Immunopathology

Diseases of the natural defense system that usually resists infections.
Immunity

- Resistance to infection via the immune response to any substance perceived as foreign
  - Therefore, not always protective
Immune Response

- Natural protective mechanisms
  - Inherited
    - Independent of previous exposures to foreign substances
  - Include
    - Mechanical barriers
    - Phagocytic cells
    - Natural killer cells
    - Protective proteins
Immune Response

- **Acquired**
  - Based upon specific responses elicited by substances that act as antigens
    - **Antigens**
      - Chemical substance that can induce a specific immune response
    - Immune system activated to destroy the antigen
    - Antibodies are formed
Immune Response

- Immuno-incompetence
  - The ability of the body to mount an appropriate immune response
Cells of the Immune System

- **Lymphocytes**
  - Derived from bone marrow pre-lymphoid stem cells
  - Primary lymphoid organs
    - Thymus
      - T lymphocytes mature here
    - Bone marrow
      - B lymphocytes remain here
      - Colonize peripheral lymphoid tissue
Lymphocytes

- Secondary lymphoid organs
  - Colonized by T and B lymphocytes once they enter blood stream
- Lymph nodes
- Spleen
  - Significant percentage of the total cell population
- Gastrointestinal and Bronchial mucosa
T Lymphocytes

- Lymphocytes that have matured in the thymus
  - T helper /inducer
    - Actively participate in the immune response to antigens, helping B cells produce antibodies
  - T suppressor/cytotoxic cells
    - Suppress unwanted antibody production
    - Mediate killing cells that are recognized by the body as foreign
T Lymphocytes

- T-cells have a surface receptor
  - TCR
    - Used to recognize antigens, essential for the activity of T cells.
    - Inherited gene in all cells of body
      - Active only in T cells
T Lymphocytes

- NK cells
  - Natural killer cells
  - Not involved in T and B cell mediated immune reactions
  - React against virus-infected cells and to kill tumor and foreign cells without previous infection
B Lymphocytes

- Lymphocytes that primed to differentiate into immunoglobulin-producing plasma cells
  - Plasma cells
    - Mature descendants
    - Contain an abundance of ribosomes
    - Secrete immunoglobulins
Antibodies

- Serum proteins of the immunoglobulins
  - Secreted by the plasma cells
Antibody Production

- Begins with contact between antigen and the cells of the immune system
  - Substances identified as foreign could serve as antigens and incite an immune response
Changes to Immunity With Age

- Skin thinning
- Decreased acidity of GI tract
- Shallower breathing
- Slowing function of phagocytes
- Difficulty with defense of newly encountered organisms
Factors Affecting Immunity

- Nutrition
- Prior/other illness/injury
- Medications
- Removal of spleen
- Stress
Hypersensitivity Reactions

- An abnormal immune response to exogenous antigens
- A reaction to endogenous auto-antigens
- Basis of hypersensitivity diseases
Types of Hypersensitivity Diseases

- **Type I**
  - Anaphalactic type reaction
    - Sensitization to foreign antigens
      - Triggers release of vasoactive substances
        - histamine
    - Late phase response can also occur
      - Occurs 4-6 hours after exposure to allergens
  - Hay fever, allergic rhinitis, bronchial asthma, atopic dermatitis
Anaphylactic Type Reaction

- Anaphylactic Shock (type I)
  - Life threatening
    - Massive release of histamine and other vasoactive substances
      - Choking (laryngeal edema)
      - Wheezing (bronchial spasm)
      - Pulmonary edema
      - Systemic circulatory collapse & fainting
        - Hypotension due to vasodilation and increased leakage of fluid from hyperpermeable blood vessels.
Type II-Hypersensitivity

- **Cytotoxic Antibody Reaction**
  - Mediated by cytotoxic antibodies that react with antigens in cells or tissue components, such as basement membranes.
    - Antibody may be
      - Extrinsic
      - Intrinsic
        - Autoimmune diseases
Type II Hypersensitivity Diseases

- Intrinsic antibodies
  - Macromolecules:
    - Proteins
    - RNA
    - DNA
  - Idopathic
Type II Hypersensitivity Diseases

- Foreign antigens
  - Drugs
  - Simple chemicals
  - Hypersensitivity occurs upon re-exposure to the pathogenic antigen
    - Persistent antigens
Type II Hypersensitivity Diseases

- Hemolytic anemia
- Grave’s Disease
  - hyperthyroidism
- Myasthenia Gravis
  - Severe muscle weakness,
    - Mediated by antibodies to the receptor for acetylcholine on the surface of striated muscle cells
      - No messages reach the muscle
Type III Hypersensitivity

- Mediated by immune complexes that are formed between antigens and appropriate antibodies
- Most reactions are short lived however
- Sustained production of immune complexes leads to chronic conditions
  - Lupus
  - Rheumatoid arthritis
Type IV Hypersensitivity

- Cell mediated hypersensitivity
  - T lymphocytes become sensitive to presence of antigen and produce delayed response when exposed to this antigen
    - Tuberculous granulomas - provide the ability to test to see whether someone has been exposed to TB
    - Contact dermatitis
      - allergy to allergens; rubber gloves, poison ivy,
    - Candida albicans
Vaccine

- Expose body to harmless version of pathogen
- Body creates antibodies to the disease, but not the actual symptoms/pathology of the disease
Transplantation

- Donor tissues must be immunologically similar enough to the recipient to avoid rejection
- Recipient’s immune system cannot react against foreign antigens
  - Immunosuppressive drugs
Transplantation

- Types
  - Autograft
    - Patient is both the donor and recipient
      - Skin grafts
      - Hair transplantation
      - Blood vessels
Transplantation

- **Types**
  - Isograft
    - Transplantation between genetically identical individuals of the same species
    - Identical twins
    - Do not elicit a transplant reaction
      - The recipient does not recognize the tissue as foreign.
Transplants

- Types
  - Homograft or allograft
    - Between individuals of the same species who are not genetically identical
    - Must be:
      - Histocompatible
      - Human leukocyte antigens
      - Same blood group
  
  - BEST WITH RELATIVES OR SIBLINGS
Transplant Rejection

- All homografts invariably evoke some transplant rejection
  - Pre and postoperative use of immunosuppressive drugs can reduce this response
Transplant Rejection

- Hyper-acute reaction
  - Recipient has pre-formed antibodies to the donor’s antigens
  - Reaction occurs during the surgery
Transplant Rejection

- Acute Rejection
  - Occurs within the first few weeks of transplantation or later when immunosuppressive treatment becomes ineffective
Transplant Rejection

- Chronic transplant rejection
  - evolves slowly over a period of several months or years
  - Ultimate deterioration of the function of the transplanted organ
Blood Transfusion

- From one person to another is a form of transplantation
  - RBCs significantly outnumber WBCs
  - RBC Blood group antigens make or break the success of the exchange
    - Major antigens
    - Minor antigens
    - Rh antigens
Blood Group Antigens

- Major blood group antigens
  - Blood type
    - AA, AB, AO, BO, BB, OO
      - A & B genes are dominant over the O gene
        - This leaves 4 blood groups
          - A, B, AB and O
Blood Group Antigens

- Minor Blood Group Antigens
  - ABO antigens have corresponding natural antibodies:
    - “A” contain anti-B
    - “B” contain anti-A
    - “O” contain both anti-A and anti-B
Blood Group Antigens

- Minor blood group antigens
  - AB = universal recipients
  - O = universal donor
Transfusion Reaction

- Incorrect infusion causes:
- Hemolysis of donor blood by the recipient is a serious consequence
  - may lead to renal failure
  - Intravascular coagulation
- Type II hypersensitivity
Blood Group Antigens

- Rh blood antigens
  - Expressed on the surface of human RBCs
    - There are no natural antibodies
    - Positive or negative
      - Hemolysis results when there is a difference
Auto-immune Diseases

Breakdown of auto-tolerance results in auto-immune disease
Autoimmune Disease

- More common in women than men
- Genetic factor
- May be organ specific or systemic
Autoimmune Disease

• Examples:
  • Systemic Lupus Erythmatosus (SLE)
  • Multiple Sclerosis (MS)
  • Myasthenia gravis
  • Rheumatoid arthritis (RA)
  • Systemic sclerosis
Systemic lupus Erythematosus

- Multisystemic involvement
- Epidemiology
  - 10 times more common in women
  - May occur at any age, but most often young adults
  - More severe in African Americans
SLE

- **Etiology**
  - Poorly understood
  - Malfunctioning of supressor T cells

- **Clinical Symptoms** *(highly variable)*
  - Inflammation of the joints
  - Organ involvement
  - CNS problems
  - Vision problems
  - “Butterfly” rash

- **Prognosis**
  - More than 30% of the patients are alive 10 years post dx
Clinical Significance

- Generalized fatigue
- Energy conservation
- Joint protection
- Exercise plan
Acquired Immunodeficiency Syndrome

- AIDS
  - Develops as a consequence of a severe acquired immunosuppression caused by:
    - Human immunodeficiency viruses
      - HIV
        - Small RNA viruses
        - “1% of all college-aged people (18-25 years of age) have serologic evidence of HIV infection.”
AIDS

- **Pathogenesis**
  - RNA retrovirus that cannot survive outside of human cells
  - Humans are the only source of infection
  - Virus is transmitted through close contact with fluid exchange
    - *Blood transfusion or contacts that transfer blood from one person to another*
AIDS

- Pathogenesis
  - Sexual secretions and sperm also contain HIV
  - Can be transferred from mother to child transplacentally
AIDS

Clinical Presentation

1. those with acute infection
2. those with asymptomatic infection
3. those with persistent generalized lymphadenopathy
4. those with other diseases superimposed on the viral infection
AIDS

- **Clinical Presentation: Acute Illness**
  - Approximately 50% of HIV infected persons, 3-6 weeks after exposure
    - Fever
    - Night sweats
    - Nausea
    - Myalgia
    - Headache
    - Sore throat
    - Skin rash
    - Mild lymph node enlargement
      - 2-3 weeks, may develop antibodies to HIV
AIDS

- Clinical Presentation: Asymptomatic Infection
  - Few months- years
  - Pt. carries the virus and is infectious
  - Approximately 50% of HIV infected patient develop AIDS within 10 years of initial diagnosis
AIDS

Clinical Presentation: Opportunistic Infections

- Gastrointestinal disorders
- Central nervous system involvement
- Neoplasia
  - Kaposi’s Sarcoma
  - Lymphoma
- Skin infections
AIDS

- Clinical significance
  - Use standard precautions
    - Hand washing
    - Covering broken skin
    - Protective barriers for bodily fluids
  - Aerobic exercise
  - Strength training/PREs