Type I

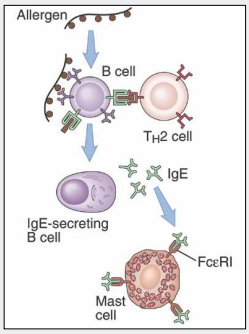
- Allergy (atopy)
- Individual becomes "sensitized" to an allergen
  - Usually harmless environmental protein antigens
- IgE response
  - Histamine, etc.: rapid effect on smooth muscle & blood vessels
  - Inflammation follows

Type I

- Why is IgE produced in response to allergen?
  - Genetic basis
  - T_H2 is dominant response to some Ag's in "allergy-prone" (atopic) individuals
    - No strong T_H2 response to Ag in most people
    - Many genes involved
    - Inherit susceptibility to allergies, not a particular allergy
  - Some evidence that immune system "priming" by parasites prevents development of atopy

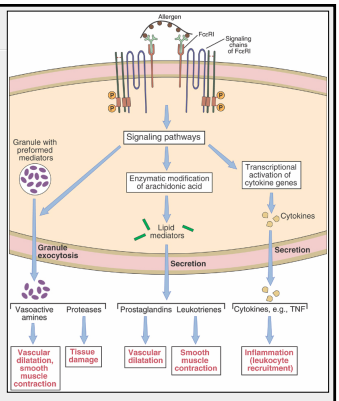
Type I

- Sensitization:
  - Activation of T_H2 and B cells specific for allergen → IgE
  - IgE binds high-affinity FcεRI receptors on mast cells
    - Found in connective tissues (bronchi, intestine)
    - Essentially irreversible
    - Mast cells with "receptors" for allergens



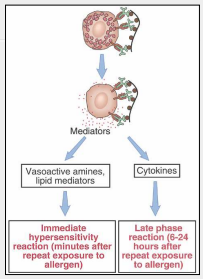
Type I

- Repeat exposure:
  - ≥2 IgE bind allergen
  - Vasoactive molecules released
    - Degranulation
    - Secretion
  - Immediate response
  - Histamine dilates blood vessels and stimulates smooth muscle
  - Prostaglandins dilate blood vessels
  - Leukotrienes stimulate smooth muscle



Type I

- Repeat exposure:
  - TNF and other inflammatory mediators recruit leukocytes
    - eosinophils
    - neutrophils
    - T_H2 cells
  - Symptoms of inflammation in 6-24 h
    - "Late phase reaction"



Type I

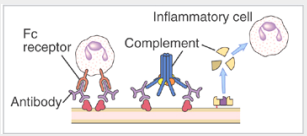
- Results:
  - Vasodilation: swelling, reddening
  - Mucus secretion
  - Muscle contration
    - Constriction of airways
    - Peristalsis in gut
    - Tissue damage due to inflammation
- Symptoms:
  - Upper respiratory: sneezing, coughing, nose running, etc.
  - Lower respiratory: wheezing, difficulty breathing (asthma)
  - Ingested: diarrhea, vomiting
  - Skin: hives, eczema
  - Systemic (anaphylaxis): b.p. drop, swelling, shock, airway obstruction

Type I

- Therapy:
  - Symptomatic
    - Antihistamines
    - Epinephrine
    - Anti-inflammatory steroids
  - Suppression
    - e.g., inhaled suppressive steroids for hayfever
  - Desensitization ("allergy shots")
    - Injection of specific allergens to stimulate production of neutralizing IgG/IgA
    - May result in anergy of IgE-producing B cells

Type II

- Antibody-mediated cytotoxicity
  - Ab produced against human cell with foreign Ag (or autoAg)
  - Tissue damage resulting from:
    - Lysis by complement
    - ADCC
    - Opsonization



Type II

- Why would one of our cells have a foreign Ag?
  - Transfusion reaction
    - RBCs with foreign Ag
    - A-B-O, M-N, Rh, etc.
    - 2-6 days
  - Drug-induced hemolytic anemia
    - Drugs react with RBC surface molecules to make new Ags
    - Penicillin, quinidine, methyldopa
    - Not the same as a drug allergy

Type III

- Immune complex disorders
  - Ab-Ag complex triggers complement → inflammation
  - Tissue damage occurs where complexes are deposited in high concentration:
    - joints
    - blood vessel walls
    - kidney
    - chloroid plexus of brain
  - Example: serum sickness
    - injection of animal IgG

Type IV

- Delayed-type hypersensitivity (DTH):
  - T-cell response
    - T_H1 cells → cytokines → macrophages, inflammation
    - T_C cells → CTL-mediated killing (usually autoimmunity)
  - Develops 48-72 hours after exposure
  - Requires large amount of Ag

Type IV

- Contact sensitivity
  - Poison ivy or oak, cosmetics, metals (e.g. Ni)
  - Allergen is a small molecule (not protein)
    - Binds self proteins, creating new epitopes
    - Processed by APCs
    - T_H1 cells activated
    - Attract and activate macrophages