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

Review Questions

Allergy & 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 16: Biology of Eosinophils
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1. Which of the following substances are contained within eosinophilic “specific” or secondary granules?
   a. Charcot-Leyden crystal protein
   b. major basic protein
   c. CD11b
   d. acid phosphatase

2. Eosinophil production and lineage differentiation is dependent on which transcription factor?
   a. GATA-1
   b. GATA-3
   c. GATA-6
   d. GATA-8

3. Eosinophil proliferation and differentiation is dependent upon interleukin-3 (IL-3), granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-5 (IL-5). Committed eosinophil precursors in the bone marrow can be identified by their expression of which of the following?
   a. IL-3 receptor and CCR5
   b. IL-5 receptor and CCR3
   c. IL-3 receptor and CCR7
   d. IL-5 receptor and CXCL13

4. Eosinophils are primarily located in tissues including the thymus, uterus, mammary glands, and gastrointestinal tract (except the esophagus) where their life span is about 2-5 days. In the peripheral blood, eosinophil half-life is about 8-18 hours. Measurement of eosinophils in the blood are the highest at what time of day?
   a. early morning
   b. late morning
   c. mid afternoon
   d. evening
5. A correlation between the concentration of this specific granule protein measured in bronchoalveolar lavage fluid with the severity of bronchial hyper-reactivity has been observed in patients with asthma:
   a. major basic protein
   b. eosinophil cationic protein
   c. eosinophil derived neurotoxin
   d. eosinophil peroxidase

6. Which of the following lipid mediators is the predominant metabolite of the 5-lipoxygenase pathway, generated by eosinophils?
   a. LTB$_4$
   b. LTC$_4$
   c. LTD$_4$
   d. LTE$_4$

7. Monoclonal anti-IL-5 therapies for asthma exert several effects on the biology of eosinophils. Which of the following eosinophil-derived substances induces tissue damage and remodeling?
   a. LTC$_4$
   b. RANTES and GM-CSF
   c. TGF-beta and MMP-9
   d. MBP, ECP, EDN, EPX

8. The most potent eosinophil chemo-attractants include platelet activating factor (PAF), LTD$_4$, C5a and CCL11 (eotaxin-1) and CCL5 (RANTES). Which of the following is implicated in the pathogenesis of eosinophilic esophagitis?
   a. PAF
   b. LTD$_4$
   c. eotaxin-1
   d. RANTES

9. Extracellular release of eosinophil granule contents is a major effector function, implicated in host defense and pathologic disease processes. Which of the following granule release forms involves granule fusion with the cell membrane, leading to sudden large increments in release?
   a. sequential release
   b. compound exocytosis
   c. piecemeal degranulation
   d. cytolysis

10. In addition to protection from helminths, eosinophils are purported to serve a role against certain viral infections. An increase in eosinophil number and concentration of eosinophil granule proteins can be found in the respiratory tracts of patients infected with this virus:
    a. respiratory syncytial virus
    b. adenovirus
    c. rhinovirus
    d. influenza A
1. b) **Major basic protein** (page 265 and page 267). Primary granules contain Charcot Leyden crystal protein. Secondary granules contain major basic protein, eosinophil peroxidase, eosinophil cationic protein, and eosinophil derived neurotoxin. Small granules contain acid phosphatase and arylsulfatase. Secretory vesicles contain membrane bound cytochrome b558, CD11b, albumin, and the alpha chain or beta-2 integrin.

2. a) **GATA-1** (page 265 and Figure 16-3). Production of eosinophils depends on different transcription factors including GATA-1, PU.1, and C/EBP members. PU.1 determines distinct cell lineage fates and GATA-1 and PU.1 synergistically induce eosinophil lineage differentiation. GATA-1 binding site deletion in mice has demonstrated a specific loss of eosinophils.

3. b) **IL-5 receptor and CCR3** (page 266). In the bone marrow, committed eosinophil precursors can be identified by their expression of IL-5 receptor and the chemokine receptor CCR3.

4. d) **evening** (page 266). Eosinophils exhibit diurnal variation. In the peripheral blood, the lowest levels are detected in the morning and the highest levels are seen in the evening.

5. a) **major basic protein** (page 268). Major basic protein has several roles; it disrupts *Schistosoma* membrane and is also toxic to *Trichinella*, *Trypanosoma*, *Staphylococcus aureus*, and *E. coli* as well as tumor cells. The concentration of MBP in the BAL fluid has been correlated with bronchial hyperreactivity in patients with asthma. MBP also increases airway responsiveness to inhaled methacholine. Eosinophil cationic protein has neurotoxic and antiviral properties. Eosinophil-derived neurotoxin is extremely neurotoxic; it also enhances Th2 responses through TLR-2 dependent mechanisms. Eosinophil peroxidase along with hydrogen peroxide and halide is anti-microbial against several pathogens.

6. b) **LTC$_4$** (page 269). In eosinophils, the predominant metabolite of the 5-LO pathway is LTC$_4$, which in turn, is metabolized to LTD$_4$ and LTE$_4$. Eosinophils also produce large amounts of 5-HETE. Together, these mediators lead to contraction of smooth muscle airways, mucus secretion, and eosinophil and neutrophil infiltration into tissues.

7. c) **TGF-beta and MMP-9** (Figure 16-6). In the pathogenesis of asthma: MBP, ECP, EDN, and EPX induce epithelial injury, MMP-9 induces tissue damage and remodeling, LTC$_4$ results in smooth muscle airway contraction, GM-CSF and RANTES are cytokines/chemokines which enhance eosinophil recruitment and activation, and TGF-beta induces tissue remodeling and fibrosis. Anti-IL-5 therapies reduce the pathologic effects of these substances.

8. c) **eotaxin-1** (page 272-274). PAF is a potent and effective chemoattractant for eosinophils and also evokes the release of granule proteins from eosinophils. LTD$_4$ is a chemoattractant for eosinophils which can be blocked by CysLT1 antagonists.

9. b) **compound exocytosis** (page 274). Sequential release is seen in *vitro* and is demonstrated with a patch-clamp technique. Compound exocytosis results in sudden, large increments in capacitance which leads to individual granule fusion with the cell membrane. Piecemeal degradation involves numerous small vesicles budding off from larger granules and moving to the plasma membrane for fusion. Cytolysis is a not well understood mechanism.
10. a) **respiratory syncytial virus** (page 276). There are increased numbers of eosinophils and increased concentration of eosinophil granule proteins in the respiratory tracts of patients with RSV. In animal models infected with parainfluenza, treatment with anti-IL-5 and subsequent reduction in eosinophil levels lead to an increase in viral content in the airways.