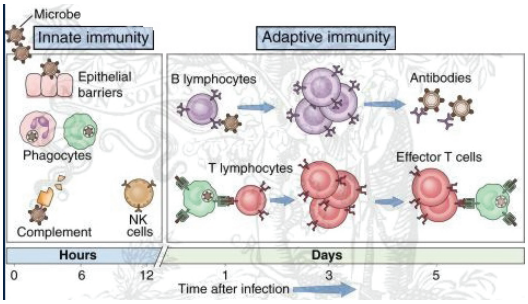
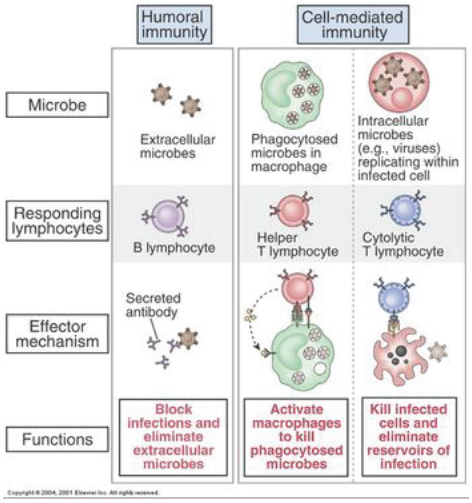
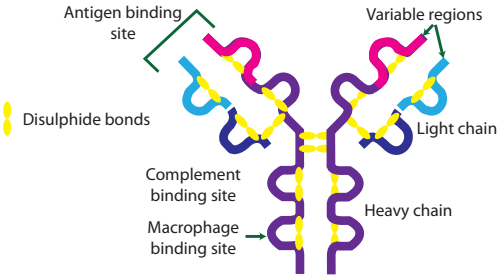
IMMUNOLOGY

The immune system is characterised by having three main characteristics. It has recognition, and is able to distinguish between self and non self as well as chemical differences between one pathogen and another. This recognition is then converted into an appropriate effector response to enable neutralisation or elimination of the organism, malignancy or foreign tissue. Finally the immune system develops a memory to a pathogen which results in a more rapid or effective response upon subsequent exposures to the same antigen. It is functionally divided into the innate (or non specific) system and the adaptive (or acquired) system. The innate and adaptive systems may be further categorised by the wether they are body fluid based (humoral) or cell based. With regard to the innate system the body fluid based components are complement (which is a collection of heat labile protiens important in the regulation of inflammation), the acute phase protiens such as CRP, alpha-1 antitrypsin, and fibronectin, and lyzosomes. The cell based components of the innate system include neutrophils, monocytes and phagocytes, NK cells, eosinophils, mast cells and basophils. The adaptive system is further categorised into the humoral system (which is characterised by antibody release from B lymphocytes and complement activation) and the cell mediated system (which is characerised by direct T lymphocyte cell actions stimulated by antigens). It should definitely be noted that this classification is based on convenience and there is significant interaction between systems.

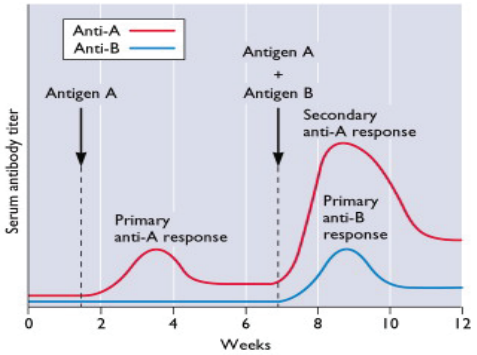




The adaptive immune system is separated into humoral (body fluid) component and the cell mediated component.



Antibodies or immunoglobulins are B lymphocyte produced molecules that combine specifically with antigens. Ab molecules consist of two identical light and heavy chains that are linked by disulphide bonds. The ends are variable regions and the stems are constant. The unique heavy chain constant regions determine the class IgA, IgE, IgM, IgG and IgD.



During the first encounter with a virus, a primary antibody response occurs. IgM antibody appears first, followed by IgA on mucosal surfaces or IgG in the serum. The IgG antibody is the major antibody of the response and is very stable, with a half-life of 7 to 21 days. When an infection occurs with the same or a similar virus, a rapid antibody response occurs that is called the secondary antibody response. The specificity and memory of the antibody response are illustrated in the following graph.

Inflammation the inflammatory response to tissue damage of invasion by pathological organisms results in vasodilation, increased capillary permiability, an influx of phagocytic cells. The inflammatory response is initiated by a series of interactions that involve several chemical mediators produced by invading organisms or damaged cells and the cells of the immune system and plasma enzyme systems. These include complement, CRP, and other acute phase protiens, histamine, kinins, and bacterial cell wall products such as endotoxin and exotoxin. Cytokines produced by macrophages and other cells of the innate immune system mediate the inflammatory response. These cytokines include TNF alpha and beta, and IL-1 and 6. The inflammatory response is characterized by the following symptom: redness, heat, swelling, pain, and possible dysfunction of the organs or tissues involved.

Apoptosis is the process of programmed cell death. The process of apoptosis is controlled by a diverse range of cell signals, which may originate either extracellularly (extrinsic inducers) or intracellularly (intrinsic inducers). Extracellular signals may include toxins, hormones, growth factors, nitric oxide or cytokines, that must either cross the plasma membrane or transduce to effect a response. Apoptosis is initiated by a family of protiens called caspases. When cells do not undergo a programmed death cell contents are often released in an uncontrolled manner leading to unwanted side effects such as inflammation and electrolyte disturbances. Unplanned cell death is called necrosis.

Non immune host defences may be considered in terms of physiochemical barriers that prevent micro-organisms from gaining access to the body. These include skin and mucous membranes, mucus, cilia and hydrochloric acid produced by the stomach. The skin forms an excellent physical barrier and prevents bacteria growth by secreting antibacterial substances (lactic acid and fatty acids). Mucus traps bacteria and foreign particles that are then removed by cilliary motion. Gastric juice is bacteriacidal. The high flow of urine, saliva, tear and secretions in biliary and lower respiratory tracts also physically remove foreign material.

Wound healing and tissue repair

- Acute inflammation
  - **Initial response to tissue damage**
  - **Relatively nonspecific response – eliminate dead tissue, protect against local infection, allow immune system access THEN . . .**
- Restitution - ideal outcome
  - **Damaged area replaced by organized tissue identical in structure/function as original tissue**
  - **Damaging agent removed; destroyed cells regenerate**
- Fibrous repair – scar tissue
  - **Cells cannot regrow and/or tissue architecture completely destroyed**
  - **Non-specialized; most frequent outcome of substantial tissue damage**
- Chronic inflammation
  - **Damaging agent persists AND continuing tissue destruction AND attempts to heal by fibrous repair AND immune responses**

2

Gell and Coombs classification of immunologic reactions

Type	Description	Mechanism	Clinical features
I Immediate reaction (within 1 hour)	IgE-mediated, immediate-type hypersensitivity	Antigen exposure causes IgE-mediated activation of mast cells and basophils, with release of vasoactive substances such as histamine, prostaglandins, and leukotrienes.	Anaphylaxis Angioedema Bronchospasm Urticaria (hives)
II	Antibody-dependent cytotoxicity	An antigen or hapten that is intimately associated with a cell binds to antibody, leading to cell or tissue injury	Hemolytic anemia Thrombocytopenia Neutropenia
III	Immune complex disease	Damage is caused by formation or deposition of antigen-antibody complexes in vessels or tissue. Deposition of immune complexes causes complement activation and/or recruitment of neutrophils by interaction of immune complexes with Fc IgG receptors	Serum sickness
IV	Cell-mediated or delayed hypersensitivity	Antigen exposure activates T cells, which then mediate tissue injury. Depending upon the type of T cell activation and the other effector cells recruited, different subtypes can be differentiated (ie, Types IVa-IVd)	Contact dermatitis, some morbilliform reactions, severe exfoliative dermatoses (eg, SJS/TEN), AGEP, DRESS/DiHS, interstitial nephritis, drug-induced hepatitis, other presentations

Christopher Andersen 2012