failure. Furthermore, some clinical studies have shown that congestive heart failure can develop in a small percentage of individuals taking...
verapamil.

Amlodipine (choice A) is also a calcium channel blocker used in the treatment of both hypertension and vasospastic angina. However, it does not have a negative inotropic effect on the heart and does not cause signs and symptoms of heart failure. Furthermore, amlodipine is generally well tolerated in heart failure patients.

Captopril (choice B) is an ACE inhibitor used in the treatment of both hypertension and congestive heart failure. Therefore, this agent would not potentiate signs and symptoms of congestive heart failure.

Furosemide (choice C) is a diuretic commonly used to treat the congestion and edema associated with heart failure. It can also be used to treat hypertension.

Hydralazine (choice D) is a vasodilator used primarily to treat signs and symptoms associated with heart failure. The use of this agent in patients with angina is not recommended because it can potentiate the angina.

A 57-year-old man is brought to the emergency room for a suspected myocardial infarction. An electrocardiogram indicates the appearance of a wide-complex ventricular tachycardia with a rate of 126 beats per minute. The physician prescribes a drug to decrease SA node automaticity, increase AV node refractoriness, and decrease AV node conduction velocity. Which of the following agents was most likely prescribed?

A. Amiodarone
B. Disopyramide
C. Lidocaine
D. Propranolol
E. Verapamil

Explanation:

The correct answer is D. The patient has a ventricular tachycardia as indicated by the electrocardiogram: the appearance of a wide-complex ventricular tachycardia with a rate of 126 beats per minute. Propranolol is a Type II antiarrhythmic agent that acts by decreasing SA node automaticity, increasing AV nodal refractoriness, and decreasing AV nodal conduction velocity. Propranolol is indicated for the treatment of ventricular tachycardias, supraventricular arrhythmias, and for slowing the ventricular rate during atrial fibrillation and atrial flutter.

Amiodarone (choice A) is a Type III antiarrhythmic that acts by prolonging the action potential duration in tissue with fast-response action potentials. Amiodarone is indicated for the treatment of refractory ventricular arrhythmias that are unresponsive to other antiarrhythmics.

Disopyramide (choice B) is a Type IA antiarrhythmic that reduces the maximal velocity of phase 0 depolarization by blocking the inward sodium current in tissue with fast-response action potentials. It also increases the action potential duration. Disopyramide is indicated for the treatment of atrial and ventricular extrasystoles and atrial and ventricular tachyarrhythmias.

Lidocaine (choice C) is a Type IB agent that attenuates phase 4 depolarization, decreases automaticity and cases a decrease in excitability and membrane responsiveness. This agent raises the ventricular fibrillation threshold as well as suppresses arrhythmias casued by abnormal automaticity. Lidocaine is used in the
treatment of the acute management of ventricular arrhythmias that occur during periods of cardiac ischemia, such as cardiac surgery or secondary to an acute MI.

Verapamil (choice E), a Type IV antiarrhythmic agent, blocks calcium channels, thereby decreasing conduction velocity and increasing refractoriness in tissue with slow-response action potentials. Verapamil is indicated for the treatment of atrial fibrillation and flutter as well as other atrial tachycardias.

A 54-year-old man is brought to the emergency department after experiencing several syncopal episodes. The patient states that he is currently taking erythromycin for treatment of bronchitis and another medication for treatment of gastroesophageal reflux disease (GERD). If an electrocardiogram reveals torsades de pointes, the patient is most likely taking which of the following medications for treatment of his reflux disease?

A. Cisapride
B. Famotidine
C. Lansoprazole
D. Metoclopramide
E. Sucralfate

Explanation:
The correct answer is A. This question is about an important drug interaction occurring between erythromycin and cisapride (used for gastroesophageal reflux disease-GERD). Serious cardiac arrhythmias, including torsades de pointes, QT interval prolongation, ventricular tachycardia, and ventricular fibrillation, have been reported in patients taking cisapride with medications that inhibit cytochrome P450 3A4. Examples of medications other than cisapride that have a similar interaction with erythromycin include ketoconazole, fluconazole, clarithromycin, nefazodone, and indinavir. It is important to note that QT prolongation, torsades de pointes, cardiac arrest, and sudden death have occurred in patients taking only cisapride. None of the other agents listed interact with erythromycin to produce these proarrhythmic effects.

Famotidine (choice B) is an H2 receptor antagonist used in the treatment of GERD and gastric ulcers; this agent is generally well tolerated with very little incidence of drug interactions.

Lansoprazole (choice C) is a proton pump inhibitor indicated for the treatment of gastric ulcerations and GERD. When this agent is administered with phenytoin, the clearance of phenytoin is decreased by 15%, leading to an extension of the therapeutic effect.

Metoclopramide (choice D) is a prokinetic agent indicated for the treatment of GERD and diabetic gastroparesis. When given with cyclosporine, the toxic effects of cyclosporine are more pronounced. Furthermore, when metoclopramide is administered with levodopa, it decreases the effectiveness of levodopa.

Sucralfate (choice E) is a basic aluminum salt indicated for the treatment of duodenal ulcer. When sucralfate is administered with digoxin, anticoagulants, ketoconazole, fluoroquinolones, and tetracyclines, there is a dramatic decrease in the absorption of these agents from this intestinal tract.

A 46-year-old woman visits her podiatrist to have several bunions removed from her right foot. She chooses conscious sedation rather than general anesthesia for this procedure. She is given intravenous midazolam to supplement the local anesthetics that are injected into her foot. Midway through the surgery, she suddenly becomes agitated, combative, and exhibits involuntary movements. The anesthesiologist determines that she is having a paradoxical reaction to the midazolam and immediately administers
A. flumazenil
B. glucagon
C. naloxone
D. nitrite
E. protamine

Explanation:
The correct answer is A. Flumazenil is a benzodiazepine antagonist and has been approved to hasten the recovery from benzodiazepines used in anesthetic and diagnostic settings and to reverse the CNS depressant effects following an overdose with benzodiazepines. Flumazenil can only be used for benzodiazepines and is not useful to reverse the effects of other CNS depressants such as barbiturates and ethanol.

Glucagon (choice B) is an antidote for beta-blocker overdose.

Naloxone (choice C), an opioid receptor antagonist, is an antidote for opioid overdose.

Nitrite (choice D), or sodium nitrite, is an antidote for cyanide poisoning.

Protamine (choice E) is an antidote for heparin overdose.

A 50-year-old stockbroker presents with a chief complaint of generalized "stiffness" lasting a few hours each morning. The patient acknowledges a recent 10 pound weight loss and a past medical history of duodenal ulcers. On examination, his temperature is 100.5 degrees Fahrenheit, there is lymphadenopathy and mild splenomegaly. Subcutaneous "nodules" are palpable over selected bony prominences. Based on this information, which of the following would be most recommended for the treatment of his acute pain symptoms?

A. Acetaminophen
B. Celecoxib
C. Indomethacin
D. Methotrexate
E. Sulfasalazine

Explanation:
The correct answer is B. Rheumatoid arthritis (RA) is a chronic, multisystem inflammatory disorder of unknown etiology. The primary feature of RA is persistent inflammatory synovitis, symmetrically involving the peripheral joints. The synovial inflammation leads to cartilage destruction and bone erosions, which can cause substantial joint deformities. In around 10-20% of patients, the onset of RA is acute, and accompanied by constitutional symptoms, such as fever, lymphadenopathy, splenomegaly, and weight loss. Subcutaneous nodules (Heberden's nodes), pleuritis, pulmonary fibrosis, pericarditis, nerve entrapment syndromes, ocular changes,
and vasculitis may also be seen. Morning stiffness > 1 hr is one of the distinguishing factors of inflammatory arthritis as compared to non-inflammatory arthritis. The question is essentially asking for the most appropriate agent for the alleviation of the patient's acute signs and symptoms. Celecoxib is a selective cyclooxygenase-2 (COX-2) inhibitor with anti-inflammatory, analgesic, and antipyretic effects. COX-1 is involved in the production of prostaglandins that protect the GI lining, while COX-2 is important for the synthesis of prostaglandins involved in inflammation and pain. Therefore, a selective COX-2 inhibitor can be used for management of RA in a patient with a past history of ulcers.

Acetaminophen (choice A) has analgesic and antipyretic effects, but not anti-inflammatory effects. Therefore, this agent would not be indicated for treatment of a patient with RA.

Indomethacin (choice C) is a non-steroidal anti-inflammatory drug indicated for the treatment of acute pain caused by inflammation. Although indomethacin can be used in the treatment of RA, it would not be recommended in a patient with a past medical history of ulcers.

Both methotrexate (choice D) and sulfasalazine (choice E) are used in the chronic management of RA as part of disease-modifying antirheumatic drug (DMARD) therapy; however, these agents take several weeks to months to elicit their beneficial effects. Therefore, these agents should not be used in the acute management of rheumatoid arthritis.

A patient with tuberculosis develops bright orange-red urine and calls his physician in a panic because he is afraid he is bleeding into the urine. The patient has no other urinary tract symptoms. Which of the following medications is most likely to produce this side effect?

A. Ethambutol
B. Isoniazid
C. Pyridoxine
D. Rifampin
E. Streptomycin

Explanation:
The correct answer is D. While not of major medical concern, urine color changes as a result of medications can be very distressing to patients. These changes are consequently worth learning so that you can warn patients when you prescribe the medicine. Rifampin is a safe drug that is used both for prophylaxis and for active tuberculosis therapy. In addition to discoloring urine, rifampin and its metabolites can discolor feces, saliva, sweat, and tears (and apparently can stain soft contact lenses).

Ethambutol (choice A) is an antituberculosis agent that is added if isoniazid-resistance is suspected and does not alter urine color.

Isoniazid (choice B) remains the principle antituberculosis agent and does not alter urine color.

Pyridoxine (choice C) is used principally in prophylaxis against tuberculosis and does not alter urine color.

Streptomycin (choice E), which must be given intramuscularly, is sometimes used as an adjunctive agent very early in antituberculosis therapy and has sometimes been lifesaving in critically ill patients. It does not cause a urine color change.
A 63-year-old man has taken an antidepressant for the past 3 months. He is on no other medications and is generally in good health. After attending a graduation party for his son at which he consumes wine, bread, and cheese, he is rushed to the emergency room with tachycardia, headache, and a blood pressure of 200/100 mm Hg. Which antidepressant is he most likely taking?

A. Fluoxetine
B. Imipramine
C. Phenelzine
D. Trazodone
E. Venlafaxine

Explanation:
The correct answer is C. This patient is clearly exhibiting the classic interaction of tyramine-containing foods (e.g., cheese, beer, wine) with monoamine oxidase inhibitors (MAOIs). When a patient is on an MAOI, gastrointestinal and hepatic MAO is inhibited, thus allowing large quantities of ingested tyramine to reach the systemic circulation. The tyramine enters the synaptic terminals of postganglionic sympathetic neurons, displacing massive amounts of norepinephrine from them; neuronal MAO is also inhibited, so that the released norepinephrine cannot be metabolized. These events can lead to a potentially lethal sympathetic crisis. The only MAOI listed is phenelzine.

All of the other drugs listed are antidepressants, but none have interactions with tyramine.

Fluoxetine (choice A) is a selective serotonin reuptake inhibitor (SSRI).

Imipramine (choice B) is a tricyclic antidepressant.

Trazodone (choice D) and venlafaxine (choice E) are heterocyclic antidepressants.

A 72-year-old woman with mild heart failure is treated overzealously with a thiazide diuretic. A few days later, the woman complains of muscle weakness, and laboratory tests demonstrate hypokalemia. Which of the following is most likely increased in this woman?

A. Arterial H+ concentration
B. Plasma aldosterone
C. Plasma sodium
D. Potassium retention
E. Sodium retention
Explanation:

The correct answer is B. Diuretics lead to aldosterone excess and hypokalemia by a variety of mechanisms. (1) Diuretic induces volume depletion stimulates the formation of angiotensin II, which, in turn, causes a secondary increase in plasma aldosterone concentration. This increase in plasma aldosterone stimulates potassium excretion, contributing to the hypokalemia. (2) The saline diuresis increases sodium delivery to the collecting tubule. The increased availability of sodium along with the elevated plasma aldosterone augments sodium reabsorption in the collecting tubule, thereby raising luminal negativity. This high luminal negativity in the collecting tubule promotes secretion of cations, especially hydrogen ions, which raises bicarbonate reabsorption. (3) The saline diuresis causes rapid fluid flow in the distal tubule, which, in turn, keeps luminal potassium concentration low by carrying it away and thus preventing the accumulation of any potassium that enters the lumen. This low luminal concentration of potassium creates a steep concentration gradient for additional potassium losses in the urine.

The treatment of edema with thiazide or loop diuretics is the most common cause of metabolic alkalosis. Arterial pH is increased and arterial H+ concentration (choice A) is decreased with metabolic alkalosis.

Sodium depletion tends to decrease plasma sodium (choice C) levels, although the effect is usually small.

Overuse of the thiazide diuretic has caused depletion of sodium and potassium by the kidneys, not retention of sodium and potassium (choices D and E).

A 16-year-old female patient presents with complaints of a non-productive cough, low-grade fever, and a headache. The physician also notes a non-purulent otitis media. She is treated with an antibiotic that inhibits the translocation of the growing peptide chain along the mRNA. The antibiotic the patient was given was

- A. chloramphenicol
- B. cycloheximide
- C. erythromycin
- D. puromycin
- E. streptomycin
- F. tetracycline

Explanation:

The correct answer is C. This patient was infected with M. pneumoniae, the most common cause of pneumonia in young adults. The disorder is usually characterized by a non-productive cough, low-grade fever, and a headache as well as non-purulent otitis media or bullous myringitis in about 20% of the patients. It is usually treated with erythromycin, azithromycin, tetracyclines, or fluoroquinolones. Erythromycin acts to inhibit the translocation step of ribosomal protein synthesis.

Chloramphenicol (choice A) inhibits ribosomal peptidyl transferase in prokaryotes.

Cycloheximide (choice B) inhibits ribosomal peptidyl transferase in eukaryotes.

Puromycin (choice D) acts to inhibit elongation by binding to the "A" site and prematurely terminating chain growth in both eukaryotes and prokaryotes.
Streptomycin (choice E) causes misreading of the code during initiation in prokaryotes.

Tetracycline (choice F) acts on prokaryotes to prevent binding of the aminoacyl-tRNA to the ribosome, thereby inhibiting initiation.

During a follow-up visit to her psychiatrist, a 17-year-old female admits that she is contemplating suicide. She has been morbidly depressed for the past 2 months; she denies drug abuse or excessive drinking. After a complete evaluation, her physician prescribes imipramine. This drug acts by

A. increasing dopamine release
B. inhibiting monoamine oxidase
C. inhibiting the reuptake of serotonin and norepinephrine
D. potentiating GABA
E. selectively inhibiting the reuptake of serotonin

Explanation:
The correct answer is C. Imipramine is a tricyclic antidepressant that works by blocking the reuptake of serotonin and norepinephrine, thereby increasing the levels of these neurotransmitters in the synaptic space.

Increasing central nervous system dopamine release (choice A) is a mechanism of action of indirect-acting sympathomimetics such as amphetamine and cocaine.

Monoamine oxidase inhibitors (choice B) such as tranylcypromine, phenelzine, iproniazid, and isocarboxazid are another class of antidepressants.

Benzodiazepines and barbiturates are sedative-hypnotics that act by potentiating GABA (choice D).

Selective serotonin reuptake inhibitors (SSRIs) (choice E) such as fluoxetine, paroxetine, and sertraline are another class of antidepressants.

Spironolactone acts at which of the areas of the nephron indicated in the diagram above?
A. A
B. B
C. C
D. D
E. E

Explanation:

The correct answer is E. Potassium-sparing diuretics act as antagonists at the intracellular aldosterone receptor located in the collecting tubule. By doing so, they decrease the expression of the genes for sodium channels and the Na+/K+ ATPase.

No known diuretics act at the glomerulus (choice A).

Carbonic anhydrase inhibitors, such as acetazolamide, inhibit sodium bicarbonate reabsorption from the proximal tubule (choice B).

Ethacrynic acid is a loop diuretic that acts by inhibiting the Na+/K+/2Cl- transporter located in the ascending loop of Henle (choice C).

Thiazide diuretics inhibit the Na+/Cl- transporter in the early segment of the distal convoluted tubule (choice D).

Which of the following drugs used in the treatment of noninsulin-dependent diabetes mellitus (NIDDM) has no effect on the secretion of insulin?

A. Acetohexamide
B. Chlorpropamide
C. Glyburide
D. Metformin
E. Tolbutamide

Explanation:

The correct answer is D. Metformin is a drug that is often used in conjunction with oral hypoglycemic agents for the treatment of NIDDM. Its mechanism of action is two-fold: (1) it decreases the production of glucose in the liver; (2) it increases the uptake of glucose in the liver. Metformin has no effect on the secretion of pancreatic insulin.

Acetohexamide (choice A) is an oral hypoglycemic agent that is a sulfonylurea derivative. It stimulates secretion of insulin from the pancreas.
Chlorpropamide (choice B) is an oral hypoglycemic agent that is a sulfonylurea derivative. It stimulates secretion of insulin from the pancreas.

Glyburide (choice C) is a sulfonylurea derivative that stimulates insulin secretion from the pancreas.

Tolbutamide (choice E) is a sulfonylurea derivative that stimulates insulin secretion from the pancreas.

A 54-year-old man presents to the emergency room with intense pain in his right eye. Examination reveals a red ring surrounding his iris and an elevated intraocular pressure in the same eye. After obtaining a careful history with the aid of the man's wife, the emergency room physician concluded that this episode was triggered by which of the following agents?

A. Amitriptyline
B. Cimetidine
C. Diazepam
D. Malathion
E. Propranolol

Explanation:
The correct answer is A. There are three facts that are necessary to know in order to answer this question: what disease the patient is suffering from, what pharmacological properties can trigger an attack, and what drug has these pharmacological properties. The patient described is suffering from an attack of acute or narrow angle glaucoma. These attacks can be precipitated by drugs with anticholinergic actions because muscarinic receptors on the pupillary constrictor muscle of the iris are blocked. This causes pupillary dilation, which further "narrows" the angle in the anterior chamber of the eye. Amitriptyline is a tricyclic antidepressant with significant anticholinergic side effects.

Cimetidine (choice B) is an H2 antagonist that reduces gastric acid release. Its trade name is Tagamet and is now available over the counter. It has no significant anticholinergic side effects.

Diazepam (choice C) is a benzodiazepine. Its trade name is Valium and it has no significant anticholinergic side effects.

Malathion (choice D) is an organophosphorus cholinesterase inhibitor that is used as an insecticide. This agent would increase levels of ACh, thereby widening the angle.

Propranolol (choice E) is a non-selective, beta-adrenergic antagonist. If anything, it would help to prevent an attack by blocking beta-receptors on the ciliary body, thereby diminishing aqueous humor production.

Which of the following drugs antagonizes both the vascular and cardiac actions of norepinephrine?

A. Atenolol
B. Esmolol
C. Labetalol
D. Metaproterenol
E. Prazosin

Explanation:
The correct answer is C. Norepinephrine (NE) is an agonist at alpha1-, alpha2- and beta1-receptors. NE exerts its vascular actions via alpha (predominantly alpha1) receptors and its cardiac actions via beta1-receptors. Labetalol is a nonselective antagonist at alpha- and beta-receptors, and therefore, could prevent all actions of NE.

Atenolol (choice A) is a selective beta1 antagonist, and therefore would block only norepinephrine's cardiac effects.

Esmolol (choice B) is a selective beta1 antagonist, and therefore would block only norepinephrine's cardiac effects. Metaproterenol (choice D) is a selective beta2 agonist and so would not block NE's effects.

Prazosin (choice E) is a selective alpha1 antagonist and would therefore block most of norepinephrine's actions in the vasculature, but would not antagonize other effects.

A 67-year-old man is being treated for atrial fibrillation with digoxin. If his serum digoxin levels are above the therapeutic range, he is at highest risk for developing digoxin toxicity if he also develops

A. hypokalemia
B. hyponatremia
C. hypophosphatemia
D. vitamin B12 deficiency
E. vitamin K deficiency

Explanation:
The correct answer is A. Digoxin is a cardiac glycoside indicated for the treatment of congestive heart failure, atrial fibrillation, and atrial flutter. The therapeutic drug serum levels for digoxin are 0.5-2.2 ng/mL. Toxicity typically occurs when digoxin levels are greater than 2.5 ng/mL; if the patient is hypokalemic, however, toxicity can occur at any therapeutic concentration. Hypokalemia sensitizes the myocardium to digoxin and may reduce the positive inotropic effects of the medication. Other signs and symptoms of digoxin toxicity include nausea, vomiting, anorexia, and appearance of yellow-green halos in the visual field, as well as the development of cardiac arrhythmias.

Although hyponatremia (choice B) and hypophosphatemia (choice C) can result in the development of other pathological disturbances, they do not potentiate digoxin toxicity.

Vitamin B12 deficiency (choice D) is associated with the development of pernicious anemia.
Vitamin K deficiency (choice E) is associated with the development of clotting disorders. Vitamin K deficiency also can potentiate warfarin toxicity.

A 57-year-old alcoholic is hospitalized in the intensive care unit after a multivehicle accident. Twenty hours after the accident, the patient develops a fever and a cough productive of purulent sputum. If a chest radiograph shows lobar consolidation and the sputum reveals the presence of gram-negative encapsulated rods, the most appropriate initial therapy would be

A. cefotaxime (IV)
B. erythromycin (IV)
C. gentamicin (IV) + vancomycin (IV)
D. ticarcillin-clavulanic acid (IV) + vancomycin (IV)
E. trimethoprim-sulfamethoxazole (PO)

Explanation:
The correct answer is A. The patient is presenting with signs and symptoms of pneumonia. Since the patients signs and symptoms are appearing 20 hours after admission, his pneumonia is most likely a "community-acquired" pneumonia; one of the criteria for diagnosing a nosocomial infection is that the infection must not occur before 48 hours after admission. The appearance of plump gram-negative encapsulated rods in an alcoholic is highly suggestive of Klebsiella pneumonia. The most appropriate treatment of Klebsiella pneumonia in this patient is the administration of a third-generation cephalosporin, such as cefotaxime, ceftriaxone, or ceftazidime.

Erythromycin (choice B) is a macrolide antibiotic used in the treatment of a variety of gram-negative and gram-positive infections. Although it is not the treatment of choice in this patient, it is the treatment of choice of Legionella pneumonia.

Gentamicin (choice C) is an aminoglycoside antibiotic that is generally added to improve the efficacy of broad spectrum antibiotics, such as penicillin and cephalosporins, in the treatment of Pseudomonas and Enterococcus infections.

Vancomycin (choices C and D) is an antibiotic used in the treatment of life-threatening infections caused by gram-positive infections; the use of this agent in a gram-negative infection is inappropriate.

Because of the severe nature of this infection, the use of an oral agent, such as trimethoprim-sulfamethoxazole (choice E), would be inappropriate.

A new antifungal medication is being tested in Phase I clinical trials. Examination of the pharmacokinetic properties of the drug reveals that the half-life of the drug is 6 hours. If a continuous intravenous infusion of this drug were started on a research subject, how long would it take to reach 75% of steady state?

A. 3 hours
B. 6 hours
C. 9 hours
D. 12 hours
E. 18 hours
F. 24 hours

Explanation:

The correct answer is D. The rule of thumb is that the plasma concentration will reach 50% in one half-life, 75% in two half-lives, 87.5% in three half-lives, etc., so that the difference between the current drug level and 100% halves with each half-life. In this instance, it takes two half-lives to reach 75%. The half-life of this drug is 6 hours, so two half-lives is 12 hours.

A 39-year-old executive presents with a chief complaint of insomnia. He is given a prescription for pentobarbital, and uses it as prescribed to induce sleep in the evening. When he runs out of the medication he has a great deal of difficulty falling asleep. When he finally does fall asleep, he experiences a multitude of intense, colorful dreams. This is an example of

A. hypnopompic hallucinations
B. night terrors
C. REM rebound
D. sensitization
E. tolerance

Explanation:

The correct answer is C. Barbiturates, alcohol, phenothiazines, and MAO inhibitors decrease the amount of REM sleep while the patient is taking them. Withdrawal of the agent then allows the body to compensate for "missed" REM sleep, and REM rebound develops. This phenomenon is characterized by an increase in the number and intensity of dreams for several days after discontinuation of the drug in question.

Hypnopompic hallucinations (choice A) occur as the patient is awakening, not while in a deep sleep.

Night terrors (pavor nocturnus; choice B) generally occur in children, and are not characterized by vivid, colorful nightmares, as they occur in stage 4 rather than in REM sleep.

Sensitization (choice D) is a process in which prior exposure to an agent leads to an increased effect upon readministration of that agent. This effect is generally associated with psychostimulant drugs.

Tolerance (choice E) refers to a progressive decrement in the effectiveness of a particular dose of a drug.
A 62-year-old Type 2 diabetic patient presents with complaints of malaise, myalgias, respiratory distress, and increased somnolence. If laboratory examination reveals an anion gap of 26 mmol/L, HCO3- of 17 mmol/L and an arterial blood pH of 7.27, the patient is most likely receiving

A. glyburide  
B. metformin  
C. repaglinide  
D. miglitol  
E. troglitazone

Explanation:

The correct answer is B. Lactic acidosis, characterized by elevated blood lactate, decreased arterial blood pH, decreased bicarbonate, and electrolyte imbalances with an elevated anion gap (normal = 10 - 12), is a rare but serious complication of metformin administration. The onset of lactic acidosis is usually accompanied by several non-specific signs and symptoms including malaise, myalgias, respiratory distress and increased somnolence. There may be associated hypothermia, hypotension, and resistant bradyarrhythmias as the condition progresses.

Glyburide (choice A) is a sulfonylurea associated with the development of hypoglycemia and cholestatic jaundice (a rare complication).

Miglitol (choice C) is an alpha-glucosidase inhibitor commonly associated with the development of abdominal discomfort and flatulence.

Repaglinide (choice D) is the non-sulfonylurea moiety of glyburide; it is commonly associated with hypoglycemia, nausea and vomiting.

Idiosyncratic hepatocellular injury has been reported during the usage of troglitazone (choice E). The hepatic injury is usually reversible, but rare cases of hepatic failure requiring liver transplantation or leading to death have been reported with this agent.

Genetic analysis of a female baby with a broad, enlarged neck extending almost to the baby's shoulders demonstrates an XO karyotype. When the baby reaches puberty, hormone replacement therapy should be begun with which of the following agents?

A. Estrogen only  
B. Estrogen and progestin  
C. Insulin  
D. Progestin only  
E. Thyroid hormone
Explanation:

The correct answer is B. The baby has Turner's syndrome, in which only one sex chromosome, the X chromosome, is present as a result of chromosomal loss early after fertilization of the egg. The chromosome loss can either occur in all cells, or only in part of the body, due to random X-chromosome inactivation, producing the variant known as a Turner mosaic. Affected babies often have a prominent "webbed" neck related to lymphatic stasis in the neck, sometimes producing a frank cystic hygroma (large cystic mass composed of dilated lymphatic channels); edema of the dorsum of the hands and feet caused by similar mechanisms is also seen in these babies. A baby with these clinical features should have a chromosomal analysis. Affected babies should also be carefully checked for cardiac anomalies (notably preductal coarctation of the aorta and aortic stenosis with endocardial fibroelastosis), since congenital heart disease can cause early death. By puberty, the neck and extremity edema has resolved, but careful physical examination often reveals residual redundant skin of the neck and shoulders, producing the mature form of webbed neck. Mosaic patients and patients with partial deletions of one X chromosome may present only at puberty with the combination of short stature and primary amenorrhea. The ovaries (usually not biopsied in obvious cases) lose all of their oocytes by 2 years of age ("menopause before menarche") and become atrophic fibrous strands without ova or follicles ("streak ovaries"). Hormonal replacement in Turner patients should include both estrogens and progestins, since unopposed estrogens (choice A) can cause atypical adenomatous hyperplasia of the endometrium.

Insulin (choice C) replacement is not required in these patients.

Replacement of progestin alone (choice D) is not recommended.

Thyroid hormone (choice E) replacement is not required in these patients.

A 33-year-old man receiving chemotherapy for testicular carcinoma develops signs of renal tubular damage. Which of the following drugs is most likely responsible for this nephrotoxicity?

A. Bleomycin
B. Cisplatin
C. Cyclophosphamide
D. Vinblastine
E. Vincristine

Explanation:

The correct answer is B. Cisplatin is an antineoplastic drug used in the treatment of carcinomas of the testes (along with bleomycin and vinblastine), ovaries, bladder, and lung (especially small cell). Along with the typical side effects of nausea, vomiting, and bone marrow suppression, cisplatin is notable for its dose-limiting nephrotoxicity and its ototoxicity.

The other answer choices also have unique, USMLE test-worthy side effects:

Bleomycin (choice A) is very effective against testicular tumors and is used in combination with cisplatin and vinblastine. The most noteworthy (and test-likely) side effect of bleomycin is pulmonary toxicity that can progress to pulmonary fibrosis.
Cyclophosphamide (choice C) is a commonly used chemotherapeutic that is effective in the treatment of lymphomas, multiple myeloma, lymphoblastic leukemias, carcinomas (e.g., breast, ovary, lung, cervix), mycosis fungoides, and neuroblastoma. Note that it is not used in the treatment of testicular cancer. In addition, its most notable side effect is hemorrhagic cystitis (not nephrotoxicity).

Vinblastine (choice D) is used for the treatment of testicular tumors. It is also used for Hodgkin's disease, lymphomas, and Kaposi's sarcoma. Vinblastine is notable for its dose-limiting bone marrow suppression.

Vincristine (choice E) is used as part of the MOPP regimen (it is also called Oncovin) for the treatment of Hodgkin's disease. It is also used in the treatment of acute lymphocytic leukemia (ALL), sarcoma, CNS tumors, and Wilms tumor. Vincristine's noteworthy side effect is its dose-limiting neurotoxicity.

A 32-year-old TV cameraman complains of weakness and blurred vision. He notes that these symptoms are typically worsened with effort and improve with rest. Physical examination is remarkable for ptosis and weakness of limb muscles on repetitive testing. What is the mechanism of action of the agent that is commonly prescribed for the long-term amelioration of these symptoms?

A. Carbamylation of acetylcholinesterase
B. Competitive inhibition of acetylcholinesterase
C. Dephosphorylation of acetylcholinesterase
D. Direct muscarinic receptor agonist
E. Direct muscarinic receptor antagonist
F. Direct nicotinic receptor agonist
G. Direct nicotinic receptor antagonist
H. Phosphorylation of acetylcholinesterase

Explanation:
The correct answer is A. The patient described suffers from myasthenia gravis (MG), a disorder in which autoantibodies to skeletal muscle nicotinic acetylcholine receptors cause a reduction in the receptor number, leading to easy fatigability, weakness of extraocular and facial muscles, and difficulty eating. Symptomatic improvement in these patients can be obtained with acetylcholinesterase inhibitors. Two of the most common drugs given are neostigmine and pyridostigmine, both of which act by carbamylating the acetylcholinesterase enzyme. This temporarily inhibits the enzyme, thus preventing the degradation of acetylcholine and allowing greater stimulation of the nicotinic acetylcholine receptors on skeletal muscle.

Edrophonium (Tensilon) is a short-acting competitive inhibitor of acetylcholinesterase (choice B), used in the diagnosis of MG. The physician selects a weak muscle and then administers edrophonium to the patient. If the test is positive, the patient will exhibit increased strength in that muscle for about two minutes. Edrophonium is not useful for the treatment of MG because of its short duration of action.

Pralidoxime (2-PAM) is an acetylcholinesterase reactivating agent that dephosphorylates acetylcholinesterase (choice C). It is used if an individual is exposed to a phosphorylating acetylcholinesterase inhibitor (e.g., parathion or nerve gases). 2-PAM has a higher affinity for phosphorus than the enzyme, and thus can bind the acetylcholinesterase inhibitor and release the enzyme if "aging" of the phosphate bond has not occurred. This
allows the active enzyme to be regenerated.

A direct muscarinic agonist (choice D) such as pilocarpine or bethanechol would cause enhanced parasympathetic effects such as increased activity in the bowel and bladder, pupillary miosis and accommodation for near vision. These agents are used clinically to activate bowel and bladder smooth muscle, and in the treatment of glaucoma. They have no place in the treatment of MG.

A direct muscarinic antagonist (choice E) such as atropine could be used as an antidote for an anticholinesterase inhibitor because it blocks the excessive parasympathetic side effects that would occur with elevated acetylcholine.

Direct-acting nicotinic receptor agonists (choice F) do not have therapeutic applications except for succinylcholine, a depolarizing skeletal muscle relaxant used in surgery.

Direct nicotinic receptor antagonists (choice G), such as curare and pancuronium, are skeletal muscle relaxants. These drugs block the skeletal muscle nicotinic receptor (NM). Antagonists at the ganglionic nicotinic receptor (NN), such as hexamethonium or trimethaphan, interrupt sympathetic and parasympathetic outflow. Neither type of agent would be used in the treatment of MG.

Agents that phosphorylate acetylcholinesterase (choice H), such as echothiophate, cause irreversible inhibition of acetylcholinesterase and are not useful in the treatment of MG. Insecticides (e.g., malathion, parathion) and nerve gases are also phosphorylating agents.

A pharmacy fellow is trying to determine what the plasma concentration of an experimental antiarrhythmic agent (Drug X) will be at steady-state. A continuous intravenous infusion of the agent began 6 hours earlier at a rate of 3 mg/min. Drug X has a half-life of 3 hours, a volume of distribution of 120 L, and a clearance of 0.6 L/min. If the rate of infusion remains constant, what will the plasma concentration be at steady-state?

A. 0.005 mg/L
B. 0.4 mg/L
C. 2.0 mg/L
D. 5.0 mg/L
E. 40.0 mg/L
F. 200.0 mg/L

Explanation:
The correct answer is D. This is actually a pretty straightforward question. The most difficult aspect is to determine which values given in the stem are necessary to answer this question. The patient is given a constant intravenous infusion (maintenance dose) of a drug and the clearance is known. This is all that is necessary to determine the plasma concentration at steady state.

The equation to use is:
Maintainace DOSE =
Cp = plasma concentration at steady state

CL = clearance

F = bioavailability

In this instance, the bioavailability is one (100%) because the drug is given intravenously, so all of the drug is "absorbed." Now you simply need to "plug and chug":

\[ 3 \text{ mg/min} = \text{Cp} \times 0.6 \]

A 70-year-old man with a history of atrial fibrillation is started on an oral anticoagulant. His prothrombin time is monitored on a regular basis. A few months into his therapy, he begins treatment for a duodenal ulcer and he develops symptoms of a bleeding diathesis. Which of the following ulcer medications is most likely responsible for this change in his hemostatic status?

A. Cimetidine
B. Famotidine
C. Misoprostol
D. Omeprazole
E. Ranitidine

Explanation:

The correct answer is A. Warfarin is the oral anticoagulant the patient was most likely taking. This drug is commonly prescribed to patients with atrial fibrillation to prevent the formation of atrial thrombi. Warfarin increases prothrombin time (PT) because it interferes with the synthesis of the vitamin K clotting factors of the liver (II, VII, IX, and X) and therefore necessitates regular monitoring of the PT. Cimetidine is an H2-blocker that inhibits hepatic enzymes, including those that metabolize warfarin. Consequently, coadministration of warfarin and cimetidine results in enhanced warfarin activity, producing pronounced anticoagulation and the bleeding diathesis in the patient in question. Cimetidine has one of the worst side effect profiles of all the H2-blockers and may also result in gynecomastia in men.

Famotidine (choice B) is an H2-blocker that does not affect liver metabolism.

Misoprostol (choice C) is a prostaglandin E1 analog used in peptic ulcer disease. It does not affect hepatic metabolism.

Omeprazole (choice D) is a proton-pump inhibitor used to decrease acid production in patients with peptic ulcer disease or reflux. It does not affect drug metabolism by the liver.

Ranitidine (choice E) is another H2-blocker. It does not inhibit liver enzymes as strongly as cimetidine does.

A 69-year-old man is brought by ambulance to the emergency room because of fever, chills, and a productive cough for four days. On physical examination, the man appears quite ill; his blood pressure is 110/70, his heart rate is 102, his respiratory rate is 24, and his temperature is 101.7 degrees Fahrenheit. There is dullness to percussion, and decreased breath sounds over the left lung base. Sputum Gram's stain reveals abundant
neutrophils, a few epithelial cells, and numerous gram-positive diplococci. Which of the following antibiotics would be the most appropriate choice for empiric therapy of this man's infection?

A. Ceftazidime
B. Ciprofloxacin
C. Erythromycin
D. Penicillin G
E. Trimethoprim-sulfamethoxazole

Explanation:
The correct answer is D. Streptococcus pneumoniae (pneumococcus) is the likely organism causing this man's pneumonia, based on the clinical presentation as well as the Gram's stain results. Given this patient's age and symptoms, intravenous antibiotics should be given in a hospital setting. Despite the occurrence of resistance of pneumococcus to penicillin, this is still the antibiotic of choice for empiric treatment of this organism.

Ceftazidime (choice A), a third generation cephalosporin with antipseudomonal activity, is less effective than first generation cephalosporins or other third generation cephalosporins (e.g., ceftriaxone) against gram-positive cocci.

Ciprofloxacin (choice B) is a fluoroquinolone with activity against gram negative-organisms. It is not reliably effective against the pneumococci.

Erythromycin (choice C) is useful for a variety of organisms, but there is a high level of macrolide resistance among community-acquired pneumococci.

Trimethoprim-sulfamethoxazole is useful for many urinary tract pathogens, Pneumocystis carinii, Shigella, Salmonella and Serratia, but pneumococci show a significant amount of resistance to the combination (choice E).

A 34-year-old woman is prescribed an antidepressant, which she has taken for the past 3 months. She is on no other medications and is in generally good health. After attending a party, at which she consumed wine and cheese, she is rushed to the emergency room with tachycardia, headache, and a blood pressure of 200/100. Which antidepressant is she most likely taking?

A. Amitriptyline
B. Fluoxetine
C. Phenelzine
D. Sertraline
E. Trazodone

Explanation:
The correct answer is C. Wine and cheese (and many other fermented foods) contain tyramine, an indirect sympathomimetic that can trigger excess catecholamine release and lead to a hypertensive crisis when ingested by patients taking MAO inhibitors. The only such drug listed among the answer choices is phenelzine. Other MAO inhibitors with similar effects include tranylcypromine, isocarboxazid, and iproniazid. Whenever this particular drug class is mentioned in a question stem, consider the possibility of interactions with foods or other medications the patient may have taken.

Amitriptyline (choice A) is a tricyclic antidepressant. Tricyclic antidepressant drugs (particularly amitriptyline) are known for their anticholinergic side effects. They also produce postural hypotension (because they block alpha-adrenergic receptors) and are sedative.

Fluoxetine and sertraline (choices B and D) are antidepressants that are selective serotonin reuptake inhibitors (SSRIs). Fluoxetine is also useful in treatment of obsessive-compulsive disorders.

Trazodone (choice E) is an atypical antidepressant with substantial sedative side effects. Its most serious side effect is priapism, a medical emergency.

A 57-year-old man presents with a steady, severe pain in the right hypochondrium, nausea, vomiting, and a temperature of 102 F. He states that his signs and symptoms began shortly after eating his favorite pizza with extra cheese, pepperoni, and sausage. Laboratory examination reveals a white blood cell count of 13,400/μL and a serum bilirubin value of 2.8 mg/dL. If hepatobiliary imaging reveals an obstructed cystic duct, which of the following agents would be the drug of choice for the treatment of this patient's pain?

A. Meperidine
B. Morphine
C. Naproxen
D. Oxycodone
E. Propoxyphene

Explanation:

The correct answer is A. The patient is presenting with signs and symptoms of acute cholecystitis, which is associated with gallstones in more than 90% of all cases. This condition occurs when a stone becomes impacted in the cystic duct and inflammation develops behind the obstruction. The acute attack is often precipitated by a large fatty meal, and is characterized by the sudden appearance of severe, steady pain localized to the epigastrium or right hypochondrium. Laboratory findings often include elevated white blood cells (2,000 - 15,000/μL). Total serum bilirubin values of 1-4 mg/dL may be seen in some instances, and serum amylase may be elevated. In noncomplicated cases, treatment often includes IV alimentation, analgesics, and antibiotics, as well as withholding of oral feedings. Meperidine is the narcotic of choice since it is least likely to cause spasm of the sphincter of Oddi, probably because of its antimuscarinic properties. It is therefore preferred over morphine (choice B), oxycodone (choice D), and propoxyphene (choice E). Furthermore, propoxyphene is a narcotic agonist with mild analgesic properties; hence, it would most likely not be able to effectively treat this patient's severe pain.

Naproxen (choice C) is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of mild to moderate pain; this agent would most likely not provide sufficient pain control for this patient.
An 82-year-old woman with congestive heart failure and a creatinine clearance (CrCl) of 17 mL/min needs a diuretic for treatment of peripheral edema. Which of the following diuretics would be most appropriate in this patient?

A. Furosemide  
B. Hydrochlorothiazide  
C. Indapamide  
D. Spironolactone  
E. Triamterene  

Explanation:

The correct answer is A. The key to this question is understanding that the effectiveness of each diuretic is dependent on the creatinine clearance (CrCl). For example, the "loop" diuretics are effective down to a CrCl of around 10 mL/min. However, the thiazide and potassium-sparing diuretics are effective only down to a CrCl of around 40 mL/min. Therefore, on the basis of this patient's CrCl of 17 mL/min, only a loop diuretic would be recommended. Furosemide is a loop diuretic that is indicated for the treatment of edema associated with congestive heart failure, hepatic cirrhosis, and renal disease.

Hydrochlorothiazide (choice B) and indapamide (choice C) are thiazide diuretics and therefore would not be recommended for patients with such a low CrCl.

Spironolactone (choice D) and triamterene (choice E) are potassium-sparing diuretics and therefore would not be recommended for a patient with a CrCl of 17 mL/min.

A 72-year-old female with a painful, swollen right leg, is admitted to the hospital to rule out deep vein thrombosis (DVT). An infusion of heparin is begun with the goal of maintaining the patient's activated partial thromboplastin time (APTT) at 1.5 times the normal value. A diagnosis of DVT is confirmed on the second day and it is decided that the patient should receive long-term anticoagulation therapy with heparin. Which of the following conditions is the patient at an increased risk of developing if heparin therapy is continued for 14 days?

A. Agranulocytosis  
B. Anaphylactic reaction  
C. Eosinophilia  
D. Protein C deficiency  
E. Thrombocytopenia  

Explanation:

The correct answer is E. Heparin is the most common cause of drug-induced thrombocytopenia, which can occur in up to 30% of all patients receiving heparin therapy. The risk for development of thrombocytopenia (TCP) seems to increase as the duration of therapy increases, especially when heparin is used for more than
10 days. The risk for developing TCP appears to be greater with full-dose therapy, but it has been reported in all dosage ranges. Some patients with heparin-induced TCP may develop antibodies that deposit on vascular endothelial cells, leading to thrombus formation. These thrombotic episodes tend to occur in a small percentage of patients.

Agranulocytosis (choice A) is an acute condition characterized by profound leukopenia with a substantial reduction of polymorphonuclear leukocytes; heparin is not associated with the development of this condition.

Anaphylactic reactions (choice B) can occur in patients taking heparin. However, the appearance of these allergic reactions is typically evident at the onset of therapy, not the end of therapy.

Eosinophilia (choice C) is a condition characterized by an increased number of circulating eosinophils; heparin is not associated with the development of this condition.

Protein C deficiency (choice D) is a condition that can produce a state of hypercoagulability and thrombosis in the cutaneous microvasculature, leading to skin necrosis. Warfarin, a coumarin anticoagulant, is associated with the development of protein C deficiency; heparin is not.

The pharmacokinetic properties of a new antihistamine are being studied in normal volunteers during phase I clinical trials. The clearance and half-life of the drug are determined to be 4.0 L/hour and 10 hours, respectively. Which of the following values is the approximate volume of distribution for this drug?

A. 0.06 L  
B. 14 L  
C. 45 L  
D. 60 L  
E. 130 L

Explanation:
The correct answer is D. The volume of distribution of a drug can be determined using the following equation:

t1/2 = (0.693 x Vd)/CL

Therefore, 10 hours = (0.693 x Vd)/(4.0 L/hour),

40 hours = 0.693 x Vd,

Vd = 58 L which is approximately 60 L

A 34-year-old male patient with a long history of asthma is referred to a pulmonologist. The physician decides to place the patient on zileuton. The mechanism of action of this drug is to

A. antagonize LTD4 receptors
B. inhibit 5-lipoxygenase
C. inhibit phosphodiesterase
D. inhibit phospholipase A2
E. stimulate beta-2 receptors

Explanation:

The correct answer is B. Zileuton is a recently approved inhibitor of 5-lipoxygenase, the first enzyme that converts arachidonic acid to leukotrienes. Thus zileuton, which is taken orally, interrupts the leukotriene pathway. Leukotrienes are synthesized in many inflammatory cells in the airways, such as mast cell macrophages, eosinophils and basophils. LTC4 and LTD4 are thought to be responsible for many of the symptoms of asthma, including bronchoconstriction, increased bronchial reactivity, hypersecretion of mucus, and mucosal edema. In addition, LTB4 is a potent chemotactic agent for neutrophils. Zileuton and similar agents are efficacious in the treatment of asthma because of their inhibition of leukotriene production.

Zafirlukast is another drug that is used to interrupt the leukotriene pathway. This drug acts as an LTD4 antagonist (choice A); it is taken orally.

Methylxanthines, such as theophylline, inhibit phosphodiesterase (choice C), thus increasing intracellular levels of cAMP. This results in smooth muscle relaxation. At therapeutic doses, methylxanthines also block adenosine receptors.

Corticosteroids prevent the release of arachidonic acid from cell membranes by inhibiting phospholipase A2 (choice D). This reduces the production of both leukotrienes and prostaglandins. Corticosteroids also inhibit the production of cytokines which are thought to play an important role in initiating the inflammatory cascade provoked by antigen inhalation and viral infection. Examples of corticosteroids include beclomethasone, budesonide, flumisolide, fluticasone and triamcinolone.

Beta-2 agonists (choice E), such as albuterol, terbutaline, metaproterenol and bitolterol, cause smooth muscle relaxation by increasing intracellular levels of cAMP.

A 51-year-old female presents with marked hyperventilation. Laboratory evaluation reveals a blood pH of 7.22, a serum bicarbonate level of 14 mEq/L, a serum lactate level of 7 mmol/L and an anion gap of 19 mEq/L. Her past medical history is significant for non-insulin dependent diabetes, hypertension, and renal insufficiency. Which of the following medications most likely caused this patient's signs and symptoms?

A. Clonidine
B. Enalapril
C. Furosemide
D. Glyburide
E. Metformin

Explanation:
The correct answer is E. Lactic acidosis is a condition characterized by the accumulation of excess lactic acid in the blood. Normally, the principle sources of lactic acid are erythrocytes, skeletal muscle, and the integument. Lactic acidosis is not uncommon in any severely ill patient suffering from respiratory or hepatic failure, cardiac decompensation, septicemia, or bowel infarction. Cases of lactic acidosis have also occurred in patients taking metformin. Metformin is a biguanide oral hypoglycemic agent used as an adjunct to diet in the treatment of non-insulin dependent diabetes. The risk for developing this disorder is increased in renally impaired patients, such as the patient in this question. Furthermore, lactic acidosis occurs more frequently in those taking nephrotoxic medications such as aminoglycosides and radiological contrast dyes. The other medications are not associated with the development of lactic acidosis.

Clonidine (choice A) is a centrally acting antihypertensive agent typically used in the treatment of refractory hypertension.

Enalapril (choice B) is an angiotensin-converting enzyme inhibitor used in the management of hypertension and congestive heart failure.

Furosemide (choice C) is a loop diuretic used in the management of hypertension and various edematous states.

Glyburide (choice D) is a sulfonylurea antidiabetic agent that is used as an adjunct to diet to lower blood glucose levels in patients with non-insulin dependent diabetes mellitus.

\[ V_d \text{ (volume of distribution)} = 60 \text{L} \]
\[ CL \text{ (clearance)} = 30 \text{mL/min} \]
\[ F \text{ (bioavailability)} = 50\% \]
\[ t_1 \text{ (half life)} = 23 \text{hours} \]

A new antibiotic is being tested in phase III clinical trials. The following pharmacokinetic parameters had been determined in earlier trials:

This antibiotic is administered orally and the target plasma concentration (Cp) is 2 mg/L.

What is the appropriate loading dose for this drug?

A. 15 mg
B. 30 mg
C. 60 mg
D. 120 mg
E. 240 mg

Explanation:
The correct answer is E. In order to achieve the desired drug plasma level rapidly, a loading dose can be given to "load" the volume of distribution. Therefore, the only necessary information to answer this question is the volume of distribution, the desired plasma concentration, and how well the drug is absorbed into the body (bioavailability).

The equation to calculate loading dose is as follows:

\[ \text{Loading dose} = C_p \times \frac{V_d}{F} \]

In this case, \( 2 \text{mg/L} \times \frac{60 \text{L}}{0.5} = 240 \text{mg} \)

Note that clearance is important to calculate maintenance dose. In order to maintain target plasma levels, it is important to administer the amount of drug that is being cleared by the patient. Maintenance doses are typically given every half-life.

A 67-year-old woman is being treated for metastatic ovarian cancer with cisplatin and cyclophosphamide. To prevent nausea and vomiting, she is given an agent that selectively antagonizes 5-hydroxytryptamine-3 (5-HT3) receptors. Which of the following drugs is this patient most likely taking?

A. Dimenhydrinate
B. Dronabinol
C. Metoclopramide
D. Ondansetron
E. Prochlorperazine

Explanation:

The correct answer is D. Cisplatin is an antineoplastic commonly used in the treatment of metastatic ovarian and testicular cancers, as well as advanced bladder cancer. This medication is associated with profound nausea and vomiting; in fact, it is considered to be one of the most emetogenic agents on the pharmaceutical market. The selective 5-hydroxytryptamine-3 (5-HT3) receptor antagonists are potent antinauseant and antiemetogenic agents indicated for prevention of nausea and vomiting associated with cancer chemotherapy. Examples of 5-HT3 receptor antagonists include ondansetron, granisetron, and dolasetron.

Dimenhydrinate (choice A) is an antihistamine with anticholinergic activity; it is indicated for the treatment of nausea and vomiting associated with motion sickness.

Dronabinol (choice B) is the principle psychoactive substance present in Cannabis sativa (marijuana). The mechanism of its antiemetic action is largely unknown; it is indicated for the treatment of severe nausea and vomiting when conventional therapies are ineffective.

Metoclopramide (choice C) is a prokinetic agent indicated for the treatment of gastroesophageal reflux disease and diabetic gastroparesis. Since this agent blocks dopaminergic receptors in the chemotrigger zone, it is also
effective in the treatment of severe nausea and vomiting.

Prochlorperazine (choice E) is a phenothiazine antiemetic that exerts its action by blocking dopaminergic receptors in the chemotrigger zone.

An 82-year-old woman presents to her physician complaining of difficulty sleeping and problems coping throughout the day since the recent death of her husband. She requests a medication which will help her through this time of her life. Her physician decides to prescribe oxazepam. The most likely rationale behind prescribing this drug is that oxazepam

A. does not deplete liver glutathione
B. does not have first pass metabolism
C. does not require phase I metabolism
D. does not require phase II metabolism
E. induces cytochrome P450

Explanation:
The correct answer is C. Phase I metabolism, which is accomplished largely by cytochrome P450, becomes less efficient with age. Phase II metabolism, which conjugates drugs to yield polar, inactive metabolites, is not generally affected by age. Oxazepam is a benzodiazepine which does not require phase I metabolism; it simply undergoes conjugation, making it a useful drug for an elderly individual. Lorazepam is the other benzodiazepine which only undergoes phase II metabolism. These two drugs are also useful for patients with liver failure; phase I metabolism can be severely affected by liver failure.

A 52-year-old man with peptic ulcer disease has been on drug therapy for 3 months. While on this regimen, he noticed changes in his bowel habits, increasing headaches, dizziness, skin rashes, loss of libido, and gynecomastia. The drug most likely responsible for these effects is

A. cimetidine
B. famotidine
C. metronidazole
D. omeprazole
E. sucralfate

Explanation:
The correct choice is A. Cimetidine, an H2-receptor antagonist, can produce all of the side effects exhibited when taken in high doses over a long period of time. In addition, cimetidine can alter the hepatic metabolism of
several drugs.

Famotidine (choice B) is also an H2-receptor antagonist, but it does not have the side effects of cimetidine.

Metronidazole (choice C) is an antibacterial and antiprotozoal drug that may present with the adverse effects of headaches, dizziness, diarrhea, and rashes, but not gynecomastia.

Omeprazole (choice D) and sucralfate (choice E) are a proton pump inhibitor and a physical barrier to gastric acid, respectively. Neither have reported effects on sexual function or breast development.

A 74-year-old woman with multiple myeloma is being treated with high doses of doxorubicin (Adriamycin). She has also received cyclophosphamide and prednisone recently. During his examination, the physician should check the patient for

A. abdominal tenderness
B. bladder distention
C. limitation of movement
D. papilledema
E. pulmonary rales

Explanation:
The correct answer is E. Doxorubicin (Adriamycin) is an anthracycline antibiotic which, when given in high doses (> 550mg/m2), can produce cardiomyopathy leading to congestive heart failure, accompanied by pulmonary edema and rales. This complication is especially likely if the patient is over 70 years of age, has received cardiac irradiation, has underlying heart disease or hypertension, or has received cyclophosphamide.

Abdominal tenderness (choice A), bladder distention (choice B), limitation of movement (choice C), or papilledema (choice D) are not typically associated with administration of doxorubicin. Doxorubicin does, however, cause alopecia and suppresses the bone marrow.

A 47-year-old woman presents with complaints of nervousness and increased sensitivity to hot weather. She is diagnosed with hyperthyroidism and prescribed propylthiouracil. What is the principal mechanism by which this drug acts?

A. Decreasing the efficacy of TSH binding to the thyroid TSH receptor
B. Decreasing the rate of proteolysis of thyroglobulin
C. Increasing the amount of 3,3',5'-triiodothyronine (reverse T3; rT3)
D. Inhibiting deiodination of thyroxine (T4)
E. Inhibiting the uptake of iodide into the thyroid gland
The correct answer is D. Propylthiouracil works primarily by inhibiting the peripheral conversion of T4 to T3. The thyroid extracts iodide from the plasma and, in an oxidative process, iodinates tyrosine residues in thyroglobulin molecules. Monoiodotyrosines and diiodotyrosines are formed and then coupled to produce either thyroxine (tetraiodothyronine, T4) or triiodothyronine (T3). Proteolytic cleavage of thyroglobulin molecules leads to free T3 or T4, which is then released into the circulation; T3 is several times more potent than T4. Peripheral deiodination of T4 at the 5' position leads to T3 formation (mainly in the liver); this step is inhibited by propylthiouracil.

Decreasing the efficacy of TSH binding (choice A), decreasing the rate of thyroglobulin proteolysis (choice B), increasing the amount of rT3 formation (choice C), and inhibiting the uptake of iodide into the thyroid (choice E), would all tend to decrease the formation of thyroid hormones in the thyroid itself.

A pharmacologist is determining the pharmacokinetic parameters of a novel antibiotic in order to determine the proper dosage. The drug is a weak organic acid with a pKa of 3.0. Assuming a pH of 2.0 in the stomach, approximately what percent of the drug will be in a form that can be rapidly absorbed from the stomach?

A. 0.1
B. 1
C. 10
D. 50
E. 90
F. 99

The correct answer is E. First, it is necessary to know that it is the uncharged, lipid-soluble form that can be rapidly absorbed. For an acid: HA $\rightleftharpoons$ H+ + A-. Therefore, the protonated form is uncharged. The Henderson-Hasselbalch equation is:

\[ \text{pH} = \text{pKa} - \log\left[\frac{\text{protonated form}}{\text{unprotonated form}}\right] \]

In this case,

\[ 2.0 = 3.0 - \log \left[ \frac{\text{HA}}{\text{A-}} \right] \]

\[ 1.0 = \log \left[ \frac{\text{HA}}{\text{A-}} \right] \]

\[ 10 = \frac{\text{HA}}{\text{A-}} = 10/1 \]

\[ \frac{\text{HA}}{\text{HA} + \text{A-}} = \frac{10}{10 + 1} = 91\%, \text{ or approximately 90\%} \]

A 68-year-old woman presents for a routine check-up. Her only complaint is that she occasionally experiences a little swelling in her ankles. Her serum potassium is 3.5 mEq/L, so the physician wants to avoid unnecessary potassium losses. Which of the following diuretics would be most appropriate for this patient?
A. Furosemide
B. Hydrochlorothiazide
C. Indapamide
D. Metolazone
E. Spironolactone

Explanation:
The correct answer is E. Potassium is responsible for maintenance of intracellular tonicity, transmission of nerve pulses, contraction of muscle (striated and smooth), and maintenance of renal function. The normal blood level of potassium ranges from 3.5 to 5.0 mEq/L. In potassium depletion, a decrease in the blood potassium level by 1 mEq/L equals a loss of 100-200 mEq from potassium stores in the body. Depletion can result in the development of muscular weakness, paralysis, and mental confusion. Since this patient is borderline hypokalemic, she should receive a potassium-sparing diuretic, such as spironolactone, amiloride, or triamterene. These agents are all indicated for the treatment of edematous states as well as the prophylaxis and treatment of hypokalemia. These agents are commonly combined with other non-potassium-sparing diuretics to prevent the appearance of hypokalemia during therapy.

Furosemide (choice A) is a loop diuretic indicated for the treatment of edematous states in hypertension and is commonly associated with the development of hypokalemia.

Hydrochlorothiazide (choice B), indapamide (choice C), and metolazone (choice D) are thiazide diuretics indicated for the treatment of edematous states in hypertension and are also commonly associated with the development of hypokalemia.

A 38-year-old man has his blood pressure measured on 3 different occasions in clinic, yielding values of 145/95, 160/105, and 150/100. A careful history reveals that he has had problems with asthma since childhood. The decision is made to treat the patient with a beta-blocker. Which of the following drugs should the physician prescribe?

A. Atenolol
B. Labetalol
C. Nadolol
D. Prazosin
E. Timolol

Explanation:
The correct answer is A. Beta1-selective antagonists are often used to control hypertension in patients, such as asthmatics, who might experience bronchoconstriction with non-selective beta antagonists (e.g., propranolol).
Remember that beta1 receptors predominate in the heart, while beta2 receptors predominate in the lungs. A mnemonic to help you remember the main beta1 (cardioselective) blockers is "A BEAM": acebutolol, betaxolol, esmolol, atenolol, metoprolol.

Labetalol (choice B) blocks alpha1, beta1, and beta2 receptors, and is useful in treating hypertensive emergencies and the hypertension of pheochromocytoma.

Nadolol (choice C) blocks both beta1 and beta2 receptors, and is known for its very long half-life (14-24 hours).

Prazosin (choice D) blocks alpha1 receptors, and is used primarily in the treatment of hypertension.

Timolol (choice E) blocks both beta1 and beta2 receptors and is frequently used for the treatment of open-angle glaucoma.

A 78-year-old woman with type 2 diabetes, diabetic nephropathy, and hyperuricemia presents to her physician for a physical examination, which is remarkable for hypertension. Which of the following drugs would be best for the initial treatment of this woman's hypertension?

A. Atenolol
B. Captopril
C. Hydrochlorothiazide
D. Indapamide
E. Minoxidil

Explanation:

The correct answer is B. The question is essentially asking, "Which of the following agents would be recommended in a women with diabetic nephropathy and hyperuricemia?" The angiotensin-converting enzyme (ACE) inhibitors, such as captopril, are commonly recommended for the treatment of hypertension in diabetic patients, especially those with renal complications, since these agents have been shown to delay the progression of renal disease. Furthermore, these agents are generally well tolerated.

Atenolol (choice A) is a beta-1 adrenergic antagonist that is generally not recommended for diabetic patients since it can "block" the appearance of the normal signs and symptoms of hypoglycemia.

The thiazide diuretics, such as hydrochlorothiazide (choice C) and indapamide (choice D), are commonly associated with hyperuricemia. Furthermore, they can precipitate an acute gout attack in patients with hyperuricemia.

Minoxidil (choice E) is a direct acting vasodilator most commonly used in the treatment of severe refractive hypertension because of its profound side effect profile. This agent is rarely used as an initial treatment agent.

A patient with essential hypertension is starting diuretic therapy. He has a history of calcium oxalate renal stones. Which of the following diuretics would be most appropriate to give this patient?
A. Acetazolamide
B. Furosemide
C. Hydrochlorothiazide
D. Spironolactone
E. Triamterene

Explanation:
The correct answer is C. A thiazide diuretic would be the drug of choice for this patient because it is the only class of diuretic which decreases urinary secretion of calcium. Thiazide diuretics, like hydrochlorothiazide, inhibit the Na+/Cl− cotransporter in the distal convoluted tubule and promote the reabsorption of calcium.

Acetazolamide (choice A), a carbonic anhydrase inhibitor, and furosemide (choice B), a loop diuretic, both induce diuresis at the expense of all three major cationic electrolytes (Na+, K+, and Ca2+) which are secreted in increased amounts.

Spironolactone (choice D) and triamterene (choice E), so-called potassium sparing diuretics, block Na+/K+ exchange in the collecting duct. Although they decrease K+ secretion, Na+ and Ca2+ secretion are elevated.

A 72-year-old man presents with fatigue and exertional and nocturnal dyspnea. Physical examination is remarkable for rales and a gallop rhythm. Chest x-ray films demonstrate cardiac enlargement. Which of the following drugs would likely serve to delay the progression of this man's disorder?

A. Captopril
B. Digoxin
C. Furosemide
D. Hydrochlorothiazide
E. Verapamil

Explanation:
The correct answer is A. The patient is presenting with the classic signs and symptoms of congestive heart failure (CHF). Heart failure is a pathologic state in which an abnormality of cardiac function produces a failure of the heart to pump blood throughout the body at a rate sufficient to meet the requirements of the metabolizing tissues. Some of the adaptive mechanisms to compensate for the "failing heart" are increasing pre-load (through the Frank-Starling mechanism), development of myocardial hypertrophy (to restore the increased ventricular wall stress to within normal limits), redistribution of cardiac output from nonvital organs to vital organs, and neurohumoral adjustments. The major criteria for diagnosing heart failure are the appearance of paroxysmal nocturnal dyspnea, neck vein distension, rales, cardiomegaly, acute pulmonary edema, S3 gallop, increased venous pressure (> 16 cm H2O), and positive hepatojugular reflex. Of the agents listed, only captopril is proven to delay the progression of this condition by protecting the ventricles from remodeling. Captopril is an ACE inhibitor that is now considered to be a standard therapy for the treatment of CHF. In addition to the protective effects, this agent causes vasodilation and blocks the detrimental neurohormonal activity associated
with the disorder. None of the other agents have been proven to protect the failing heart in this condition.

Digoxin (choice B) is an agent that produces a positive inotropic effect by increasing the force and velocity of myocardial contraction.

Furosemide (choice C) is also considered to be a first-line agent in the treatment of heart failure. This agent is indicated for the treatment of edema associated with CHF, hepatic cirrhosis, and renal disease, as well as treatment of hypertension (furosemide and torsemide).

Hydrochlorothiazide (choice D) is used in the treatment of heart failure. This agent is indicated for the treatment of edema associated with CHF as well as treatment of hypertension.

Verapamil (choice E) is a calcium channel blocker indicated for the treatment of hypertension and a variety of cardiac arrhythmias. This agent is contraindicated in the treatment of heart failure, since it has a strong negative inotropic effect on the heart.

A 54-year-old man has a total cholesterol of 272 and LDL level of 210. His therapy is initiated with dietary modification and an exercise regimen, but he is unresponsive and so is prescribed nicotinic acid (Niacin). Which of the following symptoms will this patient likely experience from this drug?

A. Bradycardia
B. Facial flushing
C. Hyperalbuminemia
D. Hypoglycemia
E. Renal dysfunction

Explanation:
The correct answer is B. Niacin, or vitamin B3, is an agent that results in the following physiologic changes: LDL reductions tend to occur in 5-7 days with the maximal effect seen in 3-5 weeks; triglycerides and VLDL are reduced by 20% to 40% in 1-4 days; and HDL levels can increase by 20%. This agent is indicated as adjunctive therapy in patients with elevated cholesterol and triglycerides when diet and other nondrug therapies are inadequate. The most common adverse effect of this agent is generalized flushing with a sensation of warmth, especially in the facial area. This reaction may be so severe in some patients that they discontinue therapy. Other common adverse effects include hepatotoxicity, tachycardia (compare with choice A), hypoalbuminemia (compare with choice C), hyperglycemia (compare with choice D), nausea, vomiting, hyperuricemia, glucose intolerance, pruritus, peptic ulcer disease, and dry skin.

A 35-year-old man is found to have a blood pressure of 150/120 mm Hg on routine physical examination. Ultrasound studies demonstrate massively enlarged kidneys with many cysts of varying sizes. Which of the following drug classes would act by directly interrupting the probable mechanism by which the hypertension was produced?

A. ACE inhibitors
B. Calcium channel blockers
C. Centrally acting sympatholytics
D. Nitrates
E. Thiazide diuretics

Explanation:

The correct answer is A. The disease is adult polycystic kidney disease. The cysts impair perfusion of glomeruli, which triggers the secretion of renin by the juxtaglomerular complexes. The renin secretion triggers the renin/angiotensin/aldosterone system. ACE (angiotensin-converting enzyme) inhibitors directly interrupt this system by blocking the conversion of angiotensin I to angiotensin II.

Calcium channel blockers (choice B) (e.g., nifedipine, verapamil, diltiazem) control hypertension by blocking calcium entry into cells, thereby inhibiting vascular smooth muscle contraction.

Centrally acting sympatholytics (choice C) (e.g., clonidine) lower blood pressure by blocking adrenergic receptors in the brain, thus reducing sympathetic outflow.

Nitrates (choice D) (e.g., nitroglycerin) release nitric oxide in smooth muscle cells, stimulating guanylate cyclase. The subsequent increase in cGMP leads to smooth muscle relaxation and vasodilation.

Thiazide diuretics (choice E) (e.g., hydrochlorothiazide) act on the early distal tubule, and would not directly address the cause of the hypertension.

Pharmacokinetic parameters of a new antimicrobial agent are being determined during Phase I clinical trials. It has recently been determined that the half-life of this new agent is 9 hours, and studies to determine the safe limits of the clinical dose range are now being performed. One subject given a high drug dose began to seize when the drug reached steady state levels. The drug was immediately discontinued. How long will it take until his plasma drug levels are approximately 6% of steady state levels?

A. 9 hours
B. 18 hours
C. 27 hours
D. 36 hours
E. 45 hours
F. 54 hours

Explanation:

The correct answer is D. The rule of thumb is that the levels decrease by half every half-life. Therefore, 50% will remain after one half-life, 25% will remain after two half-lives, 12.5% will remain after three half-lives, and 6.25% will remain after four half-lives. The half-life of this drug is 9 hours, so it will reach approximately 6% of steady state levels in 36 hours.
A 30-year-old woman with a history of tonic-clonic seizures complains of double vision, thickened gums, and growth of facial hair since starting a new medication. Which of the following anticonvulsant medications is most likely responsible for her symptoms?

A. Carbamazepine  
B. Ethosuximide  
C. Phenobarbital  
D. Phenytoin  
E. Valproic acid

Explanation:
The correct answer is D. Diplopia, gingival hyperplasia, and hirsutism are classic side effects of phenytoin. Other side effects include nystagmus, sedation, ataxia, and enzyme induction. Phenytoin is used in the treatment of grand mal and tonic-clonic seizures. It is not used for absence seizures.

Carbamazepine (choice A) does produce diplopia, but not the other symptoms in this vignette. It can also produce ataxia, enzyme induction, and blood dyscrasias. It is useful in tonic-clonic and partial seizures and tic douloureux.

Ethosuximide (choice B) causes gastrointestinal distress, headache, and lethargy as side effects. It is used exclusively for absence seizures.

Phenobarbital (choice C), which is used for grand mal and partial seizures, causes sedation, enzyme induction, and dependence.

Valproic acid (choice E) causes gastrointestinal distress, hepatotoxicity, and inhibition of drug metabolism. It can be used for all seizure types, but is particularly useful in myoclonic and petit mal seizures.

A 28-year-old woman presents to a court-ordered drug treatment center because of methamphetamine abuse. She tells the drug counselors that she initially started taking methamphetamine because she was trying to work two jobs and needed to try to stay awake and remain productive. She found that she liked the euphoric effects of the drug and kept taking methamphetamine to reexperience the "high." Which of the following mechanisms of action is most likely responsible for the reinforcing effects of methamphetamine?

A. Blocks the metabolism of both dopamine and norepinephrine  
B. Directly stimulates dopamine receptors  
C. Directly stimulates adrenergic receptors  
D. Induces dopamine release
E. Induces norepinephrine release

Explanation:

The correct answer is D. Methamphetamine (and amphetamine) acts by gaining entrance to dopamine and norepinephrine (and serotonin) nerve terminals, causing the release of these neurotransmitters via the uptake carriers. Dopamine is believed to play an important role in the reward system of the brain, and is thought to be a significant factor in the reinforcing effects of stimulants. One area of the brain that is thought to be involved in this reward system is the dopaminergic projection from the ventral tegmental area of the midbrain to the nucleus accumbens of the forebrain.

Although methamphetamine is a weak inhibitor of monoamine oxidase (MAO), and would therefore weakly block the metabolism of catecholamines (choice A), this is not the primary mechanism of action of this drug.

Methamphetamine acts as an indirect-acting agonist, via the release of neurotransmitter, not as a direct agonist (choices B and C).

Methamphetamine does induce norepinephrine release (choice E), but this plays a role in the production of systemic side effects (e.g., hypertension), rather than in the central effect of reinforcement.

A 24-year-old migrant farm worker is rushed to a nearby emergency room after an accidental exposure to parathion. He is in respiratory distress and is bradycardic. Which of the following drugs can be given to increase the activity of his acetylcholinesterase?

A. Atropine
B. Deferoxamine
C. Dimercaprol
D. N-acetylcysteine
E. Physostigmine
F. Pralidoxime

Explanation:

The correct answer is F. Pralidoxime (2-PAM) is an acetylcholinesterase (AChE) reactivating agent. It is only useful for counteracting AChE inhibitors which act by phosphorylating the enzyme (organophosphates). Pralidoxime can remove the phosphate group from AChE, thus regenerating the enzyme. This must be done in a timely fashion because normally after the phosphate group is bound to the enzyme, it undergoes a chemical reaction known as "aging." Once this bond ages, pralidoxime will no longer be effective.

Atropine (choice A) is a nonselective muscarinic antagonist. Although atropine would be an appropriate agent for this patient, it acts by preventing the excess ACh from stimulating muscarinic receptors rather than altering the activity of AChE.

Deferoxamine (choice B) is a chelator used for iron poisoning.

Dimercaprol (choice C) is a chelator used alone for arsenic, mercury and gold poisoning, and also in
conjunction with edetate calcium disodium (EDTA) for the treatment of severe lead poisoning.

N-acetylcysteine (choice D) is used to treat acetaminophen overdose.

Physostigmine (choice E) is a carbamylating acetylcholinesterase inhibitor that can be used to treat antimuscarinic overdose. This drug would certainly exacerbate this patient's symptoms.

A clinical pharmacologist is gathering pharmacokinetic data during clinical trials of a new antimicrobial agent. He has already determined that the half-life of this drug is 4 hours. He began a continuous intravenous drip 24 hours ago at a rate of 10 mg/min. Blood tests after 24 hours reveal that the patient's drug plasma concentration is 20 mg/L. What is the clearance of this agent?

A. 0.5 L/min
B. 2 L/min
C. 10 L/min
D. 50 L/min
E. 200 L/min

Explanation:
The correct answer is A. You must be familiar with the maintenance dose equation to answer this question:

M.D. = Cl x Cpss/F, where

M.D. = maintenance dose
Cl = clearance
Cpss = plasma concentration at steady state
F = bioavailability

In this case, M.D. is 10 mg/min; F, or how much drug is absorbed, is 1 (100%) because drugs administered I.V. are completely absorbed. (F becomes important when drugs are given orally.) Cpss = 20 mg/L; it takes 4 -5 half-lives to achieve steady state, so this drug has been administered for a time period equaling 6 half-lives.

Solving,

10 mg/mL = Cl x 20 mg/mL

Cl = 0.5 L/min

A 57-year-old man presents to the emergency department with a nosebleed for the past 2 hours. The patient received a prosthetic heart valve 5 months ago and is currently taking warfarin (7.5 mg per day) and oral antibiotics. Laboratory evaluation reveals an INR (international normalized ratio, the ratio of patient to normal prothrombin times) of 6.4. Which of the following antibiotics is the patient most likely taking?
A. Ampicillin  
B. Cephalexin  
C. Nitrofurantoin  
D. Norfloxacin  
E. Phenazopyridine

Explanation:

The correct answer is D. The patient is most likely experiencing a potentiation of the effects of warfarin by norfloxacin, which decreases the metabolism of the warfarin. The increased warfarin effect produces an increase in the INR. (The target INR for patients with prosthetic heart valves is usually 1.5-4, depending on the type of valve.) Although norfloxacin is the most likely drug among the choices given to cause this effect in this patient, the antibiotics most commonly associated with this type of interaction are the macrolides, such as erythromycin, metronidazole, and the sulfonamide antibiotics.

Oral doses of penicillins, such as ampicillin (choice A), are generally not associated with a potentiation of warfarin's effect, although large IV doses of penicillin may be.

Cephalexin (choice B) is a first-generation cephalosporin that can be used in the treatment of acute cystitis. Although this agent is generally not associated with an increased hypoprothrombinemic effect when given with warfarin, the cephalosporins with a methyltetrazolethiol side chain, such as cefazolin, cefmetazole, and cefoperazone, are known to increase warfarin's therapeutic effect.

Nitrofurantoin (choice C) is a urinary anti-infective agent that does not interact with warfarin.

Phenazopyridine (choice E) is a urinary tract analgesic that does not interact with warfarin, although it commonly changes the color of urine to a bright orange/red color, which the patient may mistake as blood in the urine.

Which of the following antihistamines would be the most appropriate treatment for an airline pilot with hay fever?

A. Chlorpheniramine  
B. Diphenhydramine  
C. Meclizine  
D. Pyrilamine  
E. Terfenadine

Explanation:

The correct answer is E. Terfenadine is the only drug listed that does not cross the blood-brain barrier and therefore does not cause sedation (a bad thing for someone flying an airplane). Other drugs from the same
class (piperidines) include astemizole and loratadine.

All of the other choices have some degree of sedation as a side effect and therefore would not be recommended for someone who is flying an airplane or operating any kind of machinery.

A medical student is performing experiments on an anesthetized animal for her pharmacology class. An arterial line is inserted to monitor blood pressure, and the animal is given an intravenous dose of epinephrine. The injection produces an increase in blood pressure. The student then injects an unknown drug, followed fifteen minutes later by readministration of epinephrine. The second administration of epinephrine now produces a decrease in blood pressure. To which of the following classes does the unknown drug belong?

A. Acetylcholinesterase inhibitor
B. Nicotinic ganglionic blocker
C. Nonselective alpha receptor agonist
D. Nonselective alpha receptor antagonist
E. Nonselective beta receptor antagonist

Explanation:
The correct answer is D. This classic drug response, called epinephrine reversal, is a favorite on the USMLE and in pharmacology classes. Epinephrine, a nonselective alpha and beta adrenergic agonist, increases blood pressure. The unknown drug is an alpha adrenergic antagonist, such as phentolamine, which blocks epinephrine's vasoconstrictive action on arterioles. Subsequent administration of epinephrine produces only beta receptor stimulation, causing vasodilation in skeletal muscle, leading to a decrease in blood pressure. Epinephrine, for all practical purposes, now acts like the nonspecific beta agonist, isoproterenol. This effect is called epinephrine reversal because of the fact that epinephrine originally increases BP and then produces the opposite effect after phentolamine administration.

An acetylcholinesterase inhibitor (choice A) should not affect the subsequent administration of epinephrine.

A nicotinic ganglionic blocker (choice B) may prevent a potential decrease in heart rate due to baroreceptor reflexes, but epinephrine would still cause an increase in blood pressure because its access to end organ receptors would be unaltered.

A nonselective alpha agonist (choice C) might not affect a second administration of epinephrine fifteen minutes later because the agonist effect would probably be gone. But, if there was still some agonist on board at the time of the second administration, it would only serve to enhance epinephrine's increase in blood pressure.

A nonselective beta receptor antagonist (choice E) would enhance epinephrine's increase in blood pressure. After administration of a beta antagonist such as propranolol, epinephrine would only produce alpha receptor stimulation. This would increase blood pressure to a greater extent than epinephrine alone.

A 42-year-old male suddenly develops dysuria and frequency despite the absence of bacteriuria; microscopic hematuria is noted. Over the course of the next few days, gross hematuria is seen. The patient is being treated for non-Hodgkin's lymphoma with a nitrogen mustard-type antineoplastic agent. Which of the following agents could have been administered to prevent the onset of the patient's symptoms?
A. Allopurinol
B. Leucovorin
C. Mesna
D. Penicillamine
E. Sodium thiosulfate

Explanation:

The correct answer is C. The patient is presenting with signs and symptoms of hemorrhagic cystitis. This condition is characterized by a sudden onset of dysuria and frequency in the absence of bacteriuria. In severe cases of cystitis, large segments of bladder mucosa may be shed and the patient can have prolonged periods of gross hematuria. Furthermore, there may be bladder obstruction secondary to the development of blood clots. This disorder is most often seen in patients taking ifosfamide and cyclophosphamide, both of which are nitrogen mustards. Hemorrhagic cystitis can be prevented in patients taking ifosfamide and cyclophosphamide by administering mesna. Mesna reacts chemically with the urotoxic metabolites produced when both agents are metabolized. Mesna is not effective for prophylaxis of other types of hemorrhagic cystitis.

Allopurinol (choice A) is an antigout agent used prophylactically to reduce the severity of hyperuricemia associated with both antineoplastic and radiation therapy.

Leucovorin (choice B) is primarily used to prevent or diminish toxicity associated with the use of antineoplastic folic acid antagonists, particularly methotrexate.

Penicillamine (choice D) is a chelating agent used to promote the renal excretion of excess copper in Wilson's disease. It is also used for lead poisoning and treatment of rheumatoid arthritis in patients who have failed to respond to conventional antirheumatic therapies.

Sodium thiosulfate (choice E) is an antidote for cyanide poisoning.

A 54-year-old man is admitted to the hospital with chest pain. Based on serial enzyme determinations and his electrocardiogram, he is diagnosed with a myocardial infarction. He is hospitalized for three days and recovers, but left ventricular dysfunction remains. He is prescribed several medications on discharge. A week later, he complains to his doctor about a dry, non-productive, persistent cough. Which of the following medications is most likely responsible for the appearance of this symptom?

A. Aspirin
B. Captopril
C. Metoprolol
D. Procainamide
E. Warfarín
Explanation:

The correct answer is B. Captopril, an angiotensin-converting enzyme inhibitor (ACE inhibitor), reduces the mortality associated with myocardial infarction. ACE inhibitors decrease the amount of ventricular remodeling after infarction and reduce the risk of congestive heart failure; they may also diminish the risk of a second heart attack. ACE inhibitors are known to frequently cause a dry cough. They also cause headache, diarrhea, fatigue, nausea, and dizziness. All of the other agents might be prescribed in this setting, but dry cough is only associated with captopril.

Aspirin (choice A) is a nonsteroidal anti-inflammatory drug associated with increased bleeding time, gastrointestinal bleeding, and tinnitus.

Metoprolol (choice C), a beta-1 antagonist, can cause hypoglycemia, peripheral vasoconstriction, and CNS side effects.

Procainamide (choice D) is a group IA antiarrhythmic that can cause antimuscarinic and direct depressant effects on the heart, and may produce a reversible syndrome similar to lupus erythematosus.

Warfarin (choice E) is an oral anticoagulant that can cause bleeding at therapeutic doses, and bone defects in the developing fetus.

A 68-year-old woman is taking L-dopa and carbidopa for Parkinson's disease. She presents to her physician complaining of a worsening tremor. Her neurologist decides to add trihexyphenidyl to her drug regimen but warns her about the potential side effects of this drug. Which of the following side effects will this patient most likely experience?

A. Diaphoresis
B. Diarrhea
C. Dry mouth
D. Miosis
E. Urinary incontinence

Explanation:

The correct answer is C. Trihexyphenidyl is a muscarinic antagonist used as adjunctive therapy in Parkinson's disease. It can improve tremor and rigidity, but has little effect on bradykinesia. Trihexyphenidyl is given to block cholinergic tone in the striatum, and therefore, helps to maintain the dopamine/acetylcholine balance in this region. However, this drug and similar agents that block muscarinic receptors also block parasympathetic tone to peripheral end organs, producing a number of side effects. One such side effect is a reduction of salivation, leading to a dry mouth.

Trihexyphenidyl would cause decreased sweating, not diaphoresis (choice A), by blocking sympathetic cholinergic (muscarinic) tone to sweat glands.

Trihexyphenidyl would cause constipation, not diarrhea (choice B), by blocking parasympathetic tone to the gut.

Trihexyphenidyl would cause mydriasis, not miosis (choice D), by blocking parasympathetic tone to the pupillary sphincter muscle of the eye.
Trihexyphenidyl would cause urinary retention, not urinary incontinence (choice E), by blocking parasympathetic tone to the bladder.

A 48-year-old woman goes to her dermatologist to have a mole removed. The patient tells her physician that she had an allergic reaction to a local anesthetic the last time she had dental work performed. Examination of her dental records by her dentist reveals that the patient received procaine for a tooth extraction. Which of the following drugs would be appropriate for the present procedure?

A. Benzocaine  
B. Chloroprocaine  
C. Cocaine  
D. Mepivacaine  
E. Tetracaine

Explanation:

The correct answer is D. There are two classes of local anesthetics: esters and amides. The rule of thumb is that if you are allergic to one drug in a given class (usually the ester class), you also will be allergic to other drugs of the same class. The proper course of action would be to switch over to the other drug class. In this question, the patient received procaine, which is an ester. Therefore, you need to identify the amide in the list of answers. The only amide listed is mepivacaine. Other amide local anesthetics include lidocaine, bupivacaine, etidocaine, prilocaine, and ropivacaine.

A 48-year-old man presents with a complaint of nonbloody diarrhea and right lower quadrant pain with a palpable mass and tenderness. He states that this "flare-up" is one of the worst he has ever experienced. Radiographic examination reveals evidence of ulceration, stricturing, and fistula development of the colon and small bowel. Which of the following drugs would be most useful for treating this patient?

A. Diphenoxylate and atropine  
B. Hydrocortisone suppositories  
C. Hyoscyamine  
D. Mesalamine  
E. Prednisone

Explanation:

The correct answer is E. The patient is presenting with signs and symptoms suggestive of Crohn's disease, which is an idiopathic inflammatory process that can affect any portion of the alimentary tract. This condition is often characterized by intermittent bouts of low-grade fever, diarrhea, malaise, and weight loss, as well as focal
tenderness and a palpable tender mass in the lower abdomen. There is radiographic evidence of ulceration, stricturing, or fistulas of the small intestine and colon. Nonpharmacologic therapy can be efficacious in some cases, but more severe cases may require corticosteroids, such as prednisone, which dramatically suppress the clinical signs and symptoms.

Antidiarrheal agents (eg, diphenoxylate with atropine (choice A) or loperamide) should be used very cautiously in these patients since there is a very high risk of toxic megacolon.

Hydrocortisone suppositories (choice B) are indicated for the treatment of distal ulcerative colitis, not Crohn's disease.

Hyoscyamine (choice C) is an anticholinergic agent that may alleviate the postprandial abdominal pain of a patient with irritable bowel syndrome when administered 30-60 minutes before a meal.

Mesalamine (choice D) is a 5-aminosalicylic acid derivative indicated for the treatment of ulcerative colitis. Although this agent may provide some benefit in the treatment of Crohn's disease, prednisone is the drug of choice for treatment of acute "flare-ups" seen in patients with this disease.

A research scientist is studying calcium fluxes in cultured cells using confocal laser scanning microscopy. The magnitude of the signal (brightness) is proportional to the strength of the calcium flux. Stimulation of which of the following receptor types would be expected to produce the strongest signal?

A. Alpha-1 adrenergic receptor
B. Beta-1 adrenergic receptor
C. Dopamine-1 receptor
D. Muscarinic-2 acetylcholine receptor
E. Nicotinic acetylcholine receptor

Explanation:

The correct answer is A. Alpha-1 receptors activate phospholipase C via the G protein Gq. Phospholipase C cleaves the membrane phospholipid phosphatidylinositol 4,5-bisphosphate to produce the products, inositol triphosphate (IP3) and diacylglycerol (DAG). IP3 releases intracellular calcium from the endoplasmic reticulum, and would therefore generate a robust signal. DAG activates protein kinase C.

Beta-1 adrenergic receptors (choice B) stimulate adenylate cyclase via the G protein Gs, leading to an increase in intracellular cAMP. All beta adrenergic receptors share a common mechanism of action.

Dopamine-1 receptors (choice C) stimulate adenylate cyclase via the G protein Gs. This leads to an increase in intracellular cAMP.

Muscarinic-2 acetylcholine receptors (choice D) inhibit adenylate cyclase via the G protein Gi. This leads to an decrease in intracellular cAMP. Muscarinic receptors also stimulate the opening of potassium channels in the heart, via the beta and gamma subunits of Gi.

Nicotinic acetylcholine receptors (choice E) are ligand-gated ion channels. When stimulated, they allow sodium ions to enter the cell.
A 69-year-old woman develops an atrial tachyarrhythmia. Which of the following agents could be used to slow conduction through the AV node?

A. Atropine  
B. Digitalis  
C. Nicotine  
D. Norepinephrine  
E. Quinidine

Explanation:
The correct answer is B. Digitalis is a cardiac glycoside that slows conduction through the AV node via parasympathomimetic actions, which can be blocked by atropine.

Atropine (choice A) blocks cardiac muscarinic receptors, thereby increasing conduction through the AV node.

Nicotine (choice C) increases conduction by stimulating sympathetic autonomic ganglia and the adrenal medulla.

Norepinephrine (choice D) increases conduction by stimulating cardiac β receptors.

Quinidine (choice E) acts centrally to decrease vagal tone, thereby increasing AV conduction.

A 41-year-old woman presents with chronic widespread musculoskeletal pain, fatigue, and frequent headaches. She states that her musculoskeletal pain improves slightly with exercise. On examination, painful trigger points are produced by palpitation of the trapezius and lateral epicondyle of the elbow. If objective signs of inflammation are absent and laboratory studies are normal, this patient would most likely be responsive to which of the following drugs?

A. Amitriptyline  
B. Cefaclor  
C. Naproxen  
D. Oxycodone  
E. Prednisone

Explanation:
The correct answer is A. The patient is presenting with signs and symptoms of fibrositis (fibromyalgia). This disorder is most commonly seen in women between the ages of 20 and 50, and is associated with widespread chronic musculoskeletal pain that improves with exercise, chronic fatigue, and sometimes, severe headaches.
Examination typically reveals painful trigger points produced by palpation of the trapezius and the lateral epicondyle of the elbow. Objective signs of inflammation are absent and laboratory studies are normal. Patients with this disorder are likely to respond to treatment with tricyclic antidepressants or skeletal muscle relaxants with strong anticholinergic side effects, such as cyclobenzaprine. One of the most effective agents in the treatment of this disorder is amitriptyline, a tricyclic antidepressant commonly used in the treatment of depression, and as an adjunctive pain medication.

Cefaclor (choice B) is a second generation cephalosporin. Since fibromyalgia is not an infectious disorder, this agent would be ineffective in this patient.

Naproxen (choice C) is a non-steroidal anti-inflammatory drug indicated for the treatment of mild-to-moderate pain. NSAIDs are generally ineffective in the treatment of this disorder.

Oxycodone (choice D) is an opioid analgesic indicated for the treatment of moderate to severe pain; opioids are ineffective in the treatment of fibromyalgia.

Prednisone (choice E) is a corticosteroid indicated for the treatment of a variety of disorders caused by inflammation. Since this disease is not an inflammatory condition, prednisone would be not be indicated for this patient.

A 72-year-old patient presents complaining of shaking in his right hand and trouble starting movements. On physical examination, the patient has a resting tremor of the right hand that decreases with active movement. The man's face is expressionless, and his voice is very soft. Cogwheel rigidity is noted in both arms. He also has a slightly stooped posture, and a slow, shuffling gait. Which of the following treatments for this disease works by inhibiting the metabolism of dopamine?

A. Benztropine
B. Bromocriptine
C. Levodopa
D. Pergolide
E. Selegiline

Explanation:

The correct answer is E. This clinical vignette is classic for Parkinson's disease and all the answer choices are drugs used in the treatment of this disorder. Selegiline (deprenyl) inhibits monoamine oxidase B (MAO-B). This form of MAO preferentially metabolizes dopamine, whereas MAO-A preferentially metabolizes norepinephrine and serotonin. Selegiline slows the breakdown of dopamine, thereby prolonging the clinical effects of levodopa. Some studies show that selegiline may slow the progression of Parkinson's disease.

Benztropine (choice A) is an antimuscarinic drug that may improve the tremor and rigidity of parkinsonism, although it has little effect on the bradykinesia. It is thought to help maintain the balance of cholinergic and dopaminergic neurotransmission in the neostriatum.

Bromocriptine (choice B) and pergolide (choice D) are both dopamine receptor agonists. If you did not know how these drugs worked, but you knew that they belonged to the same drug class, you could have still eliminated both answers as wrong.
Levodopa (choice C) is the most effective drug for the treatment of Parkinson's disease and is the mainstay of treatment. Levodopa is a dopamine precursor that increases circulating dopamine levels in the striatum.

An elderly man presents with complaints of ringing in his ears, blurred vision and upset stomach. He is taking multiple medications. His wife states that he has had a few episodes of confused, delirious behavior over the last few weeks. Which of the following agents might be responsible for this man's symptoms?

A. Allopurinol
B. Hydralazine
C. Niacin
D. Spironolactone
E. Quinidine

Explanation:
The correct answer is E. The collection of symptoms described above, tinnitus, blurred vision, GI upset, and delirium, are known as cinchonism, a side effect of quinidine toxicity. EKG changes such as prolongation of the QT and QRS intervals may also occur. Quinidine is an antiarrhythmic used for the treatment of ventricular arrhythmias and atrial fibrillation.

Allopurinol (choice A) is used in the treatment of gout. Its side effects include rash and fever.

Hydralazine (choice B) is a vasodilator used for the treatment of hypertension. Side effects include tachycardia, headache, nausea, and a lupus-like syndrome.

Niacin (choice C) is used in the treatment of hyperlipidemia. Its side effects include cutaneous flushing and pruritus.

Spironolactone (choice D) is a potassium sparing diuretic that blocks the effect of aldosterone at its receptor. Side effects include hyperkalemia and gynecomastia.

A patient goes to his family doctor complaining of persistent and severe headaches. His physician diagnoses migraine headaches and prescribes sumatriptan. What is the mechanism of action of this drug?

A. Dopamine1 agonist
B. GABA antagonist
C. Muscarinic3 antagonist
D. Non-selective beta antagonist
E. Serotonin1D agonist
Explanation:

The correct answer is E. Sumatriptan is a serotonin1D agonist that is used to abort migraine headaches. It is also effective in the treatment of cluster headaches.

Currently, no dopamine1 (D1) agonists (choice A), GABAB antagonists (choice B), or muscarinic3 (M3) antagonists (choice C) are used clinically.

Propranolol is an example of a non-selective beta antagonist (choice D).

A 47-year-old man with a history of type 2 diabetes, depression, and hypertension presents to the emergency department with spontaneous priapism. Which of the following drugs is the most likely cause of his current condition?

A. Atenolol
B. Furosemide
C. Glyburide
D. Paroxetine
E. Trazodone

Explanation:

The correct answer is E. Priapism is characterized by the development of a painful erection for an extended period of time. When untreated, priapism can cause severe penile damage that can culminate in impotence. Administration of the antidepressant drug trazodone has been associated with priapism in a number of patients. In patients with prolonged or inappropriate penile erection, this medication should be discontinued and medical attention should be sought immediately. Injection of alpha-adrenergic stimulants, such as norepinephrine or epinephrine, may be successful in treating the priapism. Surgical intervention is necessary for the treatment of trazodone-induced priapism in many instances.

Atenolol (choice A) is a beta-1 adrenergic antagonist indicated for the treatment of hypertension. This agent is commonly associated with impotence in males.

Furosemide (choice B) is a loop diuretic indicated for the treatment of edema and hypertension; electrolyte abnormalities are the most common side effects seen with this agent.

The sulfonylurea glyburide (choice C) is an oral hypoglycemic agent indicated for the treatment of type 2 diabetes; hypoglycemia is the most common side effect of this agent.

Paroxetine (choice D) is a selective serotonin reuptake inhibitor (SSRI) used for the treatment of depression. This agent is commonly associated with impotence in males.

A 24-year-old woman on her honeymoon presents to the cruise ship physician with a dilated right pupil and complains that she could not read the lunch menu with the same eye. Which of the following drugs is most likely responsible for her symptoms?
A. Phenylephrine  
B. Physostigmine  
C. Pilocarpine  
D. Scopolamine  
E. Tetrahydrozoline  
F. Timolol  

Explanation:

The correct answer is D. The question is asking for a drug that dilates the pupil (mydriasis) and prevents accommodation by paralyzing the ciliary muscle (cycloplegia). Scopolamine would produce both of these actions by blocking muscarinic acetylcholine receptors on the pupillary constrictor muscle (leading to mydriasis) and on the ciliary muscle (producing cycloplegia). An additional hint to arrive at this answer is the fact that she is on a cruise ship. Scopolamine patches are used to prevent motion sickness. The woman most likely applied the patch and subsequently rubbed her eye.

Phenylephrine (choice A), an alpha1-adrenergic agonist, could produce mydriasis by acting on receptors present on the radial dilator muscle. This would constrict the radial dilator muscles without affecting the ciliary muscles, which have muscarinic receptors (and a few beta-adrenergic receptors).

Physostigmine (answer B) is an intermediate-acting carbamylating inhibitor of acetylcholinesterase; it would increase cholinergic tone to the pupillary constrictor muscle, producing miosis, and cause ciliary muscle contraction to focus for near vision. It is used in the treatment of glaucoma. Pilocarpine (answer C) is a nonspecific muscarinic agonist and would therefore produce miosis and contraction of the ciliary muscle to focus for near vision. It is used in the treatment of glaucoma.

Tetrahydrozoline (answer E) is an alpha1-adrenergic agonist and is the active ingredient in Visine. It "takes the red out" by vasoconstricting vessels of the eye. It could cause some mydriasis by acting on alpha1 receptors on the radial dilator muscle; however, it would not have an effect on the ciliary muscle.

Timolol (choice F) is a nonspecific beta-adrenergic antagonist. It is used in chronic open angle glaucoma because it diminishes aqueous humor production from the ciliary body. It is well tolerated because it does not affect one's ability to focus. It would also not affect pupil size.

Which of the following local anesthetics would be most dangerous to use in a patient who has had allergic reaction to bupivacaine?

A. Benzocaine  
B. Cocaine  
C. Lidocaine  
D. Procaine  
E. Tetracaine
Explanation:

The correct answer is C. Bupivacaine is an amide-type local anesthetic, and allergic reactions to local anesthetics tend to cross-react only within groups (ester-type cross-reacts with ester-type and amide-type cross-reacts with amide-type). The only example in the answer choices of an amide-type local anesthetic, which would be metabolized by hepatic amidases, is lidocaine. Other members of this group include mepivacaine, etidocaine, and prilocaine.

Benzocaine (choice A), cocaine (choice B), procaine (choice D), and tetracaine (choice E) are all ester-type local anesthetics, which can be metabolized by plasma cholinesterases and hepatic esterases. They will usually not cross-react with antibodies produced to an amide anesthetic.

A 58-year-old woman had a mitral valve replacement, and was placed on anticoagulants and prophylactic antibiotics following her surgery. Five days after her surgery, she developed a sharply demarcated, erythematous rash on her left thigh. Two days after the rash appeared, large hemorrhagic bullae began to form in the area of the rash. Which of the following medications most likely caused the patient's rash?

A. Aspirin
B. Cefazolin
C. Heparin
D. Vancomycin
E. Warfarin

Explanation:

The correct answer is E. Warfarin is a coumarin anticoagulant used for the prophylaxis and treatment of thromboembolic complications associated with cardiac valve replacement and atrial fibrillation, as well as the prophylaxis and treatment of venous thrombosis and pulmonary embolism. Warfarin may cause necrosis of the skin (typically on the breasts, thighs, and buttocks) generally between the third and tenth days of therapy. The lesions are initially sharply demarcated, erythematous, and purpuric. They may resolve or progress to large, irregular, hemorrhagic bullae that can eventually lead to necrosis. The mechanism for this reaction is related to warfarin's ability to deplete protein C, which can lead to a state of hypercoagulability and thrombosis in the cutaneous microvasculature.

Aspirin (choice A) is commonly used for its antiplatelet effect; however, it would not be indicated for anticoagulation of a patient with a recent cardiac valve replacement. Furthermore, aspirin is not associated with the development of this type of skin necrosis.

Cefazolin (choice B) is a first-generation cephalosporin antibiotic commonly used as a perioperative prophylactic agent. If the patient was allergic to this antibiotic, an erythematous rash might have appeared. However, the rash would not lead to the appearance of large, hemorrhagic bullae.

Heparin (choice C) is an intravenous anticoagulant indicated for the prophylaxis and treatment of thromboembolic complications associated with cardiac valve replacement and atrial fibrillation. It is also indicated for the prophylaxis and treatment of venous thrombosis, pulmonary embolism, and for treatment of some coagulopathies. Although heparin is associated with the development of thrombocytopenia, it is not
associated with skin necrosis.

Vancomycin (choice D) is an antibiotic typically reserved for treatment of life-threatening infections caused by gram-positive organisms. If vancomycin is administered too rapidly via the intravenous route, a maculopapular rash may appear on the chest and on the extremities. However, once the administration is complete, the rash usually disappears in a few hours.

A 43-year-old, insulin-dependent diabetic patient is diagnosed with hypertension and begins therapy with an antihypertensive agent. Three days later, he measures his blood glucose at home and finds that it is 53 mg/dL. He recalibrates his glucose testing apparatus and repeats the test, only to find that the first reading was accurate. He is concerned that his hypoglycemia did not produce the normal premonitory signs and symptoms. Which of the following medications was most likely prescribed to treat his hypertension?

A. Captopril  
B. Diltiazem  
C. Methyldopa  
D. Prazosin  
E. Propranolol

Explanation:  
The correct answer is E. Beta-adrenergic blockade may blunt or prevent the premonitory signs and symptoms (e.g., tachycardia, blood pressure changes) of acute episodes of hypoglycemia. Non-selective beta-blockers, such as propranolol, may even potentiate insulin-induced hypoglycemia. Even though this effect is less likely with cardioselective agents, the use of either cardioselective or non-selective beta-blockers in diabetics is not recommended due to their "masking" effect of the normal warning signs and symptoms of hypoglycemia. None of the drugs listed in the other choices will blunt the premonitory signs and symptoms of hypoglycemia.

Captopril (choice A) is an angiotensin-converting enzyme (ACE) inhibitor that can be safely used for the treatment of hypertension in diabetic patients.

Diltiazem (choice B) is a calcium channel blocker that is also considered to be safe and effective for the treatment of hypertension in diabetic patients.

Both methyldopa (choice C), a centrally acting alpha-adrenergic agonist, and prazosin (choice D), an alpha1-adrenergic antagonist, can be safely used to treat hypertension in diabetic patients. However, due to the side effect profile of these medications, they are generally used only in diabetic patients who are unresponsive to ACE inhibitors and calcium channel blockers.

A 54-year-old male with acute lymphocytic leukemia develops a blast crisis. He is treated with intensive systemic chemotherapy. Following treatment, the patient will be at increased risk for the development of

A. bile pigment gallstones  
B. cholesterol gallstones  
C. cystine kidney stones
D. struvite kidney stones
E. uric acid kidney stones

Explanation:

The correct answer is E. Uric acid kidney stones in patients with leukemia are secondary to increased production of uric acid from purine breakdown during periods of active cell proliferation, especially following treatment. Vigorous hydration and diuresis are generally instituted after the diagnosis of acute leukemia is made. Uric acid kidney stones are also associated with inborn errors of purine metabolism, such as gout.

Pigment gallstones (choice A) are associated with hemolytic disease. The incidence of this type of gallstone is not increased in treated leukemias.

Cholesterol gallstones (choice B) are associated with diabetes mellitus, obesity, pregnancy, birth control pills, and celiac disease.

Cystine kidney stones (choice C) are rare; they are found in cystinuria.

Struvite kidney stones (choice D) are associated with infection by urea-splitting organisms, such as Proteus.

A patient is brought to the emergency room in a coma due to diabetic ketoacidosis. Insulin therapy is begun immediately. Which of the following therapies should also be begun immediately?

A. Calcium supplementation
B. Creatinine supplementation
C. Magnesium supplementation
D. Potassium supplementation
E. Sodium supplementation

Explanation:

The correct answer is D. Therapy of diabetic ketoacidosis requires more than insulin. Intravascular volume is often depleted, and initial fluids to restore volume should include isotonic saline or lactated Ringer's solution. If arterial blood pH is less than 7.1 or if severe hyperkalemia is present, bicarbonate supplementation should be used. IV fluids containing 5-10% dextrose (glucose) should be used when the serum glucose levels fall to 200-300 mg/dL, since high doses of rapidly acting insulin can cause life-threatening hypoglycemia. Additionally, the serum potassium concentration should be watched very carefully, since potassium is cotransported into cells with glucose in the presence of insulin. It is often the case that hyperkalemia is present initially, secondary to decreased cellular uptake of potassium with decreased cellular uptake of glucose. However, this can rapidly change when insulin drives glucose (with potassium) into cells, and a life-threatening hypokalemia can develop.

Supplementation with calcium (choice A) is not required with insulin administration.

Creatinine (choice B) is a waste product, rather than a nutrient.
Supplementation with magnesium (choice C) is not required with insulin administration.

Sodium supplementation (choice E) is not required during therapy with insulin.

The pharmacokinetic properties of a new drug are being studied in normal volunteers during phase I clinical trials. The volume of distribution and clearance determined in the first subject are 40 L and 2.0 L/hour, respectively. The half-life of the drug in this subject is approximately

A. 2 hours
B. 6 hours
C. 14 hours
D. 21 hours
E. 40 hours

Explanation:
The correct answer is C. The half-life of a drug can be determined using the following equation:

\[ t_{1/2} = \frac{0.693 \times V_d}{Cl} \]

Therefore, \( t_{1/2} = \frac{0.693 \times 40}{2.0} \) hours and \( t_{1/2} = 14 \) hours

A 45-year-old man presents to his physician with acute onset of muscle spasms in his lower back. The physician prescribes cyclobenzaprine. The side effects of this drug are most similar to those of which of the following drugs?

A. Amitriptyline
B. Dantrolene
C. Doxycycline
D. Ibuprofen
E. Lorazepam

Explanation:
The correct answer is A. Cyclobenzaprine is a centrally acting skeletal muscle relaxant that is structurally and
pharmacologically related to tricyclic antidepressants (eg, amitriptyline). It is used short-term as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute musculoskeletal conditions. Like tricyclic antidepressants, the most common side effects are dry mouth, drowsiness, dizziness, weakness, fatigue, tachycardia, urinary retention, and abdominal cramping.

Dantrolene (choice B) is also a centrally acting skeletal muscle relaxant; however, it is structurally and pharmacologically related to hydantoin derivatives, such as phenytoin. Although dantrolene produces the same CNS effects as cyclobenzaprine, it does not produce anticholinergic side effects, such as dry mouth and urinary retention.

Doxycycline (choice C) is an antibiotic used primarily in the treatment of various sexually transmitted diseases and acne. Its major side effects include diarrhea, gastrointestinal upset, and phototoxicity.

Ibuprofen (choice D) is a nonsteroidal anti-inflammatory drug used in the treatment of mild-to-moderate pain caused by inflammation; its most common side effects are intestinal discomfort and dizziness.

Lorazepam (choice E) is a benzodiazepine used in the management of anxiety disorders and for the short-term relief of anxiety. Side effects include drowsiness, sedation, dizziness, and weakness.

A 57-year-old male with a 10-year history of hypertension visits his physician for a routine physical examination. Laboratory test results indicate that the patient has a plasma renin activity 3-4 times higher than normal. The patient is given a prescription for losartan. Following administration of losartan, which of the following would be expected to increase in this patient?

A. Ability of the kidneys to excrete sodium
B. Aldosterone
C. Arterial pressure
D. Atrial natriuretic peptide
E. Total peripheral resistance

Explanation:

The correct answer is A. Losartan competitively inhibits angiotensin II at the AT-1 receptor. Angiotensin II is the most powerful sodium-retaining hormone of the body. The effects of angiotensin II can be attributed to (1) direct stimulation of sodium reabsorption in the proximal and distal tubules of the kidney; (2) stimulation of aldosterone secretion, which is another sodium-retaining hormone; and (3) constriction of the efferent arterioles in the kidney, which increases peritubular colloid osmotic pressure, thereby enhancing reabsorption of salt and water from the proximal tubule. Therefore, when the effects of angiotensin II are blocked with losartan, the ability of the kidneys to excrete sodium increases greatly.

Because angiotensin II normally stimulates aldosterone (choice B) secretion, losartan decreases plasma aldosterone levels.

The decrease in arterial pressure (choice C) caused by losartan (because of its effect to increase the loss of salt and water) should also decrease the total peripheral resistance by an autoregulatory mechanism. That is, when arterial pressure is lowered, the arterioles dilate, which maintains blood flow at a constant level in the peripheral tissues.
Overstretching of the two atria, usually as a result of increased blood volume, causes atrial natriuretic peptide (choice D) to be released into the blood. Because losartan increases the ability of the kidneys to excrete sodium (and therefore water), the blood volume should decrease, and the plasma levels of atrial natriuretic peptide should decrease.

Angiotensin II is a potent vasoconstrictor. Blocking its effects with losartan would be expected to decrease total peripheral resistance (choice E).

A 72-year-old male is noted as having a 9-pound weight loss over the past few weeks. His past medical history is significant for oat cell carcinoma of the lung, without known metastases, for which he is currently undergoing treatment. The patient states that even though his wife is preparing his favorite meals, he is not hungry. Which of the following would be the best treatment option to improve his eating habits?

A. Amitriptyline  
B. Megestrol acetate  
C. Methotrexate  
D. Neostigmine  
E. Prochlorperazine

Explanation:

The correct answer is B. One of the most common side effects of any antineoplastic therapy is weight loss secondary to decreased appetite and/or nausea and vomiting. Furthermore, weight loss due to decreased food intake tends to occur more frequently in elderly patients receiving antineoplastic therapy. One medication that has consistently helped to increase appetite in such patients is megestrol acetate. This agent is a progestational hormone with antineoplastic properties used in the treatment of advanced carcinoma of the breast and endometrium. Megestrol, when given in relatively high doses, can substantially increase the appetite in most individuals, even those with advanced cancer.

Amitriptyline (choice A) is a tricyclic antidepressant used in the treatment of depression. There is nothing mentioned in the case study to suggest that the patient is clinically depressed; hence, this agent would provide no benefit.

Methotrexate (choice C) is an antimetabolite and folic acid antagonist commonly used in various neoplastic disorders and in the treatment of rheumatoid arthritis. Since nausea, vomiting, and ulcerative stomatitis are common side effects of this medication, its usage in this patient would not be recommended.

Neostigmine (choice D) is a carbamylating acetylcholinesterase inhibitor that would not increase appetite.

Prochlorperazine (choice E) is a phenothiazine derivative used primarily to control severe nausea and vomiting. This patient is not experiencing nausea. Furthermore, this agent does not possess appetite-stimulating properties.

A 58-year-old woman arrives at her physician's office complaining of moderate anxiety. Which of the following drugs will help relieve her anxiety, with a minimum of unwanted sedative side effects?
A. Buspirone
B. Chlordiazepoxide
C. Lorazepam
D. Trazodone
E. Zolpidem

Explanation:

The correct answer is A. Buspirone is a nonbenzodiazepine anxiolytic that is devoid of the sedative (or anticonvulsive and muscle relaxant) properties typically associated with the benzodiazepines. It is a partial agonist at 5-HT1A receptors.

Chordiazepoxide (choice B) and lorazepam (choice C) are benzodiazepines that are useful anxiolytics, but which produce sedation.

Trazodone (choice D) is a very sedating atypical antidepressant.

Zolpidem (choice E) is a nonbenzodiazepine hypnotic used for the treatment of insomnia.

A 34-year-old asthmatic male presents for a check-up. He has been taking low dose oral prednisone for over 10 years and although his asthma is well controlled, he is concerned about steroid-induced osteoporosis, because his grandfather, a type 1 diabetic, recently fell and broke his hip. A comprehensive metabolic profile as well as a dual energy x-ray absorptiometry test (DEXA) of the spine and hip are ordered. Which of the following additional tests would be recommended?

A. 1,25-dihydroxy vitamin D
B. C-terminal PTH
C. Intact PTH
D. Serum glucose
E. Serum protein electrophoresis

Explanation:

The correct answer is D. This patient has a family history of diabetes. Steroid-induced diabetes mellitus is a frequent consequence of long-term corticosteroid therapy. It can be triggered by prednisone with or without a family history, but a predisposition may increase the risk. Symptoms such as polyuria and weight loss may be masked by the disease for which the patient is taking steroids.

Measurement of 1,25-dihydroxy vitamin D (choice A), the active vitamin D metabolite, would not be recommended. Corticosteroids can alter calcium balance mainly due to vitamin D deficiency secondary to impaired intestinal absorption of calcium, but 25-hydroxy vitamin D is a better marker for assessing nutrition.
PTH, an 84 amino acid polypeptide, can be cleaved into an active N-terminal fragment and an inactive C-terminal fragment. Measurement of C-terminal PTH (choice B) is not recommended. Although PTH is a regulator of calcium homeostasis, these fragment molecule measurements have not been found to correlate well with true PTH activity on bone.

Although PTH is a calcium regulator in the body, it is not considered a major contributor to corticosteroid-induced bone loss, so measurement of intact parathyroid hormone (choice C) is not the best choice. It is only significant if a person has underlying malabsorption such as inflammatory bowel disease.

Serum protein electrophoresis (choice E) is used mainly for the diagnosis of multiple myeloma in patients with pathologic fractures or a high clinical suspicion of myeloma.

A 44-year-old businessman presents to a physician because of a markedly inflamed and painful right great toe. He states that he just returned from a convention, and had noticed increasing pain in his right foot during his plane trip home. Physical examination is remarkable for swelling and erythema of the right great toe as well as small nodules on the patient's external ear. Aspiration of the metatarsal-phalangeal joint of the affected toe demonstrates needle-shaped negatively birefringent crystals. Which of the following agents would provide the most immediate relief for this patient?

A. Allopurinol
B. Aspirin
C. Colchicine
D. Probenecid
E. Sulfinpyrazone

Explanation:

The correct answer is C. The patient has gout, which is due to precipitation of monosodium urate crystals in joint spaces (notably the great toe) and soft tissues (causing tophi, which are often found on the external ears). Colchicine reduces the inflammation caused by the urate crystals by inhibiting leukocyte migration and phagocytosis secondary to an effect on microtubule assembly.

Allopurinol (choice A) and its metabolite, oxipurinol, inhibit xanthine oxidase, the enzyme that forms uric acid from hypoxanthine. Therapy with this agent should be begun 1-2 weeks after the acute attack has subsided.

Aspirin (choice B) competes with uric acid for tubular secretion, thereby decreasing urinary urate excretion and raising serum uric acid levels. At high doses (more than 2 gm daily) aspirin is a uricosuric.

Probenecid (choice D) and sulfinpyrazone (choice E) are uricosuric agents, increasing the urinary excretion of uric acid, hence decreasing serum levels of the substance. Therapy with these agents should be begun 1-2 weeks after the acute attack has subsided.

An overweight 48-year-old male presents with complaints of increased thirst and frequent urination. Laboratory examination reveals a blood glucose level of 180 mg/dL. The patient's past medical history is unremarkable, except for an anaphylactic reaction that occurred one year ago when he was given trimethoprim-sulfamethoxazole for a sinus infection. Based on this information, which of the following agents should be prescribed?
A. Chlorpropamide
B. Glipizide
C. Glucagon
D. Metformin
E. Propranolol

Explanation:
The correct answer is D. The patient's initial presentation strongly suggests Type 2 diabetes mellitus (NIDDM), which usually begins in middle or late life. Symptoms often develop gradually, and the diagnosis is frequently made when an asymptomatic or mildly symptomatic patient is found on routine laboratory examination to have an elevated blood glucose level. Therapy with an oral hypoglycemic agent would be appropriate in this case. Since the patient had a documented anaphylactic reaction to trimethoprim-sulfamethoxazole, he should not take any "sulfa" drugs, including the sulfonylurea type oral hypoglycemic agents such as chlorpropamide (choice A) and glipizide (choice B). Metformin is a biguanide oral hypoglycemic agent, chemically distinct from the sulfonylureas. This medication is indicated as monotherapy or in conjunction with other oral hypoglycemic agents in the treatment of NIDDM.

Glucagon (choice C) is the drug of choice for the treatment of severe hypoglycemia; this agent would worsen the patient's hyperglycemia.

Propranolol (choice E) is a non-selective beta blocking agent used for the treatment of hypertension and cardiac arrhythmias. Beta blockers are contraindicated since they "blunt" the appearance of the premonitory signs and symptoms of hypoglycemia.

A 72-year-old female is brought to the emergency room after the development of periorbital edema, a maculopapular rash on her chest, and a fever of 101°F (38.3°C). Laboratory examination reveals a blood urea nitrogen of 77 mg/dL and a serum creatinine of 3.1 mg/dL. Urinalysis shows mild proteinuria and eosinophils, but is negative for glucose and ketones. The patient's past medical history is significant for hypertension, diabetes, and osteoarthritis. Which of the following medications most likely caused the appearance of her signs and symptoms?

A. Acarbose
B. Clonidine
C. Ibuprofen
D. Metformin
E. Metoprolol

Explanation:
The correct answer is C. Acute interstitial nephritis is due to a hypersensitivity reaction usually caused by a
Drugs implicated in the pathogenesis of acute interstitial nephritis include non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and indomethacin; beta-lactam antibiotics, such as cephalothin and methicillin; sulfonamides; diuretics, such as furosemide and thiazides; and drugs like phenytoin, cimetidine, and methyldopa. The typical presentation for acute interstitial nephritis is the development of acute renal failure, fever, a maculopapular rash, and eosinophilia. The patient's periorbital edema and wheezing are also consistent with acute interstitial nephritis. Ibuprofen is the most likely causative agent for the development of the patient's signs and symptoms. Although the exact mechanism by which NSAIDs cause this disorder is not fully understood, it is believed to be related to their ability to decrease prostaglandin formation, which leads to a reduction in renal blood flow. None of the other medications are associated with the development of acute interstitial nephritis.

Acarbose (choice A) is an antidiabetic agent that delays the absorption of glucose from the intestinal tract.

Clonidine (choice B) is a centrally-acting antihypertensive agent used in the treatment of hypertension and prophylaxis of migraines. It has been shown to be efficacious in ameliorating symptoms of alcohol, tobacco, opiate, and benzodiazepine withdrawal. It is also used in the treatment of attention deficit disorder with hyperactivity.

Metformin (choice D) is an antidiabetic agent that increases the binding of insulin to its receptor. One important side effect of metformin is the development of lactic acidosis.

Metoprolol (choice E) is a beta-blocker used in the treatment of hypertension.

A 33-year-old woman presents with profound nausea, vomiting, sweating, hyperventilation, tachycardia, and vertigo. She states that she was out with a couple of friends having a few glasses of wine when she suddenly became ill. She has been previously diagnosed with a duodenal ulcer and is currently taking medication for her condition. Which of the following medications is most likely responsible for her latest symptoms?

A. Amoxicillin
B. Bismuth subsalicylate
C. Metronidazole
D. Omeprazole
E. Tetracycline

Explanation:

The correct answer is C. Helicobacter pylori (HP) is an acid-labile, spiral-shaped, gram-negative rod that resides in the mucosal layer and surface epithelial cells in the stomach. There is a strong association between HP and peptic ulcer disease (PUD). Since this organism is difficult to eradicate with a single agent, a multiple medication regimen, including metronidazole, bismuth subsalicylate, omeprazole, and tetracycline or amoxicillin, is often used. The patient's signs and symptoms are highly suggestive of a disulfiram-like reaction caused by metronidazole. When alcohol is ingested by patients taking metronidazole, nausea, vomiting, sweating, hyperventilation, tachycardia, chest pain, dyspnea, hypotension, blurred vision, and facial flushing can occur.

Amoxicillin (choice A) is a penicillin antibiotic most commonly associated with the development of diarrhea and mild intestinal irritation.

Bismuth subsalicylate (choice B) is used primarily for control of indigestion and diarrhea; its most common side effects are the appearance of "black-tongue" and "black tar-like" stools.
Omeprazole (choice D) is a proton pump inhibitor indicated for the treatment of gastric ulcerations and gastroesophageal reflux disease; this agent is generally well tolerated with very little incidence of side effects.

Tetracycline (choice E) is an antibiotic most commonly associated with photosensitivity, mild epigastric distress, and mild dizziness.

A worried mother complains to her pediatrician that both she and her 6-year-old son's teacher have noticed that the child has become inattentive. She states that her son frequently stops what he is doing and "stares blankly into space" before resuming his activities. Electroencephalography reveals a 3/second spike and slow wave pattern of discharges. Which of the following agents would most effectively treat this child's disorder?

A. Carbamazepine
B. Diazepam
C. Ethosuximide
D. Methylphenidate
E. Phenytoin

Explanation:

The correct answer is C. The child is suffering from absence (petit mal) seizures. The age of onset is typically from 3 to 7 years; seizures may continue into adolescence, but generally subside before adulthood. These seizures have been known to occur up to 100 times a day. Ethosuximide is indicated for this type (but no other type) of seizure. Other drugs used in the treatment of absence seizures are valproic acid, clonazepam, and a new agent, lamotrigine.

Carbamazepine (choice A) is used in the treatment of tonic-clonic (grand mal) and partial (focal) seizures.

Diazepam (choice B) has long been the drug of choice for status epilepticus. Recently, lorazepam (a shorter acting benzodiazepine) has also been accepted as a drug for this condition. Intravenous phenytoin is used if prolonged therapy is required. Phenobarbital has also been used, especially in children. If the status epilepticus is very severe and does not respond to these measures, general anesthesia may be used.

Methylphenidate (Ritalin; choice D) is a stimulant used to treat children with attention deficit disorder. This child has no history of hyperactivity, and the underlying cause of his "inattentiveness" is his seizure disorder.

Phenytoin (choice E) is effective in all seizure types except for the one in this question (absence). Note that phenytoin has some idiosyncratic, test-worthy side effects, including hirsutism and gingival hyperplasia.

A 67-year-old woman is brought to the emergency department with complaints of persistent fever, malaise, and the recent appearance of a malar "butterfly" rash on the face, as well as numerous oral ulcers. The patient states that she is taking one medication for treatment of arrhythmias. If the antinuclear antibody test is positive and the patient is mildly anemic, which of the following medications is she most likely taking?
A. Digoxin
B. Disopyramide
C. Flecaainide
D. Mexiletine
E. Procainamide

Explanation:

The correct answer is E. The patient is presenting with signs and symptoms of drug-induced lupus. This complication is associated with procainamide and other agents, including hydralazine, chlorpromazine, isoniazid, methyldopa, and quinidine. Procainamide is a class IA agent, similar in action to quinidine, and is indicated for the treatment of ventricular arrhythmias. This agent is also been associated with agranulocytosis, bone marrow depression, neutropenia, hypoplastic anemia, and thrombocytopenia.

Digoxin (choice A) is a cardiac glycoside used for congestive heart failure (CHF), atrial fibrillation, and atrial flutter. Signs and symptoms of digoxin toxicity include nausea, vomiting, anorexia, appearance of yellow-green halos in the visual field, and the development of cardiac arrhythmias.

Disopyramide (choice B) is a class IA agent indicated for the treatment of documented ventricular arrhythmias. It possesses strong anticholinergic effects and is associated with the development of atrial tachyarrhythmias, heart block, and conduction abnormalities.

Flecainide (choice C) is a class IC agent indicated for the treatment of life-threatening ventricular arrhythmias. It is associated with paresthesias, ataxia, flushing, vertigo, tinnitus, depression, and a worsening of cardiac arrhythmias.

Mexiletine (choice D) is a class IB agent indicated for the treatment of life-threatening ventricular arrhythmias. It is associated with the development of palpitations, chest pain, CHF, edema, arrhythmias, tremor, nervousness, blurred vision, CNS stimulation, and convulsions.
A pharmacologist is examining a new drug with potential antipsychotic properties. He begins by analyzing the pharmacokinetic properties of the drug. Studies of the drug's rate of elimination reveal the data above. Which of the following drugs has similar kinetics to the drug being studied?

A. Amitriptyline  
B. Cimetidine  
C. Ethanol  
D. Fluoxetine  
E. Phenobarbital

Explanation:

The correct answer is C. This drug is exhibiting zero-order kinetics, also known as saturation kinetics. This means that a constant amount of drug is eliminated per unit time, regardless of the plasma concentration. This is in contrast to first-order kinetics, which implies that a constant fraction of drug is eliminated per unit time, so that drug elimination is dependent on the plasma concentration. Drugs with zero-order kinetics and first-order kinetics can be distinguished from each other by examining a graph depicting the time course of the disappearance of the drug from the plasma. With zero-order kinetics, the drug concentration falls linearly, as exemplified by the data in this question. With first-order kinetics, the drug declines in an exponential fashion. Therefore, when the Y-axis is plasma concentration (linear concentration scale), the curve shows exponential decay; when the Y-axis is the logarithm of the plasma concentration (logarithmic concentration scale), a straight line is observed. Very few drugs actually exhibit zero-order kinetics; notable examples are ethanol, phenytoin, and salicylate. All of the other drugs listed exhibit first-order kinetics.

A patient treated for months with large doses of broad spectrum antibiotics would be most likely to develop which of the following?

A. Bleeding in joints  
B. Bony abnormalities  
C. Decreased night vision  
D. Neurologic deficits  
E. Scurvy

Explanation:

The correct answer is A. To answer this question you have to identify two pieces of information. First, you have to recognize that it is about vitamin deficiency acquired by antibiotic therapy (vitamin K is made by bacteria in the gut) and then recognize the deficiency syndrome that would be produced (bleeding tendency secondary to the inability to make clotting factors II, VII, IX, X, and proteins C and S). The other vitamin/syndrome associations are as follows:
A 62-year-old man presents to the emergency department with acute onset of severe ocular pain accompanied by blurred vision that is associated with halos around lights. On examination, the left eye is red and hard; the cornea is described as having a steamy appearance, and mydriasis is noted. The most appropriate agent for the treatment of this patient's acute signs and symptoms is

A. acetazolamide (IV)
B. dorzolamide (topical)
C. epinephrine (IV)
D. latanoprost (topical)
E. timolol (topical)

Explanation:

The correct answer is A. The patient is clearly presenting with signs and symptoms of acute angle-closure glaucoma. Primary acute angle-closure glaucoma occurs because of closure of a preexisting narrow anterior chamber angle, as is commonly found in the elderly, hyperopes, and Asians. Patients often seek immediate medical attention because of the intense pain and blurred vision. The blurred vision is characteristically associated with halos around lights. The eye is often very red and steamy, and the pupil is dilated and nonreactive to light; tonometry reveals elevated intraocular pressure. The treatment considerations are as follows: immediate lowering of intraocular pressure (IOP) is achieved with a single dose of 500 mg IV acetazolamide, followed by 250 mg PO qid. Osmotic diuretics such as oral glycerol and IV urea or mannitol may also be used. Acetazolamide is an agent that inhibits the enzyme carbonic anhydrase, leading to reduced production of aqueous humor and a concomitant reduction in IOP.

Dorzolamide (choice B) is also a carbonic anhydrase inhibitor. This agent is indicated for the chronic lowering of IOP in patients with open-angle glaucoma.

Epinephrine (choice C) is indicated for lowering of IOP in patients with open-angle glaucoma in combination with miotics, beta blockers, hyperosmotics, or carbonic anhydrase inhibitors. However, this agent is contraindicated in patients with narrow-angle glaucoma.

Latanoprost (choice D) is a prostaglandin F2 analog that is believed to reduce IOP by increasing the outflow of aqueous humor. It is indicated for lowering IOP in patients with open-angle glaucoma and ocular hypertension who are intolerant to other agents.

Timolol (choice E) is a beta adrenergic receptor antagonist that has peak ocular hypotensive effects at 1-2 hours post-dosing. This agent decreases IOP with little or no effect on pupil size or accommodation. It is indicated for chronic lowering of IOP in patients with open-angle glaucoma.
A 52-year-old male presents to his physician with a chief complaint of a substantial increase in the size of his breasts over the past few months. Three months ago he was diagnosed with hypertension, and placed on antihypertensive medication. Which of the following medications was most likely prescribed?

A. Captopril
B. Furosemide
C. Hydrochlorothiazide
D. Metoprolol
E. Spironolactone

Explanation:
The correct answer is E. All of the medications listed as answer choices can be effectively used in the treatment of hypertension. Spironolactone is a "potassium-sparing" diuretic that exerts its action primarily as a competitive inhibitor of aldosterone receptors in the distal nephron. One of the reported side effects of spironolactone is gynecomastia. None of the other choices have gynecomastia as a side effect.

Captopril (choice A) is an angiotensin-converting enzyme (ACE) inhibitor that causes a decrease in plasma angiotensin II concentration, resulting in decreased aldosterone secretion.

Furosemide (choice B) is a "loop diuretic" that acts by inhibiting the reabsorption of sodium and chloride ions in the loop of Henle as well as in the proximal and distal renal tubules.

Hydrochlorothiazide (choice C) is a "thiazide diuretic" that inhibits the reabsorption of sodium and chloride ions in the distal renal tubules.

Metoprolol (choice D) is a beta-adrenergic receptor-blocking agent that has a preferential effect on beta1 adrenoreceptors, which are mostly located in cardiac muscle.

A 62-year-old man with well-controlled Parkinson's disease and type 2 diabetes presents with akinesia, a festinating gait, rigidity, and loss of postural reflexes. The patient states that his symptoms began shortly after starting a new "stomach" medication. On the basis of this information, the patient is most likely receiving

A. cisapride
B. metoclopramide
C. nizatidine
D. omeprazole
E. sucralfate

Explanation:
The correct answer is B. The patient is presenting with an exacerbation of his Parkinson's secondary to the administration of metoclopramide; the mechanism of this side effect is related to metoclopramide's ability to antagonize dopamine receptors. Metoclopramide is a prokinetic agent indicated for the treatment of gastroesophageal reflux disease (GERD) and diabetic gastroparesis.

Cisapride (choice A) is a prokinetic agent indicated for the treatment of GERD. This agent is associated with cardiac arrhythmias, nervousness, diarrhea, and abdominal cramping.

Nizatidine (choice C) is an H2 receptor antagonist used in the treatment of GERD and gastric ulcers; this agent is generally well tolerated with very few side effects.

Omeprazole (choice D) is a proton pump inhibitor indicated for the treatment of gastric ulcerations and GERD; this agent is generally well tolerated with very few side effects.

Sucralfate (choice E) is a basic aluminum salt that forms an ulcer-adherent complex at the site of the ulcer and is indicated for the treatment of duodenal ulcer. Constipation is the most common side effect.

Following the treatment of an oral abscess with clindamycin, a patient develops a greenish, foul-smelling watery diarrhea with left lower quadrant pain. Other signs and symptoms include fever, leukocytosis, and lethargy. If the toxin produced by Clostridium difficile is detected in the stool, the patient would most appropriately be treated with

A. cisapride
B. gentamicin
C. loperamide
D. metronidazole
E. sulfasalazine

Explanation:

The correct answer is D. Antibiotic-induced colitis (pseudomembranous colitis) is characterized by severe persistent greenish, foul-smelling diarrhea and severe abdominal cramps, as well as fever, leukocytosis, and lethargy. This condition is caused by the toxin produced by Clostridium difficile. This disorder is generally seen toward the end of clindamycin therapy; however, it may begin up to several weeks after discontinuation of therapy. The treatment of this form of colitis is to discontinue medication, provide fluid and electrolyte replacement, and give corticosteroids (systemic and/or via enema), as well as metronidazole or vancomycin. Metronidazole is the treatment of choice for treatment of antibiotic-induced colitis since it is less expensive than vancomycin and does not encourage the emergence of vancomycin-resistant bacteria.

Cisapride (choice A) is a prokinetic agent indicated for the treatment of reflux esophagitis; the primary side effect of this agent is diarrhea.

Gentamicin (choice B) is an aminoglycoside antibiotic primarily used in the treatment of life-threatening infections caused by gram-negative infections; this agent would be ineffective in the treatment of C. difficile infection.

Loperamide (choice C) is an antidiarrheal. The use of this agent in patients with antibiotic-induced colitis is contraindicated, as it may prolong the disease by delaying the elimination of the toxin.
Sulfasalazine (choice E) is a locally acting sulfonamide indicated for the treatment of ulcerative colitis and mild regional enteritis. This agent is ineffective in the treatment of antibiotic-induced colitis.

A 41-year-old woman with glaucoma is treated with acetazolamide. Several weeks later the woman has an arterial pH of 7.34, an arterial PCO2 of 29 mm Hg, and a plasma HCO3− of 15 mEq/L. Which of the following abnormalities has this woman most likely developed?

A. Metabolic acidosis
B. Metabolic alkalosis
C. Mixed acidosis
D. Mixed alkalosis
E. Respiratory acidosis
F. Respiratory alkalosis

Explanation:
The correct answer is A. The laboratory results indicate that the arterial pH, arterial PCO2, and plasma HCO3− concentrations are all low. These changes clearly demonstrate metabolic acidosis, which occurs commonly when a carbonic anhydrase inhibitor is administered. The carbonic anhydrase enzyme attached to the brush border of the tubular epithelial cells normally catalyzes the dissociation of carbonic acid into water and carbon dioxide. Inhibition of carbonic anhydrase prevents the removal of bicarbonate ions from the tubular fluid, which initially increases urine pH. The result is heavy spillage of bicarbonate in the urine, which is the hallmark of type 2 RTA (renal tubular acidosis). However, once the plasma levels of bicarbonate have decreased sufficiently, the bicarbonaturia ceases and the plasma HCO3− levels stabilize at a lower than normal level. Consequently, the urine pH falls typically to 4.5-5.0.

The following table shows changes in plasma pH, plasma HCO3−, and arterial PCO2 characteristic of the various acid-base abnormalities.

<table>
<thead>
<tr>
<th></th>
<th>Plasma pH</th>
<th>Plasma HCO3−</th>
<th>Arterial PCO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis (choice A)</td>
<td>low</td>
<td>low</td>
<td>low</td>
</tr>
<tr>
<td>Metabolic alkalosis (choice B)</td>
<td>high</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td>Mixed acidosis (choice C)</td>
<td>low</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>Mixed alkalosis (choice D)</td>
<td>high</td>
<td>high</td>
<td>low</td>
</tr>
<tr>
<td>Respiratory acidosis (choice E)</td>
<td>low</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td>Respiratory alkalosis (choice F)</td>
<td>high</td>
<td>low</td>
<td>low</td>
</tr>
</tbody>
</table>

**TABLE**
Which of the following chemotherapeutic agents is specific for the M phase of the cell cycle?
Explanation:

The correct answer is E. Vincristine (and vinblastine) are Vinca alkaloids that bind to tubulin, a component of cellular microtubules. This leads to disruption of the mitotic spindle apparatus and results in metaphase arrest since the chromosomes are unable to segregate. Since these drugs interfere with mitosis, they are considered cell-cycle specific for the M phase.

Cytarabine (choice A) belongs to the class of antineoplastics that are antimetabolites. This drug class interferes with normal metabolic pathways by competing for enzymatic sites. Specifically, cytarabine (Ara-C) is a pyrimidine nucleoside analog. It interrupts DNA synthesis and function by inhibiting DNA polymerase and incorporating into the DNA or RNA of the cell. As you would expect, this drug is cell-cycle specific for the S phase.

Daunorubicin (choice B) is one of the antibiotic antineoplastic agents (others include dactinomycin, doxorubicin, bleomycin, plicamycin, and mitomycin). These agents work by disrupting DNA functioning. Daunorubicin binds to DNA between base pairs on adjacent strands, resulting in uncoiling of the helix and destruction of the DNA template. While this drug has its maximum effect during the S phase, it is not cell-cycle specific. (Note: the only antibiotic that is cell-cycle specific is bleomycin.)

Hydroxyurea (choice C) works by interfering with ribonucleoside diphosphate reductase, the enzyme responsible for generating the deoxyribonucleotides needed for DNA synthesis. It is S-phase specific.

Mechlorethamine (choice D) is a nitrogen mustard. The nitrogen mustards (mechlorethamine, cyclophosphamide, melphalan, chlorambucil) belong to the larger class of alkylating agents. These agents work by alkylating DNA (along with RNA and proteins). The alkylating agents are generally NOT cell-cycle specific.

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A 52-year-old woman presents to her physician for a check-up. She is recovering from a wrist fracture after a fall. Dual energy x-ray absorptiometry of the hip had shown her to have osteoporosis. She became menopausal at age 50 and did not begin hormone replacement therapy because of a strong family history of breast cancer. She now fears a future hip fracture and would like to begin a bone loss prevention regime. Which of the following pharmaceutical agents is most appropriate for this patient?

A. Calcitonin nasal spray
B. Oral conjugated estrogen
C. Raloxifene
D. Tamoxifen
E. Transdermal estradiol
The correct answer is C. Raloxifene is a selective estrogen receptor modulator that helps prevent osteoporosis by lessening bone resorption and reducing bone turnover. It lowers risk for vertebral fractures by 40% to 50%. It is a bone-preserving alternative for women who prefer to avoid estrogen. Raloxifene does not cause breast pain and may lessen the risk for breast cancer in menopausal women. There is also a favorable effect on LDL and cholesterol.

Calcitonin nasal spray (choice A) is an osteoclastic bone resorption inhibitor that modestly increases bone mineral density and reduces the incidence of vertebral fracture. Although it is an estrogen alternative for bone preservation, its impact on hip fracture is not known. It is also lacks the anti-breast cancer properties of raloxifene.

Oral conjugated estrogen (choice B) and transdermal estradiol (choice E) are not the best choices, as this patient wants to avoid estrogen because of a strong family history of breast cancer. The route of administration of estrogen has been shown to have similar effects on bone preservation, even though the transdermal dosage is generally half that of the oral dosage. Breast cancer risk, however, is slightly increased with the unopposed higher dosage oral estrogen replacement.

Tamoxifen (choice D), while indicated in the long-term care of breast cancer patients, is not alone useful for treatment or prevention of osteoporosis. Tamoxifen is an anti-estrogen agent that competes with estrogen for binding sites.

Explaination:

A 48-year-old male presents for a routine evaluation 3 months after starting on an antihypertensive medication. His physical examination is unremarkable and blood pressure is 128/83. Laboratory results reveal the following lipid profile: total cholesterol 280 mg/dL, HDL 34 mg/dL, LDL 188 mg/dL, and triglycerides 191 mg/dL. His lipid profile was normal prior to beginning his antihypertensive medication. Which of following medications most likely caused the patient's dyslipidemia?

A. Benazepril
B. Diltiazem
C. Guanfacine
D. Metoprolol
E. Prazosin

Explaination:

The correct answer is D. The question states that the patient began antihypertensive therapy 3 months earlier and now has elevated total cholesterol, LDL, and triglyceride levels, as well as a low HDL level. Therefore, there is a strong possibility that the antihypertensive medication caused the dyslipidemia. Metoprolol is a beta-adrenergic blocking agent that is known to cause dyslipidemias in patients. None of the other medications are associated with the development of dyslipidemias.

Benazepril (choice A), an ACE inhibitor, and diltiazem (choice B), a calcium-channel blocker, are both used to treat essential hypertension, and are not associated with the development of dyslipidemias.

Both guanfacine (choice C), a centrally acting alpha-2-receptor agonist, and prazosin (choice E), a peripherally acting alpha-1-receptor blocking agent, can be used to treat hypertension. However, due to their side-effect profiles, these agents are generally used in patients unresponsive to other antihypertensive therapies.
In an experiment, norepinephrine was injected intravenously and smooth muscle contraction was measured (control curve). Curves X, Y and Z are the result of three separate experiments, in which norepinephrine was administered shortly after an unknown pharmacological agent. What are the three most likely drugs (X,Y,Z) used in the three consecutive experiments?

A. Cocaine, prazosin, phenoxybenzamine
B. Fluoxetine, propranolol, phenoxybenzamine
C. Phenoxybenzamine, cocaine, fluoxetine,
D. Prazosin, phentolamine, phenoxybenzamine
E. Propranolol, cocaine, prazosin

Explanation:

The correct answer is A. The graph is that of a log dose response curve of norepinephrine on alpha-1 receptors of vascular smooth muscle. Norepinephrine alone (control curve) is expected to show an increased response as the dose is increased. A shift to the left indicates potentiation (less norepinephrine is needed to give the same size response), a shift to the right indicates antagonism (more norepinephrine is needed to see a given response).

Curve X shows potentiation, curve Y shows competitive antagonism and curve Z shows non-competitive blockade of the alpha-1 receptors found on vascular smooth muscle. The answer must therefore include an indirect agonist, a competitive blocker, and a non-competitive blocker of alpha-1 receptors.

Cocaine is an indirect agonist that acts by blocking monoamine reuptake, thereby allowing norepinephrine to stay longer and at higher concentration in its synapse, potentiating its action (curve X). (It also blocks the reuptake of dopamine and serotonin, potentiating them in the same way.) Prazosin is a competitive alpha-1 receptor blocker...
used in treatment of hypertension because of its vasodilatory effect, and would produce a right-shift of the
dose-response curve (curve Y). Phenoxybenzamine is the only non-competitive alpha-1 blocker used
therapeutically in cases of malignant hypertension and pheochromocytomas. The excessive vasodilation produced
by this agent is the result of irreversible binding to the receptor, thereby decreasing the efficacy (decreased curve
height) of norepinephrine (curve Z).

Fluoxetine (choices B and C) is a serotonin specific reuptake blocker that would potentiate the action of serotonin,
but not norepinephrine. It is also a weak alpha-1 blocker, which explains its side-effect of orthostatic hypotension.

Propranolol (choices B and E) is a non-selective beta-blocker that would not directly effect the norepinephrine
response at alpha-1 receptors. Although norepinephrine is also a beta-1 receptor agonist, beta-1 receptors are
not present on blood vessels.

Phentolamine (choice D) is a non-selective competitive alpha-blocker that has been largely supplanted by more
selective alpha-1 blockers.

A 32-year-old male, infected with HIV, is diagnosed with Hodgkin's lymphoma. If the patient's CD4 count is
505/mm3, which of the following agents would be suitable for the treatment of this patient's lymphoma without
further compromising his immune system?

A. Busulfan
B. Cisplatin
C. Cyclophosphamide
D. Paclitaxel
E. Vincristine

Explanation:
The correct answer is E. Bone marrow suppression, diarrhea, and alopecia are the most common side effects
seen with cancer chemotherapy regimens. Vincristine, a mitotic inhibitor, is a chemotherapeutic agent that is not
associated with the development of bone marrow suppression and would be the most appropriate agent to use
in this patient. Vincristine is effective in the treatment of acute lymphoblastic leukemia and other leukemias,
Hodgkin's disease, lymphosarcoma, neuroblastoma, and various other types of cancer. Bleomycin is another
antineoplastic agent that does not cause bone marrow suppression.

Busulfan (choice A) is an alkylating agent primarily used in the palliative treatment of chronic myelogenous
leukemia; it is known to cause severe bone marrow suppression. As a general rule, the alkylating agents
typically produce severe immunosuppressive effects.

Cisplatin (choice B) is another alkylating agent indicated for the treatment of metastatic testicular and ovarian
tumors in combination with other agents. This agent can also cause profound bone marrow suppression.

Cyclophosphamide (choice C) is classified as a nitrogen mustard, a subcategory of the alkylating agents. It is
primarily used to treat breast, testicular, and other solid tumors, as well as leukemia and lymphoma. This drug
suppresses bone marrow.

Paclitaxel (choice D) is an antimicrotubule agent typically used in the treatment of ovarian and breast cancer.
Profound neutropenia is typically seen with this agent.
A 58-year-old alcoholic with chronic obstructive lung disease secondary to cigarette smoking is presently receiving theophylline as a bronchodilator for his lung disease. Serum levels of theophylline are persistently lower than expected for the prescribed dose the patient is receiving. The patient's wife is responsible for administering the medicine each day and states that she has not missed any of the doses. Which of the following is the most likely explanation for these laboratory findings?

A. Cirrhosis of the liver  
B. Decreased absorption  
C. Enhanced liver metabolism  
D. Increased urinary clearance  
E. Noncompliance

Explanation:

The correct answer is C. The patient is an alcoholic, and alcohol normally enhances the cytochrome P450 system in the smooth endoplasmic reticulum (SER) of the liver. This system is responsible for the metabolism of drugs, hence, the low theophylline levels are most likely due to enhanced liver metabolism. The hepatocyte SER undergoes hyperplasia as a response to alcohol ingestion and synthesizes the enzyme gamma-glutamyl transferase (GGT). An elevation of GGT in this particular patient would help confirm the likelihood of increased hepatic drug metabolism as the cause of low drug levels.

Cirrhosis of the liver (choice A) would likely increase the serum levels of theophylline because of poor metabolism of the drug.

Decreased absorption of the drug (choice B) in the gastrointestinal tract is a possible choice. However, the history of excess alcohol intake and lack of a history of malabsorption suggest increased hepatic metabolism.

Increased clearance of theophylline in the urine (choice D) implies an increase in the glomerular filtration rate, which would not be expected in this patient.

Since the patient's wife is administering the medication, noncompliance (choice E) is highly unlikely. However, in most circumstances, the lack of an expected response to a medication is due to patient noncompliance until proven otherwise.

A 32-year-old female presents with amenorrhea for the past several months. She also states that there is a "watery secretion" coming from both her nipples. On examination, there is a non-puerperal, watery secretion that does not contain white or red blood cells. Laboratory examination reveals elevated serum prolactin levels. Which of the following medications most likely caused this patient's signs and symptoms?

A. Captopril  
B. Hydrochlorothiazide  
C. Indomethacin
D. Nortriptyline
E. Warfarin

Explanation:
The correct answer is D. Galactorrhea is a condition in which there is a non-puerperal, watery or milky breast
secretion that contains neither pus nor red blood cells. This condition is most commonly associated with
hyperprolactinemia. The secretion, occurring with galactorrhea, can occur spontaneously or on breast
examination. Hyperprolactinemia can also cause oligomenorrhea or amenorrhea. Hyperprolactinemia can be
caused by medications that affect normal pathways for dopamine and norepinephrine. Medications most
commonly associated with this disorder include tricyclic antidepressants such as nortriptyline, tranquilizers,
methyldopa, narcotics, and phenothiazines. Nortriptyline is a tricyclic antidepressant used to treat endogenous
depression. The other medications listed are not associated with the development of hyperprolactinemia.

Captopril (choice A) is an angiotensin-converting enzyme inhibitor used in the treatment of hypertension and
congestive heart failure.

Hydrochlorothiazide (choice B) is a thiazide diuretic used in the treatment of various edematous states.

Indomethacin (choice C) is a non-steroidal, anti-inflammatory drug used in the treatment of mild-to-moderate
pain.

Warfarin (choice E) is a coumarin anticoagulant used for prophylaxis and treatment of deep venous thrombosis
or pulmonary embolism.

A 64-year-old white female who was diagnosed with rheumatoid arthritis two years ago has been taking
salicylates and other NSAIDs for the past 18 months without adequate relief of her symptoms. Her physician
decides to institute methotrexate therapy. Over the next seven weeks she receives prednisone as a form of
"bridging therapy" to help prevent pain and inflammation while waiting for the pharmacological benefits of
methotrexate to begin. Which of the following is she most likely to experience secondary to her glucocorticoid
therapy?

A. Dehydration
B. Hyperkalemia
C. Hypocalcemia
D. Hypoglycemia
E. Hyponatremia

Explanation:
The correct answer is C. Methotrexate is a type of disease-modifying antirheumatic drug (DMARD). DMARDs
are a varied group of drugs, including methotrexate, azathioprine, penicillamine, hydroxychloroquine and
chloroquine, organic gold compounds, and sulfasalazine, which are thought to slow the progression of
rheumatoid arthritis by modifying the disease itself. However, these drugs can take several weeks to several
months to produce therapeutic effects. In rheumatoid arthritis, prednisone is used when persistent synovitis is
seen in multiple joints despite sufficient dosage of NSAIDs. It is also used for "bridge" therapy when DMARD therapy with methotrexate is first initiated. Because it takes a long time for the therapeutic effect of DMARDs to become evident, agents like prednisone are needed to "bridge the gap" between NSAID therapy and DMARD therapy.

The major disadvantage of using glucocorticoids for an extended period of time is the severe side effect profile. For example, long term use of prednisone is associated with hypocalcemia (choice C), fluid retention (not dehydration, choice A), hypokalemia (not hyperkalemia, choice B), hyperglycemia (not hypoglycemia, choice D), and hypernatremia (not hyponatremia, choice E). Other adverse reactions include adrenal suppression, muscle weakness and atrophy, gastritis, nausea, vomiting, Cushingoid state (moon face, buffalo hump, central obesity), immunosuppression, hypertension, psychosis, osteoporosis, glaucoma, and posterior subcapsular cataracts.

A 62-year-old man with congestive heart failure (CHF) and poorly controlled hypertension presents with new onset of anginal symptoms during periods of exertion. His physician prescribes a calcium channel blocker for angina prophylaxis and for his hypertension. Which of the following drugs would be most likely to exacerbate the patient's heart failure?

   A. Amlodipine
   B. Diltiazem
   C. Felodipine
   D. Isradipine
   E. Verapamil

Explanation:

The correct answer is E. Verapamil is a "first-generation" calcium channel blocker that has been associated with an accelerated progression of CHF in certain patients. This agent has a strong negative inotropic effect, which leads to a decrease in the force and velocity of myocardial contraction. Hence, this agent would most likely exacerbate the patient's heart failure. As a general rule, the use of calcium channel blockers in CHF is reserved for patients who also have hypertension and/or anginal symptoms.

Amlodipine (choice A) and felodipine (choice C) are the most commonly used calcium channel blocking agents in patients with CHF. These two medications may actually produce a small increase in myocardial contractility and cardiac output.

Diltiazem (choice B) is generally avoided in patients with CHF, since it has mild-to-moderate negative inotropic effects leading to a small decrease in myocardial contractility. However, the negative inotropic effects of verapamil are much greater than those seen with diltiazem.

Isradipine (choice D) is a calcium channel blocker that can safely be used at lower doses in patients with CHF; it seems to have no net effect on myocardial contractility.

A 50-year-old man with moderate familial hypertriglyceridemia is treated with gemfibrozil. What is the primary mechanism of action of this drug?

   A. Binding of bile acids in the intestine
B. Inhibition of hepatic VLDL secretion
C. Inhibition of HMG-CoA reductase
D. Stimulation of HDL production
E. Stimulation of lipoprotein lipase

Explanation:

The correct answer is E. Gemfibrozil (as well as clofibrate) works by increasing the activity of lipoprotein lipase, leading to increased clearance of VLDLs, which are elevated in familial hypertriglyceridemia. This question gives us the opportunity to review the mechanism of action of the drugs used in the treatment of hyperlipidemia.

Binding of bile acids (choice A) is the mechanism of action of resins such as cholestyramine. They cause the liver to use cholesterol for the synthesis of new bile acids.

Inhibition of hepatic VLDL secretion (choice B) is the mechanism of action of niacin.

Inhibition of HMG-CoA reductase (choice C) is the mechanism of action of lovastatin and simvastatin.

Stimulation of HDL production (choice D) may occur with both gemfibrozil and niacin, but it is not the main mechanism of action.

A 33-year-old newlywed presents to her physician with a sharp, burning epigastric pain. She had recently begun a regimen of non-steroidal antiinflammatory agents to help relieve pain caused by rheumatoid arthritis. Her physician recommends misoprostol to relieve her gastric distress. Before prescribing this drug, the physician should first obtain the results of a(n)

A. antinuclear antibody test
B. barium swallow
C. esophageal manometry
D. osmotic fragility test
E. pregnancy test

Explanation:

The correct answer is E. Misoprostol, a methyl analog of prostaglandin E1, is approved for the prevention of ulcers caused by the administration of nonsteroidal anti-inflammatory agents. Because this drug is a potential abortifacient, it should not be given to pregnant women, or to women who are attempting to conceive.

Antinuclear antibodies (choice A) are associated with autoimmune diseases such as systemic lupus erythematosus, scleroderma, Sjögren's syndrome, and inflammatory myopathies. The test would be of no value in this case.

A barium swallow (choice B) is not indicated prior to the administration of misoprostol.

Esophageal manometry (choice C) is used to evaluate the competency of the lower esophageal sphincter, and
to assess esophageal motor activity.

The osmotic fragility test (choice D) is performed by placing erythrocytes into a low-salt solution. An increased susceptibility to osmotic lysis is found in hereditary spherocytosis.

A 60-year-old male with angina comes to the emergency room with severe chest pain unresponsive to sublingual nitroglycerin. An EKG shows ST segment elevation in the anterolateral leads, and thrombolytic therapy is initiated. If streptokinase is given to this patient, it may produce thrombolysis after binding to which of the following proteins?

A. Antithrombin III
B. Fibrin
C. Plasminogen
D. Protein C
E. Thrombomodulin

Explanation:

The correct answer is C. The fibrinolytic activity of streptokinase is due to its ability to bind and cleave plasminogen, producing plasmin. Plasmin directly cleaves fibrin, both between and within the fibrin polymers, thus breaking up thrombi and potentially restoring blood flow to ischemic cardiac muscle. This same mechanism of fibrinolysis is shared by urokinase and tissue-plasminogen activator (tPA).

Antithrombin III (choice A) is a coagulation inhibitor that binds to and inactivates thrombin. Antithrombin III is anticoagulant, not fibrinolytic.

Fibrin (choice B) is not directly acted upon by streptokinase. It is indirectly cleaved through the action of plasmin.

Protein C (choice D) is a glycoprotein that modulates coagulation by inhibiting the procoagulant activities of factors V/Va and VIII/VIIIa. Protein C has no inherent fibrinolytic activity.

Thrombomodulin (choice E) is an anticoagulant protein that binds to thrombin and diminishes its capacity to activate fibrinogen, Factor V, and platelets. Thrombomodulin has no fibrinolytic activity.

A 29-year-old epileptic sanitation engineer is maintained on primidone. Ultrastructural examination of a liver biopsy reveals increased amounts of smooth endoplasmic reticulum. This change is most closely related to increases in the activity of which of the following?

A. P-450 system
B. Purine degradation
C. Pyrimidine synthesis
D. Tricarboxylic acid (Krebs) cycle

E. Urea cycle

Explanation:

The correct answer is A. The cytochrome P-450 mixed-function oxidase system is located on smooth endoplasmic reticulum in liver cells. This system is involved in the detoxification of some drugs and other exogenous compounds (barbiturates, carcinogenic hydrocarbons, steroids, carbon tetrachloride, alcohol, insecticides), and its growth can be stimulated by exposure (particularly chronic exposure) to these agents. As a consequence, cells adapted to one drug can more rapidly metabolize the other drugs and compounds handled by the P-450 system.

While rescuing a child from a burning home, a firefighter was burned over 60% of his body. He is rushed to the emergency room and quickly taken into surgery. During the surgery, the anesthesiologist notices tall, peaked T waves and prolongation of the PR interval, accompanied by progressive widening of the QRS complex so that it appears to merge with the T waves. The patient goes into ventricular fibrillation, then asystole, and cannot be resuscitated. Which of the following agents is most likely responsible for this patient's electrocardiographic changes?

A. Atracurium
B. Baclofen
C. Cyclobenzaprine
D. Succinylcholine
E. Tubocurarine

Explanation:

The correct answer is D. The electrocardiogram strongly suggests that this patient is suffering from hyperkalemia. Hyperkalemia is a potentially life-threatening complication of succinylcholine. Because succinylcholine is a depolarizing skeletal muscle relaxant, during prolonged muscle depolarization, the muscle can release substantial amounts of K+. Patients with burns, extensive soft tissue injuries, spinal cord injury, or muscular dystrophies are at great risk of succinylcholine-induced hyperkalemia, and succinylcholine should either be avoided or used with extreme caution.

Atracurium (choice A) and tubocurarine (choice E) are nondepolarizing skeletal muscle relaxants, and do not increase the risk of hyperkalemia.

Baclofen (choice B) is a spasmolytic, and would not be used in a surgical setting.

Cyclobenzaprine (choice C) is used to relieve acute temporary muscle spasm that is caused by strain or local trauma. It would never be used as a skeletal muscle relaxant in a surgical setting.
A cardiovascular pharmacologist is researching the effects of new compounds on arteriolar resistance. Drug X maximally increases vascular resistance by 50% at a dose of 20 mg/mL. Drug Y maximally increases vascular resistance by 75% at a dose of 40 mg/mL. Which of the following conclusions can the researcher draw from this experiment?

A. Drug X has a smaller volume of distribution than Drug Y  
B. Drug X has a shorter half-life than Drug Y  
C. Drug X is less efficacious than Drug Y  
D. Drug X is less potent than Drug Y  
E. Drug X has a lower LD50 than Drug Y

Explanation:

The correct answer is C. The only conclusion that can be drawn from this data is that Drug X is less efficacious than Drug Y. Efficacy is defined as the maximum effect that can be produced by a drug, regardless of dose. Drug X can only produce a 50% change in resistance, whereas Drug Y can produce a 75% change in resistance. Therefore, Drug X is less efficacious than Drug Y.

A volume of distribution (choice A) is the ratio of the amount of drug in the body to its plasma concentration. In this experiment, we do not know the total amount of drug used or the plasma concentration. For that matter, we do not even know if this is an in vivo experiment. Thus, no conclusions can be drawn about volume of distribution.

The half-life (choice B) is the time it takes for the concentration of a drug to fall 50% from its previous measurement. There is no information given to determine half-life.

The potency (choice D) is the dose or concentration required to produce 50% of the drug's maximal effect. We cannot determine the potency of Drug Y from this question.

The LD50 (choice E) is the dose that causes death in 50% of a population of subject. The experiment described above does not describe a population study, nor does it give any indication about the toxicity of the drug.

A 32-year-old stockbroker suffers from myoclonic jerking, but is not afflicted by other seizure types. He does not appear to have any other neurological deficits. When discussing possible pharmacological therapies with his physician, he says that because of the demanding nature of his line of work he would prefer a drug with minimal sedative properties. Which of the following drugs will his physician most likely prescribe?

A. Carbamazepine  
B. Clonazepam  
C. Ethosuximide  
D. Phenobarbital  
E. Valproic acid
Explanation:

The correct answer is E. Valproic acid is the drug of choice for specific myoclonic syndromes because it very effective and it is nonsedating.

Carbamazepine (choice A), ethosuximide (choice C), and phenobarbital (choice D) are not used for the treatment of this disorder.

Clonazepam (choice B), a benzodiazepine, can be effective in this disorder, but high doses are generally required, causing marked sedation.

A 15-year-old boy presents to the emergency room with agitation, mydriasis, and hot, dry skin. Physical examination reveals decreased bowel sounds and tachycardia. Assuming that he is suffering from a drug overdose, which class of drugs is most likely responsible for his symptoms?

A. Anticholinergic
B. Cholinomimetic
C. Opioid
D. Salicylate
E. Sedative-hypnotic
F. Stimulant

Explanation:

The correct answer is A. This patient is most likely suffering from an anticholinergic overdose, which would produce the symptoms described in the question. The probable culprit is Jimson weed, a naturally growing plant that contains antimuscarinic agents. This plant is often cultivated or field-collected and its leaves brewed in a tea.

Cholinomimetics (choice B), such as those in insecticides, can cause miosis, excessive salivation and sweating, hyperactive bowel sounds with abdominal cramping and diarrhea, anxiety, agitation, seizures, and coma. Muscle fasciculations may occur, followed by flaccid paralysis. Death may result from flaccid paralysis of respiratory muscles.

Opioids (choice C) can cause sleepiness, lethargy, or coma, miosis, cool skin, hypoventilation, hypotension, bradycardia, and decreased bowel sounds.

Salicylates (choice D) can cause hyperventilation, hyperthermia, anion gap metabolic acidosis, dehydration, potassium loss, and confusion, lethargy, or coma.

Sedative-hypnotics (choice E) can cause disinhibition at low doses, and increasing central nervous system depression (lethargy, stupor, coma) with higher doses.

Stimulants (choice F) can cause agitation, mydriasis, and tachycardia. The best way to distinguish stimulant overdose from anticholinergic overdose is the skin, which is sweaty with stimulants and dry with anticholinergics.
Stimulants can also cause arrhythmias, seizures, psychosis, and hyperthermia.

An electrophysiologist is performing intracellular recordings on neuronal cells in culture. He is trying to identify a drug that would reliably increase the firing rate in the cultured cells. Assuming the cells in question express all of the following receptor types, an agonist at which of the following receptors would most likely produce an increase in firing rate?

A. Alpha-2 adrenergic
B. Beta-1 adrenergic
C. Gamma-aminobutyric acid
D. Glycine
E. N-methyl-D-aspartate

Explanation:
The correct answer is E. The answer options contain a mix of ligand-gated ion channel receptors and G protein coupled receptors. A receptor that would reliably produce excitation, thus increasing in firing rate, would be an excitatory amino acid receptor. The N-methyl-D-aspartate (NMDA) receptor is an example of this type of receptor. The NMDA receptor is a ligand-gated ion channel that would permit the influx of cations (sodium and calcium). The rule of thumb is that cations entering the cell through ion channels produce depolarization, and anions entering the cell cause hyperpolarization.

The alpha-2 adrenergic receptor (choice A) is coupled to Gi, and would lead to a decrease in cAMP levels.

The beta-1 adrenergic receptor (choice B) is coupled to Gs, and would lead to an increase in cAMP levels.

The gamma-aminobutyric acid (GABA) (choice C) and glycine (choice D) receptors are inhibitory amino acid receptors. They are ligand-gated ion channel receptors that allow chloride influx. This could cause hyperpolarization, or at least membrane potential stabilization, thus preventing excitation of the cell.

A 49-year-old alcoholic businessman complains of 2 days of severe worsening pain with redness and swelling of his first metatarsophalangeal joint. He has no history of injury or trauma. He is afebrile with no constitutional symptoms. Which of the following drugs would likely be prescribed for this patient?

A. Allopurinol
B. Colchicine
C. Colestipol
D. Pravastatin
E. Probenecid
Explanation:

The correct answer is B. This patient is experiencing an acute attack of gout. The association of gout with alcoholism is well documented. Gout is caused by an overproduction or underexcretion of uric acid. Precipitation of sodium urate (uric acid is ionized at body pH) in joint fluid causes an acute inflammatory synovitis with synovial edema and leukocytic infiltrate. It usually affects the joints of the lower extremity, most commonly, the large toe. Formation of tophi (urate deposits surrounded by inflammatory cells, including foreign body giant cells) is pathognomonic.

Colchicine is an anti-gout drug that binds to microtubule proteins and interferes with microtubule assembly. In this way, it impairs leukocyte chemotaxis, thus preventing the migration of granulocytes to the inflammatory site. Colchicine is the drug of choice for attacks of acute gout. Note that NSAIDs can also be used in the treatment of acute gout. They are as efficacious as colchicine; however, symptomatic improvement takes longer.

Allopurinol (choice A) is an anti-gout drug that is indicated for the treatment of chronic gout. Allopurinol functions to inhibit the enzyme xanthine oxidase, which results in a decreased production of uric acid from its immediate precursor, xanthine. It lowers both serum and urinary concentrations of uric acid.

Cholestipol (choice C) is a bile acid sequestrant that is useful in lowering cholesterol levels in familial hyperlipidemias. It is not used for the treatment of gout.

Pravastatin (choice D) is an HMG-CoA reductase inhibitor useful in the treatment of familial hyperlipidemias. It is not used for the treatment of gout.

Probenecid (choice E) is indicated for the treatment of chronic gout. Probenecid inhibits uric acid reabsorption and therefore increases the urinary excretion of uric acid.

A 32-year-old pregnant woman is told by her physician to avoid taking aspirin. Use of aspirin is contraindicated, especially during the last part of pregnancy, because aspirin affects which of the following hematologic parameters?

- A. Activated partial thromboplastin time
- B. Bleeding time
- C. Platelet count
- D. Prothrombin time
- E. Thromboplastin time

Explanation:

The correct answer is B. Aspirin irreversibly acetylates platelet cyclooxygenase, thereby inactivating this enzyme and preventing the production of thromboxane A2. In this manner, aspirin therapy interferes with secondary aggregation. The result is a prolonged bleeding time related to platelet dysfunction rather than to dysfunction of the coagulation process, as would be implied by prolongation of the activated partial thromboplastin time (choice A), prothrombin time (choice D), or thromboplastin time (choice E). The platelet count (choice C) is not affected by aspirin.
A 46-year-old male with non-insulin dependent diabetes presents with a recent onset of nausea, vomiting, abdominal pain, anorexia, and dark-colored urine. Laboratory examination reveals an AST = 136 U/L and an ALT = 142 U/L. Based on these findings, which of the following oral hypoglycemic agents is the patient most likely taking?

A. Acarbose  
B. Glipizide  
C. Metformin  
D. Repaglinide  
E. Troglitazone

Explanation:

The correct answer is E. Cases of severe idiosyncratic hepatocellular injury have been reported following the administration of troglitazone. The hepatic injury is usually reversible, but rare cases of hepatic failure leading to death or liver transplantation have been reported. The initial signs and symptoms of hepatic dysfunction include recent onset of nausea, vomiting, abdominal pain, anorexia, and a dark colored urine. Once these signs and symptoms begin to appear, the patient taking troglitazone should have liver function tests performed. An AST and ALT of greater than 3 times the normal limits and/or the appearance of jaundice are typical.

Acarbose (choice A) is an alpha-glycosidase inhibitor used as an adjunctive treatment measure for NIDDM; the most common side effects are abdominal discomfort and flatulence.

Glipizide (choice B) is a sulfonylurea oral hypoglycemic agent associated with the development of hypoglycemia and cholestatic jaundice (a rare complication).

Metformin (choice C) is a biguanide oral hypoglycemic agent associated with the development of lactic acidosis and malabsorption of amino acids.

Repaglinide (choice D) is the non-sulfonylurea moiety of glyburide; it is commonly associated with hypoglycemia, nausea and vomiting.

A 63-year-old man presents to the emergency department with precordial chest pain. He states that this pain is often precipitated by stress or exertion and is generally relieved quickly by rest and/or nitrates. On examination, there is electrocardiographic evidence of ischemia during stress testing. Angiography demonstrates narrowing of several major heart vessels. Which of the following would be most likely to worsen the patient's angina?

A. Acebutolol  
B. Atenolol  
C. Metoprolol  
D. Nadolol  
E. Propranolol
Explanation:

The correct answer is A. The patient meets the criteria for exertional angina: precordial chest pain precipitated by stress or exertion, generally quickly relieved by rest and/or nitrates. The beta-adrenergic blocking agents prevent angina by decreasing myocardial oxygen requirements during exertion and stress through the reduction of heart rate, myocardial contractility, and blood pressure. Beta-blockers are the only antianginal agents that have been proven to prolong life in patients with coronary disease and are considered to be first-line agents in the treatment of chronic angina. Beta blockers with intrinsic sympathomimetic activity (acebutolol and pindolol) are generally not recommended for patients with angina since they may exacerbate the angina in some patients.

Currently in the U.S., agents indicated for treatment of angina include atenolol (choice B), metoprolol (choice C), nadolol (choice D), and propranolol (choice E).

A 65-year-old man with mild heart failure is treated with a loop diuretic. A few days later the man complains of muscle weakness. Laboratory results are shown below.

- Arterial PCO2: 48 mm Hg
- Arterial pH: 7.49
- Plasma HCO3⁻: 35 mEq/L

Which of the following is most likely decreased in this man?

A. Plasma angiotensin  
B. Plasma potassium  
C. Potassium excretion  
D. Renin secretion  
E. Sodium excretion

Explanation:

The correct answer is B. The data shown in the table indicate that the man has developed metabolic alkalosis (increased PCO2, pH, and HCO3⁻), which occurs commonly with overuse of diuretics (thiazides and loop diuretics). The overuse of a loop diuretic increases the excretion of sodium (choice C) by the kidneys. The increase in potassium excretion leads to a decrease in plasma potassium levels (choice B). The sodium depletion stimulates renin secretion (choice D), which in turn raises angiotensin II (choice A) levels in the plasma (which also stimulates aldosterone secretion).

A 58-year-old female develops a rather sudden onset of orthopnea, paroxysmal nocturnal dyspnea, and nocturia. On examination, the patient is tachycardic and both pulmonary rales and a third heart sound (S3) are noted. If the patient is receiving antineoplastic therapy for treatment of breast cancer, which of the following agents did she most likely receive?
A. Bleomycin
B. Carmustine
C. Cisplatin
D. Doxorubicin
E. Methotrexate

Explanation:

The correct answer is D. Dilated (congestive) cardiomyopathy results in a diminution in the contractile function of the left, right, or even both ventricles of the heart. The loss of heart muscle function frequently results in the development of congestive heart failure. This patient is presenting with classic signs and symptoms of congestive cardiomyopathy/congestive heart failure; orthopnea, paroxysmal nocturnal dyspnea, nocturia, tachycardia, pulmonary rales, and a third heart sound (S3) are noted. The anthracycline antibiotics doxorubicin and daunomycin both are commonly associated with the development of congestive cardiomyopathy; however, the incidence is much higher with doxorubicin therapy. Doxorubicin is an antibiotic antineoplastic agent commonly used in the treatment of sarcomas, multiple myeloma, malignant lymphoma, acute leukemias, and ovarian, breast, testicular, gastric, bladder, and throat cancer.

Bleomycin (choice A) is classified as an anticancer antibiotic and is one of the few chemotherapeutic agents that does not cause bone marrow suppression. Bleomycin, along with busulfan, carmustine (BCNU), and methotrexate, are commonly associated with the development of pulmonary toxicity. Bleomycin is indicated for the treatment of squamous cell carcinomas of the head, neck, penis, cervix, and vulva, as well as several types of lymphomas.

Carmustine (BCNU; choice B) is an alkylating agent commonly used in the treatment of Hodgkin's disease and other lymphomas. The most notable side effects of this agent are "delayed" myelosuppression and pulmonary toxicity.

Cisplatin (choice C) is an alkylating agent indicated for the treatment of metastatic testicular and ovarian tumors in combination with other agents. This agent can cause severe bone marrow suppression as well as profound renal toxicity.

Methotrexate (choice E) is an antimetabolite and folic acid antagonist commonly used in various neoplastic disorders, such as pediatric acute lymphocytic leukemia, Burkitt's lymphoma, non-Hodgkin's lymphoma, breast, head, neck, and small cell lung cancer. The most common side effects seen with this agent are mucositis, gastrointestinal ulcer, hepatotoxicity, bone marrow suppression, and pulmonary toxicity.

The pharmacokinetic properties of a new drug are being studied in normal volunteers during phase I clinical trials. The volume of distribution and clearance determined in the first subject are 80 L and 4.0 L/hr, respectively. The half-life of the drug in this subject is approximately

A. 0.03 hours
B. 14 hours
C. 78 hours
D. 139 hours
E. 222 hours

Explanation:
The correct answer is B. The half-life of a drug can be determined using the following equation:

\[ T_{\frac{1}{2}} = 0.693 \times \frac{Vd}{Cl} \]

\[ T_{\frac{1}{2}} = 14 \text{ hours} \]

A 5-year-old male with no previous medical history is brought to the ER by his mother because he accidentally ingested a large dose of rat poison. He is conscious but appears quite agitated. On physical exam, he is found to have a blood pressure of 110/70 and a heart rate of 90. Labs are significant for an elevated PT but a normal PTT. The patient should be immediately treated with

A. atropine
B. flumazenil
C. N-acetylcysteine
D. protamine
E. vitamin K

Explanation:
The correct answer is E. As you might have guessed from his elevated PT level, the active ingredient in rat poison is warfarin. It acts as an anticoagulant by interfering with the normal hepatic synthesis of the vitamin K-dependent clotting factors II, VII, IX, and X. The most important adverse effect of warfarin is bleeding. The action of warfarin can be reversed with vitamin K.

Atropine (choice A) is used as an antidote for anticholinesterase toxicity (e.g., ingestion of organophosphates).

Flumazenil (choice B) is used as an antidote for benzodiazepine toxicity (e.g., Valium).

N-acetylcysteine (choice C) is used as an antidote for acetaminophen toxicity.

Protamine (choice D) is used as an antidote for heparin overdose. Note that heparin enhances the activity of antithrombin III, producing its anticoagulant effect. Heparin toxicity would have resulted in an elevated PTT.

A migrant worker presents to the emergency room in respiratory distress. He had been spraying parathion in the fields for several days, and today he began to feel sweaty and dizzy. By the time he got to the hospital he was drooling, gasping, and becoming agitated. These symptoms are due to the actions of parathion on which of the following?

A. Acetylcholinesterase
B. Muscarinic receptors
C. Neuronal lipid bilayer
D. Nicotinic receptors
E. Voltage-gated sodium channels

Explanation:

The correct answer is A. Organophosphate insecticides such as parathion function as acetylcholinesterase inhibitors, producing increased acetylcholine levels at all cholinergic synapses. Although both muscarinic and nicotinic receptors are stimulated, the muscarinic effects are usually identified first. Treatment with atropine is generally indicated with organophosphate intoxication.

Muscarinic (choice B) and nicotinic (choice D) receptors are not directly affected by organophosphates. The drug's actions are completely indirect; increased stimulation is due to the lengthened half-life of acetylcholine at the synapse.

The neuronal lipid bilayer (choice C) is disturbed by inhalational anesthetic drugs. Although the mechanism of action is poorly understood, it is believed to be a consequence of altered neuronal transmission and ion channel dysfunction.

Nerve conduction is blocked when local anesthetics bind to and inactivate voltage-gated sodium channels (choice E).

A patient with severe systemic lupus erythematosus is receiving long-term glucocorticoid therapy. She should consequently receive supplemental therapy with which of the following?

A. Calcium
B. Carotene
C. Folate
D. Iron
E. Vitamin B12

Explanation:

The correct answer is A. Long-term corticosteroid use can cause osteopenia with vertebral compression factors. This can be minimized with oral calcium supplementation. If the patient is a post-menopausal woman, estrogen therapy is also useful. More controversial are the use of vitamin D, thiazide diuretics, calcitonin, and diphosphonates. Exercise, in moderation may stimulate bone formation.

Carotene (choice B) is an antioxidant, and has no role in the amelioration of bone loss due to long-term corticosteroid treatment.
Some patients with lupus develop hemolytic anemia, and extra nutritional support with folate (choice C) or iron (choice D) may be helpful, but this is a feature of the disease itself, rather than of the steroid therapy.

Supplementation with Vitamin B12 (cobalamin; choice E) is not indicated with glucocorticoid therapy.

A 66-year-old man complains of frequent urination, nocturia, and dysuria. Rectal examination reveals an enlarged prostate. Prostatic specific antigen (PSA) levels are slightly increased, but prostatic biopsy fails to reveal evidence of malignancy. The patient receives treatment with finasteride and has significant improvement of symptoms. Clinical improvement in this case is most likely attributable to

- A. blocking of \( \alpha \)-adrenergic receptors
- B. blocking of androgen receptors
- C. inhibition of bacterial growth
- D. inhibition of 5\( \alpha \)-reductase
- E. inhibition of pituitary LH secretion

Explanation:

The correct answer is D. Prostatic hyperplasia predominantly affects the periurethral zone, leading to compression of the urethra. It should be emphasized that hyperplasia involves all tissue components to varying degrees, increasing the mass of not only the glandular component, but also the fibrous tissue and smooth muscle in the stroma. Obstruction of urinary flow produces difficulty in urination and subsequent distention of the urinary bladder. Prostatic hyperplasia is mediated in part by dihydrotestosterone (DHT), a metabolite of testosterone synthesized by the action of 5\( \alpha \)-reductase. Finasteride, the drug used to treat this patient, acts by inhibiting 5\( \alpha \)-reductase, thus decreasing the trophic influence of DHT on the prostate.

Blockade of \( \alpha \)-adrenergic receptors (choice A) inhibits contraction of prostatic smooth muscle. Thus, treatment with \( \alpha \)-blockers leads to significant improvement of urinary problems, probably because of inhibition of smooth muscle activity within the prostatic gland, which is also partly responsible for urethral compression.

Flutamide and other drugs are used to treat prostatic hyperplasia because of their ability to block androgen receptors (choice B), thus inhibiting hormonal stimulation of prostatic growth.

Inhibition of bacterial growth (choice C) by antibiotic therapy is not beneficial in prostatic hyperplasia, unless there is superimposed bacterial prostatitis.

Inhibition of pituitary LH secretion (choice E) can be produced with drugs like leuprolide and megestrol acetate (by an unknown mechanism), resulting in diminished secretion of testosterone and reduced androgenic trophic influences on the prostate.

The reflex change in heart rate in response to intravenous isoproterenol would be enhanced by which of the following drugs?
A. Dobutamine
B. Esmolol
C. Hexamethonium
D. Phenylephrine
E. Pirenzepine

Explanation:
The correct answer is A. The first thing you need to know to answer this question is what effect isoproterenol has on blood pressure. Isoproterenol, a nonselective beta agonist, decreases blood pressure primarily because of beta2-induced vasodilatation. This would lead to a reflex increase in heart rate by stimulating the sympathetic nervous system and inhibiting the parasympathetic nervous system. The next step is to determine which drug would enhance this increase in heart rate. Of all the drugs listed, only dobutamine would increase heart rate. Dobutamine is a beta1 agonist, typically given intravenously in a hospital setting, which would increase heart rate by stimulating cardiac receptors.

Esmolol (choice B) is a beta1 antagonist. This would prevent some of the reflex increase in heart rate by blocking beta1-receptors on the heart.

Hexamethonium (choice C) is a ganglionic blocker that acts by blocking nicotinic receptors at peripheral ganglia. This would prevent any baroreceptor reflexes by blocking all sympathetic and parasympathetic outflow.

Phenylephrine (choice D) is an alpha1-selective agonist. This would not have a direct effect on the heart and, if anything, would diminish the isoproterenol-induced baroreceptor reflex because it would cause peripheral vasoconstriction.

Pirenzepine (choice E) is a selective muscarinic1 (M1) antagonist. This would not have an effect on the heart because M2 receptors are the subtype of muscarinic receptor that resides on the heart. Atropine, a nonselective muscarinic antagonist, would enhance the reflex increase in heart rate.

A 48-year-old non insulin-dependent diabetic patient on daily extended-release glipizide presents with complaints of polyuria and polydipsia. Laboratory evaluation reveals a blood glucose of 192 mg/dL. She states that her diabetes had been well-controlled and she had been symptom-free for the past 8 years, until recently, when she began taking a medication for hypertension. Which of the following medications is she most likely taking for hypertension?

A. Diltiazem
B. Enalapril
C. Hydrochlorothiazide
D. Methyldopa
E. Terazosin
The correct answer is C. The fact that the patient had well-controlled diabetes until the addition of an antihypertensive medication suggests that the new agent is responsible for increasing the blood glucose level. Hydrochlorothiazide is a thiazide diuretic that is known to increase fasting blood glucose in diabetic patients. Dosage adjustments of both oral hypoglycemic agents, like glipizide, and insulin may be required to maintain euglycemia. None of the other agents in this patient would directly increase the blood glucose level. Thus, all of these agents are considered to be safe and effective for the treatment of hypertension in diabetic patients.

Diltiazem (choice A), a calcium channel blocker, and enalapril (choice B), an ACE inhibitor, can both be used in the treatment of hypertension in diabetic patients. Since these agents have favorable side effect profiles, their use in the initial treatment of hypertension would be recommended.

Both methyldopa (choice D), a centrally acting alpha receptor agonist, and terazosin (choice E), a peripherally acting alpha receptor blocking agent, can be used to treat hypertension in diabetic patients. However, due to their side effect profiles, these agents should be used after other more tolerable agents have been attempted.

A 57-year-old man presents for a routine physical. His blood pressure is 161/98 mm Hg. The patient's only complaint is that over the past several months he has had difficulty urinating. His urine stream is intermittent, and he has recently begun experiencing nocturia and profound urinary urgency. Digital rectal exam reveals diffuse enlargement of the prostate. Which of the following agents would be most likely to effectively treat the man's urinary tract symptoms as well as his hypertension?

A. Finasteride
B. Guanfacine
C. Hydralazine
D. Labetalol
E. Terazosin

The correct answer is E. The patient is presenting with hypertension and signs and symptoms of benign prostatic hyperplasia (BPH). The essential diagnostic characteristics of BPH include a decrease in the force and caliber of the urinary stream, nocturia, high post-void residual volume, urinary retention, and azotemia. Terazosin is an alpha-adrenergic antagonist that selectively blocks alpha-1 receptors in vascular smooth muscle producing relaxation. It is indicated for the treatment of both hypertension and BPH.

Finasteride (choice A) is a specific inhibitor of 5-alpha reductase, an enzyme that converts testosterone into the potent androgen dihydrotestosterone (DHT) in the prostate gland. This agent is indicated only for the treatment of BPH.

Guanfacine (choice B) is a centrally acting alpha-2 agonist indicated for the treatment of mild to moderate hypertension.

Hydralazine (choice C) is a vasodilator indicated for the treatment of hypertension and to decrease afterload in patients with congestive heart failure.

Labetalol (choice D) is both an alpha- and beta-receptor blocking agent indicated for the treatment of
A 25-year-old woman is despondent that her husband left her for another woman. She attempts suicide by ingesting 25 tablets of extra strength acetaminophen. Her mother finds her and the empty bottle a couple of hours later and immediately rushes her to the emergency room. Which of the following drugs will most likely be given to this patient?

A. Acetylcysteine  
B. Atropine  
C. Penicillamine  
D. Pralidoxime  
E. Protamine

Explanation:

The correct answer is A. Acetylcysteine (N-acetylcysteine) is the antidote for acetaminophen overdose. It likely acts by replenishing hepatic stores of glutathione, which become depleted in the effort to metabolize the acetaminophen. It is most effective if administered within 10 hours of acetaminophen ingestion.

Atropine (choice B) is a muscarinic receptor antagonist used in the treatment of cholinesterase inhibitor poisoning.

Penicillamine (choice C) is a chelating agent used to treat poisoning with copper, lead, arsenic, and gold.

Pralidoxime (choice D) is an acetylcholinesterase reactivating agent that is used in organophosphorus cholinesterase inhibitor poisoning.

Protamine (choice E) is used for heparin overdose. Protamine is a basic peptide that binds heparin to form a stable complex devoid of anticoagulant activity.

A 48-year-old female is being treated for breast carcinoma. Over the past few days, she has been complaining of dysuria and frequency. Laboratory examination revealed the presence of microscopic hematuria. The next day the patient developed gross hematuria. Which of the following agents most likely caused the development of these signs and symptoms?

A. Cyclophosphamide  
B. Mitomycin  
C. Paclitaxel  
D. Tamoxifen  
E. Vincristine
Explanation:

The correct answer is A. Cyclophosphamide is metabolized to acrolein, which is excreted in the urine. If the patient's urine is concentrated, the toxic metabolite may cause severe bladder damage. Early symptoms of bladder toxicity include dysuria and frequency. This can be distinguished from a urinary tract infection, since there is no bacteriuria with cyclophosphamide-induced bladder toxicity. However, microscopic hematuria is often present on urinalysis. In severe hemorrhagic cystitis, large segments of the bladder mucosa may be shed which can lead to prolonged, gross hematuria. The incidence of cyclophosphamide-induced hemorrhagic cystitis can be decreased by ensuring that the patient maintains a high fluid intake. Cyclophosphamide is an alkylating agent used in the treatment of breast carcinoma, malignant lymphoma, multiple myeloma, and adenocarcinoma of the ovary, as well as various other forms of cancer. The major toxic reactions commonly seen with this agent include mucositis, nausea, hepatotoxicity, sterile hemorrhagic and non-hemorrhagic cystitis, leukopenia, neutropenia, and interstitial pulmonary fibrosis.

Mitomycin (choice B) is an antibiotic antineoplastic agent used in the treatment of breast carcinoma, adenocarcinoma of the pancreas and stomach, as well as various other forms of cancer. The major toxic reactions commonly seen with this agent include bone marrow depression, nausea, hepatotoxicity, acute bronchospasm, thrombocytopenia, and interstitial pneumonitis.

Paclitaxel (choice C) is an antineoplastic agent primarily used in the treatment of ovarian and breast cancer. The major toxic reactions commonly seen with this agent include bone marrow depression, nausea, hepatotoxicity, bronchospasm, thrombocytopenia, and neutropenia.

Tamoxifen (choice D) is an antineoplastic hormone primarily used in the palliative treatment of estrogen-receptor positive breast cancer patients. The major toxic reactions commonly seen with this agent include depression, dizziness, thrombosis, mild leukopenia or thrombocytopenia.

Vincristine (choice E) is a mitotic inhibitor antineoplastic agent used in the treatment of breast cancer, Hodgkin's disease, non-Hodgkin's lymphoma, advanced testicular cancer and various other types of cancer. The major toxic reactions commonly seen with this agent include mental depression, hemorrhagic enterocolitis, bone marrow depression, nausea, thrombocytopenia, and leukopenia.

A 62-year-old white male complains of left thigh and leg pain and swelling which is exacerbated by walking. One week earlier the patient had a cardiac catheterization procedure performed. The patient is currently vacationing, and has spent the last 28 hours in a car. Which of the following drugs, which might be prescribed in this instance, works by inhibiting the enzyme epoxide reductase?

A. Acetylsalicylic acid  
B. Dipyridamole  
C. Heparin  
D. Streptokinase  
E. tPA  
F. Warfarin

Explanation:
The correct answer is F. This patient has deep venous thrombi (DVT). He has several risk factors for the development of DVT, including a recent hospitalization that likely included catheterization in the femoral region, and a recent period of prolonged stasis. The enzyme epoxide reductase is responsible for converting vitamin K into its active quinone form. The drugs that inhibit epoxide reductase are the vitamin K antagonists such as warfarin. Clotting factors II, VII, IX, and X and proteins C and S are all dependent on vitamin K, which acts as a cofactor for carboxylation reactions. Carboxylation makes factors II, VII, IX, and X better able to interact with calcium, and thus better able to form clots.

Acetylsalicylic acid (choice A) acts as a platelet aggregation inhibitor by decreasing thromboxane A2 production, which under normal circumstances causes platelet aggregation.

Dipyridamole (choice B) is also a platelet aggregation inhibitor that increases cAMP levels by inhibiting cyclic nucleotide phosphodiesterase. This causes inhibition of thromboxane A2 production in platelets and may potentiate the effects of prostacyclin, causing decreased platelet adhesion to thrombogenic surfaces. Dipyridamole may be used in combination with warfarin, in contrast to acetylsalicylic acid, which may cause an unpredictable potentiation of anticoagulation.

Heparin (choice C) is used in cases of DVT, but is limited to parenteral use because it does not readily cross membranes. It acts by potentiating the activity of antithrombin III, which is a suicide inhibitor of thrombin and factors IXa, Xa, XIa, and XIIa.

Streptokinase (choice D) is also used in cases of DVT, but it is limited to intravenous, intra-arterial, and intracoronary use. It is a protein produced by β-hemolytic streptococci that converts plasminogen to plasmin, which is involved in digesting fibrin clots.

tPA (choice E) is also a thrombolytic agent used intravenously. Its mechanism of action is similar to that of streptokinase. tPA has the advantage of not being rapidly inactivated by antibodies from a previous streptococcal infection (as streptokinase can be) because it is a recombinant human enzyme. It is very expensive.

Which of the following diuretics acts at the nephron's distal tubule?

A. Ethacrynic acid  
B. Furosemide  
C. Hydrochlorothiazide  
D. Mannitol  
E. Spironolactone

Explanation:
The correct answer is C. The thiazide diuretics (e.g., hydrochlorothiazide, chlorothiazide, benzthiazide) promote diuresis by inhibiting reabsorption of NaCl, primarily in the early distal tubule.

Ethacrynic acid (choice A) and furosemide (choice B) are both loop diuretics. They act by inhibiting electrolyte reabsorption in the thick ascending loop of Henle. Note that even if you didn't know where these agents act, if you knew that they both belonged to the same class of diuretics, you could have eliminated them both as possibilities since there can't be more than one correct answer choice.
Mannitol (choice D) is an osmotic diuretic. It is freely filtered at the glomerulus and is not reabsorbed. Its primary action occurs at the proximal tubule.

Spironolactone (choice E) is a potassium-sparing diuretic. These agents, which also include triamterene and amiloride, act on the collecting tubule to inhibit the reabsorption of Na+ and the secretion of K+. Spironolactone is a structural analog of aldosterone that binds to its receptor (triamterene and amiloride are not aldosterone antagonists).

A 72-year-old man with prostate cancer is treated with leuprolide. What is the mechanism of action of this drug?

A. It inhibits 5α-reductase  
B. It is a competitive antagonist at androgen receptors  
C. It is a competitive inhibitor of LH  
D. It is a synthetic analog of GnRH  
E. It is a testosterone agonist

Explanation:

The correct answer is D. Leuprolide is a GnRH analog. Given long-term in a continuous fashion, it will inhibit FSH and LH release, thereby decreasing testosterone production and exacting a chemical castration in men. It can be used in the treatment of prostate cancer, polycystic ovary syndrome, uterine fibroids, and endometriosis.

Inhibition of 5α-reductase (choice A) is the mechanism of action of finasteride. It thereby inhibits the production of dihydrotestosterone. It is used in the treatment of benign prostatic hyperplasia (BPH).

Flutamide is another drug used in the treatment of prostate cancer. It is a competitive antagonist at androgen receptors (choice B).

Since LH activates interstitial cells to secrete testosterone, a synthetic analog of LH (choice C) would not be appropriate treatment for prostatic cancer. The same goes for a testosterone analog (choice E).

Here is a brief chart that will aid you in remembering the actions of these similar sounding drugs:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuprolide</td>
<td>GnRH analog</td>
<td>Prostate CA</td>
</tr>
<tr>
<td>Flutamide</td>
<td>Competitive androgen antagonist</td>
<td></td>
</tr>
<tr>
<td>Finasteride</td>
<td>5α-reductase inhibitor</td>
<td>BPH</td>
</tr>
</tbody>
</table>

Remember, "loo"prolide and "flo"tamide are both used for prostate cancer. Finasteride is used for BPH.
A 71-year-old female is seen by a cardiologist, who obtains an electrocardiogram that reveals the presence of atrial fibrillation. The cardiologist wants to decrease conduction through the atrioventricular node. Which of the following medications would he most likely prescribe?

A. Atropine
B. Digoxin
C. Lidocaine
D. Procainamide
E. Quinidine

Explanation:
The correct answer is B. The effect of digoxin on the myocardium is dose-related and involves both a direct and indirect action on the cardiac muscle. The indirect actions involve a vagomimetic action, which decreases the conduction rate through the atrioventricular node (AV node), and a depression of the sinoatrial node. Digoxin is indicated for the treatment of atrial fibrillation, especially when the ventricular rate is elevated. Digoxin is also indicated for the treatment of congestive heart failure and atrial flutter, although electrical cardioversion is often the treatment of choice for atrial flutter.

Atropine (choice A) is an anticholinergic agent that has been used in the treatment of atrioventricular heart block to increase conduction through the AV node when increased vagal tone is a major factor in the conduction defect.

Lidocaine (choice C) is an antiarrhythmic agent indicated for the treatment of ventricular arrhythmias. Lidocaine has a variable effect on AV node conduction. For the most part, conduction through the AV node remains unchanged.

Procainamide (choice D) is a class IA antiarrhythmic agent indicated for the treatment of ventricular arrhythmias. It often causes AV node conduction to be slightly increased.

Quinidine (choice E) is indicated for the conversion of atrial fibrillation/flutter. However, quinidine exerts an indirect anticholinergic effect that will decrease vagal tone and may facilitate conduction in the AV node.

A 29-year-old medical student developed a positive PPD (purified protein derivative) test. She was started on isoniazid (INH) and rifampin prophylaxis. Three months into her therapy, she began to experience muscle fasciculations and convulsions. Administration of which of the following vitamins might have prevented these symptoms?

A. Niacin
B. Pyridoxine
C. Riboflavin
D. Thiamine

E. Vitamin C

Explanation:

The correct answer is B. Pyridoxine, or vitamin B6, is sometimes depleted with isoniazid (INH) use. Patients with pyridoxine deficiency may experience neurologic symptoms, such as convulsions and fasciculations. The treatment of this disorder is slow IV administration of 2-5 g of pyridoxine.

Niacin (choice A) deficiency, also known as pellagra, is a disease that involves several organs, including the skin, the gastrointestinal system, and the nervous system. A useful mnemonic for remembering the symptoms of pellagra is the "4 D's": dermatitis, dementia, diarrhea, and death. These symptoms are not consistent with the patient history described in the question.

Riboflavin (choice C) deficiency is not typically seen alone, but rather in conjunction with other vitamin deficiencies. Dermatitis and glossitis are the most frequent clinical manifestations.

Thiamine (choice D) deficiency, or beri-beri, presents with dry skin and paralysis, rather than convulsions. Severe thiamine deficiency produces Wernicke's encephalopathy, with disorientation, ataxia, and ophthalmoplegia. This deficiency is typically seen in alcoholic patients.

Vitamin C (choice E) deficiency, or scurvy, causes defective growth and maintenance of gums, blood vessels, joints, and teeth. These symptoms are due to impaired collagen hydroxylation, a process that requires vitamin C.

A 68-year-old man with renal insufficiency and hypertension is prescribed enalapril. This agent is most likely to cause which of the following electrolyte disturbances?

A. Hyperkalemia
B. Hypernatremia
C. Hyperphosphatemia
D. Hypokalemia
E. Hypophosphatemia

Explanation:

The correct answer is A. The angiotensin-converting enzyme (ACE) inhibitors are indicated for the treatment of hypertension, heart failure, and diabetic nephropathy. These agents may cause hyperkalemia and mild hyponatremia (compare to choice B), as well as neutropenia, anaphylactoid reactions, angioedema, chronic cough, and fetal abnormalities. Laboratory evaluation should be performed periodically, especially for patients at risk for the development of hyperkalemia. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and use of potassium-containing products, including salt substitutes. These agents do not affect phosphate (choices C and E) blood levels.
A 38-year-old construction worker presents with constant back pain that is exacerbated by movement. After being discharged from the emergency room, the man gets a prescription filled, and takes the recommended dose of the medication. After about 45 minutes, he begins to feel sleepy, has a dry mouth and can feel his heart "racing.” Based on this information, which of the following drugs was most likely prescribed?

A. Baclofen  
B. Cyclobenzaprine  
C. Diclofenac  
D. Methocarbamol  
E. Rofecoxib

Explanation:

The correct answer is B. When patients present with either a muscle spasm or a "strained" muscle, a centrally acting skeletal muscle relaxant is typically prescribed. In addition to these agents, a nonsteroidal anti-inflammatory drug is often added for additional pain control. Although somnolence can be seen with any of the agents listed, xerostomia (dry mouth), mydriasis and tachycardia are classic anticholinergic side effects. Cyclobenzaprine is a centrally acting skeletal muscle relaxant that is structurally related to tricyclic antidepressants, which are known for their strong anticholinergic side effects. Additional common anticholinergic side effects seen with this agent include blurred vision, urinary retention, and constipation. Less common side effects include agitation, respiratory depression, disorientation, tachycardia, and widening of the QRS complex.

Baclofen (choice A) is a centrally acting skeletal muscle relaxant that produces muscle relaxation by inhibition of both monosynaptic and polysynaptic reflexes at the spinal level. This agent is indicated for the treatment of spasticity resulting from multiple sclerosis or secondary to spinal cord injuries; it has also been used in the treatment of trigeminal neuralgia. The most common side effects include transient drowsiness, fatigue, and hypotension.

Diclofenac (choice C) is a non-steroidal anti-inflammatory drug indicated for the treatment of a variety of disorders associated with pain and inflammation. The most common side effects include dyspepsia, nausea, vomiting, abdominal cramps, and dizziness.

Methocarbamol (choice D) produces muscle relaxation by general CNS depression; it does not have a direct action on the contractile mechanism of striated muscle or nerve fibers. This agent is indicated as an adjunct to rest, physical therapy, and other measures for relief of discomfort in various musculoskeletal conditions. Reported side-effects include dizziness, vertigo, ataxia, headache, irritability, bradycardia, hypotension, and syncope.

Rofecoxib (choice E) is a selective cyclooxygenase-2 (COX-2) inhibitor with anti-inflammatory, analgesic, and antipyretic effects. This agent is used in adults for relief of pain and inflammation caused by osteoarthritis and rheumatoid arthritis, as well other inflammatory conditions. The most common side effects are nausea, vomiting, diarrhea, abdominal distress, flatulence, and anorexia.

A 30-year-old female with a 15-year history of asthma presents to the emergency room with left elbow pain. Physical examination reveals tenderness and swelling over the olecranon process. An x-ray of the left arm reveals a fracture. Her medications include oral prednisone and albuterol aerosol. By which of the following mechanisms might corticosteroids have contributed to her fracture?

A. Reduced collagen synthesis  
B. Inhibition of matrix metalloproteinase activity  
C. Suppression of osteoblast function  
D. Induction of osteoclast differentiation  
E. Suppression of interleukin-1 production
A. Decreased osteoblastic bone formation only
B. Decreased osteoblastic bone formation and osteoclastic bone resorption
C. Increased osteoclastic bone resorption only
D. Increased osteoclastic bone resorption and decreased osteoblastic bone formation
E. Increased osteoclastic bone resorption and osteoblastic bone formation

Explanation:
The correct answer is D. Corticosteroids inhibit the proliferation and function of osteoblasts, which are modified mesenchymal cells. These agents stimulate osteoclasts to differentiate from bone marrow macrophages and also stimulate their activity. The net effect is maximal bone loss with increased resorption and decreased formation.

A 24-year-old woman attempts suicide by taking an overdose of diazepam. She is rushed to the emergency department, where the attending physician will most likely order which of the following treatments?

A. Acetylcysteine
B. Atropine
C. Bicarbonate
D. CaNa2EDTA chelation
E. Deferoxamine
F. Ethanol
G. Flumazenil
H. Physostigmine
I. Pralidoxime
J. Protamine

Explanation:
The correct answer is G. Flumazenil is an antagonist at the benzodiazepine receptor. It has no effect on other CNS depressants, such as barbiturates or alcohol.

Acetylcysteine (choice A) is the drug of choice for treatment of overdose of acetaminophen, the active ingredient in Tylenol.

Atropine (choice B) is a muscarinic antagonist used in cases of acetylcholinesterase inhibitor overdose.
Bicarbonate (choice C) infusions may be given to alkalinize the urine and enhance the excretion of acidic drugs (e.g., aspirin).

CaNa2EDTA (choice D) is used as a chelator in lead poisoning.

Deferoxamine (choice E) is an effective chelator for poisoning with iron salts.

Ethanol (choice F) is used in cases of methanol and ethylene glycol poisoning. Administration of EtOH in cases of diazepam overdose would be completely inappropriate because CNS depressants are additive.

Physostigmine (choice H) is used in cases of anticholinergic agent overdose.

Pralidoxime (choice I) is an acetylcholinesterase reactivating agent used in cases of organophosphorus acetylcholinesterase inhibitor overdose.

Protamine (choice J) is administered to reverse the anticoagulant effects of heparin overdose.

IV administration of drug X to an anesthetized animal produces an increase in blood pressure. After administration of drug Y, readministration of drug X produces a decrease in blood pressure. Which of the following pairs of drugs could produce this sequence of events?

<table>
<thead>
<tr>
<th>Drug X</th>
<th>Drug Y</th>
</tr>
</thead>
</table>
| A. Acetylcholine  
Neostigmine       |        |
| B. Epinephrine  
Phentolamine      |        |
| C. Isoproterenol  
Atropine           |        |
| D. Norepinephrine  
Propranolol        |        |
| E. Phenylephrine  
Hexamethonium      |        |

Explanation:

The correct answer is B. First, eliminate all answers in which Drug X does not produce an increase in blood pressure (BP). Choice A should be eliminated because acetylcholine stimulates the noninnervated muscarinic (M3) receptors that are located on endothelial cells of the vasculature. Stimulation of these receptors releases endothelial-derived relaxing factor (EDRF; nitric oxide), which produces a relaxation of the neighboring smooth muscle cells, leading to a decrease in BP. Choice C should be eliminated because isoproterenol (a nonspecific beta agonist) decreases BP by stimulating beta-2 receptors in the vasculature.

Epinephrine, norepinephrine, and phenylephrine all increase BP, so the remaining answers must be eliminated by examining the effects of Drug Y on Drug X. Start with choice B: Epinephrine is an agonist at alpha-1, alpha-2, beta-1, and beta-2 receptors; phentolamine is an antagonist at alpha-1 and alpha-2 receptors. Therefore, after
the administration of phentolamine, epinephrine can stimulate only beta receptors, which would produce a
decrease in BP. Epinephrine is now acting like isoproterenol. This is called epinephrine reversal (the name stems
from the fact that epinephrine originally increases BP and then produces the opposite effect after phentolamine
administration). Therefore, choice B is correct.

Choice D: Norepinephrine is an agonist at alpha-1, alpha-2, and beta-1 receptors; propranolol is a nonselective
beta antagonist. After administration of propranolol, norepinephrine can stimulate only alpha receptors, which will
still cause vasoconstriction (primarily via alpha-1 stimulation in the vasculature) and therefore increase BP.

Choice E: Phenylephrine is an alpha-1 agonist; hexamethonium is a nicotinic ganglionic blocker. Hexamethonium
administration would be predicted to eliminate the baroreceptor response after the second phenylephrine
administration by blocking the peripheral ganglia. However, phenylephrine will still reach the alpha-1 receptors on
the vasculature to produce an increase in blood pressure.

A 55-year-old male with hypertension and a past medical history of myocardial infarction is prescribed atenolol.
This medication will lower his blood pressure by

A. blocking catecholamine release
B. blocking the conversion of angiotensin I to angiotensin II
C. decreasing cardiac output
D. decreasing intravascular volume
E. increasing renin release from the kidney

Explanation:
The correct answer is C. Atenolol is a beta-adrenergic receptor blocking agent used in the treatment of
hypertension. Medications in this drug class lower blood pressure by reducing both cardiac output (choice C)
and decreasing renin release from the kidney (to a lesser extent).

Blocking catecholamine release from peripheral sympathetic nerves (choice A) is the antihypertensive effect
seen with peripherally acting adrenergic neuron blockers (e.g., guanethidine and bretylium).

Angiotensin converting enzyme (ACE) inhibitors block the conversion of angiotensin I to angiotensin II (choice
B). Diuretics decrease intravascular volume (choice D), which ultimately leads to a reduction in blood pressure.

Increasing renin release from the kidney (choice E) would increase, not decrease, blood pressure.

A 38-year-old pregnant woman with a past medical history significant for chronic hypertension presents with a
blood pressure of 158/105 mm Hg. Which of the following antihypertensive agents would be most suitable for initial
therapy in this patient?

A. Bumetanide
B. Fosinopril
C. Hydrochlorothiazide

D. Methyldopa

E. Valsartan

Explanation:
The correct answer is D. Pregnant women with chronic hypertension "require" antihypertensive therapy when the diastolic pressure is greater than 100 mm Hg; however, some clinicians may decide to treat patients with diastolic blood pressures less than 100 mm Hg. For the initiation of therapy, methyldopa is still considered to be the agent of choice. Methyldopa is converted intraneuronally to \( \alpha \)-methylnorepinephrine, an alpha-2 adrenergic agonist, which is subsequently released. Release of \( \alpha \)-methylnorepinephrine in the medulla leads to a decrease in sympathetic outflow, thus lowering blood pressure. Methyldopa has been safely used in the treatment of hypertension during pregnancy; this agent is not associated with the development of teratogenic or other fetal abnormalities.

Diuretics, such as bumetanide (choice A) and hydrochlorothiazide (choice C), are often avoided since these agents can produce hypovolemia, leading to reduced uterine blood flow. Although these agents can be used during pregnancy, methyldopa and hydralazine are the drugs of choice for hypertension during pregnancy.

Fosinopril (choice B) is an angiotensin-converting enzyme (ACE) inhibitor that should not be administered to pregnant women, especially in the second or third trimesters. These agents have been associated with severe fetal and neonatal injury, such as hypotension, neonatal skull hypoplasia, anuria, renal failure, and death.

Along the same lines, the use of the angiotensin II receptor antagonists, such as valsartan (choice E), is not recommended since these agents cause fetal complications similar to the ACE inhibitors.

Patency of the ductus arteriosus can be artificially prolonged after birth by administration of

A. glucocorticoids
B. indomethacin
C. insulin
D. oxytocin
E. prostaglandins

Explanation:
The correct answer is E. The ductus arteriosus is an arterial channel connecting the aorta with the pulmonary trunk during intrauterine life. Closure of this embryonal vessel occurs in the first few days after birth. Patency of the ductus is maintained by prostaglandins, more specifically prostaglandin E. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as indomethacin (choice B), promote closure of this structure since NSAIDs inhibit prostaglandin synthesis. Prostaglandin E and NSAIDs can be used therapeutically to maintain a patent ductus arteriosus or to promote its closure.

Glucocorticoids (choice A) can accelerate pulmonary maturation and stimulate production of surfactant, but do not affect the ductus arteriosus.
Insulin (choice C) inhibits surfactant production, but has no effect on the ductus arteriosus.

Oxytocin (choice D) is a hypothalamic hormone that stimulates contraction of smooth muscle in the uterus and mammary glands. It has no effect on the ductus arteriosus.

A patient was administered trimethaphan during surgery. This drug will cause which of the following responses?

A. Accommodation  
B. Hypertension  
C. Peristalsis  
D. Pupillary constriction  
E. Tachycardia

Explanation:

The correct answer is E. Trimethaphan is a ganglionic blocker that is sometimes administered during surgery to maintain controlled hypotension and to minimize blood loss. The trick to determining the effect of a ganglionic blocker is to first know the predominant tone of the end organ in question. The blocker will produce the opposite effect of the predominant tone. The vessels, arterioles and veins, are predominantly under sympathetic tone. Most everything else is under parasympathetic tone. The heart is under predominantly parasympathetic control. Parasympathetic stimulation of the heart causes bradycardia. Removal of this tone with trimethaphan would result in tachycardia.

The eye is predominantly under parasympathetic control. Parasympathetic stimulation causes the eye to accommodate (focus for near vision, choice A). Removal of this tone with trimethaphan would produce focusing for far vision.

Arterioles are predominantly under sympathetic control. Sympathetic stimulation produces vasoconstriction and possibly hypertension (choice B). Removal of this tone with trimethaphan would produce vasodilatation and hypotension.

The gut is predominantly under parasympathetic control, which increases gut motility (choice C). Removal of parasympathetic tone with trimethaphan would diminish gut motility.

The eye is predominantly under parasympathetic control. Parasympathetic stimulation causes the pupil to constrict (choice D). Removal of this tone with trimethaphan would produce mydriasis.

Which of the following drugs is a long-duration ester local anesthetic?

A. Bupivacaine  
B. Cocaine  
C. Lidocaine
D. Procaine
E. Tetracaine

Explanation:
The correct answer is E. Tetracaine is a long-duration ester local anesthetic.
Bupivacaine (choice A) is a long-duration amide.
Cocaine (choice B) is a medium-duration ester, and is also an uptake blocker.
Lidocaine (choice C) is a medium-duration amide, and is also an antiarrhythmic.
Procaine (choice D) is a short-duration ester.

A 57-year-old smoker with a long history of chronic obstructive lung disease presents to the physician with a blood pressure of 150/95. Which of the following antihypertensives is contraindicated in this patient?

A. Acebutolol
B. Atenolol
C. Esmolol
D. Metoprolol
E. Nadolol

Explanation:
The correct answer is E. The point of this question is that nonselective beta-blockers are contraindicated in patients with lung disease. This is because nonselective beta-blockers will cause bronchoconstriction by blocking the beta2-receptors responsible for promoting bronchial smooth muscle relaxation (recall that beta2 agonists are a mainstay of asthma therapy). Acebutolol (choice A), atenolol (choice B), esmolol (choice C), and metoprolol (choice D) are all cardioselective beta1-blockers that could be used in a patient with lung/airway disease. Another cardioselective blocker that is not listed is betaxolol. As for nadolol (choice E), it is a nonselective beta-blocker and should NOT be used in a patient with lung disease.

Introduction of tyramine to a postganglionic sympathetic neuron would most likely decrease the activity of which of the following enzymes?

A. Catechol-O-methyl transferase (COMT)
B. Choline acetyltransferase
C. Dopa decarboxylase
D. Monoamine oxidase
E. Tyrosine hydroxylase

Explanation:
The correct answer is E. Tyramine increases intraneuronal levels of norepinephrine. Norepinephrine negatively feeds back on tyrosine hydroxylase (the rate-limiting enzyme of catecholamine synthesis) to decrease its own synthesis.

COMT (choice A) is an extraneuronal enzyme involved in the degradation of catecholamines, and is not regulated by norepinephrine levels.

Choline acetyltransferase (choice B) is located in some postganglionic sympathetic neurons (the sympathetic cholinergics), however, tyramine would have no effect on those neurons.

Dopa decarboxylase (choice C) converts L-dopa to dopamine and is not regulated by norepinephrine.

Monoamine oxidase (choice D) is located within postganglionic sympathetic neurons and functions to degrade norepinephrine and other monoamine neurotransmitters. It is not regulated by norepinephrine. Patients on MAO inhibitors need to avoid tyramine-rich foods in order to avoid a sympathetic crisis, caused by leakage of large amounts of norepinephrine from terminals. This occurs because tyramine displaces norepinephrine, which MAO can no longer metabolize, from synaptic vesicles.

A 55-year-old diabetic man is brought to the emergency room in an unresponsive state. The following laboratory values are obtained: PCO2 19 mm Hg, HCO3 11 mEq/L, and pH 6.9. The most appropriate immediate treatment of this patient is

A. administration of an oral hypoglycemic agent
B. administration of bicarbonate
C. administration of insulin
D. close observation only

Explanation:
The correct answer is C. This patient is in a diabetic ketoacidotic coma. The goals in treating such a patient are to increase the rate of glucose utilization by insulin-dependent tissues, to reverse ketonemia and acidosis, and to replenish fluid imbalances.

Oral hypoglycemic agents (choice A) are commonly prescribed for the maintenance of NIDDM patients and would not be appropriate in an acute setting.

Treatment with bicarbonate (choice B) would result in only a transient elevation of pH.

Since this is a life-threatening condition, monitoring the patient without treatment (choice D) is unacceptable.
A 44-year-old man sustains a myocardial infarction, and is admitted to the hospital from the emergency room. Serum chemistries reveal two-fold elevation of his LDL cholesterol. He is prescribed lovastatin, which acts by inhibiting which of the following enzymes?

A. Acetyl-CoA carboxylase
B. Carbamoyl phosphate synthetase I
C. Hydroxymethyl glutaryl-CoA reductase
D. Pyruvate dehydrogenase
E. Uridyl transferase

Explanation:
The correct answer is C. Hydroxymethyl glutaryl-CoA reductase (HMG-CoA reductase) catalyzes the rate-limiting step in cholesterol synthesis, in which HMG-CoA (formed from 3 acetyl-CoA molecules) is reduced to mevalonic acid, using 2 NADPH. Lovastatin and pravastatin reduce cholesterol synthesis and lower serum cholesterol levels by inhibiting this enzyme. Lovastatin is metabolized by the CYP3A isoform of cytochrome P450. In contrast, gemfibrozil and clofibrate lower cholesterol by increasing the activity of lipoprotein lipase, which is produced by the endothelial cells of the vasculature of adipose and muscle tissue.

Acetyl-CoA carboxylase (choice A) catalyzes the first step in fatty acid synthesis.

Carbamoyl phosphate synthetase (choice B) catalyzes the rate-limiting step in urea synthesis.

Pyruvate dehydrogenase (choice D) catalyzes the transition step between glycolysis and the TCA (Krebs) cycle.

Uridyl transferase (choice E) is employed in galactose metabolism.

A 24-year-old male presents to the emergency room with hypertension, tachycardia, an elevated body temperature, diaphoresis, mydriasis, and severe agitation. His mother reports that he uses illicit drugs, although she is not sure which kind. Which of the following agents is the most appropriate therapy for this patient?

A. Atropine
B. Flumazenil
C. Fluoxetine
D. Labetalol
E. Naloxone
F. Physostigmine

Explanation:
The correct answer is D. The patient described above is probably under the influence of a central nervous system stimulant, such as methamphetamine. Labetalol is a nonselective alpha- and beta-antagonist and would block many of the dangerous peripheral side effects of CNS stimulants, such as hypertension and cardiac stimulation. Other appropriate medications that could be administered under these conditions would be antipsychotic agents (to control the agitation and psychotic symptoms) and diazepam (to control possible seizures). Supportive care should be given as needed to control the hyperthermia and to maintain respiration.

Atropine (choice A) is a muscarinic antagonist, which would be an appropriate therapy for an acetylcholinesterase inhibitor overdose. A patient presenting with an acetylcholinesterase inhibitor overdose would not be expected to have an elevated body temperature or hypertension. Their eyes would be miotic, not mydriatic. Bradycardia, not tachycardia, would be expected. They would, however, have diaphoresis because of increased cholinergic tone at the sweat glands, which are innervated by sympathetic cholinergics.

Flumazenil (choice B) is a benzodiazepine receptor antagonist. It is specifically useful in the case of a benzodiazepine overdose.

Fluoxetine (choice C) is a selective serotonin reuptake inhibitor (SSRI) type of antidepressant. It would not be indicated in the case of CNS stimulant overdose.

Naloxone (choice E) is an opioid receptor antagonist, which would be an appropriate therapy for an opiate overdose, such as heroin or morphine. A patient presenting with such an overdose would appear sleepy, lethargic, or comatose, depending on the degree of overdose. Pupils would be miotic, not mydriatic. Blood pressure and heart rate would usually be decreased. Respiration would be depressed.

Physostigmine (choice F) is an acetylcholinesterase inhibitor, which might be used for antimuscarinic drug overdose, such as atropine, scopolamine, or Jimson weed. An antimuscarinic overdose can look similar to a CNS stimulant overdose, with at least one important exception. The hyperthermia seen with an antimuscarinic overdose is accompanied by hot and dry skin (because of blockade of the sympathetic cholinergics to the sweat glands). Stimulant overdose is often characterized by profuse sweating. Tachycardia, hypertension, hyperthermia, mental changes, and mydriasis are common to both.

A 4-year-old male is brought to the emergency room with a recent onset of a rash, urticaria, and a fever of 101 degrees F. The mother also states that her son has been complaining that his "bones hurt." Physical examination reveals mild lymphadenopathy. The patient's past medical history is unremarkable except that he just finished a 10-day course of cefaclor suspension for treatment of an upper respiratory infection. The patient should be treated with

A. aspirin and diphenhydramine
B. erythromycin and diphenhydramine
C. intravenous penicillin and diphenhydramine
D. oral prednisone and diphenhydramine
E. topical betamethasone

Explanation:

The correct answer is D. Serum sickness is a condition commonly caused by hypersensitivity to drugs. It is suggested that the drug acts as a hapten, which binds to plasma proteins. This drug-protein complex is
recognized as being foreign to the body and induces the serum sickness. Common signs and symptoms of serum sickness include fever, cutaneous eruptions (morbilliform and/or urticarial), lymphadenopathy, and arthralgias. Erythema multiforme may also appear in severe cases. With respect to cefaclor, the incidence of serum sickness is much higher in infants and children than in adults. Due to the severity of the signs and symptoms in this patient, oral prednisone and diphenhydramine should be administered. The prednisone will treat the arthralgias and the skin rash and the diphenhydramine will alleviate the urticaria.

The use of aspirin (choice A) in a child with a fever is not indicated due to the risk of Reye syndrome. If the patient had not completed his antibiotic therapy and/or signs and symptoms of the infection were still present, switching the antibiotic to a non-beta lactam would be indicated.

Prescribing erythromycin (choice B) for a patient with no signs or symptoms of infection would not be indicated.

Intravenous penicillin (choice C) would not be indicated since there is no infection in this patient, and IV penicillin is reserved for serious infections. In fact, penicillin administration is the most common cause of serum sickness.

Topical betamethasone (choice E) may help to treat the rash and urticaria; however, oral prednisone and diphenhydramine would produce more symptomatic relief.

A 57-year-old man with severe bronchial asthma presents with white patches on the inside of the cheeks that can be easily wiped off, leaving a red, bleeding, sore surface. He is currently using beclomethasone and albuterol inhalers for his asthma and he is allergic to penicillin. Which of the following agents would be most appropriate for the treatment of this patient's oral condition?

A. Acyclovir
B. Amoxicillin
C. Cefixime
D. Erythromycin
E. Nystatin

Explanation:

The correct answer is E. The patient most likely has candidiasis, which can appear in any area of the oral mucosa. Inhaled corticosteroids, such as beclomethasone, are associated with the development of candidiasis in asthmatic patients, especially those who do not "wash out" their mouth with water after each usage. On the basis of the description, the patient has the pseudomembranous form of oral candidiasis or "oral thrush." There is also an erythematous form that presents with flat red and white lesions that cannot be "rubbed off." Oral candidiasis responds very well to antifungal therapy. Nystatin is an antifungal agent used locally for treatment of infections caused by many different Candida species. As a side note, the fact that the patient is penicillin allergic does not impact the treatment decision; it is only a distracter.

Acyclovir (choice A) is an antiviral agent used in the treatment of infections caused by herpes simplex virus types 1 and 2 and varicella-zoster virus. This agent would be indicated in individuals with herpes zoster infections, which typically appear as vesicular eruptions and/or ulcers on the cheek, tongue, gingiva, or palate.

If the patient presented with lymphoid hyperplasia of the posterior pharynx covered by a punctuate or coalescent exudate that is gray, yellow, or white, one might suspect streptococcal infection, which is associated with severe pharyngitis and fever. The posterior pharynx is diffusely erythematous with a gray, yellow, or white exudate. If this were the case, erythromycin (choice D), a macrolide antibiotic, would be the treatment of choice.
in a penicillin-allergic patient.

Both amoxicillin (choice B) and cefixime (choice C) are β-lactam antibiotics used to treat a wide range of bacterial infections. These agents are both known to cause allergic reactions in penicillin-allergic patients.

A 66-year-old male presents with chronic fatigue. On examination, the patient is noted to have lymphadenopathy and an enlarged liver and spleen. Laboratory examination reveals a white blood cell count of 25,000/µL with 93% lymphocytes; the lymphocytes appear small and mature. Both the hematocrit and platelet counts are within normal limits; however, hypogammaglobulinemia is also noted. Which of the following agents is indicated for treatment of this patient's condition?

A. Chlorambucil
B. Cisplatin
C. Dacarbazine
D. Tamoxifen
E. Vinblastine

Explanation:

The correct answer is A. Chronic lymphocytic leukemia (CLL) is typically a disease of the elderly, with 90% of cases occurring after the age of 50; the median age is 65. Patients will typically present with a complaint of chronic fatigue and/or lymphadenopathy. Approximately 50% of all patients with CLL present with an enlarged liver and/or spleen. CLL typically pursues an indolent course but can occasionally present as a rapidly progressive disease. The hallmark of CLL is the isolated lymphocytosis in which the white blood cell count is usually greater than 20,000/µL and between 75% and 98% of the circulating cells are small "mature" lymphocytes. Chlorambucil is classified as a nitrogen mustard, a subcategory of the alkylating agents. It is primarily used to treat chronic lymphocytic leukemia and ovarian carcinoma; it can also be used to treat Hodgkin's disease and various other lymphomas.

Cisplatin (choice B) is an alkylating agent indicated for the treatment of metastatic testicular and ovarian tumors in combination with other agents.

Dacarbazine (choice C) is a cytotoxic agent with alkylating properties. It is used as a single agent or in combination with other antineoplastics in the treatment of metastatic malignant melanoma, refractory Hodgkin's disease, and various sarcomas.

Tamoxifen (choice D) is an antiestrogen hormone used in the palliative treatment of breast cancer in patients with estrogen-receptor-positive breast cancer.

Vinblastine (choice E) is a mitotic inhibitor antineoplastic agent indicated for the treatment of Hodgkin's disease and non-Hodgkin's lymphomas, choriocarcinoma, lymphosarcoma, and neuroblastoma, as well as various other types of cancer.