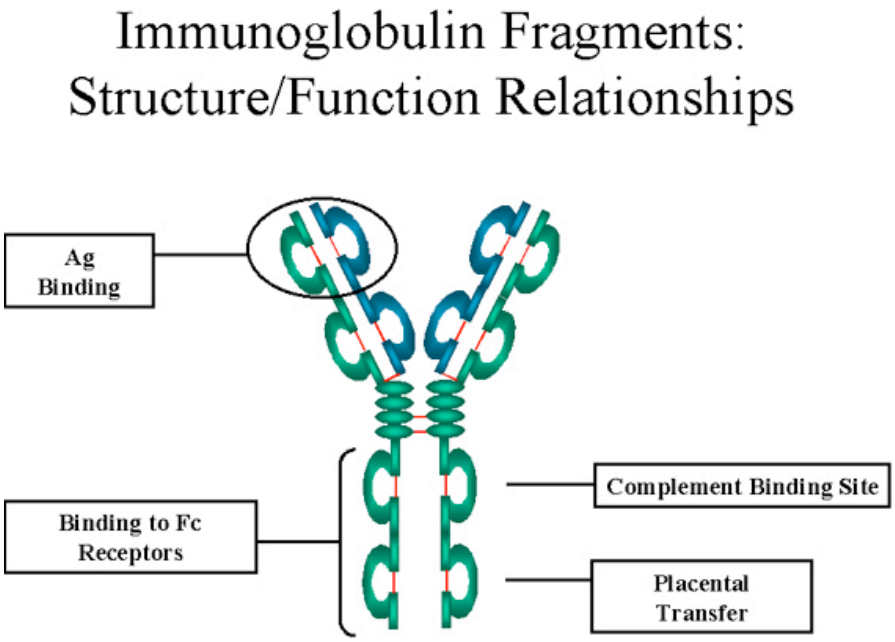
Immunoglobulins classes

Antibodies (also known as **immunoglobulins,Ig**)
Immunoglobulins are glycoprotein molecules that are produced by plasma cells in response to an immunogen and which function as antibodies. They are typically made of basic structural units—each with two large heavy chains and two small light chains to form, for example, monomers with one unit, dimers with two units or pentamers with five units. Antibodies are produced by a kind of white blood cell called a plasma cell. There are different types of antibody which are grouped into different isotypes based on which heavy chain they possess. Five different antibody isotypes are known in mammals, which perform different roles, and help direct the appropriate immune response for each different type of foreign object they encounter.



GENERAL FUNCTIONS OF IMMUNOGLOBULINS

A. Antigen binding

Immunoglobulins bind specifically to one or a few closely related antigens. Each immunoglobulin actually binds to a specific antigenic determinant. Antigen binding by antibodies is the primary function of antibodies and can result in protection of the host.

B. Effector Functions

The immunoglobulins mediate a variety of effector functions. Usually the ability to carry out a particular effector function requires that the antibody bind to its antigen. Such effector functions include:

- 1. Fixation of complement - This results in lysis of cells and release of biologically active molecules.
- 2. Binding to various cell types - Phagocytic cells, lymphocytes, platelets, mast cells, and basophils have receptors that bind immunoglobulins. This binding can activate the cells to perform some function. Some immunoglobulins also bind to receptors on placental trophoblasts, which results in transfer of the immunoglobulin across the placenta. As a result, the transferred maternal antibodies provide immunity to the fetus and newborn.

BASIC STRUCTURE OF IMMUNOGLOBULINS

The basic structure of the immunoglobulins is are built from the same basic units.

A. Heavy and Light Chains

All immunoglobulins have a four-chain structure as their basic unit. They are composed of two identical light chains (23kD) and two identical heavy chains (50-70kD)

B. Disulfide bonds

1. Inter-chain disulfide bonds - The heavy and light chains and the two heavy chains are held together by inter-chain disulfide bonds and by non-covalent interactions.

2. Intra-chain disulfide binds - Within each of the polypeptide chains there are also intra-chain disulfide bonds.

C. Variable (V) and Constant (C) Regions

When the amino acid sequences of many different heavy chains and light chains were compared, it became clear that both the heavy and light chain could be divided into two regions based on variability in
the amino acid sequences. These are the:

1. Light Chain - VL (110 amino acids) and CL (110 amino acids)
2. Heavy Chain - VH (110 amino acids) and CH (330-440 amino acids)

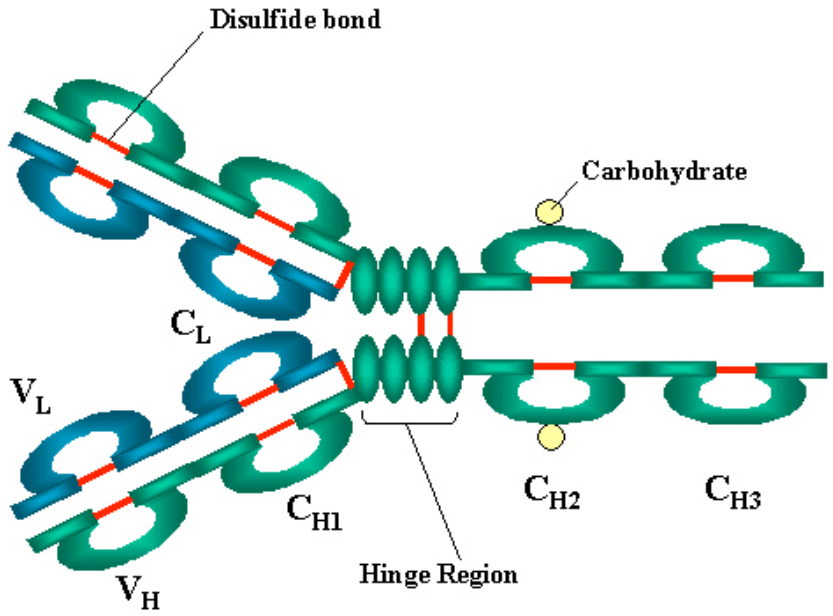
D. Hinge Region

This is the region at which the arms of the antibody molecule forms a Y. It is called the hinge region because there is some flexibility in the molecule at this point.

E. Domains

Three dimensional images of the immunoglobulin molecule show that it is not straight but, it is folded into globular regions each of which contains an intra-chain disulfide bond These regions are called domains.
1. Light Chain Domains - VL and CL
2. Heavy Chain Domains - VH, CH1 - CH3 (or CH4)

F. Oligosaccharides
Carbohydrates are attached to the CH2 domain in most immunoglobulins. However, in some cases carbohydrates may also be attached at other locations.



Immunoglobulin classes
The immunoglobulins can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains. All immunoglobulins within a given class will have very similar heavy chain constant regions. These differences can be detected by sequence studies or more commonly by serological means (*i.e.* by the use of antibodies directed to these differences).

1. IgG - Gamma heavy chains
2. IgM - Mu heavy chains
3. IgA - Alpha heavy chains
4. IgD - Delta heavy chains

5. IgE - Epsilon heavy chains

STRUCTURE AND SOME PROPERTIES OF IG CLASSES AND SUBCLASSES

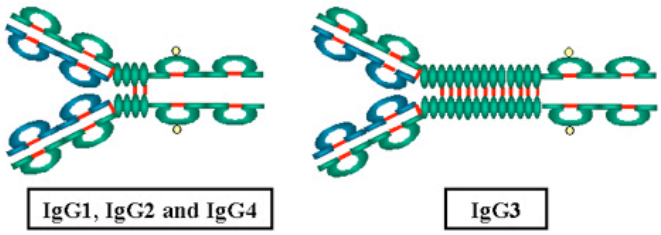
A. IgG

1. Structure

The structures of the IgG subclasses are presented in figure. All IgG's are monomers (7S immunoglobulin). The subclasses differ in the number of disulfide bonds and length of the hinge region.

IgG

- Structure
  - Monomer (7S)



2. Properties

IgG is the most versatile immunoglobulin because it is capable of carrying out all of the functions of immunoglobulin molecules.

a) IgG is the major Ig in serum - 75% of serum Ig is IgG

b) IgG is the major Ig in extra vascular spaces

c) Placental transfer - IgG is the only class of Ig that crosses the placenta. Transfer is mediated by a receptor on placental cells for the Fc region of IgG. Not all subclasses cross equally well; IgG2 does not cross well.

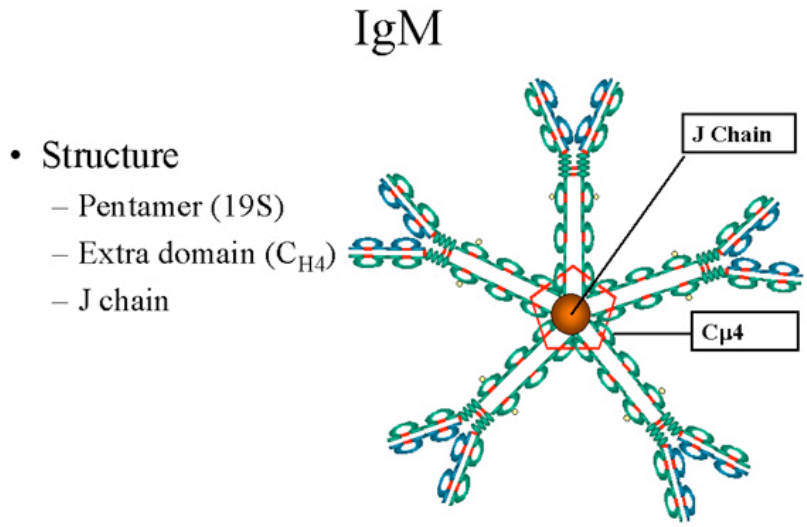
d) Fixes complement - Not all subclasses fix equally well; IgG4 does not fix complement

e) Binding to cells - Macrophages, monocytes, PMNs and some lymphocytes have Fc receptors for the Fc region of IgG. Not all subclasses bind equally well; IgG2 and IgG4 do not bind to Fc receptors. A consequence of binding to the Fc receptors on PMNs, monocytes and macrophages is that the cell can now internalize the antigen better.

B. **IgM**

1. Structure

IgM normally exists as a pentamer but it can also exist as a monomer. In the pentameric form all heavy chains are identical and all light chains are identical. IgM has an extra domain on the mu chain (CH4) and it has another protein called the J chain. This chain functions in polymerization of the molecule into a pentamer.



2. Properties

a) IgM is the third most common serum Ig.

b) IgM is the first Ig to be made by the fetus and the first Ig to be made by a virgin B cells when it is stimulated by antigen.

c) As a consequence of its pentameric structure, IgM is a good complement fixing Ig. Thus, IgM antibodies are very efficient in leading to the lysis of microorganisms.

d) As a consequence of its structure, IgM is also a good agglutinating Ig . Thus, IgM antibodies are very good in clumping microorganisms for eventual elimination from the body.

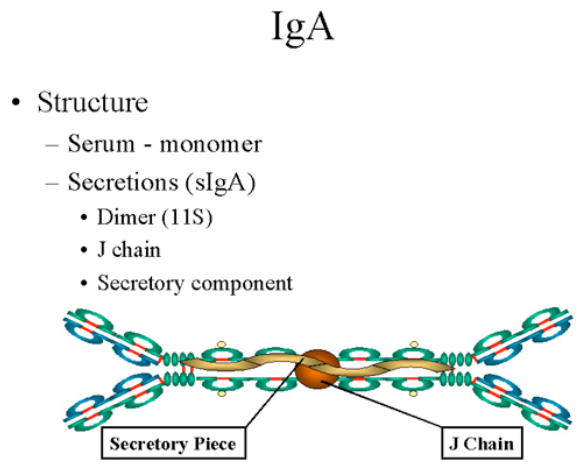
e) IgM binds to some cells via Fc receptors.

f) B cell surface Ig

C. **IgA**

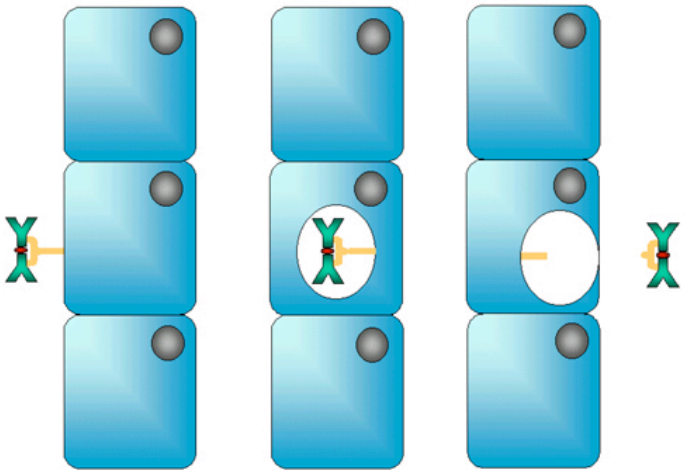
1. Structure

Serum IgA is a monomer but IgA found in secretions is a dimer as. When IgA exits as a dimer, a J chain is associated with it.



When IgA is found in secretions is also has another protein associated with it called the secretory piece; Unlike the remainder of the IgA which is made in the plasma cell, the secretory piece is made in epithelial cells and is added to the IgA as it passes into the secretions. The secretory piece helps IgA to be transported across mucosa and also protects it from degradation in the secretions.

Origin of sIgA



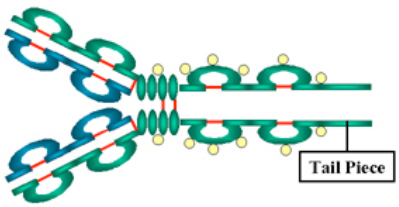
Properties
a) IgA is the 2nd most common serum Ig.
b) IgA is the major class of Ig in secretions - tears, saliva, colostrum, mucus. Since it is found in secretions secretory IgA is important in local (mucosal) immunity.
c) Normally IgA does not fix complement, unless aggregated.
d) IgA can binding to some cells - PMN's and some lymphocytes.
Figure 13 IgD Structure

D. IgD

1. Structure
2. IgD exists only as a monomer.

IgD

- Structure
  - Monomer
  - Tail piece



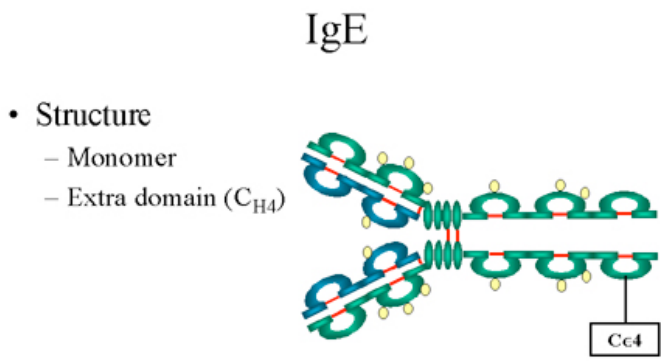
Properties
a) IgD is found in low levels in serum; its role in serum uncertain.
b) IgD is primarily found on B cell surfaces where it functions as a receptor for antigen. IgD on the surface of B cells has extra amino acids at C-terminal

end for anchoring to the membrane. It also associates with the Ig-alpha and Ig-beta chains.
c) IgD does not bind complement.

E. IgE

Structure

IgE exists as a monomer and has an extra domain in the constant region.



Properties

a) IgE is the least common serum Ig since it binds very tightly to Fc receptors on basophils and mast cells even before interacting with antigen.
b) Involved in allergic reactions - As a consequence of its binding to basophils an mast cells, IgE is involved in allergic reactions. Binding of the allergen to the IgE on the cells results in the release of various pharmacological mediators that result in allergic symptoms.
c) IgE also plays a role in parasitic helminth diseases. Since serum IgE levels rise in parasitic diseases, measuring IgE levels is helpful in diagnosing parasitic infections. Eosinophils have Fc receptors for IgE and binding of eosinophils to IgE-coated helminths results in killing of the parasite.
d) IgE does not fix complement.

Immune response

Is a complex and regulated sequence of events involving several cell types. Its triggered when an Ag enters the body and encounters a specialized class of APCs. These cells capture the Ag and processed in a form that can be recognized by helper T lymphocyte, the helper T cells activated and promote the activation of B-cells or cytotoxic T cells. The activated lymphocytes proliferate and carry out their specific function (inactivate or eliminate the Ag).

At each stage in this process, the lymphocytes and APCs communicate with one another through direct or by secreting regulatory cytokines.

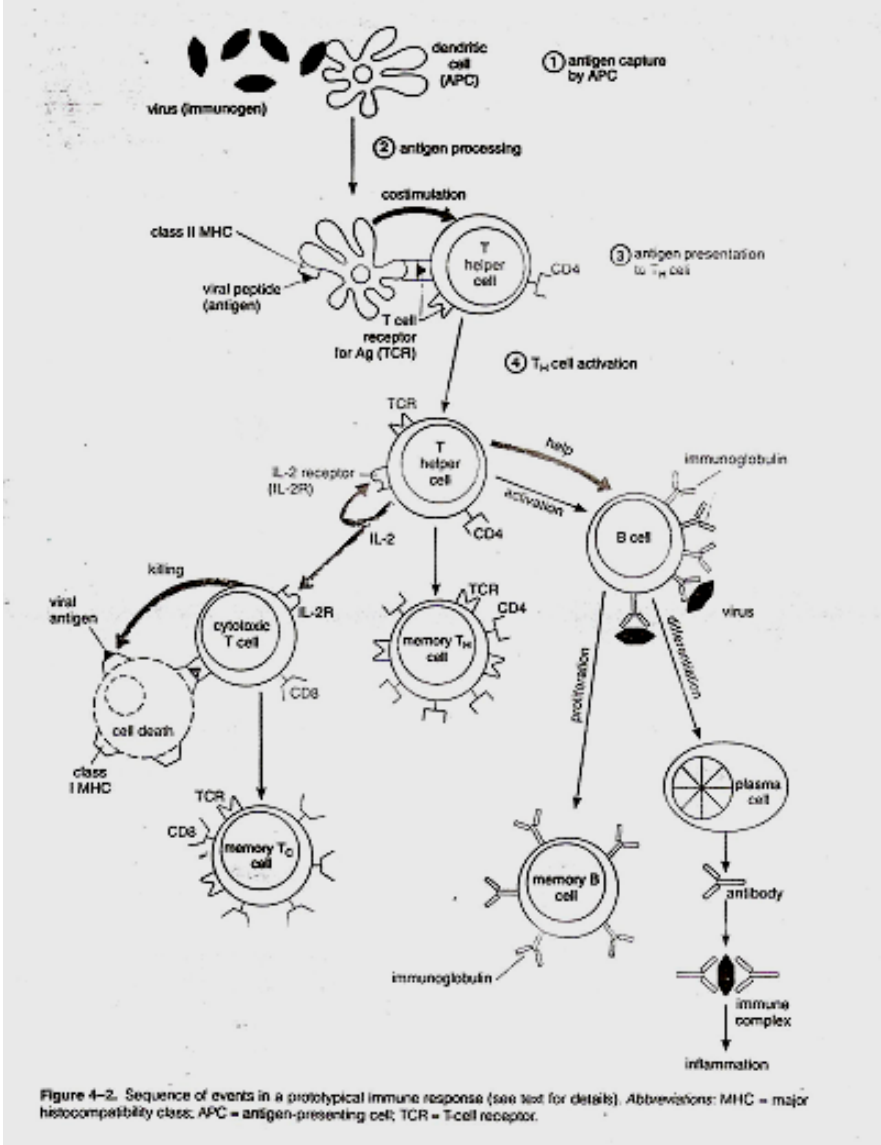


Figure 4–2. Sequence of events in a prototypical immune response (see text for details). *Abbreviations:* MHC = major histocompatibility class; APC = antigen-presenting cell; TCR = T-cell receptor.

When a person exposed to Ag B-cell response and concentration of serum Ab against that Ag rise this is divided into several phase.
1- Lag phase: time between intial exposure to immunogen and appear of Ab in the circulating which average 1-week in human.
2- Exponential phase: is rapid increase in quality of circulating Ab
3- Steady State: Ab level remains constant because secretion and degradation is in equal rates.
4- Deckling-phase: Ab level decline (no new plasma cell produced and existing plasma cell are dying).
This kind of immune response is weak, short-lived and called primary immune response. Subsequent encounters with same immunogen lead to response similar to primary but lag period is short and Ab level rise more rapidly (because of presence of primary memory T and B cells) to much higher level and the steady-state level remaining in the same for much longer periods.