Chapter 19 Disorders of the Immune System

Hypersensitivity Reactions

- Response to antigens (allergens) leading to damage
- Require sensitizing dose(s); primary exposure
- When exposed again → dangerous reaction

Type I (Anaphylactic) Reactions

- Involve IgE antibodies
- Localized: Hives or asthma contact or inhaled antigens
- Systemic: Shock from ingested or injected antigens
Type II (Cytotoxic) Reactions

- Involve IgG or IgM antibodies and complement
- Complement activation causes cell lysis or damage by macrophages
- 5-8 hours after exposure

ABO Blood Group System

<table>
<thead>
<tr>
<th>Blood Group</th>
<th>Rh Antigens on Red Blood Cells</th>
<th>Plasma Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A and B</td>
<td>Anti-A</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>Anti-B</td>
</tr>
<tr>
<td>O</td>
<td>None</td>
<td>Anti-A and Anti-B</td>
</tr>
</tbody>
</table>

Hemolytic Disease of the Newborn
Type III (Immune Complex) Reactions
- IgG antibodies and antigens form complexes that lodge in basement membranes.

Type IV (Cell-Mediated Rxns)
- Delayed-type hypersensitivities due to $T_D$ cells
- Cytokines attract macrophages and initiate tissue damage
• Clonal deletion during fetal development ensures self-tolerance
• Autoimmunity is loss of self-tolerance
• 75% of cases in women

Autoimmune Diseases

• Type I — Due to antibodies against pathogens (viruses); Hep C
• Type II — Antibodies react with cell-surface antigens; Graves
• Type III (Immune Complex) — IgM, IgG, complement immune complexes deposit in tissues; Lupus, RA
• Type IV — Mediated by T cells; MS (suspect Epstein-Barr virus)

Human Leukocyte Antigen (HLA) Complex

• Histocompatibility antigens: Self antigens on cell surfaces
• Major histocompatibility complex (MHC): Genes encoding histocompatibility antigens
• Human leukocyte antigen (HLA) complex: MHC genes in humans
Reactions to Transplantation

- Transplants may be attacked by T cells, macrophages, and complement-fixing antibodies.
- Transplants to privileged sites do not cause an immune response; cornea
- Stem cells may allow therapeutic cloning to avoid rejection.

Grafts

- Autograft: Use of one’s own tissue
- Isograft: Use of identical twin’s tissue
- Allograft: Use of tissue from another person
- Xenotransplantation product: Use of non-human tissue
- Graft-versus-host disease can result from transplanted bone marrow that contains immunocompetent cells
Cyclosporine suppresses IL-2
Mycophenolate mofetil inhibits T cell and B cell reproduction
Sirolimus blocks IL-2

Congenital: Due to defective or missing genes
- Selective IgA immunodeficiency
- Severe combined immunodeficiency: no B or T
- Agammaglobulinemia; few or no Abs
- Di George: no thymus so no T cells

Acquired: Develop during an individual's life, due to drugs, cancers, infections
- Multiple Myeloma: single plasma cell
- Macroglobulinemia: overproduce IgM

Immunosuppression

Immune Deficiencies

Immune System and Cancer
- Cancer cells possess tumor-specific antigens; Tc cells recognize and lyse
- Cancer cells may lack tumor Ags/ kill Tc cells
Immunotherapy

- Treatment of cancer using immunologic methods
- Tumor necrosis factor, IL-2, and interferons may kill cancer cells
- Immunotoxins link poisons with a monoclonal antibody directed at a tumor antigen
- Vaccines contain tumor-specific antigens

Chapter 18

Types of Vaccines

- Inactivated whole agent
  - Killed organism (formalin or phenol)
- Rabies, Influenza, Strep pneumo, cholera, Salk (polio)
Types of Vaccines

- **Attenuated whole agent**: living but weakened organism
  - Closely mimics infection
  - May be life long and 95% effective
  - Can mutate to more virulent strain; not if immunosuppressed
- MMR, TB, Typhoid, Sabin polio

- **Toxoids**: inactivated toxins from bacteria
  - Tetanus, Diphtheria

- **Subunit**: Antigenic fragments of organism that best stimulates response
  - safer
  - Hep B

- **Conjugated**: combine capsular polysaccharide with protein; deals with children’s poor response to capsular Ags (not respond until 15-24 months)
  - Haemophilus influenzae B (can protect at 2 months)
• Nucleic Acid vaccines:
  – Newest
  – Plasmids of naked DNA injected into muscle
• Adjuvants: chemical added to improve effectiveness of Ags for vaccines
  – Alum; increases effectiveness

Principal Vaccines in US

• DtaP
  – Diphtheria: Purified diphtheria toxoid
  – Pertussis: Acellular fragments of *B. pertussis*
  – Tetanus: Purified tetanus toxoid
• Meningococcal meningitis: Purified polysaccharide from *N. meningitidis*
• *Haemophilus influenzae* type b meningitis:
  Polysaccharides conjugated with protein
• Pneumococcal conjugate vaccine: *S. pneumoniae* antigens with protein