1. Read chapter

2. Review objectives (p.183)

3. Review key terms and definitions (p.183)

4. What are the indications for oral *inhaled* corticosteroids (ICS)?

5. What is the primary indication for *intranasal* corticosteroids?


7. List the primary source of natural-occurring inhaled corticosteroids.

8. Review Table 11-1

9. Review Table 11-2

10. Review Table 11-3

11. After prolonged use of steroid, adrenal suppression is common. Explain the process of adrenal suppression. (p.187)

12. Refer to the figure on next page. When the body is under stress (e.g., infection, physical stress, emotional stress, trauma), the hypothalamus is stimulated. The impulses from hypothalamus cause release of CRF (corticotropin-releasing factor). In turn, the CRF stimulates the anterior pituitary gland to secrete ACTH (adrenocorticotropic hormone). ACTH is released into the bloodstream. Once ACTH arrives at the adrenal cortex, corticosteroids are released to raise blood glucose levels to combat stress.

A biofeedback mechanism (dash line) is available to regulate the hypothalamus action (e.g., suppress hypothalamus action when circulating corticosteroid is sufficient).

Administration of systemic corticosteroid will suppress the hypothalamus action. (True or False?)
Adrenal insufficiency can occur when systemic corticosteroids are stopped abruptly. Explain.

13. Explain why corticosteroids should be used on a regular time schedule for consistent effects.

14. Corticosteroids should be used without interruption. (T/F). Explain.

15. Study the figure on the next page. Mast cells are found in tissues throughout the body, particularly in structures such as blood vessels and nerves, and in proximity close to surfaces that are exposed to the external environment (i.e., airways). Mast cells contain histamine and other chemical mediators that can cause a range of adverse reactions including bronchospasm. Mast cells become sensitized on first exposure to the antigens. Upon re-exposure to the same antigens, the mast cells rupture (degranulate) and release the histamine and other chemical mediators into the blood stream. The antigens that can cause an allergic reaction vary widely and dependent on the environment factors and the susceptibility of an individual.

16. Rupture of the mast cells leads to the release of _______.
17. What is the clinical presentation following mast cell rupture (degranulation)?

18. Study the figure below and note the early and late phase responses of mast cell rupture (degranulation). Early phase is caused by immunoglobulin E (IgE) and IgE can release inflammatory mediators such as histamine and other chemical mediators.
19. *Late* phase of mast cell rupture. Following production of arachidonic acid, the lipoxygenase pathway leads to production of leukotrienes (a group of biologically active compounds, originally isolated from leukocytes). Leukotrienes play a role in the inflammation and allergic responses in asthma. Leukotriene modifiers are used to block this late-phase responses. Three available leukotriene *modifiers* (leukotriene antagonists or leukotriene pathway blockers) are zileuton (Zyflo) 1996, zafirlukast (Accolate) 1997, and montelukast (Singulair), 1998. Zileuton (Zyflo) is an orally active *inhibitor* of 5-lipoxygenase, the enzyme that speeds up the formation of leukotrienes from arachidonic acid.

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20. Refer to the figure on the previous page. Following production of arachidonic acid, the cyclooxygenase pathway leads to production of prostaglandins (PGEs). PGE$_{2\alpha}$ is the most common prostaglandin. When stimulated, it causes bronchoconstriction and increase in mucus production. PGE$_1$ and PGE$_2$ are important to airway muscle tone. When stimulated, they cause
bronchodilation. This characteristic could lead to future application in the management of bronchoconstriction.

21. Review the individual aerosolized corticosteroids (p.190-192)

22. Review the availability of intranasal corticosteroids.

23. Describe the possible hazards and side effects of steroids.

24. Review the following drugs in relation to the sites of action in the diagram on the previous page.

These drugs inhibit the action of 5-lipoxygenase (thus the leukotriene pathway). Zileuton (Zyflo), Zafirlukast (Accolate), and Montelukast (Singulaire) are called leukotriene modifiers (or antagonists, or inhibitors).

Omalizumab (Xolair) is designed to block IgE (immunoglobulin E), a substance made by the body that plays a key role in the allergic response in allergic asthma.
Zileuton (1996)

Zafirlukast (1997)

Montelukast (1998)
Omalizumab (Xolair)