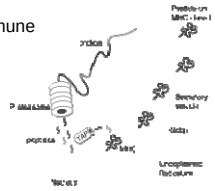
Immune System Function

Lecture Outline

- Immune System Basics & General Functions
- Functional Anatomy of the Immune System
- Physical and Chemical Barriers
- The Immune Response
  - Innate Immunity (non-specific)
  - Adaptive Immunity (acquired immunity)
- Pathogenic Differences
- Incompatibilities & Allergies

Immune System Basics

- Why do we need an immune system?
  - To protect against disease causing agents
    - Viruses, bacteria, fungi, protozoans, parasites…
- How does this work efficiently and without killin us?
  - The key to do this is recognition of what does belong in your body, or what is "self" vs. what does not belong in the body, or what is "foreign" (not self).
  - All "self" cells have a recognizable complement of surface markers
  - Foreign cells and structures have non-self markers which are capable of being recognized by our immune system
    - The component that is recognizable and initiates an immune response is the antigenic portion
  - Major Histocompatability Complexes (MHC) are molecules that present antigenic cytosolic components to the exterior for the purpose of initating an immune response
    - MHC-I which are found on all nucleated cells of the body
    - MHC-II which are found on macrophages, dendritic cells and B cells = antigen presenting cells (APCs)



Immune System General Functions

1. Protection from pathogens
   - May include microorganisms
     - Bacteria
     - viruses
     - Fungi
     - Protozoans
   - May also include macroorganisms
     - Parasites such as
       - Hookworms
       - Tapeworms
   - May also overzealously protect from non dangerous pathogens
     - Creates an allergic response

Immune System General Functions

2. Clean up!
   - Removal of dead and damaged cells and components
3. Recognition and removal of abnormal cells
   - Failure to do this can result in
     - Cancers
     - Autoimmune disorders

Lack of immune system response indicates immunodeficiency!

may be acquired through family genetics

may be acquired through infection

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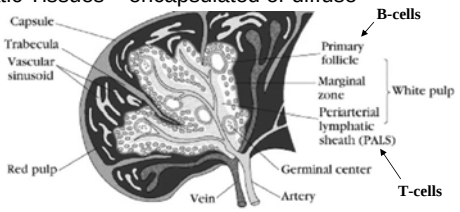
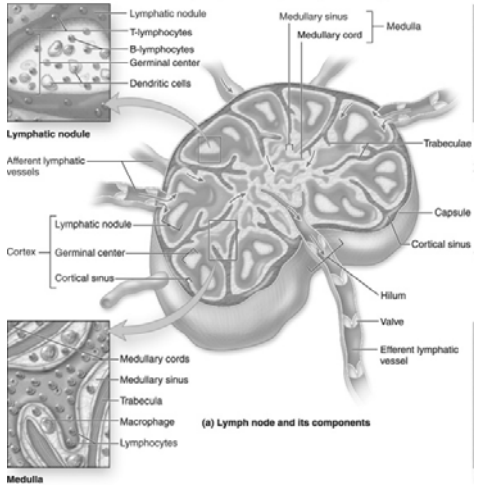
Functional Anatomy

- Highly integrated into other systems
- Two relatively identifiable aspects
  1. Lymphoid tissues
     - Primary Lymphatic Tissues – sites of production & maturation
       - Thymus
       - Bone marrow
     - Secondary Lymphatic Tissues – encapsulated or diffuse
       - Spleen
       - Lymph nodes
       - MALTs (diffuse)



Functional Anatomy



Functional Anatomy

2. Cells – Leukocytes & Derivatives

Types of Cells	 Basophils  Mast Cells	 Neutrophils	 Eosinophils	 Monocytes  Macrophages	 Lymphocytes  Plasma Cells	 Dendritic Cells
Classifications		Phagocytes				
		Granulocytes				
			Cytotoxic cells		Cytotoxic cells (some types)	
					Antigen-presenting cells	
% of WBCs in blood	Rare	50-70%	1-3%	1-6%	20-35%	NA
Subtypes and nicknames		Called "polys" or "segs." Immature forms called "bands" or "stabs."		Called the mononuclear phagocyte system	B lymphocytes Plasma cells Memory cells T lymphocytes Cytotoxic T cells Helper T cells Natural killer cells	Also called Langerhans cells, veiled cells
Primary function(s)	Release chemicals that mediate inflammation and allergic responses	Ingest and destroy invaders	Destroy invaders, particularly antibody-coated parasites	Ingest and destroy invaders. Antigen presentation	Specific responses to invaders, including antibody production	Recognize pathogens and activate other immune cells by antigen presentation

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Physical & Chemical Barriers

- Provide the 1st line of defense against pathogens
- Least specific
  - Physical/mechanical barriers
    - Skin
    - Mucus
    - Coughing/sneezing
    - Tears
    - Urination
  - Chemical barriers
    - Acid secretions
    - Sweat/Tears
    - Semen/Vaginal secretions
    - Respiratory enzymes
    - Salivary enzymes
    - Breast Milk enzymes

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The Immune Response

- Innate Immunity
  - 2nd line of defense
    - Phagocytosis – job of some leukocytes
      - Antigen presenting – specific function to activate specific immune responses (adaptive immunity)
    - NK cells
    - Cytokines
  - Macrophages, Monocytes, & Neutrophils that are both stationary and mobile
    - Must be able to recognize “non-self” aspects of pathogens & then initiate an appropriate response
      - Pathogen-Associated Mollecular Patterns (PAMPs)
        - » Allow for recognition of foreign structures from bacterial cell wall components and toxins to secretions and exposure of collage/fibrin from injured tissue area
        - » Bind to Pattern Recognition Receptors (PRRs)

The Immune Response

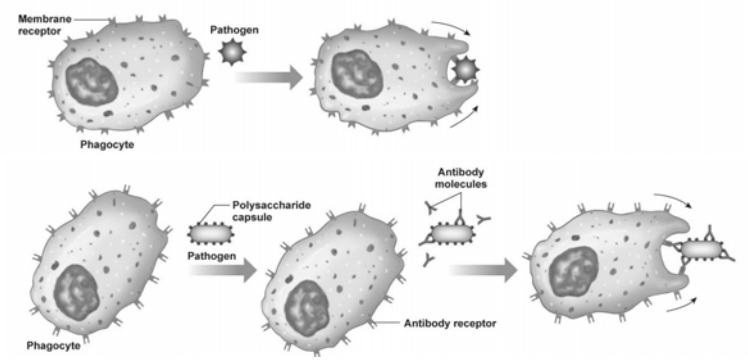
Innate Immunity

- Phagocytosis
  - Primarily the job of tissue macrophages and neutrophils
  - Options are
    - Bind and engulf pathogen directly by binding to PRRs on phagocyte
    - Pathogen gets coated (opsonized) by antibodies (Ab’s) which then bind to receptors on the phagocyte and iniatiate phagocytosis

The Immune Response

Innate Immunity

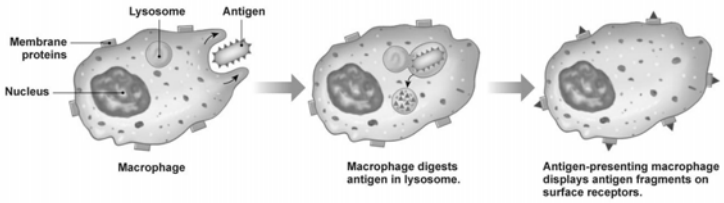
- Phagocytosis Options



The Immune Response

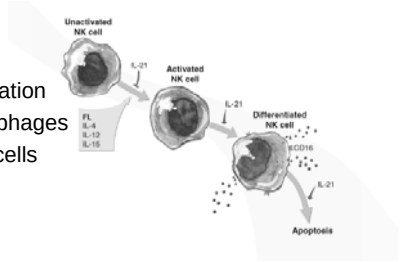
Innate Immunity

- Phagocytosis Options
  - Once the pathogen is ingested macrophages become antigen presenting cells (APCs)
    - This simply means that they process the pathogen internally and then insert the antigenic portion of the pathogen into their cell membrane and “present” it to lymphocytes
    - B lymphocytes and Dendritic cells are also capable of acting as APCs



The Immune Response
Innate Immunity

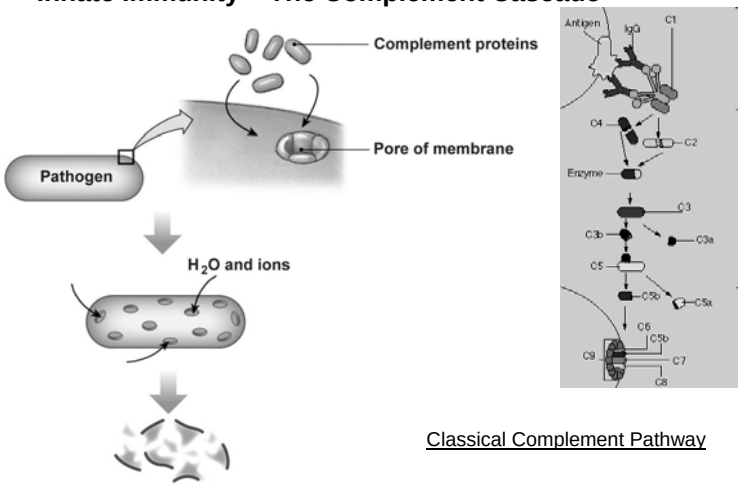
- Natural Killer Cells (NK cells)
  - A class of lymphocytes
    - Attack and induce cells to kill themselves (self induced apoptosis)
    - May also attack some tumor cells
    - Also secrete
      - Interferons
        - » Mess up viral replication and activate macrophages and other immune cells



The Immune Response
Innate Immunity

- Cytokine Function
  - Inflammation
    - Attracts additional immune cells
    - Increases physical barrier effectiveness
    - Promotes tissue repair upon removal of infectious agent
    - The cytokine players
      - Acute-phase proteins
        - » Appear quickly after injury or infection
        - » Molecules produced by the liver that act as opsonins, antiprotease molecules and C-reactive protein (involved in atherosclerotic thrombus formation – released by foam cells)
      - Histamine
        - » local vasodilator and attracts leukocytes
        - » Produced by mast cells & basophils
      - Interleukins
        - » Chemical messengers involved in communication among leukocytes
      - Bradykinin
        - » Vasodilator & pain receptor stimulator
      - Complement Proteins
        - » Cascading activation that ends with insertion of a "membrane attack complex" into the target cell, causing death by lysis

The Immune Response
Innate Immunity – The Complement Cascade



Classical Complement Pathway

The Immune Response
Adaptive Immunity

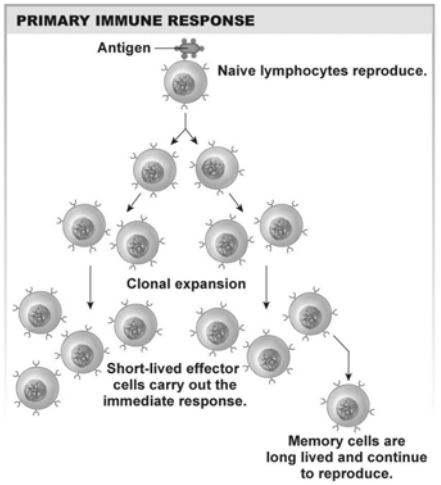
- Functions of Adaptive Immunity
  1. Recognition of "non-self" antigens from "self"
  2. Generate a tailored response to eliminate specific antigen
  3. Development of immunological memory
- Adaptive Immune responses refer to an antigen-specific response. This requires:
  - Processing the pathogen
  - Presenting the Ag to B and T cells
  - After presentation options are
    - Produce antibodies
    - Activate cytotoxic T cells
  - Creation of memory cells for long lasting immunity
- Why is adaptive?
  - Because of the capacity to generate immune responses for the nearly endless varieties of antigens
    - Through the process of recombining antigen receptor gene segments based on the antigen presented to the system

The Immune Response
Adaptive Immunity

- The players
  - B cells
    - Involve in humoral immunity
    - Differentiate into
      - plasma cells which produce antibodies for the specific antigen
      - Memory cells to provide immunological memory
  - T cells
    - cell-mediated immunity
    - Types of T cells
      - CD4 T cells or T helper cells of which there are two types
        - » Th1 and Th2
      - CD8 T cells (T killer or cytotoxic T cells)
      - NK cells (natural killer cells)
        - » Provide the “link” between innate and adaptive immunity
      - T memory cells – provide?

The Immune Response
Adaptive Immunity

- The general process:



The Immune Response
Adaptive Immunity

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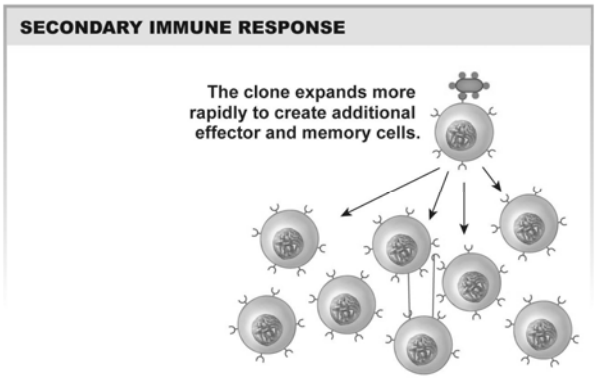

The Immune Response
Adaptive Immunity

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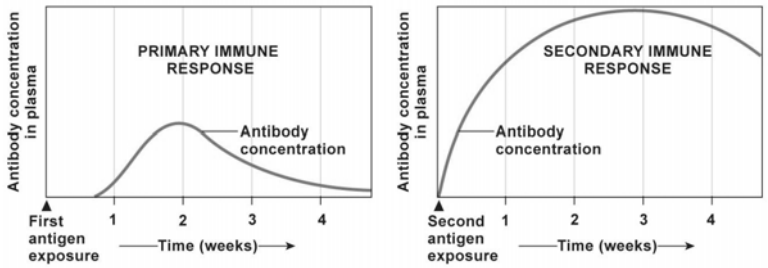
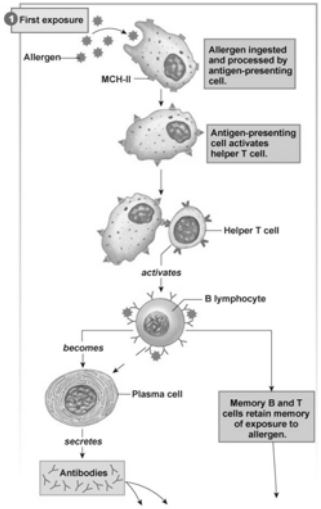


The Immune Response
Adaptive Immunity

- The general process:
  - Antigen is processed and presented
  - CD4 (T helper) cells are activated
  - B cells are activated by CD4 cells and
    - Differentiate into
      - Plasma cells
        - » Produce clonal antibodies
        - » Produce memory cells

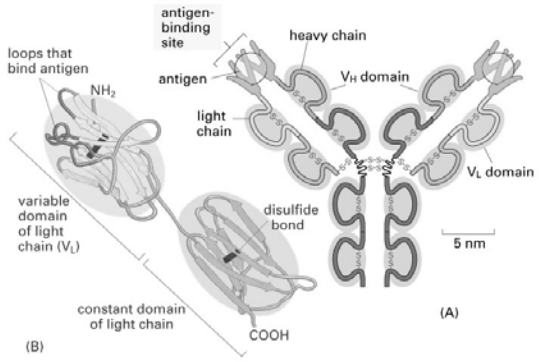
The Immune Response
Adaptive Immunity

The general process:



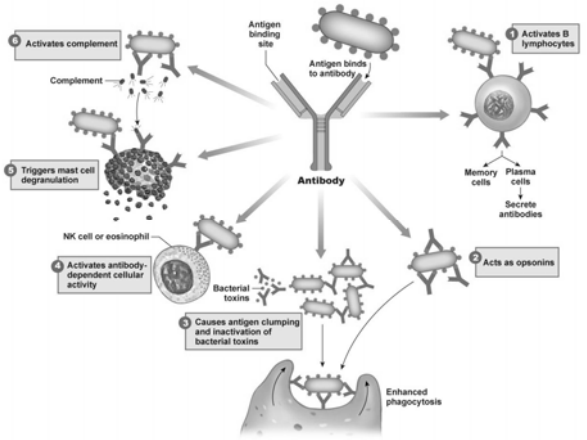
The Immune Response
Adaptive Immunity

- Antibody Structure:



The Immune Response
Adaptive Immunity

Antibody Function:



The Immune Response

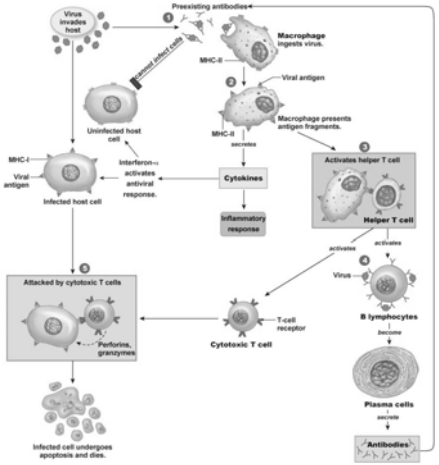
Antibody Types & Functions

Name	Description
IgA	Found in mucosal areas, such as the gut, respiratory tract and urogenital tract, and prevents colonization by pathogens. Also found in saliva, tears, and breast milk.
IgD	Functions mainly as an antigen receptor on B cells that have not been exposed to antigens. It has been shown to activate basophils and mast cells to produce antimicrobial factors.
IgG	In its four forms, provides the majority of antibody-based immunity against invading pathogens. The only antibody capable of crossing the placenta to give passive immunity to fetus.
IgE	Binds to allergens and triggers histamine release from mast cells and basophils, and is involved in allergy. Also protects against parasitic worms.
IgM	Expressed on the surface of B cells and in a secreted form with very high avidity. Eliminates pathogens in the early stages of B cell mediated (humoral) immunity before there is sufficient IgG.

The Immune Response

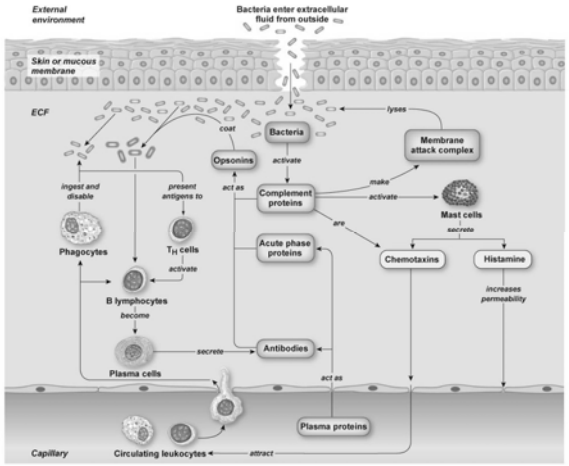
Adapative Immunity

- T cell activation



The Immune Response

The Integrated View



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The Immune Response
Pathological Differences

- What are the differences between the two major pathological entities?
  - Bacteria Vs. Viruses
    - Bacteria – 10x the bacteria as there are cells in the human body
      - Most are non-pathogenic
      - Those that are produce toxins/by products of bacterial growth and metabolism
    - Viruses – disrupt cell function by taking over the cell's DNA creating a virus producing machine

The Immune Response
Incompatabilities & Allergies

- What happens when things go wrong?
  - Incompatibility?
  - Allergies?