Welcome to the 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 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., Bruce S. Bochner, A. Wesley Burks, William W. Busse, Stephen T. Holgate, Robert F. Lemanske, Jr., Robyn E. O’Hehir

**Chapter 14: Biology of Mast Cells and Their Mediators**
Prepared by: Miriam Samstein MD PhD

1. IgE binds to which subunit of FcεRI?
   a. Alpha
   b. Beta
   c. Gamma

2. What is the best marker of systemic mast cell activation in anaphylaxis?
   a. Plasma histamine
   b. α-trypase
   c. β-trypase
   d. chymase

3. The Early Asthmatic Reaction is a decline in respiratory function within how many minutes of bronchial allergen challenge?
   a. 10-20 minutes
   b. 60-90 minutes
   c. 90-180 minutes
   d. 4 hours

4. Which of the following is an obligate mast cell growth factor?
   a. VEGF
   b. SCF
   c. GCSF
   d. GMCSF

5. The arachidonic acid metabolite prostaglandin D₂ (PGD₂) is synthesized by which pathway?
   a. Lipoxygenase pathway
   b. Pyruvate pathway
   c. IRAK
   d. cyclooxygenase
6. The generation of IP$_3$ following IgE dependent mast cell stimulation leads to:
   a. Efflux of intracellular CA$^{2+}$ and storage of Ca$^{2+}$ in the rough endoplasmic reticulum
   b. Ca$^{2+}$ mobilization from the rough endoplasmic reticulum and influx of extracellular Ca$^{2+}$
   c. Activation of the NOD2 pathway
   d. Activation of the sodium calcium transporter on the rough endoplasmic reticulum

7. Mast cells are thought to Skew T cell development towards which phenotype?
   a. Th1
   b. Th2
   c. Th17
   d. Treg

8. Anaphylaxis is primarily mediated by which two cell types?
   a. Mast cells and eosinophils
   b. Eosinophils and basophils
   c. Neutrophils and eosinophils
   d. Mast cells and basophils

9. The percentage of which type of mast cell is increased in the skin of patients with atopic dermatitis?
   a. MC$_{TC}$
   b. MC$_{TCT}$
   c. MC$_T$
   d. MC$_C$

10. Aspirin-triggered asthma is associated with?
    a. Increased LTE$_4$ in the urine
    b. Increased LTE$_4$ in nasal secretions
    c. Increased PGD$_2$ in the urine
    d. Decreased PGD$_2$ in the urine

**Answers:**
1. **A.** Page 233. Fc$\varepsilon$RI is a tetrameric structure consisting of an alpha chain that binds IgE, a beta chain signaling subunit and two gamma subunits that exist as immunoreceptor tyrosine-based activation Motif (ITAM) – containing homodimer signaling subunit.

2. **C.** Page 237. The best marker of systemic mas cell activation in anaphylaxis is an acute rise in the concentration of B-tryptase in the peripheral circulation. Alpha tryptase is released by mast cells constitutively, B tryptase is stored in mast cell granules and released after IgE-dependent activation. Histamine concentrations in blood peak within 5 minutes, the tryptase concentration is maximal between 15 and 120 minutes after the onset of symptoms.

3. **A.** Page 239. The early asthmatic response is a rapid deterioration of pulmonary function, as indicated by a fall in forced expiratory volume in 1 second, at 10 to 20 minutes following bronchial allergen challenge.
4. **B.** Page 228. Stem cell factor (SCF), or kit ligand, is an obligate mast cell growth factor that is derived from many cellular sources. Removal of SCF leads to rapid mast cell apoptosis. SCF is the ligand for kit encoded by the proto-oncogene c-kit.

5. **D.** Page 233. Newly formed metabolites of arachidonic acid are released from mast cells after IgE-dependent activation. The cyclooxygenase pathway produces PGD₂, whereas the lipoxygenase pathway form Leukotriene C₄ (LTC₄).

6. **B.** Page 234. IgE receptor activation initiates receptor aggregation with lipid rafts containing Lyn. Lyn kinase transphosphorylates tyrosine residues on the ITAMS binding to phosphorylated FCεRβ1 ITAM through the src homology 2 domain. Syk protein tyrosine kinases are recruited to the rafts and bind the phosphorylated ITAMS. They are then phosphorylated to recruit Lyn and Syk promoting an activation loop. This results in fully activated Syk, starting a cascade that activates inositol trisphosphate (IP₃). IP₃ induced CA²⁺ mobilization from the rough endoplasmic reticulum stores which initiates influx of extracellular Ca²⁺, a critical requirement for the release of preformed and newly generated mediators.

7. **B.** Page 237. Rat mast cells can skew T cell differentiation towards a Th2 phenotype through IL-4 release. Mast cells also influence the development of dendritic cells and their ability to activate T cells. Histamine increases IL-10 and decreases IL-12 production by mature dendritic cells, polarizing naïve T cells towards a Th2 phenotype.

8. **D.** p. 237. Anaphylaxis is mediated primarily by mast cells and perhaps basophils.

9. **C.** p. 239. Healthy skin contains mast cells that are approximately 90% MCₜc. The number of MCₜ increases in the skin of patients with atopic dermatitis.

10. **A.** p. 241. Aspiring-triggered asthma is associated with increased LTC₄ in the nasal secretions and increased LTE₄ in the urine.