

QUESTIONS

2. A 23-year-old woman is admitted to the emergency department with difficulty breathing. Examination reveals significant laryngeal edema. Past medical history indicates that she suffers from recurrent episodes of angioneurotic edema with release of histamine and other mediators. Which of the following drugs is the most effective physiologic antagonist of histamine in smooth muscle?
- (A) Epinephrine
(B) Loratadine
(C) Ondansetron
(D) Ranitidine
(E) Sumatriptan
3. A 20-year-old woman is taking over-the-counter diphenhydramine for severe hay fever. Which of the following adverse effects is she most likely to report?
- (A) Muscarinic increase in bladder tone
(B) Nausea
(C) Nervousness, anxiety
(D) Sedation
(E) Vertigo
4. A laboratory study of new H₂ blockers is planned. Which of the following will result from blockade of H₂ receptors?
- (A) Increased cAMP (cyclic adenosine monophosphate) in cardiac muscle
(B) Decreased channel opening in enteric nerves
(C) Decreased cAMP in gastric mucosa
(D) Increased IP₃ (inositol trisphosphate) in platelets
(E) Increased IP₃ in smooth muscle

2. The smooth muscle effects of histamine are mediated mainly by H₁ receptors. Loratadine is a *pharmacologic* antagonist of histamine at these receptors. Ondansetron is a 5-HT₃ antagonist used to prevent postsurgical and chemotherapy-induced vomiting. Sumatriptan is a 5-HT_{1D/1B} agonist. Ranitidine is a pharmacologic histamine antagonist that blocks the H₂ receptor in the stomach and the heart, not H₁ receptors in smooth muscle. Epinephrine has a *physiologic* antagonist action that reverses histamine's effects on smooth muscle. The answer is **A**.

3. H₁ blockers do not activate muscarinic receptors, mediate vasoconstriction, or cause vertigo. Some *relieve* vertigo or motion sickness. They do not cause nervousness or anxiety. Diphenhydramine is a potent sedative with H₁- and M₃-blocking actions. The answer is **D**.
4. H₂ receptors are G_s-protein-coupled receptors, like β adrenoceptors. Blockade of this system will cause a decrease in cAMP in several tissues. The answer is **C**.

1. One effect that theophylline, nitroglycerin, isoproterenol, and histamine have in common is **غير مطلوب** (not required).
- (A) Direct stimulation of cardiac contractile force
(B) Tachycardia
(C) Bronchodilation
(D) Postural hypotension
(E) Throbbing headache
2. A 23-year-old woman is using an albuterol inhaler for frequent acute episodes of asthma and complains of symptoms that she ascribes to the albuterol. Which of the following is *not* a recognized action of albuterol?
- (A) Diuretic effect
(B) Positive inotropic effect
(C) Skeletal muscle tremor
(D) Smooth muscle relaxation
(E) Tachycardia
3. A 19-year-old college student has well-controlled asthma but on reporting to the college health clinic, complains of a sore throat. On examination, he has typical signs of thrush, a fungal infection with *Candida albicans*. The asthma controller medication most likely to be associated with *Candida* infection is:
- (A) Albuterol by aerosol
(B) Beclomethasone by aerosol
(C) Ipratropium by inhaler
(D) Prednisone by mouth
(E) Theophylline in long-acting oral form

Questions 4–5. A 16-year-old patient is in the emergency department receiving nasal oxygen. She has a heart rate of 125 bpm, a respiratory rate of 40 breaths/min, and a peak expiratory flow <50% of the predicted value. Wheezing and rales are audible without a stethoscope.

4. Which of the following drugs can be used by nebulizer for a prompt direct bronchodilator effect in severe, acute asthma?
- (A) Albuterol
(B) Ipratropium
(C) Prednisone
(D) Salmeterol
(E) Theophylline
5. After successful treatment of the acute attack, the patient was referred to the outpatient clinic for follow-up treatment for asthma. Which of the following is *not* an established prophylactic strategy for asthma?
- (A) Avoidance of antigen exposure
(B) Blockade of histamine receptors
(C) Blockade of leukotriene receptors
(D) IL-5 cytokine blockade
(E) Inhibition of phospholipase A₂

6. Mr Green is a 60-year-old former smoker with cardiac disease and severe chronic obstructive pulmonary disease (COPD) associated with frequent episodes of bronchospasm. Which of the following is a bronchodilator useful in COPD and least likely to cause cardiac arrhythmia?
- (A) Aminophylline
(B) Cromolyn
(C) Epinephrine
(D) Ipratropium
(E) Metaproterenol
(F) Metoprolol
(G) Prednisone
(H) Salmeterol
(I) Zafirlukast
(J) Zileuton
7. A 22-year-old man is brought to the emergency department after suffering seizures resulting from an overdose of a drug he has been taking. His friends state that he took the drug orally and sometimes had insomnia after taking it. Which of the following is a direct bronchodilator that is most often used in asthma by the oral route and is capable of causing insomnia and seizures?
- (A) Cromolyn
(B) Epinephrine
(C) Ipratropium
(D) Metaproterenol
(E) Metoprolol
(F) Prednisone
(G) Salmeterol
(H) Theophylline
(I) Zileuton
8. Which of the following in its parenteral form is life-saving in severe status asthmaticus and acts, at least in part, by inhibiting phospholipase A₂?
- (A) Aminophylline
(B) Cromolyn
(C) Epinephrine
(D) Ipratropium
(E) Metaproterenol
(F) Metoprolol
(G) Prednisone
(H) Salmeterol
(I) Zafirlukast
(J) Zileuton
9. Which of the following has a slow onset but long duration of action and is always used in combination with a corticosteroid by inhalation?
- (A) Aminophylline
(B) Cromolyn
(C) Epinephrine
(D) Ipratropium
(E) Metaproterenol
(F) Metoprolol
(G) Prednisone/prednisolone
(H) Salmeterol
(I) Zafirlukast
(J) Zileuton
10. Oral medications are popular for the treatment of asthma in children because young children may have difficulty with the proper use of aerosol inhalers. Which of the following is an orally active inhibitor of leukotriene receptors?
- (A) Albuterol
(B) Aminophylline
(C) Ipratropium
(D) Zafirlukast
(E) Zileuton

ANSWERS

- Theophylline does not ordinarily cause headache or postural hypotension. Nitroglycerin does not cause direct cardiac stimulation but does evoke a compensatory sympathetic reflex. Histamine does not cause bronchodilation. The answer is **B**.
- Albuterol is a β_2 -selective receptor agonist, but in moderate to high doses it produces β_1 cardiac effects as well as β_2 -mediated smooth and skeletal muscle effects. **It does not cause diuresis.** The answer is **A**.
- Chronic oral corticosteroids, eg, prednisone, have important toxicities (see Chapter 39). However, they are unlikely to cause oral fungal infection. In contrast, topical, inhaled steroids, eg, beclomethasone, are associated with this adverse effect because the inhalation route results in high concentrations in the oropharynx. The answer is **B**.
- Although extremely important in severe chronic asthma and status asthmaticus, corticosteroids do not have a demonstrable direct bronchodilator action. **Salmeterol has a slow onset of action and is not suitable for an acute asthmatic attack. Ipratropium has bronchodilator action but is not the drug of first choice.** The answer is **A**.
- Histamine does not appear to play a significant role in asthma, and antihistaminic drugs, even in high doses, are of little or no value. Antigen avoidance is well established. Blockade of leukotriene receptors with montelukast or zafirlukast; inhibition of phospholipase with corticosteroids; and inhibition of cytokines are also useful. The answer is **B**.
- Ipratropium or a similar antimuscarinic agent is the bronchodilator that is most likely to be useful in COPD without causing arrhythmias. The answer is **D**.
- Theophylline is a bronchodilator that is active by the oral route. **It causes insomnia in therapeutic doses and seizures in overdose.** The answer is **H**.
- Parenteral corticosteroids such as prednisolone (the active metabolite of prednisone) are lifesaving in status asthmaticus. They probably act by reducing production of leukotrienes (see Chapter 18). The answer is **G**.
- Salmeterol is a β_2 -selective agonist that has a slow onset and long duration of action. **Used alone, it increases asthma mortality, but in combination with inhaled corticosteroids prophylactic use improves asthma control.** The answer is **H**.
- Zileuton is an inhibitor of the lipoxygenase enzyme involved in the synthesis of leukotrienes. Montelukast and zafirlukast are leukotriene antagonists at the leukotriene receptor. The answer is **D**.

QUESTIONS

- A 35-year-old woman with moderately severe arthritis has been treated with nonsteroidal anti-inflammatory drugs for 6 mo. Her arthritis symptoms have been well controlled. She now complains of heartburn and indigestion. A fecal blood test is positive. You give her a prescription for a drug to be taken along with the anti-inflammatory agent, but 2 d later she calls the office complaining that your last prescription has caused severe diarrhea and cramping that resembles her periods. Which of the following is most likely to be associated with increased gastrointestinal motility and uterine cramping?

(A) Aspirin
(B) Famotidine
(C) Leukotriene LTB_4
(D) Misoprostol
(E) Zileuton

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- Which mechanism explains aspirin's inhibition of thromboxane synthesis?

(A) Blocks cyclooxygenase
(B) Blocks lipoxygenase
(C) Blocks phospholipase A_2
(D) Blocks PGE_1 receptors
(E) Blocks PGI_2 receptors

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- A 57-year-old man has severe pulmonary hypertension and right ventricular hypertrophy. Which of the following agents causes vasodilation and may be useful in pulmonary hypertension?

(A) Acetylcholine
(B) Bradykinin
(C) Prostaglandin $\text{PGF}_{2\alpha}$
(D) Prostacyclin
(E) Thromboxane
- A 19-year-old woman complains of severe dysmenorrhea. A uterine stimulant derived from membrane lipid in the endometrium is

(A) Angiotensin II
(B) Oxytocin
(C) Prostacyclin (PGI_2)
(D) Prostaglandin $\text{PGF}_{2\alpha}$
(E) Serotonin
- Inflammation is a complex tissue reaction that includes the release of cytokines, leukotrienes, prostaglandins, and peptides. Leukotrienes involved in inflammatory processes are typically produced from arachidonic acid by which of the following enzymes?

(A) Cyclooxygenase-1
(B) Cyclooxygenase-2
(C) Glutathione-S-transferase
(D) Lipoxygenase
(E) Phospholipase A_2
- A newborn infant is diagnosed with transposition of the great vessels, wherein the aorta exits from the right ventricle and the pulmonary artery from the left ventricle. Which of the following drugs is likely to be used in preparation for surgical correction of this anomaly?

(A) Aspirin
(B) Leukotriene LTC_4
(C) Prednisone
(D) Prostaglandin PGE_1
(E) Prostaglandin $\text{PGF}_{2\alpha}$

7. A patient with a positive fecal blood test is referred to the gastroenterology clinic. He is apparently taking large amounts of an unidentified drug that inhibits platelet activity. Which of the following is taken orally and *directly* and *reversibly* inhibits platelet cyclooxygenase?
- (A) Alprostadil
 (B) Aspirin
 (C) Ibuprofen
 (D) Leukotriene LTC₄
 (E) Misoprostol
 (F) Prednisone
 (G) Prostacyclin
 (H) Zafirlukast
 (I) Zileuton
8. Which of the following is a component of slow-reacting substance of anaphylaxis (SRS-A)?
- (A) Alprostadil
 (B) Aspirin
 (C) Leukotriene LTB₄
 (D) Leukotriene LTC₄
 (E) Misoprostol
 (F) Prednisone
 (G) Prostacyclin
 (H) Zafirlukast
 (I) Zileuton
9. A 17-year-old patient complains that he develops wheezing and severe shortness of breath whenever he takes aspirin for headache. Increased levels of which of the following may be responsible, in part, for some cases of aspirin hypersensitivity?
- (A) Alprostadil
 (B) Hydrocortisone
 (C) Ibuprofen
 (D) Leukotriene LTC₄
 (E) Misoprostol
 (F) PGE₂
 (G) Prostacyclin
 (H) Thromboxane
 (I) Zileuton
10. Which of the following is a leukotriene receptor blocker?
- (A) Alprostadil
 (B) Aspirin
 (C) Ibuprofen
 (D) Leukotriene LTC₄
 (E) Montelukast
 (F) Prednisone
 (G) Prostacyclin
 (H) Zileuton
2. Hydrocortisone and other corticosteroids inhibit phospholipase. Ibuprofen and indomethacin inhibit cyclooxygenase reversibly, whereas zileuton inhibits lipoxygenase. Because aspirin inhibits cyclooxygenase irreversibly, its action is more effective in platelets, which lack the ability to synthesize new enzyme, than in the endothelium. Aspirin does not block prostaglandin receptors. The answer is **A**.
3. Prostacyclin (PGI₂) is a very potent vasodilator. Acetylcholine and bradykinin cause generalized vasodilation and many other undesirable effects; they are not useful in pulmonary or systemic hypertension. PGF_{2α} and thromboxane are vasoconstrictors. The answer is **D**.
4. Although serotonin and, in some species, histamine may cause uterine stimulation, these amines are not derived from membrane lipid. Similarly, oxytocin causes uterine contraction, but it is a peptide hormone released from the posterior pituitary. Prostacyclin relaxes the uterus (Table 18–1). The answer is **D**.
5. See Figure 18–1. Phospholipase A₂ converts membrane phospholipid to arachidonic acid. Cyclooxygenases convert arachidonic acid to prostaglandins. COX-1 products appear to be important in normal physiologic processes. Lipoxygenase is the enzyme responsible for the production of leukotrienes from arachidonic acid in inflammatory cells. The answer is **D**.
6. Infants with great vessel transposition pump venous blood to the aorta and oxygenated blood back to the lungs. Therefore, they require surgical correction as soon as they are strong enough to withstand the procedure. While awaiting surgery, they are dependent on a patent ductus arteriosus to allow some oxygenated blood to flow from the left ventricle via the pulmonary artery and ductus to the aorta. The ductus can be prevented from closing by infusing the vasodilator PGE₁. The answer is **D**.
7. Aspirin is a direct but *irreversible* inhibitor of cyclooxygenase. NSAIDs other than aspirin (such as ibuprofen) are reversible inhibitors of COX. Corticosteroids reduce the synthesis of cyclooxygenase. The answer is **C**.
8. The leukotriene C and D series are major eicosanoid components of SRS-A. Leukotriene LTB₄ is a chemotactic eicosanoid. The answer is **D**.
9. When cyclooxygenase is blocked, leukotrienes may be produced in increased amounts by diversion of prostaglandin precursors into the lipoxygenase pathway (Figure 18–1). In patients with aspirin hypersensitivity, this might precipitate the bronchoconstriction often observed in this condition. The answer is **D**.
10. Zileuton blocks the synthesis of leukotrienes. Montelukast and zafirlukast block LTD₄ receptors. The answer is **E**.

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ANSWERS

1. Aspirin and zileuton rarely cause diarrhea. LTB₄ is a chemotactic factor. Famotidine is an H₂ blocker that does not cause diarrhea (Chapter 16). Misoprostol, a PGE₁ analog, increases gastrointestinal and uterine motility. It is sometimes used as part of an abortifacient. The answer is **D**.

QUESTIONS

1. A 45-year-old homeless man presents to the emergency department with fever, weight loss, and a productive cough. Chest x-ray shows right apical infiltrate and TB is suspected. He is started on empiric INH, rifampin, and pyrazinamide. The primary reason for the use of drug combinations in the treatment of this patient's TB is:
 - (A) Delay or prevent the emergence of resistance
 - (B) Ensure patient compliance with the drug regimen
 - (C) Increase antibacterial activity synergistically
 - (D) Provide prophylaxis against other bacterial infections
 - (E) Reduce the incidence of adverse effects
- Questions 2–5.** A 21-year-old woman from Southeast Asia has been staying with family members in the United States for the last 3 mo and is looking after her sister's preschool children during the day. Because she has difficulty with the English language, her sister escorts her to the emergency department of a local hospital. She tells the staff that her sister has been feeling very tired for the last month, has a poor appetite, and has lost weight. The patient has been feeling somewhat better lately except for a cough that produces a greenish sputum, sometimes specked with blood. With the exception of rales in the left upper lobe, the physical examination is unremarkable and she does not seem to be acutely ill. Laboratory values show a white count of 12,000/ μ L and a hematocrit of 33%. Chest x-ray film reveals an infiltrate in the left upper lobe with a possible cavity. A Gram-stained smear of the sputum shows mixed flora with no dominance. An acid-fast stain reveals many thin rods of pinkish hue. A preliminary diagnosis is made of pulmonary tuberculosis. Sputum is sent to the laboratory for culture.
2. At this point, the most appropriate course of action is to
 - (A) Hospitalize the patient and start treatment with 4 antitubercular drugs
 - (B) Hospitalize the patient and start treatment with rifampin
 - (C) Prescribe isoniazid for prophylaxis and send the patient home to await culture results
 - (D) Provide no drugs and send the patient home to await culture results
 - (E) Treat the patient with isoniazid plus rifampin
 3. Which drug regimen should be initiated in this patient when treatment is started?
 - (A) Amikacin, isoniazid, pyrazinamide, streptomycin
 - (B) Ciprofloxacin, cycloserine, isoniazid, PAS
 - (C) Ethambutol, isoniazid, pyrazinamide, rifampin
 - (D) Isoniazid, pyrazinamide, rifampin, streptomycin
 - (E) PAS, pyrazinamide, rifabutin, streptomycin
 4. Which statement concerning the possible use of isoniazid (INH) in this patient is false?
 - (A) Dyspnea, flushing, palpitations, and sweating may occur after ingestion of tyramine-containing foods
 - (B) In fast acetylators, lower maintenance doses are necessary
 - (C) Peripheral neuritis may occur during treatment
 - (D) The patient should take pyridoxine daily
 - (E) The risk of the patient developing hepatitis from INH is less than 2%
 5. On her release from the hospital, the patient is advised not to rely solely on oral contraceptives to prevent pregnancy because they may be less effective while she is being maintained on antimycobacterial drugs. The agent most likely to interfere with the action of oral contraceptives is
 - (A) Amikacin
 - (B) Ethambutol
 - (C) Isoniazid
 - (D) Pyrazinamide
 - (E) Rifampin
 6. A patient with AIDS and a CD4 cell count of 100/ μ L has persistent fever and weight loss associated with invasive pulmonary disease due to *M. avium* complex (MAC). Optimal management of this patient is to **غير مطلوب**
 - (A) Choose an antibiotic based on drug susceptibility of the cultured organism
 - (B) Initiate a two-drug regimen of INH and pyrazinamide
 - (C) Prescribe rifabutin because it prevents the development of MAC bacteremia
 - (D) Start treatment with the combination of azithromycin, ethambutol, and rifabutin
 - (E) Treat with trimethoprim-sulfamethoxazole
 7. A 10-year-old boy has uncomplicated pulmonary tuberculosis. After initial hospitalization, he is now being treated at home with isoniazid, rifampin, and ethambutol. Which statement about this case is accurate?
 - (A) A baseline test of auditory function test is essential before drug treatment is initiated
 - (B) His mother, who takes care of him, does not need INH prophylaxis
 - (C) His 3-year-old sibling should receive INH prophylaxis
 - (D) Polyarthralgia is a potential adverse effect of the drugs the boy is taking
 - (E) The potential nephrotoxicity of the prescribed drugs warrants periodic assessment of renal function

8. Which statement about antitubercular drugs is accurate?
- (A) Antimycobacterial actions of streptomycin involve inhibition of arabinosyltransferases
 - (B) Cross-resistance of *M tuberculosis* to isoniazid and pyrazinamide is common
 - (C) Ocular toxicity of ethambutol is prevented by thiamine
 - (D) Pyrazinamide treatment should be discontinued immediately if hyperuricemia occurs
 - (E) Resistance to ethambutol involves mutations in the *emb* gene
9. Once-weekly administration of which of the following antibiotics has prophylactic activity against bacteremia caused by *M avium* complex in AIDS patients? غير مطلوب
- (A) Acedapson
 - (B) Azithromycin
 - (C) Clarithromycin
 - (D) Kanamycin
 - (E) Rifabutin
10. Risk factors for multidrug-resistant tuberculosis include
- (A) A history of treatment of tuberculosis without rifampin
 - (B) Recent immigration from Asia and living in an area of over 4% isoniazid resistance غير مطلوب
 - (C) Recent immigration from Latin America
 - (D) Residence in regions where isoniazid resistance is known to exceed 4%
 - (E) All of the above

ANSWERS

1. Although it is sometimes possible to achieve synergistic effects against mycobacteria with drug combinations, the primary reason for their use is to delay the emergence of resistance. The answer is **A**.
2. Despite the fact that this patient does not appear to be acutely ill, she would in most cases be treated with 4 drugs that have activity against *M tuberculosis*. This is because organisms infecting patients from Southeast Asia are commonly INH-resistant, and coverage must be provided with 3 other antituberculosis drugs in addition to isoniazid. This patient should be hospitalized for several reasons, including potential difficulties with compliance regarding the drug regimen and the fact that young children are in the home where she is living. The answer is **A**.
3. Sputum cultures will not be available for several weeks, and no information is available regarding drug susceptibility of the organism at this stage. For optimum coverage, the initial regimen should include INH, rifampin, pyrazinamide, and ethambutol. INH-resistant organisms are usually sensitive to both rifampin and pyrazinamide. Streptomycin is usually reserved for use in severe forms of tuberculosis or for infections known to be resistant to first-line drugs. Likewise, amikacin and ciprofloxacin are possible agents for treatment of multidrug-resistant strains of *M tuberculosis*. Cycloserine, PAS, and rifabutin are alternative second-line drugs that may be used in cases of failed response to more conventional agents. The answer is **C**.
4. Fast acetylators may require higher doses of the drug than others. Peripheral neuropathy caused by INH is due to pyridoxine deficiency. It is more common in the diabetic, malnourished, or AIDS patient and can be prevented by a daily dose of 25–50 mg of pyridoxine. INH can inhibit monoamine oxidase type A and has caused tyramine reactions. Hepatotoxicity is age-dependent, with an incidence of 0.3% in patients aged 21–35 years and greater than 2% in patients older than 50 years. The answer is **B**.
5. Rifampin induces the formation of several microsomal drug-metabolizing enzymes, including cytochrome P450 isoforms. This action increases the rate of elimination of a number of drugs, including anticoagulants, ketoconazole, methadone, and steroids that are present in oral contraceptives. The pharmacologic activity of these drugs can be reduced markedly in patients taking rifampin. The answer is **E**.
6. Combinations of antibiotics are essential for suppression of disease caused by *M avium* complex in the AIDS patient, and treatment should be started before culture results are available. Although rifabutin is prophylactic against MAC bacteremia when it is used as sole therapy in active disease, resistant strains of the organism emerge rapidly. MAC is much less susceptible than *M tuberculosis* to conventional antimycobacterial drugs. Currently, the optimum regimen consists of azithromycin (or clarithromycin) with ethambutol and rifabutin. The answer is **D**.
7. A baseline test of ocular (not auditory) function may be useful before starting ethambutol. None of the drugs prescribed is associated with nephrotoxicity. Polyarthralgia is a common adverse effect of pyrazinamide that was not prescribed in this case. Periodic tests of liver function may be advisable in younger patients who are treated with INH plus rifampin, especially if higher doses of these drugs are used. Prophylaxis with INH is advisable for all household members and very close contacts of patients with active tuberculosis, especially young children. The answer is **C**.
8. Arabinosyltransferase is inhibited by ethambutol (not streptomycin) and resistance involves alterations in the *emb* gene. Ocular adverse effects of ethambutol are dose-dependent and usually reversible when the drug is discontinued. Thiamine is not protective. There is minimal cross-resistance between pyrazinamide and other antimycobacterial drugs. Pyrazinamide uniformly causes hyperuricemia, but this is not a reason to halt therapy even though the drug may provoke gouty arthritis in susceptible persons. The answer is **E**.
9. Because of its long elimination half-life (3–4 d), weekly administration of azithromycin has proved to be equivalent to daily administration of clarithromycin when used for prophylaxis against *M avium* complex in AIDS patients. Acedapson is a repository form of dapson used in leprosy. The answer is **B**.
10. Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance to 2 or more drugs. All the risk factors are relevant. In the case of resistance to both INH and rifampin, initial regimens still include both drugs, plus ethambutol, pyrazinamide, streptomycin (or other aminoglycoside), and a fluoroquinolone. Continuation therapy should include at least 3 drugs shown to be active in vitro against the infecting strain. The appropriate duration of therapy has not been established. The answer is **E**.