* **Immunology**
  + Study of the components and function of the immune system
* **Immune System** 
  + Molecules, cells, tissues and organs which provide non-specific and specific protection against
    - Microorganisms
    - Microbial toxins
    - Tumor cells
  + Crucial to human survival
* Active
  + Antigens enter body naturally with response of
    - Innate and adaptive immune systems
  + Provides long term protection
* Passive
  + Antibodies pass from mother to
    - Fetus across placenta
    - Infant in breast milk
  + Provides immediate short term protection

PRINCIPAL FUNCTION OF THE IMMUNE SYSTEM

* To protect humans from pathogenic microorganisms
* Pathogenic microorganisms (Pathogens)
  + Microorganisms capable of causing infection and/or disease
* Infection
  + Ability of pathogen to enter host, multiply and stimulate an immune response
* Disease
  + Clinical manifestations associated with infection

DEFENSE MECHANISMS OF THE HUMAN HOST

* **Innate Mechanisms (Innate immunity)**
  + First line of defense
  + Non-specific
* **Adaptive Mechanisms (Adaptive immunity)**
  + Second line of defense
  + Highly specific with memory
* **Cooperation between mechanisms**

ORIGIN OF CELLS OF THE IMMUNE SYSTEM

* **Derived from common progenitor cell in bone marrow**
  + Pluripotent hematopoietic stem cell
* **Progenitor Stem Cells**
  + Erythroid lineage
    - Erythrocytes and Megakaryocytes
  + Myeloid lineage
    - Monocyte/macrophage, dendritic cells, PMN’s, mast cells
  + Lymphoid lineage
    - Small and large lymphocytes

CELLS OF INNATE AND ADAPTIVE IMMUNITY

* **Myeloid Lineage** 
  + Neutrophil
    - Principal phagocytic cell of innate immunity
  + Eosinophil
    - Principal defender against parasites
  + Basophil
    - Functions similar to eosinophils and mast cells
  + Referred to as
    - Polymorphonuclear leukocytes (PMN’s)
      * Nuclei are multilobed (2 to 5)
    - Granulocytes
      * Cytoplasmic granules

CELLS OF INNATE AND ADAPTIVE IMMUNITY

* **Myeloid lineage** 
  + Monocytes
    - Leukocytes with bean shaped or brain-like convoluted nuclei
    - Circulate in blood with half life of 8 hours
    - Precursors of tissue macrophages
  + Macrophages
    - Mononuclear phagocytic cells in tissue
    - Derive from blood monocytes
    - Participate in innate and adaptive immunity

Myeloid lineage

Dendritic cells

Cells with dendriform (star shaped) morphology

Interdigitating reticular cells (synonym)

Capture and present antigens to T lymphocytes

Mast cells

Located in mucous membrane and connective tissue throughout body

Major effector cell in allergy

* Modulation of initial immune respon**Lymphoid Lineage**
  + Large lymphocytes (large granular lymphocytes)
    - Natural killer (NK) cells (CD16, CD56)
    - Innate immunity to viruses and other intracellular pathogens
    - Participate in antibody-dependent cell-mediated cytotoxicity (ADCC)
  + Small lymphocytes
    - B cells (CD19)
    - T cells (CD3, CD4 or CD8)
    - Adaptive immunity
  + Lymphocytes refers to small lymphocytes

se**Erythrocytes (RBC) 4.0 to 5.4 M/uL**

**Thrombocytes (Platelets) 145 to 400 K/uL**

**Leukocytes (WBC) 4.8 to 10.8 K/uL**

**Neutrophils 40 to 74 %**

**Band neutrophils 0 to 9**

**Eosinophils 0 to 6**

**Basophils 0 to 1**

**Lymphocytes 15 to 47**

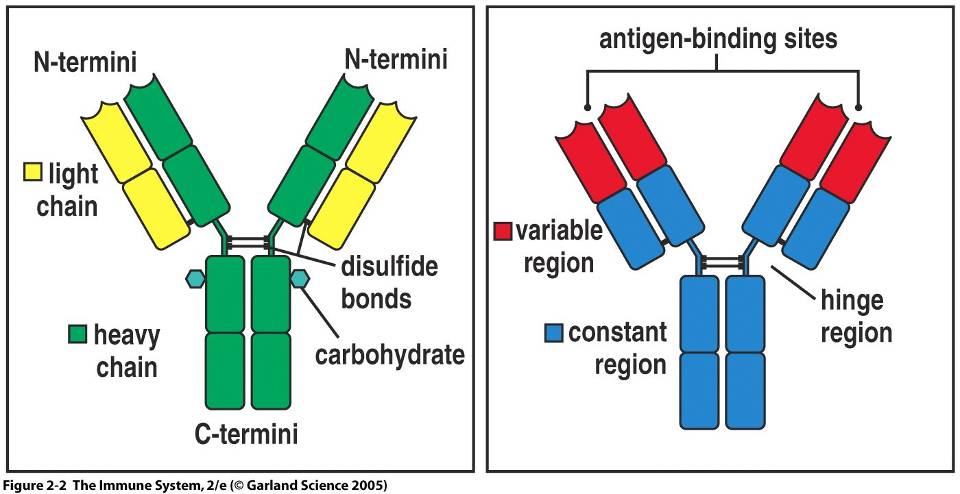
**Monocytes 0 to 12**

LYMPHOCYTES, LYMPHOID TISSUES AND ORGANS

* **Lymphocytes originate in bone marrow**
* **Lymphoid tissues and organs**
  + Primary
    - Development and maturation of lymphocytes
    - Bone Marrow (B cells) and thymus gland (T cells)
  + Secondary
    - Mature lymphocytes meet pathogens
    - Spleen, adenoids, tonsils, appendix, lymph nodes, Peyer’s patches, mucosa-associated lymphoid tissue (MALT)

THE LYMPHATIC SYSTEM

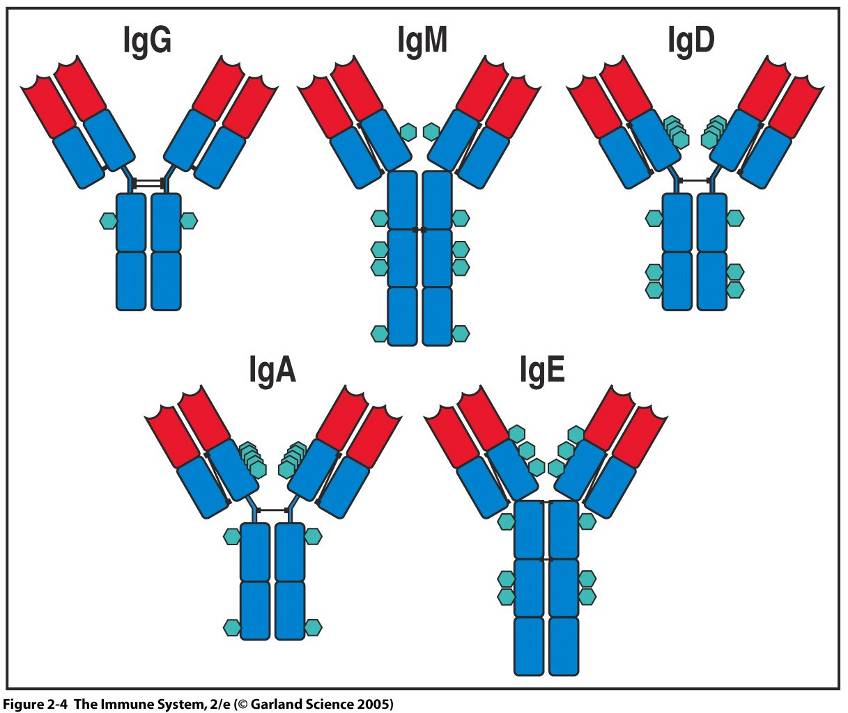
* **Lymph**
  + Fluid and cells in lymphatic vessels
* **Lymphatic vessels**
  + Collect and return interstitial fluid to blood
  + Transport immune cells throughout body
  + Transport lipid from intestine to blood
* **Lymph nodes** 
  + Kidney shaped organs at intervals along lymphatic vessels
* **Other secondary lymphatic tissues and organs**
* **Lymph**
* Fluid and cells in lymphatic vessels
* **Lymphatic vessels**
* Collect and return interstitial fluid to blood
* Transport immune cells throughout body
* Transport lipid from intestine to blood
* **Lymph nodes**
* Kidney shaped organs at intervals along lymphatic vessels
* **Other secondary lymphatic tissues and organs**
* LYMPHOCYTES AND THE LYMPH NODES
* Naïve lymphocytes circulate between blood, lymph and secondary lymph nodes
* Pathogens from infected tissue sites are picked up by lymphatic vessels and arrive at closest lymph node
* T and B cells congregate at specific regions of nodes
* Architecture and size of nodes change in response to activation of lymphocytes
* **Spleen**
* Lymphoid organ in upper left abdomen
* Functions
* Remove damaged or old erythrocytes
* Activation of lymphocytes from blood borne pathogens
* **Architecture of Spleen**
* Red pulp
* Erythrocytes removed
* White pulp
* Lymphocytes
* SECONDARY LYMPHOID TISSUES ASSOCIATED WITH MUCOUS MEMBRANES
* **Primary portals of entry for pathogens**
* Respiratory tract
* Gastrointestinal tract
* **Secondary lymphoid tissues**
* Bronchial-associated lymphoid tissue (BALT)
* Gut-associated lymphoid tissues (GALT)
* Tonsils, adenoids, appendix, Peyer’s patches
* **Pathogens are directly transferred across mucosa by “M” cells**
* THE INNATE IMMUNE RESPONSE
* Mediated (initiated) by phagocytes, NK cells and soluble proteins
* Phagocytes
* Cells specialized in the process of phagocytosis
* Macrophages
* Reside in tissues and recruit neutrophils
* Neutrophils
* Enter infected tissues in large numbers
* Recognize common molecules of bacterial cell surface using a few surface receptors
* Phagocytosis
* Capture, engulfment and breakdown of bacterial pathogen
* Inflammatory response enhances phagocytosis through acute phase proteins
* Mannose-binding lectin (MBL)
* Binds to bacterial surface with particular spatial arrangement of mannose or fucose
* C-reactive protein (CRP)
* Binds to phosphorylcholine on bacterial surface
* Complement
* Set of proteins which bind to bacterial surface
* Inflammatory response
* Accumulation of fluid and cells at infection site (swelling, redness, heat and pain)
* THE ADAPTIVE IMMUNE RESPONSE
* Creates millions of different B and T cells for specific antibody-mediated and cell-mediated immunity
* Antibody-Mediated Immunity (AMI)
* Involves B lymphocytes, plasma cells and antibodies
* Humoral immunity
* Name derives from antibodies found in body fluids (humors - old medical term)
* Cell-Mediated Immunity (CMI)
* Involves T lymphocytes, antigen-presenting cells and MHC (major histocompatibility complex) molecules
* Cellular immunity
* ANTIBODY-MEDIATED (HUMORAL) IMMUNITY
* Directed against extracellular microorganisms and toxins
* B-lymphocytes (B cells)
* Differentiate into plasma cells which produce antibodies
* Function as antigen-presenting cells (APC’s)
* Classification of Antibodies (Immunoglobulins)
* Immunoglobulin M (IgM)
* Immunoglobulin G (IgG)
* Immunoglobulin A (IgA)
* Immunoglobulin D (IgD)
* Immunoglobulin E (IgE)
* CELL-MEDIATED IMMUNITY (CMI
* Directed against intracellular microorganisms
* Non-phagocytic cells and phagocytic cells
* T-lymphocytes (T cells)
* Differentiate into effector cells following antigen presentation by antigen presenting cells (APC’s)
* Functional types of T cells
* Helper (CD4 T cells)
* TH1 and TH2 cells
* Cytotoxic (CD8 T cells)
* Regulatory
* CD4 and CD8 Tregs
* ANTIGEN
* Historically named as **anti**body **gen**erators
* Molecule which stimulates production of and binds specifically to an antibody
* Contemporary view distinguishes between
* Antigen
* Molecule which can bind to specific antibody but cannot elicit adaptive immune response
* Immunogen
* Molecule which can stimulate adaptive immune response
* Best immunogens are proteins with   
  MW > 10,000
* Carbohydrates, nucleic acids and lipids are also potential antigens / immunogens
* Hapten
* Small (low MW) molecule unable to elicit immune response
* Combines with larger carrier molecule which together function as immunogen
* Antibody may react independently with hapten following hapten/carrier adaptive immune response
* Example
* Penicillin G (MW of 372)
* Albumin (MW of 66,000)
* THE NATURE OF ANTIBODIES
* Antibodies are glycoproteins
* Exist as monomers, dimers or pentamers of basic structure
* Basic antibody structure has 4 polypeptide chains
  + 2 identical light chains
  + 2 identical heavy chains
* Regions of heavy and light chains
  + Variable
  + Constant



* Also referred to as
  + Immune globulins / Immunoglobulins (IG)
  + Immune serum globulins (ISG)
  + Gamma globulins
* Contemporary immunology
  + Antibody
    - Secreted form of IG made by plasma cells
  + Immunoglobulin
    - Antigen binding molecules of B cells
      * (B cell antigen receptors)

CLASSIFICATION OF ANTIBODIES (IMMUNOGLOBULINS

* Five (5) classes (isotypes)
  + Immunoglobulin A (IgA)
  + Immunoglobulin G (IgG)
  + Immunoglobulin M (IgM)
  + Immunoglobulin D (IgD)
  + Immunoglobulin E (IgE)
* Based on structural differences in constant regions of heavy chains
* Classes have specialized effector functions



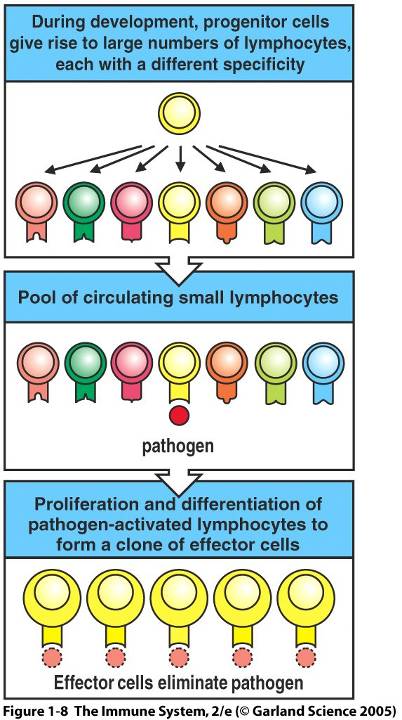
B LYMPHOCYTES AND   
HUMORAL IMMUNITY

* Originate from stem cells in bone marrow
* Maturation in bone marrow followed by migration to secondary lymphoid tissue
* Antigen exposure in secondary lymphoid tissue
* Following exposure to antigen, differentiation into plasma cells and memory cells
* Plasma cells produce antibodies of all IG classes

ACTIVATION OF ANTIBODY PRODUCING CELLS BY CLONAL SELECTION

* B lymphocytes recognize intact pathogenic microorganisms and toxins
* B lymphocytes possess specific surface receptors for recognition of specific antigen
  + IgM and IgD
* Binding of specific antigen results in proliferation of a clonal population of cells
* Antigen determines clonal proliferation

ACTIVATION OF ANTIBODY PROCDUCING CELLS BY CLONAL SELECTION



ACTIVATION OF ANTIBODY PROCDUCING CELLS BY CLONAL SELECTION

Proliferation of activated cells is followed by differentiation into

Plasma cells

Life span of

4 to 5 days

1 to 2 months

Produce 2,000 antibody molecules / second

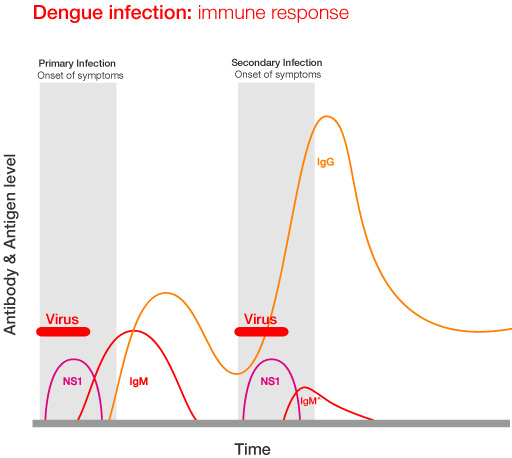
Memory cells

Life span of years to decades

Differentiate into plasma cells following stimulation by same antigen

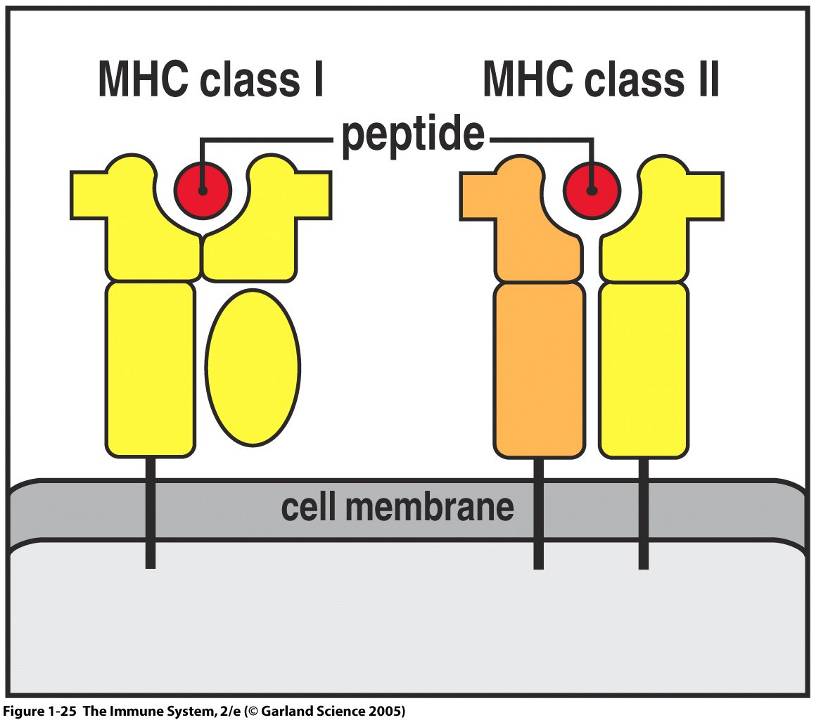
PRIMARY AND SECONDARY ANTIBODY RESPONSE

* Primary Response
  + Following exposure to an antigen, there is a slow rise in IgM followed by a slow rise in IgG
* Secondary Response
  + Following exposure to previously encountered antigen, there is a rapid rise in IgG and slow or no rise in IgM
    - Memory or anamnestic response



T LYMPHOCYTES AND CELL-MEDIATED IMMUNITY

* Originate from stem cells in bone marrow followed by migration to thymus gland
* Maturation takes place in thymus gland followed by migration to secondary lymphoid tissue
* Respond to antigens on the surface of antigen presenting cells (APC’s)
* Antigen presenting cells (APC’s)
  + Macrophages
  + Dendritic cells
  + B lymphocytes
* Antigen presenting cells (APC’s)
  + Ingest and process antigens then display fragments (short peptides) on their surface in association with molecules of major histocompatibility complex (MHC)
* Major histocompatibility (MHC) molecules
  + MHC class I molecules
    - Present antigens to CD8 T cells
  + MHC class II molecules
    - Present antigens to CD4 T cells
* T cells which encounter antigen differentiate into effector T cells



* CD8 cytotoxic T cells
  + Enter bloodstream and travel to infection site
  + Kill cells infected with viruses and other intracellular microorganisms
* CD4 TH1 helper T cells
  + Enter blood stream and travel to infection site
  + Help activate macrophages
* CD4 TH2 helper T cells
  + Work within secondary lymphoid tissues
  + Help activate B cells
  + 