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Allergy and Asthma Self-Study Module

Tuesday, February 19, 2008
3:00 PM

- 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
 - Urticaria = 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