Microbiology

Immunological Disorders

Hypersensitivities

- Immune responses that lead to host damage
- May occur in *sensitized* hosts
- Four principal types
  - Type I: *Anaphylaxis*
  - Type II: *Cytotoxic hypersensitivities*
  - Type III: *Immune complex hypersensitivities*
  - Type IV: *Delayed-type hypersensitivities*
- Types I-III involve antibodies
- Type IV involves cell-mediated response

Type I - Anaphylaxis

(a) IgE antibodies, produced in response to an antigen, coat mast cells and basophils. When an antigen bridges the gap between two adjacent antibody molecules of the same specificity, the cell undergoes degranulation and releases mediators such as histamine and leukotrienes.

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• **Systemic anaphylaxis**
  – “Anaphylactic shock”
  – Systemic allergens such as venoms
  – May lead to potentially fatal loss of blood pressure
• **Localized anaphylaxis**
  – “Atopic allergy”
  – Usually effects respiratory or gastrointestinal tissues
  – *Asthma* is a type I hypersensitivity response

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**Cytotoxic hypersensitivity**

• Immunoglobulin molecules attached to cells can lead to damage through
  – Complement activation
  – ADCC
  – Interference with normal function
• **Transfusion reactions**, involving the *ABO* antigens on erythrocytes, are a well-known example of type II hypersensitivity

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**Hemolytic disease of the newborn**

1. Rh+ father.
2. *Rh- mother carrying her first Rh- fetus. If* Rh- antigens from the developing fetus can enter the mother's blood during delivery.
3. In response to the fetal Rh antigens, the mother will produce anti-Rh antibodies.
4. If the woman becomes pregnant with another Rh- fetus, her anti-Rh antibodies will cross the placenta and damage fetal red blood cells.

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Thrombocytopenic purpura

1. Drug binds to platelet, forming hapten-platelet complex.
2. Complex induces formation of antibody against hapten.
3. Action of antibodies and complement causes platelet destruction.

Immune complex hypersensitivity

1. Immune complexes are deposited in wall of blood vessel.
2. Presence of immune complexes activates complement and attracts inflammatory cells such as neutrophils.
3. Enzymes released from neutrophils cause damage to endothelial cells of basement membrane.

Delayed-type hypersensitivity

1. Penicillin contact molecules
2. Skin protein
3. Penicillin contact molecules combined with skin proteins

T cells
T memory cells
Many active T cells

Primary Contact
Secondary Contact
Hypersensitivity and Autoimmunity

- Autoimmunity is a breakdown in self-tolerance, leading to immune responses to “self” antigens
- Tissue damage in autoimmune disease can be attributed to hypersensitivities
  - Type III immune complexes cause tissue damage in systemic lupus erythematosus (SLE) and rheumatoid arthritis
  - T cell-mediated damage of cells (type IV) is associated with type I diabetes

Transplant antigens

- MHC proteins (HLA antigens) are the major “non-self” antigens associated with transplant rejection
- Traditional tissue typing involves testing for type II hypersensitivities
- Transplant rejection is controlled by immunosuppression

Transplant Biology

- Some tissue sites are immunologically privileged; e.g., corneas are not rejected
- Classification of transplants
  - Autografts are within the same individual (e.g., some skin transplants)
  - Isografts are between genetically identical individuals
  - Allografts are between genetically nonidentical individuals
  - Xenografts are between individuals of different species
- Graft versus host (GVH) disease may occur where the transplant includes lymphocytes (e.g., bone marrow transplant)