Specific Immune Response (Chapter 17)

Involves specialized WBCs—Lyphocytes (B and T cells)
Response in highly specific
Response generates memory
Can distinguish between self and non-self
Substances that provoke response: Antigen
Immune Response product: Antibody

Types of Immunity:

Immunity:
Active: exposure to Antigen and Antibodies produced
Passive: Antibodies transferred to person/only lasts as long as Antibodies present
Can be Natural or Artificial
Natural acquired active immunity: Response to antigens encountered over lifetime/immunity may be lifelong
Natural acquired passive immunity: Antibodies transferred from mother to infant across placenta and in milk(colostrums)/lasts only as long as antibodies present
Infant: immature immune system/produces own antibodies at 6 months
Artificial acquired active immunity: vaccination
Artificial acquired passive immunity: injection of antibodies into the body/immediate immunity but short lived (Eg. after exposure to Hep A./ Neisseria meningitides)

What causes an immune response? Antigens
Usually protein or polysaccharides
Foreign substance with MW of ≥10,000
Hapten--not large enough and needs carrier molecule; antibody formed will then react with hapten only
Examples of antigens: bacterial capsules, cell walls, flagella, toxins

How are Foreign Antigens recognized as non-self?
Major histocompatibility complex (**MHC**) glycoprotein self markers
MHC I: produced by all cells; proteins are degraded into peptides which are loaded in MHC I (If cell not infected with virus or bacteria, all peptides are self.) If abnormal foreign peptides presented by MHC I Glycoprotein [fragments of antigens in groove of MHC I (bun and hot dog)] to Tcytotoxic cells→ lysis of antigen by perforin
MHC II produced by Antigen presenting cells, dendritic, B cells, T cells; Antigens are outside host cells (exogenous Antigens) and activates Thelper cells (Tℏ binds to Ag-MHC II complex and is activated to proliferate)

Antibodies: Immunoglobulin produced in response to antigen; recognizes, binds to and then neutralizes or destroys the antigen
Composed of heavy and light chains with antigen binding sites
Separated by electrophoresis into different immunoglobulin classes:
IgG: (80 % Abs)monomer (2 heavy and 2 light); crosses placenta
IgM: (5-10 %)5 monomers; can't cross placenta due to large size; First to appear then IgG; ABO
IgA: (10 -15% in blood) Most common in mucus and saliva, tears so most abundant in body
Prevents attachment of pathogens to mucosal
IgD: (0.2%) blood, lymph and on B cells (antigen receptors)
IgE: (0.002%) bound by Fc to mast cell and basophils; allergic reactions
Eg. Pollen (Ag) reacts with IgE on mast cells and basos→**histamine**→allergic rxn

Humoral Immunity: mediated by B cells

B cells exposed to free antigen
B cells are activated
B cell divides and differentiates into clone (clonal selection) of plasma cells
Plasma cells produce antibodies against the **specific** antigen (live for few days; each can produce 2000 Abs/sec)
Some B cells do no differentiate into plasma cells and become **memory** cells

Primary and Secondary Response:

Primary:
No detectable titer (amount of antibody in blood) for several days—slow rise in titer
First IgM produced, then IgG
Secondary: memory or anamnestic
Some B cells become memory cells and long lived; if exposed again to same antigen—B cells rapidly become plasma cells and produce antibodies (titer rises rapidly)

Apoptosis: "programmed cell death" Normal destruction of B cells that do not encounter antigen; does not trigger inflammation

Antigen-Antibody Reactions:

Antibody and Antigen→AB-AG complex—tag for foreign cells for removal
Antibody does not harm antigen: binds to and tags
Antigen rendered harmless by:

Agglutination: clumps more easily phagocytized
Neutralization: IgG inactivate viruses by blocking attachment to host cell
Opsonization: Abs coat and enhance ingestion and lysis by phagocytes
Antibody dependent mediated cytotoxicity: Ab coating targets
Trigger Complement attachment and activation on Ag surface→lysis

Monoclonal Antibodies:
Previously if needed antibodies:

AG → animal→ harvest Abs produced

Now combine cancerous B cells with normal AB producing B cells-→monoclonal antibodies
Use in diagnostic tests and in therapy:

Mono Abs to suppress T cells in transplant patient
Treat specific illnesses (leukemia, Crohn's, RA)
Combine mono Abs with radioisotope to target cancer cells

Cell Mediated Immunity: T cells

Dependent on **cytokines**: chemical messengers within the immune system (can inhibit and/or stimulate Response) Between WBCs—interleukins

Chemokines—chemotaxis
Interferons
TNF tumor necrosis factor

T cells arise from stem cells in bone marrow; precursors migrate to thymus and to other lymphoid tissue

T cells have antigen receptors to recognize and react with antigens; differentiate into effector cells to carry out cell-mediated immunity; proliferate

Types of T cells:

Th—Helper: influences action of other immune system cells; **activates macrophages and B cells**
Tc—Cytotoxic: **destroys target antigens on contact**; releases **perforin**
Td—Delayed hypersensitivity: certain allergies; transplant rejection
Ts—Suppressor: not well understood; may regulate immune system by "turning off" when Antigen no longer present

Non-specific Immune cells:

Macrophages: usually in resting state; activated by ingestion onf antigen or cytokines from activated Thelper cells
NK cells(natural killer): **not** immune specific/does not need to be stimulated by antigen
Lymphocytes capable of destroying other cells (not phagocytic but must be in contact with target cell such as virus infected and tumor cells, large parasites

Disorders of the Immune System (Chapter 19)

Hypersensitivity (Allergy): Antigenic response beyond normal
Previous exposure to allergen; when exposed against→dangerous reaction

Type I Anaphylactic: 2-30 min after exposure
Antigen with IgE bind to mast cells and basophils→release of 1. histamine
Swelling
Redness
Increased mucus
Smooth muscle contraction (breathing difficulty)
Chemotactic attraction of segs/eos
2. leukotrienes and prostaglandins: prolonged contact→asthma
May be Localized (hay fever, congestion, cough, sneezing)
Systemic (anaphylactic shock) with lower blood pressure/fatal within minutes: treat with epinephrine to constrict blood pressure and raise BP

Type II Cytotoxic Reactions: activate C′ and lyse cell
Transfusion reactions, HDN (hemolytic disease of newborn), Drug induced (thrombocytopenia purpura)

Type III Immune Complex Reactions: Forms when certain ratio of AB to AG occurs (usually IgG and slight excess of Ag) →complexes form and escape phagocytosis; can circulate in blood and pass into epithelial cells →damage of membrane Eg. Glomerulonephritis

Type IV Cell Mediated Reactions: Delayed type of hypersensitivity from T cells
Exposure creates memory T cells; Reexposed→memory cell→cytokines→antigens
Eg. Skin test for TB
Latex dermatitis

Autoimmune Diseases: loss of self tolerance

70 % in women

Type I: Antibodies attack self; sometimes response to virus that is similar to self proteins

Eg. Hep C → autoimmune hepatitis

Type II: cytotoxic: antibodies react with cell surface antigens

Eg. Graves disease: Abs to receptors on thyroid gland→goiter (gland swells, eyes bulge)

Type III: Immune Complexes:

Eg**. Lupus erythromatosus** (antibodies against own DNA/antinuclear Ab)

Rheumatoid Arthritis: IgM-IgG and C′ deposited in joints

Type IV: Cell mediated

Eg. **Multiple Sclerosis**: T cells and macrophages attach myelin sheath of nerves

Transplants: (First kidney transplant in 1954)

Priviledged site: some transplanted tissue will not stimulate antigenic response Eg. Cornea (Abs don't circulate)

Stem Cells: embryonic stem cells generate all types of cells; grow tissues the same as person's own

Autografts: own tissue to another location (eg. Skin grafts in burn victums)

Isografts: Between identical twins

Allografts: Between HLA matches

Xenografts: tissues or organs from animals (other species)

Bone Marrow Transplants: Graft versus Host (GVH) complication from transplanting immune cells from bone marrow; Less likely GVH if use umbilical cord blood

Rejection of transplants: caused by T cells

Immunosuppression for transplant: Cyclosporine to suppress secretion on Il-2 and disrupt Tcytotoxic cells

Immune Deficiencies:

1. Congenital: genetic or developmental abnormality
   - Agammaglobulinemia: very rare; few or no antibodies
   - Severe Combined Immunodeficiency (SCID): neither B or T cell function; die early unless Bone Marrow transplant
   - IgA deficiency: most common
   - DiGeorge syndrome: lack thymus so no cell mediated immunity; T cells absent

2. Acquired:
   - Hodgins: lowers cell mediated
   - Removal of spleen: decrease humoral response
   - Multiple myeloma: single plasma cell proliferates and its Abs increase
   - Macroglobulinemia: overproduction of IgM

Practical Applications of Immunology (Chapter 18)

Vaccines:
Suspension of organisms or parts of organisms used to induce immunity →primary immune response→ Formation of antibodies and memory cells

1. **Attenuated whole agent vaccine**: living but weaken organism:closely mimics true infection; maybe lifelong and 95% effective Eg**. MMR**, Sabin polio, TB, thypoid

2**. Inactivated whole agent**: Killed microbes (by formalin or phenol)
Eg. **Rabies**, influenzae, Salk polio, Strep pneumo, cholera

3**. Toxoid**: inactivated toxins
Eg**. Tetanus**, diphtheria

4. **Subunit**: antigenic fragments of microbe that best stimulate response; safer
Eg. **Hep B**

Conjugated: developed to deal with poor response in children to vaccines against capsular polysaccharide Ag
Combine capsular Ag and protein

Nucleic Acid (DNA) vaccines: newest, use plasmids of naked DNA to stimulate immune response

Adjuvants: chemical added to improve effectiveness of antigens for vaccines; Alum