Chapter 12
Nonsteroidal Antiasthma Agents
Study Guide and Application Exercise

1. Read chapter

2. Review objectives (p.202)

3. Review key terms and definitions (p.202) Add “Airway remodeling.”

4. What are the clinical indications for nonsteroidal antiasthma agents?

5. Cromolyn and antileukotrienes (Zileuton / Zyflo; Zafirlukast / Accolate and Montelukast / Singulair) are recommended as alternatives to ______ (high-dose, medium-dose, low-dose) inhaled corticosteroids in EPR-3 Step 2 care.

Antileukotriene is a broad term that includes (1) leukotriene inhibitor (inhibit synthesis of leukotriene, and (2) leukotriene receptor antagonist (or blocker).

6. Why is cromolyn a preferred drug over inhaled corticosteroids for infants and children in EPR-3 Step 2 care?

7. Antileukotrienes can be used with inhaled corticosteroids to reduce the steroid dose (e.g., patients with steroidal intolerance or complications). (True/False)

8. Review the drug groups (controllers and relievers) for the management of asthma. (Box 12-1) p.203.

9. Differentiate extrinsic and intrinsic asthma.

10. Airway remodeling is a permanent change to the airways in patients with chronic (long-standing) airway inflammation and bronchoconstriction.

11. Review the nonsteroidal antiasthma medications (generic and brand names). Table 12-1 FYI: Cromolyn sodium for CFC MDI (Intal) was discontinued in Dec 2010. Nebulizer Intal solution (1% solution one 2-mL ampule = 20 mg/2mL) is still available for SVN use. FYI: Nedocromil sodium CFC MDI (Tilade) was discontinued in June 2010.

12. Review the cell-mediated and antibody-mediated mechanisms involved in allergy and inflammation. (Box 12-2) p.204
13. Describe how activation of T lymphocytes leads to asthma symptoms. (p.202-203)

14. 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.

15. Briefly describe the following for *cromolyn*: general uses, dosage and administration, mode of action. (p.206-207)

16. What are two additional uses of cromolyn sodium? (p.206)

17. List the clinical application of cromolyn. (p.208)

18. Name the 3 antileukotriene agents available in the U.S.

19. Describe the biochemical pathways of these agents in #18.

20. The agent that inhibits synthesis of leukotrienes is ____________________.

21. The two agents that block the receptor for leukotrienes are ____________________ and ____________________.

22. Review Table 12-2 and compare the key features between zileuton (Zyflo), zafirlukast (Accolate), and montelukast (Singulair)

23. Briefly describe the following for *zileuton (Zyflo)*: general uses, dosage and administration, mode of action, hazards and side effects. (p.211-212)

24. Briefly describe the following for *zafirlukast (Accolate)*: general uses, dosage and administration, mode of action, pharmacokinetics, hazards and side effects. (p.212-213)

25. Briefly describe the following for *montelukast (Singulair)*: general uses, dosage and administration, mode of action, pharmacokinetics, hazards and side effects. (p.213)
26. List the three specific asthma triggers that may be prevented by antileukotrienes. (p.213-214)

27. Describe the roles of antileukotrienes in the management of chronic persistent asthma. (p.214)

28. Describe the roles of antileukotrienes when they are used concurrently with inhaled corticosteroids. (p.214)

29. Review “Summary of Clinical Use of Antileukotriene Therapy.” (p.215)

30. Describe the drug type and usage of omalizumab (Xolair).

31. Describe Xolair’s mode of action in the management of asthma.

32. Review “Respiratory Care Assessment of Nonsteroidal Antiasthma Agents” (p.216) and list the talking points during patient education on the correct use of antiasthmatic drugs.

33. Peak flow meter is a single-breath (similar to forced vital capacity) device that patients use at home to monitor the possible onset of asthma. (decreasing peak flow = progressing bronchospasm). The personal best (or green zone) is the peak flow measurement (in L/min) when asthma is very well controlled. The patient sets the green and yellow zones.

34. Review “Clinical Scenario” (p.217) and describe the clinical significance of: theophylline dose of 600 mg daily, 13% eosinophils, plasma glucose level of 281 mg/dL, usage of pirbuterol / Maxair (discontinue at end of 2013), and “headaches, upset stomach, lack of appetite, insomnia.”
Antigen (\(\gamma\)) enters respiratory tract and stimulates formation of antigen-specific antibody (\(\beta\)) IgE on mast cell. IgE then attaches to mast cell.

Sensitized mast cell

Upon re-exposure of antigen, antigen–antibody complex (\(\beta\)) is formed and stimulates rupture of mast cells and release of chemical mediators.

Histamine and other chemical mediators released

Bronchospasm
Increased mucus production

Clinical presentation can include:
- Wheezing
- Shortness of breath
- Cough
- Tight chest
- Hypoxemia

Mast Cell Rupture or Degranulation in the Airways
# 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.

# *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 response. 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.

The Late-Phase Inflammatory Response in the Airways

*Note:* Increased neutrophils, monocytes, and eosinophils migrating to inflamed airways also contribute to late-phase response.
# Refer to the figure on the previous page. Following production of arachidonic acid, the cyclooxygenase pathway leads to production of protaglandins (PGEs). PGE$_{2\alpha}$ is the most common prostglandin. 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.

(Zileuton (1996))

(Zafirlukast (1997))
Montelukast (1998)
Omalizumab (Xolair)