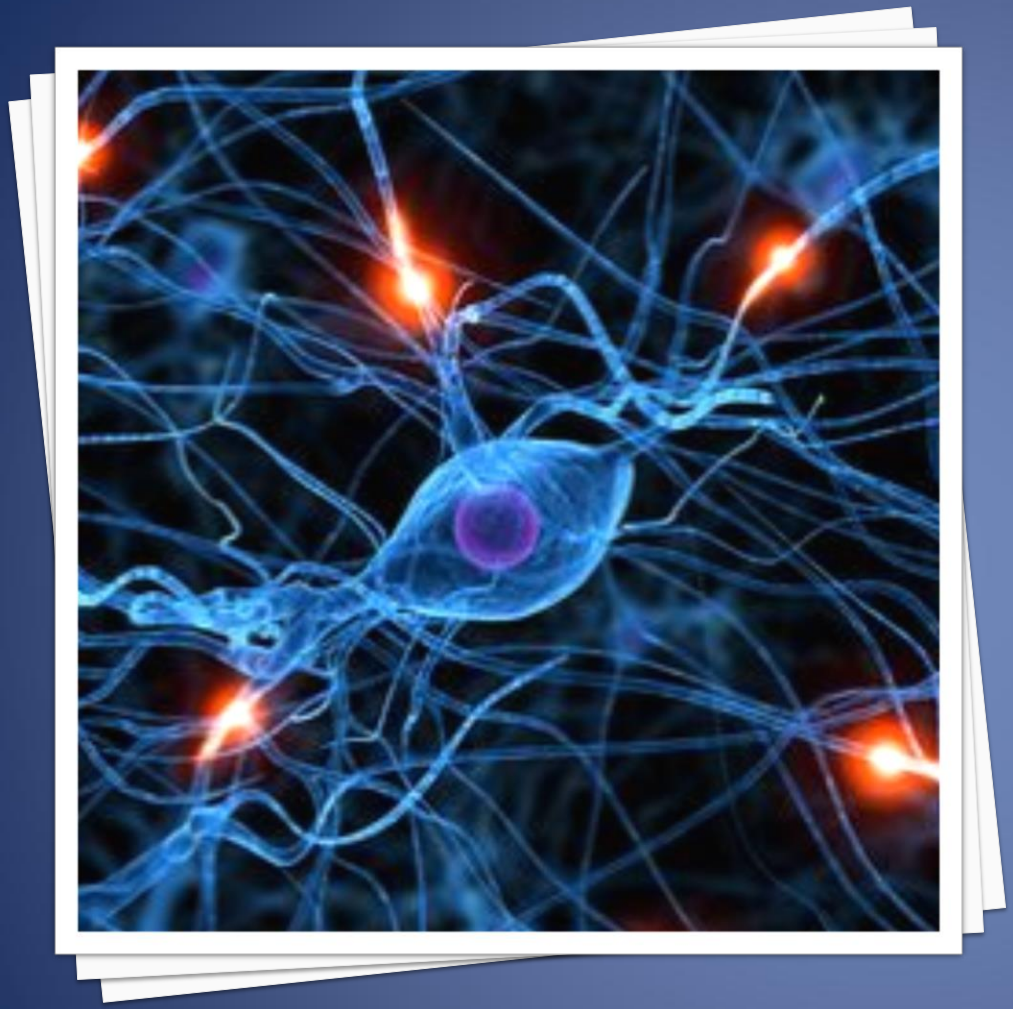


GENERAL BIOLOGY
IMMUNE SYSTEM

IMMUNE SYSTEM: (1) ORGANS

- Tonsils and adenoids
- Thymus
- Lymph nodes
- Spleen
- Payer's patches
- Appendix
- Lymphatic vessels
- Bone marrow

Immune system: (2) cells

- Lymphocytes
  - T-lymphocytes
  - B-Lymphocytes, plasma cells
  - natural killer lymphocytes
- Monocytes, Macrophage
- Granulocytes
  - neutrophils
  - eosinophils
  - basophils

IMMUNE SYSTEM: (3) MOLECULES

- Antibodies
- Complement
- Cytokines
- Interleukines
- Interferons

TWO TYPES OF IMMUNITY

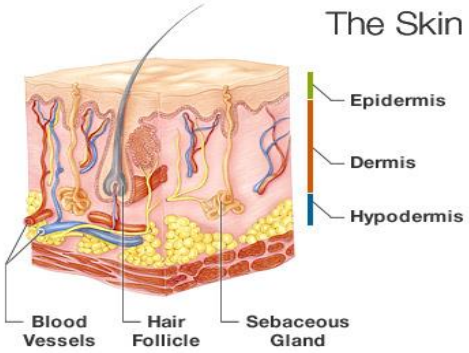
1. Innate (non-adaptive)
   - first line of immune response
   - relies on mechanisms that exist before infection
2. Acquired (adaptive)
   - Second line of response (if innate fails)
   - relies on mechanisms that adapt after infection
   - handled by T- and B- lymphocytes
   - one cell determines one antigenic determinant

INNATE IMMUNITY

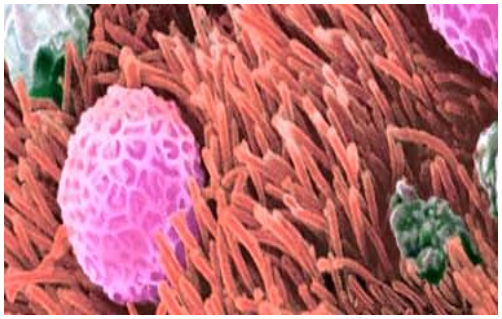
- Based on genetic make-up
- Relies on already formed components
- Rapid response: within minutes of infection
- Not specific
  - same molecules / cells respond to a range of pathogens
- Has no memory
  - same response after repeated exposure
- Does not lead to clonal expansion

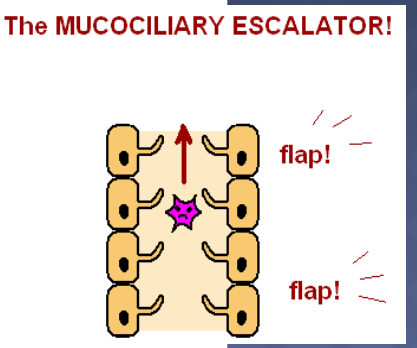
ANATOMICAL BARRIERS - MECHANICAL FACTORS

- Skin

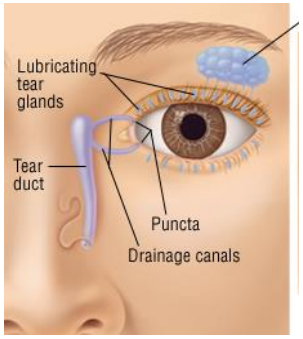


- Mucociliary escalator





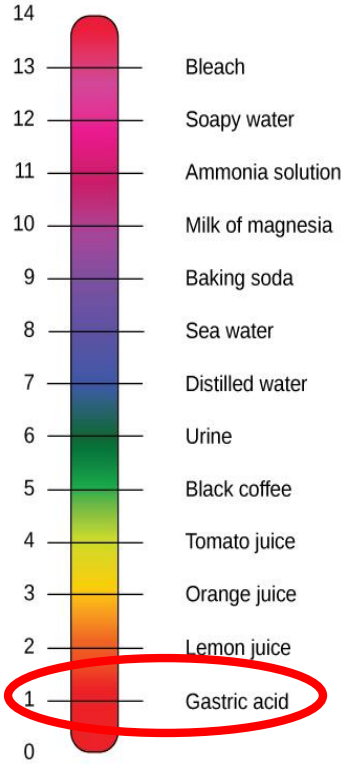
- Flushing action of saliva, tears, urine



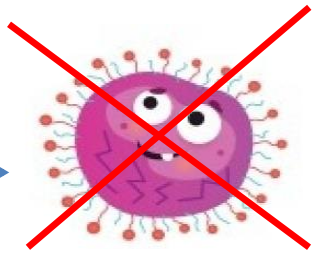
ANATOMICAL BARRIERS – CHEMICAL FACTORS

Antimicrobial Peptides in sweat

HCl in stomach



Lysozyme in tears /saliva

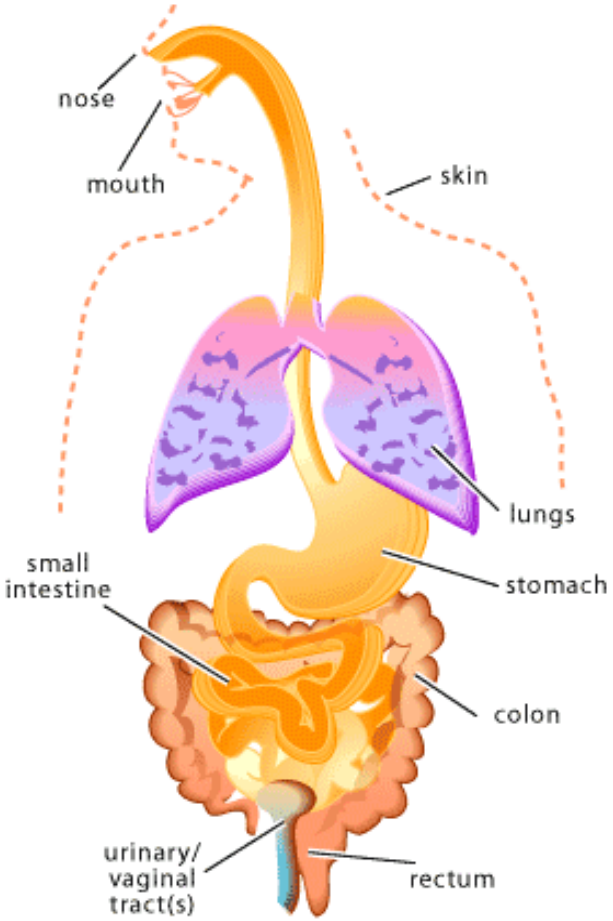


ANATOMICAL BARRIERS – BIOLOGICAL FACTORS

Normal flora – microbes in many parts of the body

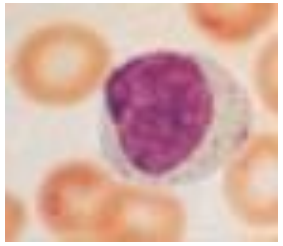
Normal flora – > 1000 species of bacteria

Normal flora – competes with pathogens for nutrients and space

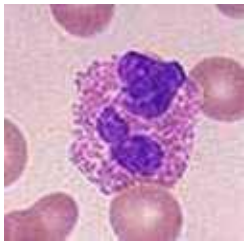


INNATE IMMUNITY: MECHANISMS

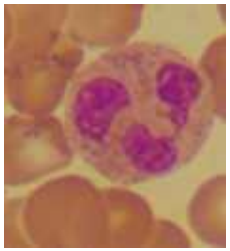
- Mechanical barriers / surface secretion
  - skin, acidic pH in stomach, cilia
- Humoral mechanisms
  - lysozymes, basic proteins, complement, interferons
- Cellular defense mechanisms
  - natural killer cells neutrophils, macrophages,, mast cells, basophils, eosinophils



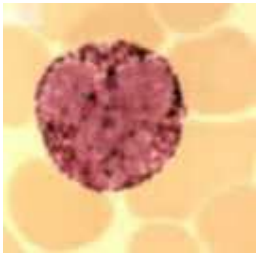
NK Cell



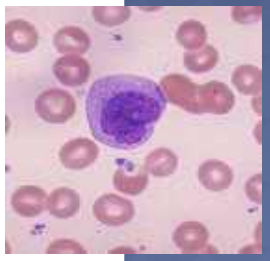
Eosinophils



Neutrophil



Basophils & Mast cells



Monocyte Macrophage

Adaptive Immunity: Second Line of Response

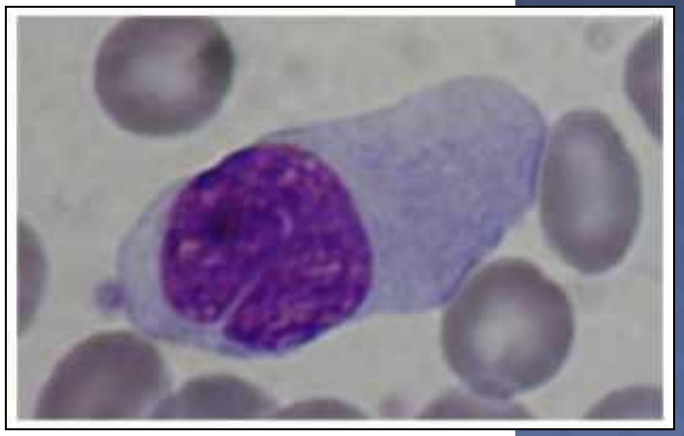
- Based upon resistance acquired during life
- Relies on genetic events and cellular growth
- Responds more slowly, over few days
- Is specific
  - each cell responds to a single epitope on an antigen
- Has anamnestic memory
  - repeated exposure leads to faster, stronger response
- Leads to clonal expansion

Adaptive Immunity: Active and Passive

	Active Immunity	Passive Immunity
Natural	clinical, sub-clinical infection	via breast milk, placenta
Artificial	Vaccination: Live, killed, purified antigen vaccine	immune serum, immune cells

ADAPTIVE IMMUNITY: MECHANISMS

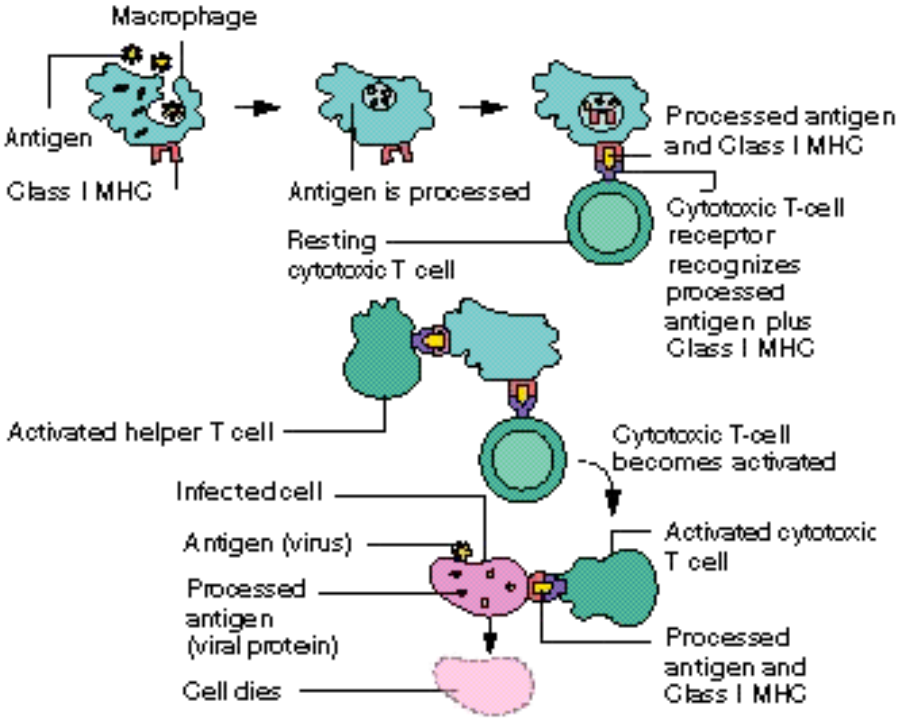
- Cell-mediated immune response (CMIR)
  - T-lymphocytes
  - eliminate intracellular microbes that survive within phagocytes or other infected cells
- Humoral immune response (HIR)
  - B-lymphocytes
  - mediated by antibodies
  - eliminate extra-cellular microbes and their toxins



Plasma cell
(Derived from B-lymphocyte, produces antibodies)

CELL-MEDIATED IMMUNE RESPONSE

1. T-cell
   - recognizes peptide antigen on macrophage in association with major histo-compatibility complex (MHC) class
   - identifies molecules on cell surfaces
   - helps body distinguish self from non-self
2. T-cell goes into effectors cells stage that is able to kill infected cells



T LYMPHOCYTES

2 types

- helper T- lymphocytes (CD4+)
  - CD4+ T cells activate phagocytes to kill microbes
- cytolytic T-lymphocyte (CD8+)
  - CD8+ T cells destroy infected cells containing microbes or microbial proteins

CELL MEDIATED IMMUNE RESPONSE

Primary response

- production of specific clones of effector T cells and memory clones
- develops in several days
- does not limit the infection

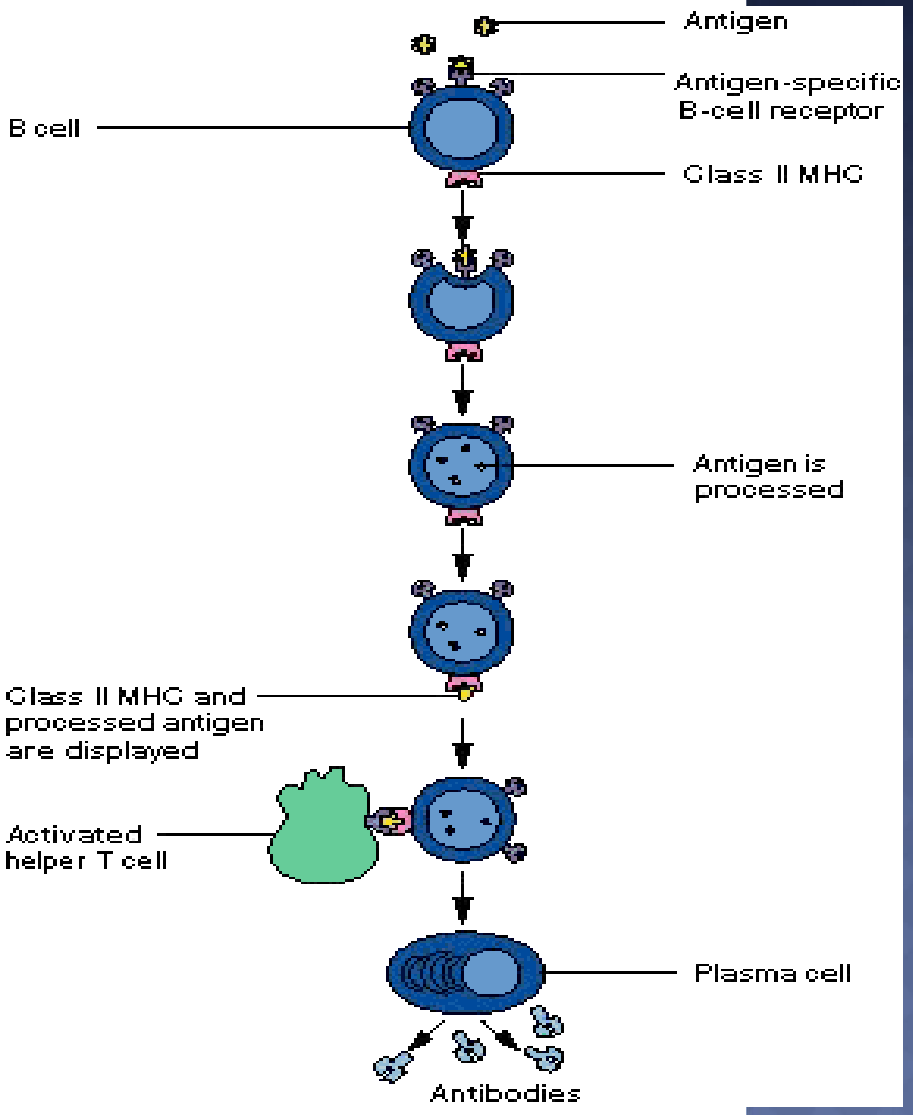
Secondary response

- more pronounced, faster
- more effective at limiting the infection

Example - cytotoxic reactions against intracellular parasites, delayed hypersensitivity (e.g., Tuberculin test) and allograft rejection

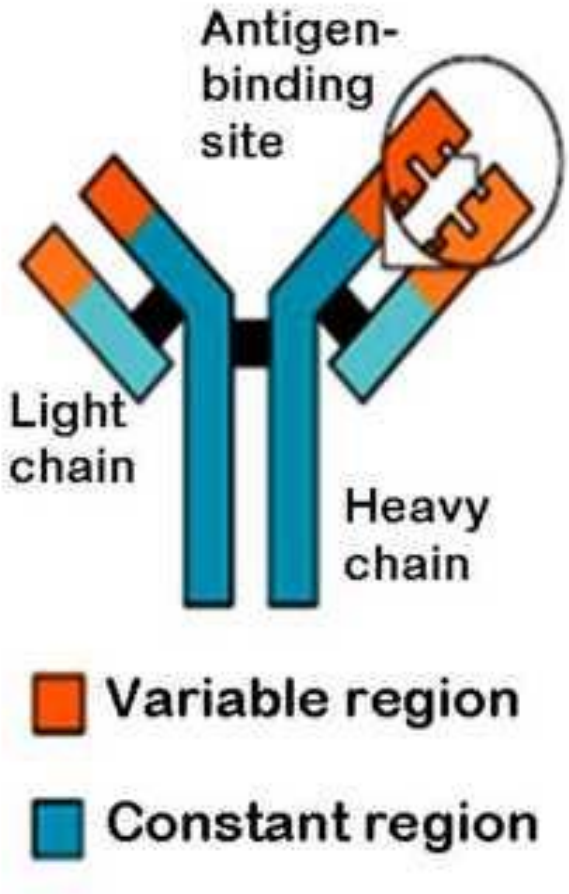
HUMORAL IMMUNE RESPONSE

1. B lymphocytes recognize specific antigens
   - proliferate and differentiate into antibody-secreting plasma cells
2. Antibodies bind to specific antigens on microbes; destroy microbes via specific mechanisms
3. Some B lymphocytes evolve into the resting state - memory cells



ANTIBODIES (IMMUNOGLOBULINS)

- Belong to the gamma-globulin fraction of serum proteins
- Y-shaped or T-shaped polypeptides
  - 2 identical heavy chains
  - 2 identical light chains
- All immunoglobulins are not antibodies
- Five kinds of antibodies
  - IgG, IgM, IgA, IgD, IgE



IGG

- 70-75% of total immuniglobulin
- Secreted in high quantities in secondary exposures
- Cross the placenta
- Major functions / applications
  - neutralize microbes and toxins
  - opsonize antigens for phagocytosis
  - activate the complement
  - protect the newborn

- 4-fold rise or fall indicates active infection
- A single positive sample indicates past exposure

IGM

- Secreted initially during primary infection
- Cannot cross the placenta
- Major functions / applications
  - secreted first during primary exposure
  - activates the complement
  - used as a marker of recent infection

- Presence in newborn means infection
- Single positive sample in serum or CSF indicates recent or active infection
- Used to detect early phase of infection

IGA

- Monomeric in serum
- Dimeric with secretory component in the lumen of the gastro-intestinal tract and in the respiratory tract
- Major function / application
  - neutralizes microbes and toxins

- Sero-diagnosis of tuberculosis
- Synthicial respiratory virus tests

IgD

- Monomeric
- Major functions / applications
  - present on the surface of B lymphocytes
  - functions as membrane receptor
  - role unclear
    - has a role in antigen stimulated lymphocyte differentiation

IgE

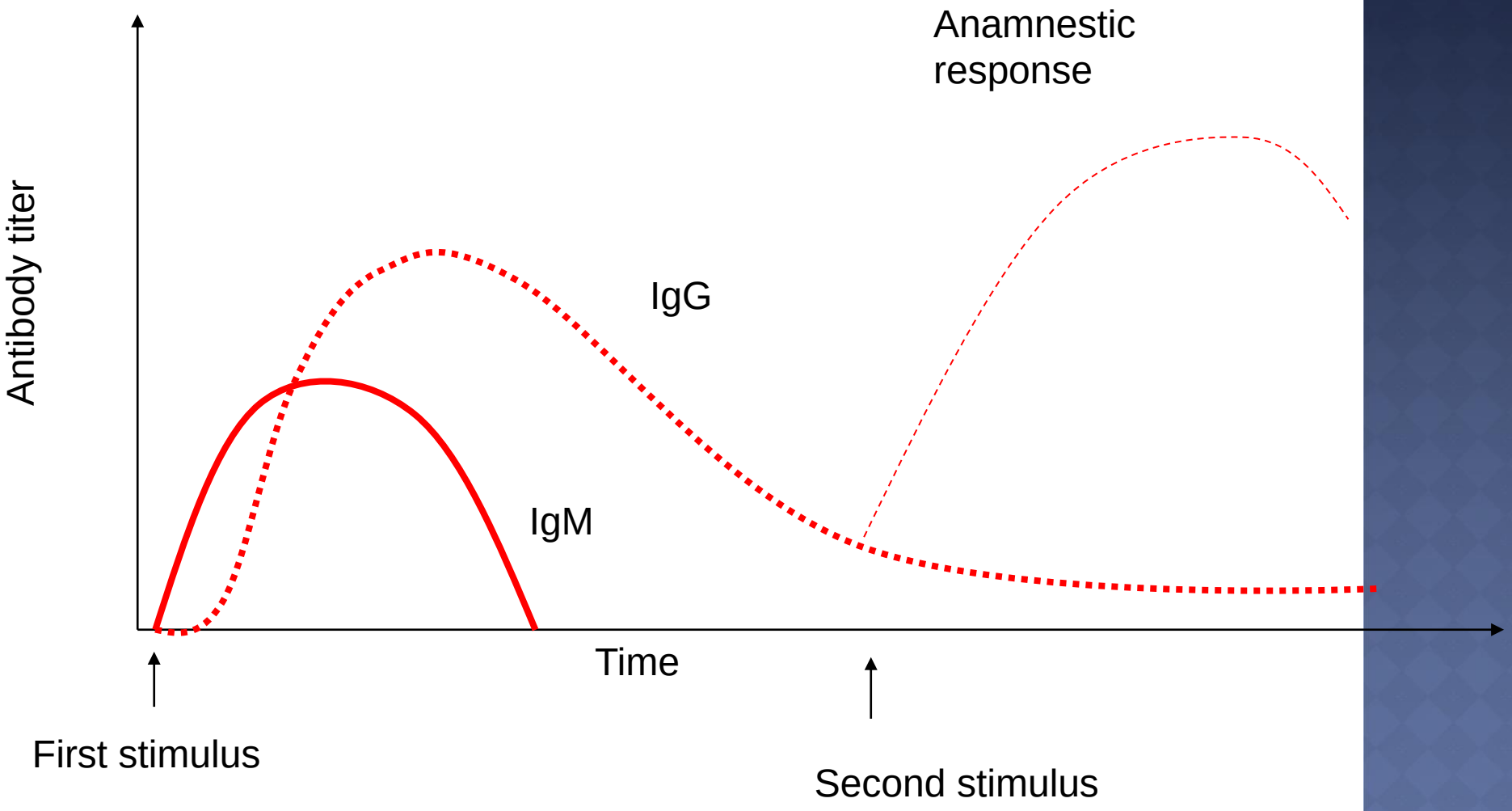
- Mediates type I hypersensitivity
- Monomeric
- Major functions / applications
  - associated with anaphylaxis
  - plays a role in immunity to helminthic parasites

Serodiagnosis of infectious and non infectious allergies (e.g., allergic bronchopulmonary aspergillosis, parasitic diseases)

SEQUENTIAL IGM-IGG HUMORAL RESPONSE

- IgM
  - produced as a first response to many antigens
  - levels remain high transiently
- IgG
  - produced after IgM
  - higher levels persist in small amounts throughout life
  - produced in large amounts during secondary response
    - persistence of antigen sensitive ‘memory cells’ after primary response

IGM - IGG SEQUENTIAL RESPONSE



FAILURE OF IMMUNE RESPONSE

- Immune response helps individuals defend against
  - microbes
  - some cancers
- Immune response can fail
  - hypersensitivity reactions
  - immunodeficiency

HYPERSENSITIVITY REACTIONS

- Cause cell damage through excessive immune response to antigens
- Hypersensitivity
  - overreaction to infectious agents
- Allergy
  - overreaction to environmental substances
- Autoimmunity
  - overreaction to self

IMMUNODEFICIENCY

- Loss or inadequate function of various components of the immune system
- Can occur in any part or state of the immune system
  - physical barrier, phagocytes, B lymphocytes, T lymphocytes, complement, natural killer cells
- The immuno-compromised host
  - has an impaired function of immune system
  - is at high risk of infection

IMMUNODEFICIENCY

- Congenital (primary) immunodeficiency
  - genetic abnormality
    - defect in lymphocyte maturation
- Acquired (secondary) immunodeficiency
  - results from infections, nutritional deficiencies or treatments
    - AIDS, chronic leukemia

ALTERED IMMUNITY: IMMUNO-COMPROMISED

		Disorder	Compromised function
Altered anatomic barrier	Mucus membrane	Reduction in IgA	Microbe binding
	Gastro-intestinal tract	Elevated pH	Bacteria killing
		Change in flora	Colonization resistance
Immune system	Innate immunity	Reduction of complement	Activates phagocytosis Opsonization of bacteria Membrane attack complex
		Neutropenia Monocytopenia	Phagocytosis Bacteria killing
	Adaptive immunity	Reduction of T cells	Activation of macrophages Activation of B lymphocytes
		Hypo-gammaglobulinemia	Neutralizes pathogens and toxins, opsonization, complement activation

SUMMARY (1)

- Innate immunity
  - relies on mechanisms already existing before microbe infects host
  - is the first line of defense
  - has no memory for subsequent exposure
  - relies on non specific mechanisms

SUMMARY (2)

- Adaptive immunity
  - develops following entry of microbe into the host
  - comes into action after innate immunity fails to get rid of microbe
  - has memory to deal with subsequent exposure
  - happens through specific cells
    - T cells (cell mediated)
    - B cells (antibody mediated)

SUMMARY (3)

- Primary immune response
  - short lasting
  - smaller in magnitude
- Secondary immune response
  - longer in duration
  - larger in magnitude
    - develop ‘memory cells’ following primary response
- Failure of immune response can result in:
  - hypersensitivity
  - immunodeficiency