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UNIVERSITY OF MICHIGAN

# Allergy and Asthma Self-Study Module

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3:00 PM

- Type I Allergic Reactions
  - Pathophysiology
    - Primarily a Th2-type of diesase
      - Cytokines secreted increase production of IgE, IL-4, IL-13, IL-5
      - Cytokines mature eosinophils and influence allergic responses
    - Mediated by IgE binding to receptor on mast cells, basophils, activated eosinophils
    - Degranulation when allergen binds to IgE to release mediators of early phase responses w/in mins
      - Changes in vascular permeability
      - Smooth muscle contraction
      - Initiation of inflammation
    - Late phase mediators result in release of more inflammatory mediators hours to days later
      - Vascular permeability
      - Smooth muscle contraction
      - Increased inflammation
      - Remodeling of connective tissue
      - Matrix
      - Mucus secretion
    - Granules (mast cell) contain heparin, histamine, proteases, TNF-α, lipid mediators, cytokines, chemokines
    - Eosinophils
      - Bilobed nucleus
      - Cytoplasm pink in eosin stain
      - Production in bone marrow enhanced by IL-5
      - Chemokines from Th2 cells chemotactic for eosinophils (presence is characteristic of chronic allergic inflammation)
    - Basophils - Stain w/ basic dyes, degranulated when binding IgE
- Antigens and Allergens
  - Allergens
    - Tend to be small, particulate proteins inhaled or exposed in small quantities
    - Can be used for benefits like vaccines or pathology of allergic responses
    - Pollens, food proteins, pet dander, dried feces of dust mites
    - Routes of exposure: airborne inhalation, contact, oral ingestion, medical injection
    - Atopic Individuals do not become allergic to proteins in vaccines
      - b/c these are encountered in different presentation, location, dose
      - Recognized by immune system to stimulate T cell memory and ultimately host protection
  - Atopy
    - Genetically determined tendency to produce IgE mediated hypersensitivity rxns against innocuous substances
    - Significant genetic component w/ several genes involved
    - Genetics
      - 60-70% inherited
      - Concordance in twins
      - Latest genome wide screen for genes contributing to asthma revealed ten different loci on different chromosomes
      - 11q and 20p significantly associated w/ asthma even by most conservative tests
      - Several genes whose products regulate Th2/Th1 balance or regulate expression of IgE

seem to contribute to atopic diseases (IL-4 receptor α for example)

- The "hygiene" hyopthesis
  - Observations that infants on farms tend to have less atopic disease than city dwellers or individuals from industrialized nations
  - Infants exposed to certain antigens may be less likely to develop allergies
  - Exposure to bacterial antigens critical to appropriate balance of Th1 and Th2 immune responses
- Clinical characteristics
  - Part of body exposed will display symptoms often
  - Response is usually in dose-dependent manner
  - Uticaria = hives caused by skin contact

- Asthma
  - Allergic response to breathed in allergen
    - Result of mast cell degranulation --> smooth muscle contraction
    - Recurrence of such problems during late phase
    - Increased secretion of mucus and fluids exacerbates problems in oxygen exchange
  - Inflamed airway
    - Vasodilated
    - Smooth muscle contraciton
    - Thickened basement membrane
    - Neutrophil, eosinophil, T-lymphocyte infiltration
    - Excessive mucus secretion
    - Airway wall edema
    - Increased capillary permeability
    - Shedding of damaged epithelial cells
  - FEV1 changes
    - Drop in 30 minutes
    - Recovery
    - Drop 8 hours later
    - Slow recovery
- Immediate phase
  - Result of mast cell degranulation
  - Causes most of the acute symptoms of allergic rxn
- Late phase
  - Due to chemokines, leukotrienes, cytokines synthesized by mast cells after IgE mediated activation by Th2 cells after restimulation by allergenic antigens
  - In asthma, late phase is more detrimental b/c it results in permanent lung damage
- Anaphylaxis
  - Some allergens in the blood stream can lead to degranulation of mast cells associated w/ blood vessels
  - Cascade causes systemic smooth muscle constriction and vascular permeability (anaphylactic shock)
  - Drug allergies, insect stings, and food can be associated w/ systemic anaphylactic shock
  - Treatment relies on EPI and medicines to restore normal cardiac and respiratory systems
- Treatment
  - Avoidance
  - Pharmacologic
    - Treatment of Symptoms
    - Antihistamines
    - Nasal corticosteroids
    - Decongestants
    - β-agonists
  - Immunotherapy
    - Desensitization by injection of allergens in form that changes nature or intensity of

immunity response

- Inducing tolerance or shifting production of antibodies away from IgE
- Usually used w/ aeroallergens and drugs, not foods