Now Presenting…Antigens
Specific Immunity and Immunization

Specific Defenses of the Host:
The Immune Response

- Innate (nonspecific)- Defenses against any pathogen
- Immunity - Specific antibody and lymphocyte response to an antigen
- Antigen (Ag)- A substances that causes the body to produce specific antibodies or sensitized T cells
- Antibody (Ab)- Proteins made in response to an antigen

Terminology

- Serology- Study of reactions between antibodies and antigens
- Antiserum- Generic term for serum because it contains Ab
- Globulins - Serum proteins
- Gamma (γ) globulin- Serum fraction containing Ab

Third line of Defense

- Specific immunity is a complex interaction of immune cells (leukocytes) reacting against antigens
  - Stages
  - Self and nonself
  - Clonal selection
  - Antigens

Stages

- Dual lymphocyte development and differentiation
- Presentation of antigens
- Challenge of B and T lymphocytes by antigens
- Production of antibodies by B cells (plasma cell)
- T lymphocyte responses

Self and non-self

- Markers
  - glycoprotein
  - located on the cell surface
  - Ex. Major histocompatibility complex (MHC)

Markers

- Host cells receptors (ex. MHC) confer specificity and identity
- Role – detection, recognition, and communication
- Lymphocyte cells recognize the host cell receptors as “self”
- Lymphocyte cells recognize microbe receptors as ‘non-self’

Major histocompatibility complex (MHC)

- Self-receptor
- Glycoprotein

- Found on all nucleated cells
- In humans – Human leukocyte antigen (HLA) is equivalent to the MHC
- Classes of MHC

Classes of MHC

- Each individual has a unique MHC profile
  - Expression of a particular combination of MHC genes
- Class I – all nucleated cells
- Class II – macrophages, dendritic cells, B cells

Clonal selection

- The synthesis of varied receptor types
  - approximately 500 genes undergo rearrangement
  - eventually one clone recognizes an antigen and expands (proliferates)
- Clone
  - each mature lymphocyte possesses a single combination or receptor specificity
- Expansion
  - a single cell is stimulated by antigen recognition
- Clonal deletion
  - cells that recognize self are removed

Lymphocytes

- Key cells controlling the immune response.
- They specifically recognize foreign material and distinguish it as non-self.
- There are two main types of lymphocytes: B cells and T cells.

B cells

- Develop in fetal liver and subsequently in the bone marrow.
- They are named after the bursa of Fabricius.
- Mature B cells carry surface immunoglobulins which act as their antigen receptor.
- They are distributed throughout the body.
- They respond to antigenic stimuli by dividing and differentiating into plasma cells.

T cells

- Develop in the thymus.
- It is seeded with lymphocytic stem cells.
- These develop T cell antigen receptors (TCRs) and differentiate into the two major T cell subsets- one with CD4, one with CD8.
- The T cell subsets each will bind to different MHC molecules.

B cell clone

- Application of immunology
- Propagate a single clone in order to synthesis monoclonal antibodies
- Monoclonal antibody
  - possess a single specificity for antigen

Receptors

- Present on B and T cells
  - Immunoglobulin molecule
    - Light chain
    - Heavy chain
    - Variable region
    - Constant region
- B cell receptors are secreted as antibodies

Antigens

- Foreign material
- Size and shape
- Alloantigens
- Superantigens

Foreign material

- Proteins and polypeptides
  - enzymes, cell surface structures, hormones, exotoxins)
- Lipids
  - cell membranes
- Glycoproteins
  - blood cell markers
- Nucleoproteins
  - DNA complexed to proteins
- Polysaccharides
  - capsules, LPS)

Size and shape

- Immunogen
  - Less than1000 daltons – no immune recognition
  - Greater than 1000 daltons – immune recognition
  - Proteins are better immunogens than polysaccharides
- Epitope
  - portion of the antigen (ex. Amino acids) recognized by lymphocyte receptor
- Haptens
  - antigens that are too small to elicit an immune response

Alloantigens

- Cell surface markers that occur in some members of the same species
  - blood typing (transfusion)
  - MHC profile (organ grafting)

Superantigen

- Bacterial toxins
- T cell activation much greater than normal antigens
- Large release of cytokines
- Results in toxic shock syndrome and some autoimmune diseases

B cells

- Activation
- Antibody
- Antibody-antigen interaction
- Response

Activation

- Clonal selection and binding of antigen
- Instruction by chemical mediators
- Transmission of signal to the nucleus
- B cell changes into a plasma cells and begins mitosis
- Clonal expansion and memory cell formation
- Antibody production and secretion

Antibody

- Product of B cell (plasma cell) activation
  - Immunoglobulin (Ig) or antibody
- Structure
  - Four polypeptides
  - Connected by disulfide bonds
  - Antigen binding fragment (Fabs)
  - Crystallizable fragment (Fc)
- Classes

Fab

- Variable (N-terminal of the heavy and light chains)
- Binds to the antigenic determinant
- Swiveling enables more efficient
- Held together by disulfide bonds

Fc

- Constant (C-terminal of heavy chain)
- Binds to macrophages
- Anchors Ig to lymphocyte
- Held together by disulfide bonds
- Responsible for class identification

Classes

- Isotypes – based on the Fc fragment
- Immunoglobulin (Ig)
  - IgM
  - IgG
  - IgA
  - IgD
  - IgE

IgM antibodies

- Pentamer
- 5-10% of serum antibodies
- Fix complement
- In blood, lymph, on B cells
- Agglutinates microbes; first Ab produced in response to infection
- Half-life = 5 days

IgG antibodies

- Monomer
- Memory cell response
- Most prevalent in tissue fluid and blood
- 80% of serum antibodies
- In blood, lymph, intestine
- Cross placenta
- Enhance phagocytosis; neutralize toxins & viruses; protects fetus & newborn
- Half-life = 23 days

IgA antibodies

- Dimer
- 10-15% of serum antibodies
- In secretions
- Mucosal protection
- Secretory IgA (mucous and serous secretions)
  - Local immunity
  - Salivary glands, intestine, nasal membrane, breast, lung, genitourinary tract
- Protection for newborns
- Half-life = 6 days

IgD antibodies

- Monomer
- 0.2% of serum antibodies
- In blood, lymph, on B cells
- On B cells, initiate immune response
- Half-life = 3 days

IgE antibodies

- Monomer
- 0.002% of serum antibodies
- On mast cells and basophils, in blood
- Fc portion binds to mast cells and basophils
  - release chemical mediators that aid inflammation
- Allergic reactions; lysis of parasitic worms
- Half-life = 2 days

Antibody-antigen interactions

- Opsonization
- Agglutination
- Neutralization
- Complement fixation
- Inflammation
- Antibody dependent cell-mediated cytotoxicity

Opsonization

- Microbes or particles coated with antibodies
- Enables macrophages to recognize and phagocytize microbe

Agglutination

- Antibodies cross-link cells or particles into clumps
- Renders microbes immobile
- Enhances phagocytosis
- Principle for certain immune tests (RBC typing)

Neutralization

- Antibody binds to
  - The microbe or virus receptor
  - Antigenic site of a molecule (Eg. Exotoxin)
- Prevents further binding of microbe or toxin

Complement fixation

- Antibodies interaction with complement proteins (Eg. Classical pathway)
- Lysis of microbial cell

Response

- Primary
- Secondary

Primary

- First exposure
  - Latent period
    - Lack of antibodies synthesis
  - Synthesis of antibodies
    - Level of synthesis (titer)
    - IgM first
    - Followed by IgG, and some IgA and IgM

Secondary

- Re-exposure to the same immunogen (Anamnestic response)
- Antibody synthesis, titer, and length of antibody persistence is rapid and amplified
  - Primarily due to memory cells

T cell

- Activation
- Types

Activation

- Cell-mediated immunity
- Antigen presenting cells
- Transformation

Cell-mediated immunity

- Direct involvement of T cells
- Produce and react to cytokines
- Activated simultaneously with B cell activation
- Subset of T cells have unique CD receptors (CD4, CD8)

Antigen presenting cells (APC)

- Macrophages and dendritic cells
  - Process and present antigen in association with MHC II
  - T cell CD receptor recognize antigen/MHC II

Transformation

- Activated T cells prepare for mitosis
- Effectors cells or types (T_H, T_C) are produced
- Memory cells are produced

Types

- Helper T cells (T_H)
- Cytotoxic T cells (T_C)

T_H

- Regulate immune reactions to antigens by releasing cytokines
- CD4 receptor
- Type of cytokine will determine subset of T_H
  - T_{H1} (activate other T cells, delayed type hypersensitivity)
  - T_{H2} (B cell differentiation)
- Cytokines also activate macrophages
- Most prevalent in the blood

T_C

- Binds and lyses cells (apoptosis)
  - microbe, viral infected cells, foreign cells, cancer cells
- CD8 receptor
- Perforins – punch holes in the membrane
- Granzymes – degrade proteins
- Natural killer (NK) cells
  - related to T_C

- attack virus infected cells and cancer cells

Specific Immunities

- Active
- Passive
- Natural
- Artificial
- Vaccines

Active

- Natural or artificial
- Antigen activates B and T cells
- Memory cells
- Long-term protection

Passive

- Natural or artificial
- Receive antibodies from another individual or animal
- No memory cells
- No antibody production
- Short-term protection

Natural

- Immunity produced by normal biological experiences, no medical intervention
  - Natural active
    - Eg. Infection
  - Natural passive
    - Eg. Mother to child

Artificial

- Immune protection through medical procedures or intervention
  - Artificial active
    - Eg. vaccination
  - Artificial passive
    - Eg. Immunotherapy

Vaccines

- Types
  - Killed whole cell or inactivated viruses
  - Live, attenuated cells or viruses
  - Antigenic molecules from bacteria or viruses
  - Genetically engineered microbes or microbial antigens

New vaccines

- DNA vaccines
  - Insert microbial DNA into plasmid

  - Inoculate recipient with plasmid
  - Host cell expresses microbial DNA
  - Immune system reacts to microbial antigen expressed on the host cell surface

Benefits of vaccinations

- Long-lasting immunity
- Herd immunity
  - Indirect protection of nonimmune
  - Prevents epidemics