• Type I Allergic Reactions
  ○ Pathophysiology
    ▪ Primarily a Th2-type of disease
      □ 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" hypothesis
  - 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 contraction
    - 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