Immunity = resistance: defense against foreign material

Innate immunity = defenses that are always present to provide instant protection against infection

Adaptive immunity = induced, adapts to a specific foreign substance, acquired memory of the infection

Antigens = substances that provoke an immune response, immunogenic molecules

Dual Nature of Adaptive Immune Response:
1. Humoral / Antibody-Mediated Immunity
   -involves antibodies produced by B cells to confer immunity
   -best against bacteria, toxins, and virus that are free in body fluids
2. Cell-Mediated Immunity
   -involves T cells that act against foreign organisms or tissues
   -involves cytokines & cytotoxicity
-works best on bacteria- or virus-infected cells, fungi, protozoa, tissue grafts and cancer

Four Types of Adaptive Immunity: (on handout)
1. Naturally Acquired Active Immunity
   - everyday exposure to antigens & disease
   - development of B and T cell responses & memory, immunity may be life long
2. Naturally Acquired Passive Immunity
   - transfer of antibodies from mother to fetus or infant across placenta or in milk
   - immunity lasts as long as antibodies, weeks to months
3. Artificially Acquired Active Immunity
   - vaccination / immunization: forced introduction of nonvirulent antigens
   - development of B and/or T cell responses & memory, immunity may be life long
4. Artificially Acquired Passive Immunity
   - injection of preformed antibodies from people or animals, called antiserum
   - immunity lasts as long as antibodies, weeks to months
Antigens:
-determine self vs. non-self
-non-self provokes immune response
-located on the surface of cells: capsules, walls, flagella, fimbriae, pentons, spikes, etc., or toxin molecules
-most are proteins or large polysaccharides
-the specific antigenic compound recognized by lymphocytes or antibodies is called the epitope / antigenic determinant
lymphocytes have receptors to recognize and specifically bind to the epitope
antibodies have specific antigen-binding sites

-a single pathogen or antigen can have hundreds of different epitopes / antigenic determinants on its surface, each of which would be recognized and bound by a different antibody or lymphocyte

**Antibodies / Immunoglobulins**
special protein produced by plasma cells (B cells) that will recognize and bind to its specific epitope of an antigen via its antigen binding sites
- Antibodies recognize and bind to specific shape of antigen’s epitope
- Antibodies have great specificity
- Affinity = strength of bond between antigen and antibody
- Each has minimum of 2 antigen binding sites: both recognize same epitope (antigen)

Antibody Molecule Structure: (on handout)
Classes of Antibodies/Immunoglobulins

**IgG antibodies**
- Monomer
- 80% of serum antibodies
- Produced on second+ exposures
- In blood, lymph
- Can enter tissues, cross placenta
- Fix complement, enhance phagocytosis, neutralize toxins & viruses, protects fetus & newborn, antiserum

**IgM antibodies**
- Pentamer
- 5-10% of serum antibodies
- Produced only on first exposure
- In blood, lymph, on B cells
- Fix complement, agglutinates antigens

**IgA antibodies**
- Dimer
- 10-15% of serum antibodies
- In secretions
- Mucosal protection

**IgD antibodies**
- Monomer
- 0.2% of serum antibodies
- Surface receptor on B cells
- Initiate humoral immune response by B cells

**IgE antibodies**
- Monomer
- 0.002% of serum antibodies
- Surface receptor on mast cells and basophils
- Inflammation, allergic reactions; lysis of parasitic worms
B cells and Humoral Immunity
-B cells produce antibodies = humoral / antibody-mediated immunity
-B cells arise from stem cells in bone marrow
-when mature, migrate to lymphoid tissue
-wait to recognize and bind to antigen to be stimulated to produce antibodies

Activation of B cells by clonal selection:
-each B cells produces only one antibody against one antigen/epitope
-recognizes antigen/epitope via IgD receptor on cell surface
-when activated it will divide to produce clones
(on handout)
Activation and Clonal Selection of B cells

T-independent Antigen

Epitope tends to be polysaccharide, produces weaker immune response than T-dependent Antigen

1. IgD antibody receptor on B cell binds its specific antigen/epitope
2. B cell is activated and undergoes clonal selection: the B cell proliferates and differentiates into two types of cell populations: Memory B cells and Plasma Cells
3. Plasma cells secrete antibodies specific for the original epitope (2000 antibody molecules per second) for 3-5 days. [Time from initial antigen binding to antibodies appearing in the blood is 7-10 days] Antibodies bind to free antigens.
4. Upon second exposure to the same antigen/epitope, memory cells bind antigen and are triggered to differentiate into plasma cells and secrete antibodies. [Time from initial antigen binding to antibodies appearing in the blood is 2-5 days]

Memory cells = long term immunity
Primary Response:
- initial exposure to antigen results in IgM production
  - peak titer 10-17 days
  - peak titer of antibodies low
Secondary/Memory Response:
- second and subsequent exposure results in IgG production
  - peak titer 2-7 days
  - much higher peak titer of antibodies

Function of Antibodies
antigen-antibody complex = antibody bound by its antigen-binding sites to the epitope
Antigen bound to IgE on Mast cells triggers histamine release and

Results of Antigen-Antibody Binding:

1. Agglutination
   Enhances phagocytosis and reduces number of infectious units to be dealt with

2. Opsonization
   Coating antigen with antibody enhances phagocytosis

3. Neutralization
   Blocks adhesion of bacteria and viruses to mucosa

4. Antibody-dependent cell-mediated cytotoxicity
   Antibodies attached to target cell cause destruction by non-specific immune system cells

5. Inflammation
   Disruption of cell by complement/reactive protein attracts phagocytic and other defensive immune system cells

6. Activation of complement
   Cell lysis

MAC
T cells and Cell-Mediated Immunity
- requires coordinated activity of specialized cells that must communicate
Communication chemicals = cytokines
- chemical messengers used within immune system (proteins or glycoproteins)
- many kinds, each has specific message
Cells = T cells
- originate from stem cells in bone marrow but mature in thymus, travel to blood & lymph
- each only recognizes one antigen
- when it binds to antigen, will undergo clonal selection to produce effector and memory cells
- effector cells: attack foreign cells or stimulate other defense cells via cytokines
- memory cells: rapid response upon second exposure, long term immunity
- T cells do not bind free antigen: must be on cell surface in association with molecules of the major histocompatibility complex (MHC)
Class I MHC
Infected cell

Class I MHC is found on all cell types and displays all antigens that are present in a cell, both self and non-self.

Class II MHC is found only on APCs and only displays antigens that have been endocytosed

Class II MHC
Antigen Presenting Cell

Antigenic fragments are displayed by Class II MHC proteins.

Endoplasmic reticulum

Lysosome action produces antigenic fragments.
Types of T cells:
1. $T_H$ (Helper T cells) / CD4 Cells
   - activated by antigen in Class II MHC
   - respond by secreting cytokines to influence other immune cells

A. $T_{H1}$: activate cells related to cell-mediated immunity ($T_C$ and Macrophages)
B. $T_{H2}$: activate B cells to make antibodies (T-dependent antigens)
Activation of Helper T Cells (on handout)

Class II TH1 TH2

APC (macrophage) Antigen Complex of MHC molecule and Ag fragment

Ag fragment (short peptides) MHC molecule

Microorganism carrying antigens

Defense against intracellular pathogens

TH1

Cytotoxic T cell

Cell-mediated immunity (attack on infected cells)

TH2

B cell

Humoral immunity (secretion of antibodies by plasma cells)

Defense against free pathogens

Defense against intracellular pathogens

Activation and cell division

Memory TH cells (inactive)

Cytokines released

Active TH cells

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2. T\textsubscript{C} (Cytotoxic T cells) / CD8 Cells
- activated by antigen in Class I MHC
- respond by secreting perforin and lysing the target cell:
- this usually requires pre-activation of the T\textsubscript{C} by cytokines produced by a T\textsubscript{H1} cell

Activation of Cytotoxic T Cells (on handout)

3. T\textsubscript{S} (Suppressor T cells) aka T\textsubscript{reg} (Regulatory T cells)
- regulate the immune response
- prevent autoimmunity
- inhibit T and B cell activity when antigen levels decline
Natural Killer Cells (NK cells)
-not immunologically specific
 -attack any abnormal antigen on eukaryotic cells: virus-infected, cancer, large parasites
 -attack cells lacking proper class I MHC
 -lyse target cell by releasing perforins to disrupt membrane

Inter-relationship of Cell-Mediated and Antibody-Mediated Immunity
T-dependent antigens:
 -more common than T-independent antigens
 -protein epitopes
 -require $T_H^2$ cells to signal B cells to produce antibodies
(on handout)
T-dependent antigens:

- activate B cell directly
- less common
- antigens: polysaccharides, lipopolysaccharides
- weaker immune response

T-independent antigens:

(previous notes)
- activate B cell directly
- less common
- antigens: polysaccharides,
  lipopolysaccharides
- weaker immune response
Most activity of the immune system requires cytokines produced by T Helper cells

Most activities of B and T cells function to enhance non-specific defenses / innate immunity (on handout)
Non-specific defenses and the immune response are integrated:
both function together for overall defense

Defense against intracellular pathogens

Defense against free pathogens