Welcome to the FIT Board Review Corner, prepared by Miriam Samstein, MD, PhD, and Timothy Chow, MD senior and junior representatives of the College’s Fellows-In-Training (FITs) to the Board of Regents. The FIT Board Review Corner is an opportunity to help hone your Board preparedness.

**Review Questions**

**Allergy and Immunology Review Corner:** Middleton’s Allergy Principles and Practice, 8th edition
N. Franklin Adkinson Jr., MD, Bruce S. Bochner, MD, A. Wesley Burks, MD, William W. Busse, MD, Stephen T. Holgate, MD, DSc, FMedSci, Robert F. Lemanske, Jr., MD and Robyn E. O’Hehir, FRACP, PhD, FRCPath

**Chapter 21: Pathophysiology of Allergic Inflammation**
Prepared by: Melissa Gans, MD

1. Which of the following is released by epithelial cells to maintain mucosal mast cells at the airway and skin surface?
   a. IL-9
   b. Stem cell factor (SCF)
   c. CCL17
   d. CCL22

2. Th2 cells release all of the following cytokines except:
   a. IL-4
   b. IL-5
   c. IL-9
   d. IL-17

3. All of the following are true about TSLP except:
   a. Epithelial cells and mast cells release TSLP.
   b. TSLP acts on immature dendritic cells to mature.
   c. TSLP directly acts on B lymphocytes and eosinophils.
   d. TSLP stimulates the release of CCL17, which attracts Th2 cells via CCR4.

4. Why is measuring exhaled nitric oxide more useful as a marker of asthma than allergic rhinitis?
   a. The local production of nitric oxide by the nasal mucosa is diluted as a consequence of the high nitric oxide production from paranasal sinuses.
   b. Nitric oxide is not elevated in patients with allergic rhinitis.
   c. Nitric oxide is not increased further during the late response to inhaled allergen.
   d. There is not increased expression of inducible nitric oxide synthase in airway epithelial cells.

5. Which of the following does not lead to increased airway mucus secretion?
   a. Stimulation by Th2 cytokines and oxidative stress.
   b. Epidermal growth factor activation.
   c. Inhibition of acetylcholine and substance P.
   d. Increased expression of mucin gene MUC5AC.
6. In resting Th2 cells, GATA3 is localized to the cytoplasm. What causes phosphorylation of GATA3 so that GATA3 is imported to the nucleus and binds to the promoter region of Th2 cytokine genes to activate gene expression and cause allergic inflammation?
   a. Interaction with antigen-presenting dendritic cells activates the T cell receptor (CD3) and costimulatory molecule CD28 causing p38 mitogen-activated protein kinase (MAPK) signal transduction.
   b. Inflammatory stimuli activate enzyme IKK2 which degrades NF-κB inhibitor.
   c. IL-4 and IL-13 stimulate Jak1 and Jak3 to phosphorylate STAT6.
   d. IL-27 activates STAT1 and IL-12 activates TSAT4 which signals T-bet in Th1 cells.

7. Which of the following is inappropriately paired with the effect on airway smooth muscle by inflammatory cell mediators?
   a. Contraction: histamine, cys-LT, kinin, prostanoid, endothelin
   b. Proliferation: PDGF, EGF, endothelin-1
   c. Secretion: cytokines, chemokines, prostanooids
   d. Neurogenic inflammation: neurotrophin, SP, CGRP

8. Th17 cells release which of the following?
   a. IL-2
   b. IL-9
   c. IFN-γ
   d. IL-22

9. All of the following are major explanations for activating airway epithelial cells to promote inflammation in asthma through eosinophil survival and chemotaxis, lymphocyte activation, smooth muscle hyperplasia, and fibroblast activation except:
   a. Viruses release oxygen and nitric oxide.
   b. Basophils release histamine.
   c. Allergens act on the FcεRII receptor.
   d. Macrophages release TNF-α, IL-1β, and IL-6.

10. Which of the following is true regarding chemokines in the recruitment of inflammatory cells in allergic disease?
    a. Chemokines do not act in sequence to determine the final inflammatory response so chemokine inhibitors will likely be very effective.
    b. The only chemokines that are chemotactic for eosinophils are CCL11 and CCL24.
    c. Chemokines work through G protein-coupled receptors.
    d. The only chemokine receptor for allergic disease is CCR3.

**Answers:**

1. **B.** p. 328, Figure 21-2. Epithelial cells release stem cell factor to maintain mucosal mast cells. CCL17 and CCL22 are released by epithelial cells to act on CCR4 to attract Th2 cells. IL-9 is released by Th2 cells to stimulate mast cell proliferation.

2. **D.** p. 329, Figure 21-3. Th2 cells release IL-4, IL-5, IL-9, and IL-13. Th17 cells release IL-17 and IL-22.

3. **C.** p. 332, Figure 21-6. TSLP does not directly act on eosinophils and B lymphocytes. TSLP directly acts on Th2 cells which then release cytokines that acts on eosinophils and B lymphocytes.
4. A. p. 333. Nitric oxide is elevated in patients with allergic rhinitis. Nitric oxide is increased further during the late response to inhaled allergen. There is increased expression of inducible nitric oxide synthase in airway epithelial cells.

5. C. p. 335, Figure 21-8. Increased release of acetylcholine and substance P cause increased mucus hypersecretion. Epidermal growth factor causes increased expression of the mucin gene MUC5AC.

6. A. p. 337, Figure 21-11. When inflammatory stimuli activate enzyme IKK2 which degrades NF-κB inhibitor, NF-κB subunits translocate to the nucleus where they bind to promoter regions of inflammatory genes. When IL-4 and IL-13 stimulate Jak1 and Jak3 to phosphorylate STAT6, GATA3 is activated (but not specifically moved from the cytoplasm to the nucleus). When IL-27 activates STAT1 and IL-12 activates TSAT4 which signals T-bet in Th1 cells, Th1 cytokines are released – GATA3 actually works against this pathway.


8. D. p. 329, Figure 21-3. Th17 cells release IL-17 and IL-22. Th1 cells release IL-2 and IFN-γ. Th9 cells release IL-9.

9. B. p. 331-330, Figure 21-4. Although basophils do release histamine, this is not believed to play a major role in asthma. Small increase in basophils has been documented in the airways of asthmatic patients, though these cells are far outnumbered by eosinophils.

10. C. p. 333. Chemokines do act in sequence in determining the final inflammatory response so inhibitors may not be effective, depending on the kinetics of the response. Examples of chemokines that are chemotactic for eosinophils include: CCL11, CCL24, CCL28, CCL5, and CCL13. CC3 and CC4 are chemokine receptors that can be targeted for their involvement in allergic disease.