

QUESTIONS: HISTAMINE & NSAIDs

1. A 23-year-old woman 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. Cetirizine
- B. Epinephrine
- C. Granisetron
- D. Ranitidine
- E. Sumatriptan

1. The answer is B. The smooth muscle effects of histamine are mediated mainly by H₁ receptors. Cetirizine is a pharmacologic antagonist of histamine. Granisetron is a 5-HT₃ antagonist. Sumatriptan is a 5-HT_{1D} agonist. Ranitidine is a histamine antagonist but 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.

2. A 20-year-old woman is taking 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. Uterine cramps

2. The answer is D. H₁ blockers do not activate muscarinic receptors, mediate vasoconstriction, or cause uterine cramping. They do not cause nervousness or anxiety. Diphenhydramine is a potent sedative.

3. A 43-year-old ship's captain complains of seasonal allergies. Which one of the following would be indicated?

- A. Cyclizine.
- B. Doxepin.
- C. Doxylamine.
- D. Hydroxyzine.
- E. Fexofenadine.

3.The answer is E. The use of first-generation H₁ antihistamines is contraindicated in the treatment of pilots and others who must remain alert. Because of its lower potential to induce drowsiness, fexofenadine may be recommended for individuals working in jobs in which wakefulness is critical.

4. Which one of the following statements concerning H₁ antihistamines is correct?
- A. Second-generation H₁ antihistamines are relatively free of adverse effects.
 - B. Because of the established long-term safety of first-generation H₁ antihistamines, they are the first choice for initial therapy.
 - C. The motor coordination involved in driving an automobile is not affected by the use of first generation H₁ antihistamines.
 - D. H₁ antihistamines can be used in the treatment of acute anaphylaxis.
 - E. Both first- and second-generation H₁ antihistamines readily penetrate the blood-brain barrier.

4.The answer is A. Second-generation H₁ antihistamines are preferred over first-generation agents because they are relatively free of adverse effects. Driving performance is adversely affected by first generation H₁ antihistamines. Epinephrine, not antihistamine, is an acceptable treatment for acute anaphylaxis. Second-generation H₁ antihistamines penetrate the blood-brain barrier to a lesser degree than the first-generation drugs.

5. Which one of the following drugs could significantly impair the ability to drive an automobile?
- A. Diphenhydramine.
 - B. Ergotamine.
 - C. Fexofenadine.
 - D. Ranitidine.
 - E. Sumatriptan.

5.The answer is A. Diphenhydramine can impair operation of an automobile by causing drowsiness and by impairing accommodation. The other agents do not have this restriction.

6. Field workers exposed to a plant toxin develop painful fluid-filled blisters. Analysis of the blister fluid reveals high concentrations of a peptide. Which of the following is a peptide that causes increased capillary permeability and edema?
- A. Angiotensin II

- B. Bradykinin
- C. Captopril
- D. Histamine
- E. Losartan

6. The answer is B. Histamine and bradykinin both cause a marked increase in capillary permeability that is often associated with edema, but histamine is not a peptide.

7. You have been treating a 50-year-old woman with moderately severe arthritis with nonsteroidal anti-inflammatory drugs for 6 months. She now complains of heartburn and indigestion. You give her a prescription for a drug to be taken along with the anti-inflammatory agent, but 2 days later she calls the office complaining that your last prescription has caused severe diarrhea. Which of the following is most likely to be associated with increased gastrointestinal motility and diarrhea??

- A. Aspirin
- B. Corticosteroids
- C. Leukotriene LTB₄
- D. Misoprostol
- E. Zileuton

7. The answer is D . Aspirin, corticosteroids, and zileuton do not cause diarrhea. LTB₄ is a chemotactic factor.

8. Which of the following drugs inhibits thromboxane synthesis much more effectively than prostacyclin synthesis?

- A. Aspirin
- B. Hydrocortisone
- C. Ibuprofen
- D. Indomethacin
- E. Zileuton

8. The answer is A . 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.

9. 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. Angiotensin II
- B. Ergotamine
- C. Prostaglandin PGF₂ α
- D. Prostacyclin
- E. Thromboxane

9. The answer is D. Prostacyclin (PGI₂) is a very potent vasodilator. All the other choices in the list are vasoconstrictors.

10. Inflammation is a complex tissue reaction that includes the release of cytokines, leukotrienes, prostaglandins, and peptides. Prostaglandins 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 A₂

10. The answer is B. Phospholipase A₂ converts membrane phospholipid to arachidonic acid. Cyclooxygenases convert arachidonic acid to prostaglandins. COX-2 is the enzyme believed to be responsible for this reaction in inflammatory cells.

11. 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 LTC₄
- C. Prednisone
- D. Prostaglandin PGE₂

E. Prostaglandin $\text{PGF}_2\alpha$

11. The answer is D. 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. In the meantime, they are dependent on a patent ductus arteriosus to allow some oxygenated blood to flow from the left ventricle via the pulmonary artery to the aorta. The ductus can be prevented from closing by infusing the vasodilator PGE₂.

12. A patient with a bleeding tendency presents in the hematology clinic. He is apparently taking large amounts of an unidentified drug that inhibits platelet activity. Which of the following directly and reversibly inhibits platelet cyclooxygenase?

A. Alprostadil

B. Aspirin

C. Ibuprofen

D. Leukotriene LTC_4

E. Misoprostol

F. Prednisone

G. Prostacyclin

H. Zafirlukast

I. Zileuton

12. The answer is C. 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.

13. Which of the following is a component of slow-reacting substance of anaphylaxis (SRS-A)?

A. Alprostadil

B. Aspirin

C. Leukotriene LTB_4

D. Leukotriene LTC_4

E. Misoprostol

F. Prednisone

G. Prostacyclin

H. Zafirlukast

I. Zileuton

13. The answer is D. The leukotriene C and D series are major components of SRS-A. Leukotriene LTB₄ is a chemotactic eicosanoid.

14. 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

14. The answer is D. When cyclooxygenase is blocked, leukotrienes may be produced in increased amounts by diversion of prostaglandin precursors into the lipoxygenase pathway. In patients with aspirin hypersensitivity, this might precipitate the bronchoconstriction often observed in this condition.

15. Which of the following is a leukotriene receptor blocker?

A. Alprostadil

B. Aspirin

C. Ibuprofen

D. Leukotriene LTC₄

E. Misoprostol

F. Prednisone

G. Prostacyclin

H. Zafirlukast

I. Zileuton

15. The answer is H. Zileuton blocks the synthesis of leukotrienes. Zafirlukast and montelukast block LTD₄ receptors.

16. In which one of the following conditions would aspirin be contraindicated?

A. Myalgia.

B. Fever.

C. Peptic ulcer.

D. Rheumatoid arthritis.

E. Unstable angina.

16. The answer is C. Among the nonsteroidal anti-inflammatory drugs, aspirin is one of the worst for causing gastric irritation. Aspirin is an effective analgesic and is used to reduce muscle pain. It also has antipyretic actions, so it can be used to treat fever. Because of its anti-inflammatory properties, aspirin is used to treat pain related to the inflammatory process (for example, in the treatment of rheumatoid arthritis). Low doses of aspirin also decrease the incidence of transient ischemic attacks.

17. Which one of the following statements concerning COX₂ inhibitors is correct?

A. The COX-2 inhibitors show greater analgesic activity than traditional NSAIDs.

B. The COX-2 inhibitors decrease platelet function.

C. The COX-2 inhibitors do not affect the kidney.

D. The COX-2 inhibitors show anti-inflammatory activity similar to that of the traditional NSAIDs.

E. The COX-2 inhibitors are cardioprotective.

17. The answer is D. The COX-2 inhibitors show similar analgesic and anti-inflammatory activity compared to traditional NSAIDs. They do not affect platelets. Like NSAIDs, COX-2 inhibitors may cause the development of acute renal failure due to renal vasoconstriction. COX-2 inhibitors have the potential for increasing the risk of myocardial infarction.

18. An 8-year-old girl has a fever and muscle aches from a presumptive viral infection. Which one of the following drugs would be most appropriate to treat her symptoms?

A. Acetaminophen.

- B. Aspirin.
- C. Celecoxib.
- D. Codeine.
- E. Indomethacin.

18. The answer is A. Aspirin should be avoided in children because of an association with Reye's syndrome. Indomethacin has antipyretic activity but is too toxic for use in these circumstances. Celecoxib is indicated for alleviation of pain, and codeine has no antipyretic effects.

19. A 70-year-old man has a history of ulcer disease. He has recently experienced swelling and pain in the joints of his hands. His physician wants to begin therapy with an NSAID. Which one of the following drugs might also be prescribed along with the NSAID to reduce the risk of activating this patient's ulcer disease?

- A. Allopurinol.
- B. Colchicine.
- C. Misoprostol.
- D. Probenecid.
- E. Sulindac.

19. The answer is C. Misoprostol is a prosta glandin analog that can reduce gastric acid and pepsin secretion and promote the formation of mucus in the stomach. It is indicated for the purpose of decreasing the risk of ulcer activation in patients taking NSAIDs. The other choices are not appropriate for alleviating the gastric irritation caused by NSAIDs.