Antibodies

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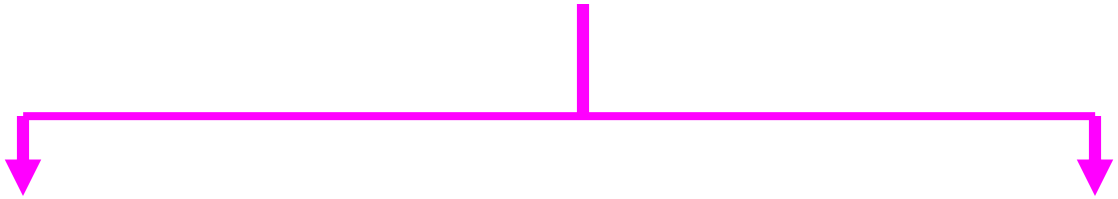
Acquired (Adaptive) Immunity

Defensive mechanisms include :

1) Innate immunity (Natural or Non specific)

2) Acquired immunity (Adaptive or Specific)



Cell-mediated immunity Humoral immunity

Aquired (specific) immunity

* The acquired immune response is more specialized than innate immune response

* The acquired immune response involves a combination of two mechanisms :

1) Humoral immune response

2) cell mediated immune response

* They interact with one another to destroy foreign body (microorganisms, infected cells, tumor cells)

Aquired (specific) immunity

Two mechanisms

1) Humoral immune response:

- **Antibodies are produced by B-lymphocytes**
- **These have the ability to recognize and bind specifically to antigen that induced their formation**

2) The cell mediated immune response (CMI)

- **It is mediated by certain types of T-lymphocytes**
- **T-lymphocytes recognize foreign material by means of surface receptors**
- **T-lymphocytes attack and destroy foreign material directly or through release of soluble mediators** i.e. cytokines

Characters Of Acquired Immune Response

1) Highly specific for the invading organism

2) Discrimination between “self and “non self” molecules

The response only occurs to “non self” molecules

3) Diversity:

- It can respond to millions of different antigens
- Lymphocytes population consists of many different clones (one cell and its progny)
- Each clone express an antigen receptor and responds only to one antigenic epitope

Mechanism of Humoral immunity

* Antibodies induce resistance through:

1) Antitoxin neutralize bacterial toxins (diphtheria,tetanus)

Antitoxin are developed actively as a result of:

a- Previous infection

b- Artificial immunization

c- Transferred passively as antiserum

* Neutralization of toxin with antitoxin prevents a combination with tissue cells

Mechanism of Humoral immunity

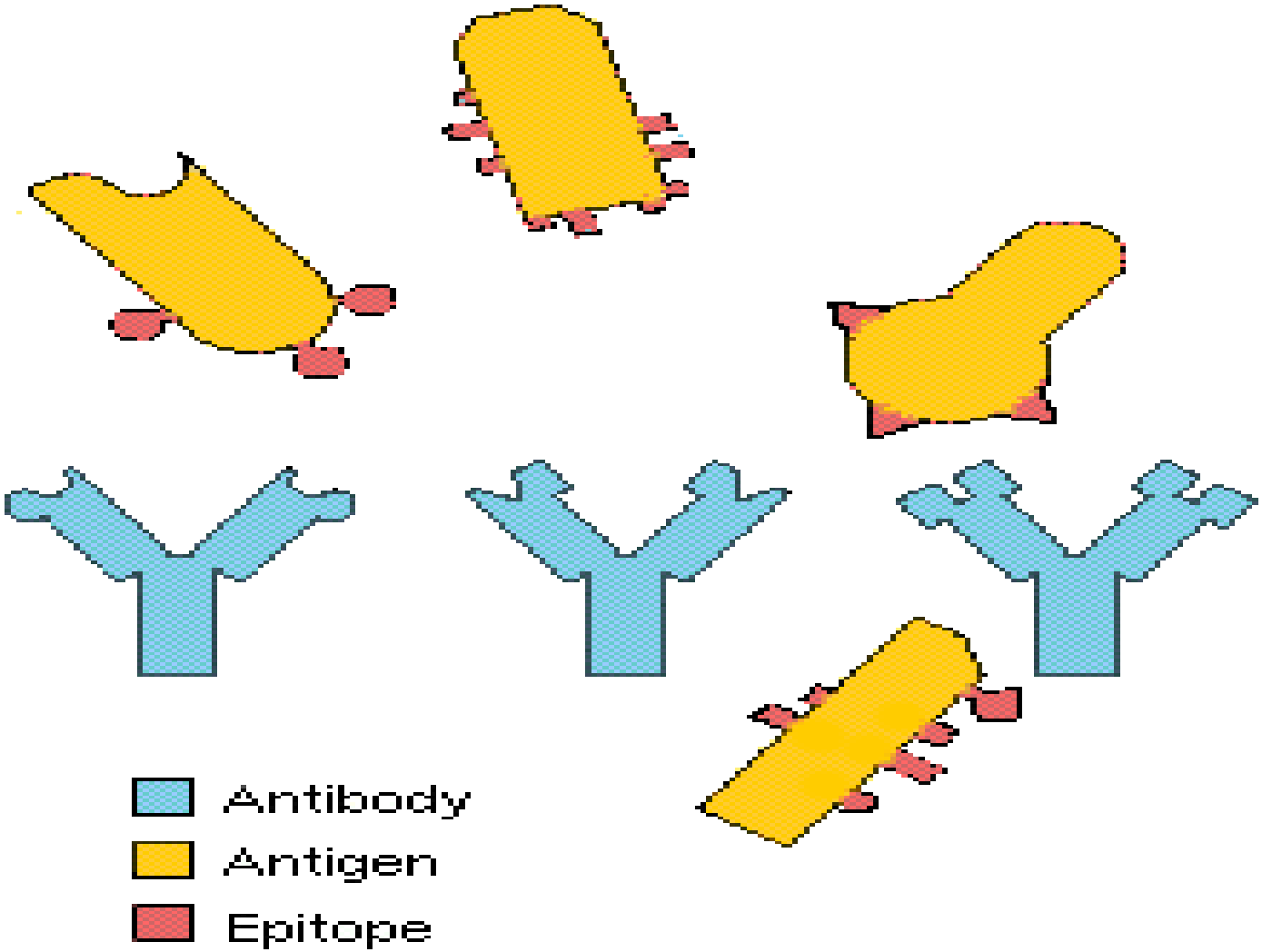
2) Antibodies attach to the surface of bacteria an

a- act as opsonins and enhance phagocytosis

b- prevent the adherence of microorganisms to their target cells, e.g. IgA in the gut

c- Activate the complement and lead to bacterial lysis

d- Clump bacteria (agglutination) leading to phagocytosis



Antibodies produced by B-cells of the immune system

recognize foreign antigens and mark them for destruction

B-lymphocytes

in bone marrow

* The lymphoid stem cells differentiate into B cells

* B-cells precursors mature, differentiate into immunocomptent B-cells with a single antigen specificity

* Immature B-cells that express high affinity receptors for self antigens, die or fail to mature

  i.e negative selection or clonal deletion

* This process induces central self tolerance and reduces autoimmune diseases

B-lympocytes

* Immature B cells express IgM receptors on the surface

* Mature B cells express IgM, IgD molecules on surfaces

* IgM and IgD molecules serve as receptors for antigens

* Memory B-cells express IgG or IgA or IgE on the surface

* B-cells bear receptors for Fc portion of IgG and a receptor for C3 component of the complement

* They express an array of molecules on their surfaces that are important in B-cells interactions with other cells such as MHC II, B7 and CD40

Antibodies or Immunoglobulins

* **Definition:**

  Glycoprotein in serum and tissue fluid

* **Produced by:** B-lymphocytes in response to exposure to antigen

* **React specifically with antigen**

* **Five classes of Antibodies:**

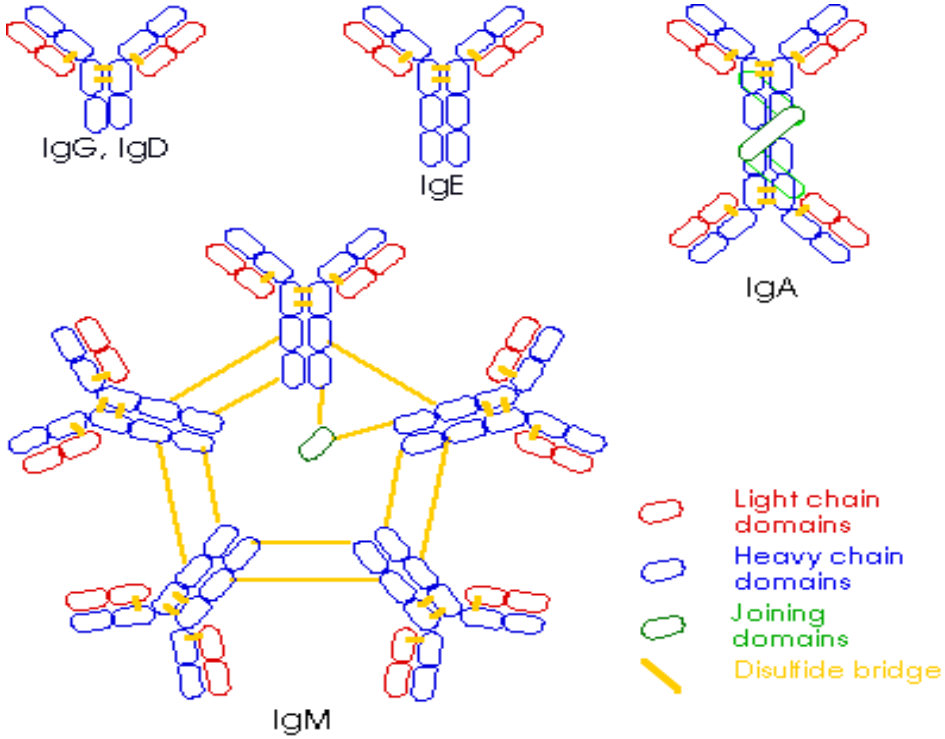
  IgG

  IgM

  IgA

  IgD

  IgE



Antibodies

- **Proteins that recognize and bind to a particular antigen with very high *specificity*.**
- **Made in response to exposure to the antigen.**
- **One virus or microbe may have several *antigenic determinant sites*, to which different antibodies may bind.**
- **Each antibody has at least two identical sites that bind antigen: *Antigen binding sites*.**
- **Valence of an antibody: Number of antigen binding sites. Most are bivalent.**
- **Belong to a group of serum proteins called immunoglobulins (Igs).**

ANTIBODY STRUCTURE

An antibody molecule is composed of two identical Ig heavy chains (H) and two identical light chains (L), each with a variable region (V) & constant region (C).

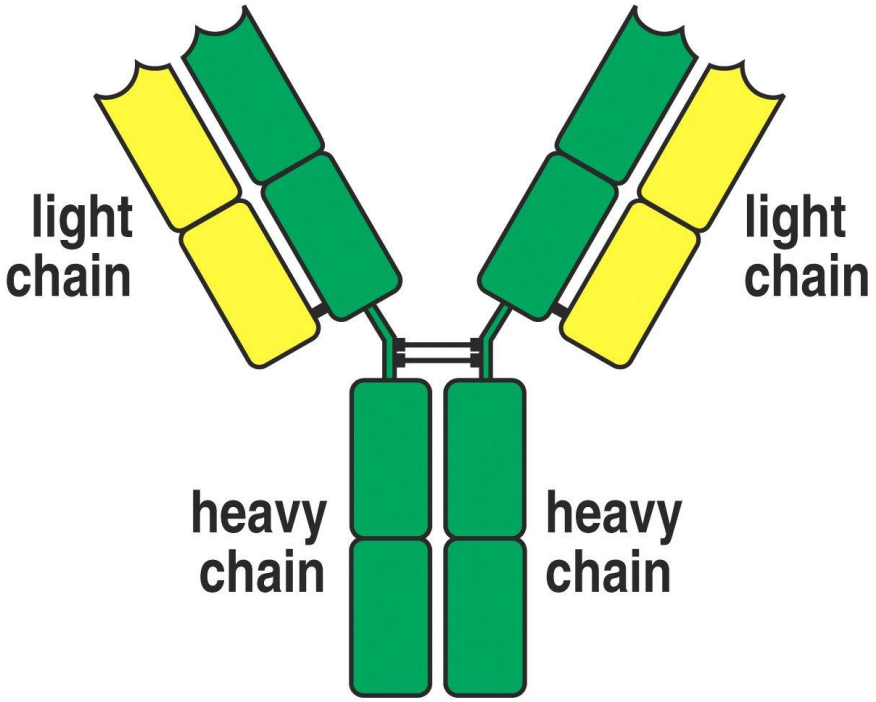


Figure 1-17 Immunobiology, 6/e. (© Garland Science 2005)

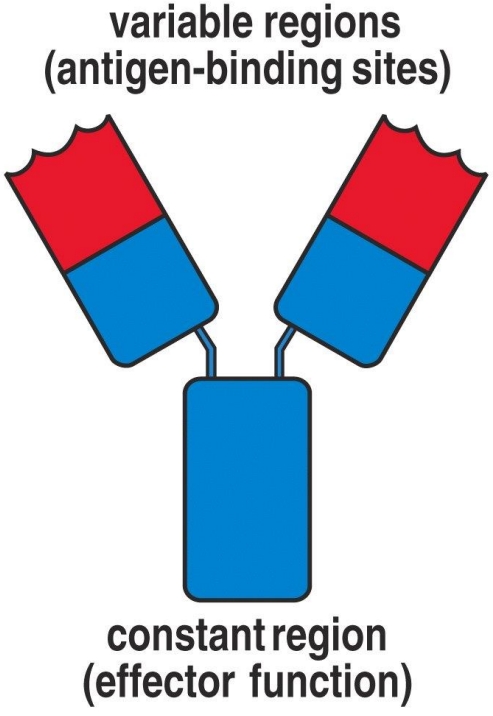


Figure 1-16 Immunobiology, 6/e. (© Garland Science 2005)

Amino acid sequences were determined from myeloma proteins.

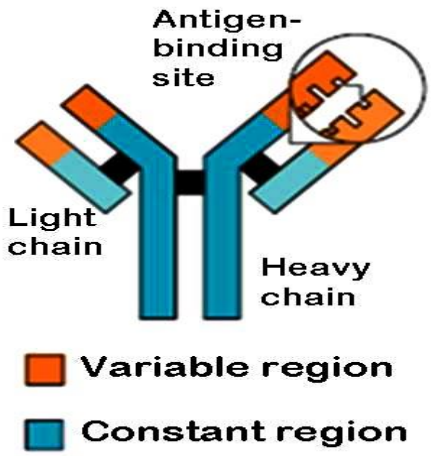
Antibody Structure

- **Monomer: A flexible Y-shaped molecule with four protein chains:**
  - **2 identical *light* chains**
  - **2 identical *heavy* chains**
- **Variable Regions: Two sections at the end of Y's arms. Contain the antigen binding sites (Fab). Identical on the same antibody, but vary from one antibody to another.**
- **Constant Regions: Stem of monomer and lower parts of Y arms.**
- **Fc region: Stem of monomer only. Important because they can bind to complement or cells.**

Antibody Structure

Immunoglobulins are glycoproteins made up of Four polypeptid chains (IgG):

a- Two light (L) polypeptide chains
b- Two heavy (H) polypeptide chains



- The four chains are linked by disulfide bonds
- Terminal portion of L-chain contains part of antigen binding site
- H-chains are distinct for each of the five immunoglobulins
- Terminal portion of H-chain participate in antigen binding site
- The other (Carboxyl) terminal portion forms Fc fragment

Variable(V) and Constant (C) Regions

- Each **H**-chain and each **L**-chain has **V**-region and **C**-region
- **V**-region lies in terminal portion of molecule
- **V**-region shows wide variation in amino a. sequences
- Hypervariable region form region complementary to Ag determinant . It is responsible for antigen binding
- **C**-region lies in carboxyl or terminal portion of molecule
- **C**-region shows an unvarying amino acid sequence. It is responsible for biologic functions

Antibody Fragments

- Fab fragment: antigen binding site
- Fc (crystallizable fragment):

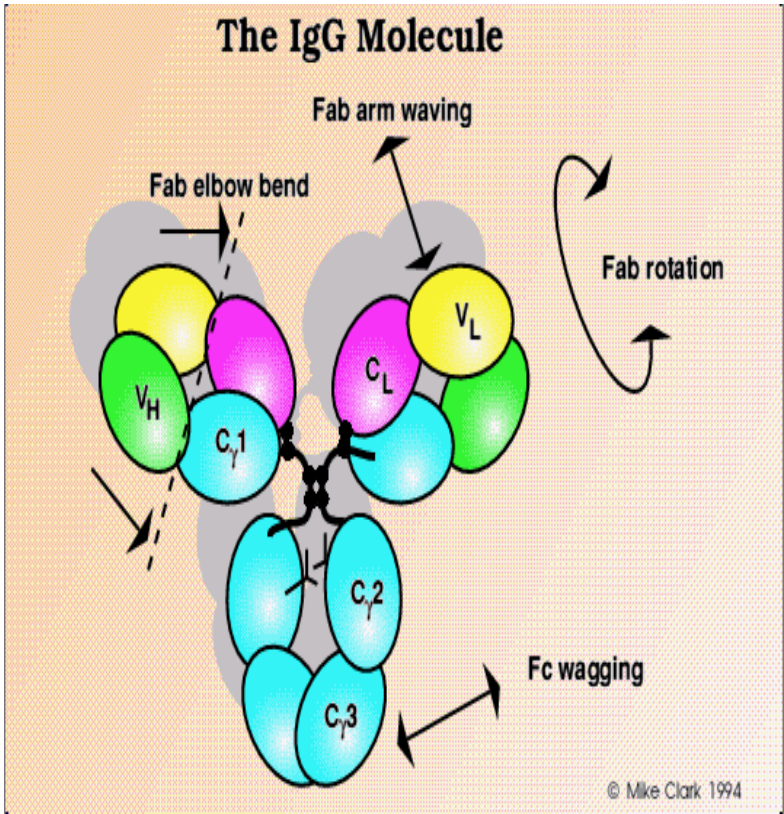
  a- Complement fixation (IgM and IgG)

  b- Opsonization (IgG)

  C- Placental attachment (IgG)

  d- Mucosal attachment (IgA)

e- Binding to mast cells (IgE)



Immunoglobulin Classes

I. IgG

- Structure: Monomer
- Percentage serum antibodies: 80%
- Location: Blood, lymph, intestine
- Half-life in serum: 23 days
- Complement Fixation: Yes
- Placental Transfer: Yes
- Known Functions: Enhances phagocytosis, neutralizes toxins and viruses, protects fetus and newborn.

IgG

Properties

- Major serum Ig
- Major Ig in extravascular spaces
- The only Placental transfer Ig
- Fixes complement
- Phagocytes - opsonization

Immunoglobulin Classes

II. IgM

- **Structure: Pentamer**
- **Percentage serum antibodies: 5-10%**
- **Location: Blood, lymph, B cell surface (monomer)**
- **Half-life in serum: 5 days**
- **Complement Fixation: Yes**
- **Placental Transfer: No**
- **Known Functions: First antibodies produced during an infection. Effective against microbes and agglutinating antigens.**

IgM

Properties

- First Ig made by fetus and B cells
- Present in colostrum and mother milk protect newly born.
- Fixes complement

Immunoglobulin Classes

III. IgA

- **Structure: Dimer**
- **Percentage serum antibodies: 10-15%**
- **Location: Secretions (tears, saliva, intestine, milk), blood and lymph.**
- **Half-life in serum: 6 days**
- **Complement Fixation: No**
- **Placental Transfer: No**
- **Known Functions: Localized protection of *mucosal* surfaces. Provides immunity to infant digestive tract**

IgA

-Found in serum and body secretion:

Tears, saliva, gastric and pulmonary secretions

- Major secretory Ig on Mucous surfaces give Local Immunity by coating m.o(bacteria or viruses) preventing their adherence to mucosal cells
- Does not fix complement (unless aggregated)
- Present in colostrum and mother milk protect newly born.

Immunoglobulin Classes

IV. IgD

- Structure: Monomer
- Percentage serum antibodies: 0.2%
- Location: B-cell surface, blood, and lymph
- Half-life in serum: 3 days
- Complement Fixation: No
- Placental Transfer: No
- Known Functions: In serum function is unknown. Or
  B cell surface, initiate immune response.

IgD

- Present in very small amount in serum
- B cell surface Ig
- Does not bind complement

Immunoglobulin Classes

V. IgE

- Structure: Monomer
- Percentage serum antibodies: 0.002%
- Location: Bound to mast cells and basophils throughout body. Blood.
- Half-life in serum: 2 days
- Complement Fixation: No
- Placental Transfer: No
- Known Functions: Allergic reactions. Possibly lysis of worms.

IgE

- Least common serum Ig
  - Binds to basophils and mast cells (Does not require Ag binding)
- Allergic and hypersensitivity reactions
- Parasitic infections (Helminths)
  - Binds to Fc receptor on eosinophils
- Does not fix complement

Properties of Immunoglobulins

Property	IgG	IgA	IgM	IgE	IgD
Heavy chain symbol	γ	α	μ	ε	δ
Molecular weight	150 KDa	170-400 KDa	900 KDa	190 KDa	180 KDa
Percentage in serum	75 %	15 %	10 %	0.004 %	% 0.2
Complement fixation	Yes	No	Yes	No	No
Transplacental passage	Yes	No	No	No	No
Opsonization	Yes	No	No	No	No

Immunological Memory

Antibody Titer: **The amount of antibody in the serum.**

Pattern of Antibody Levels During Infection

Primary Response:

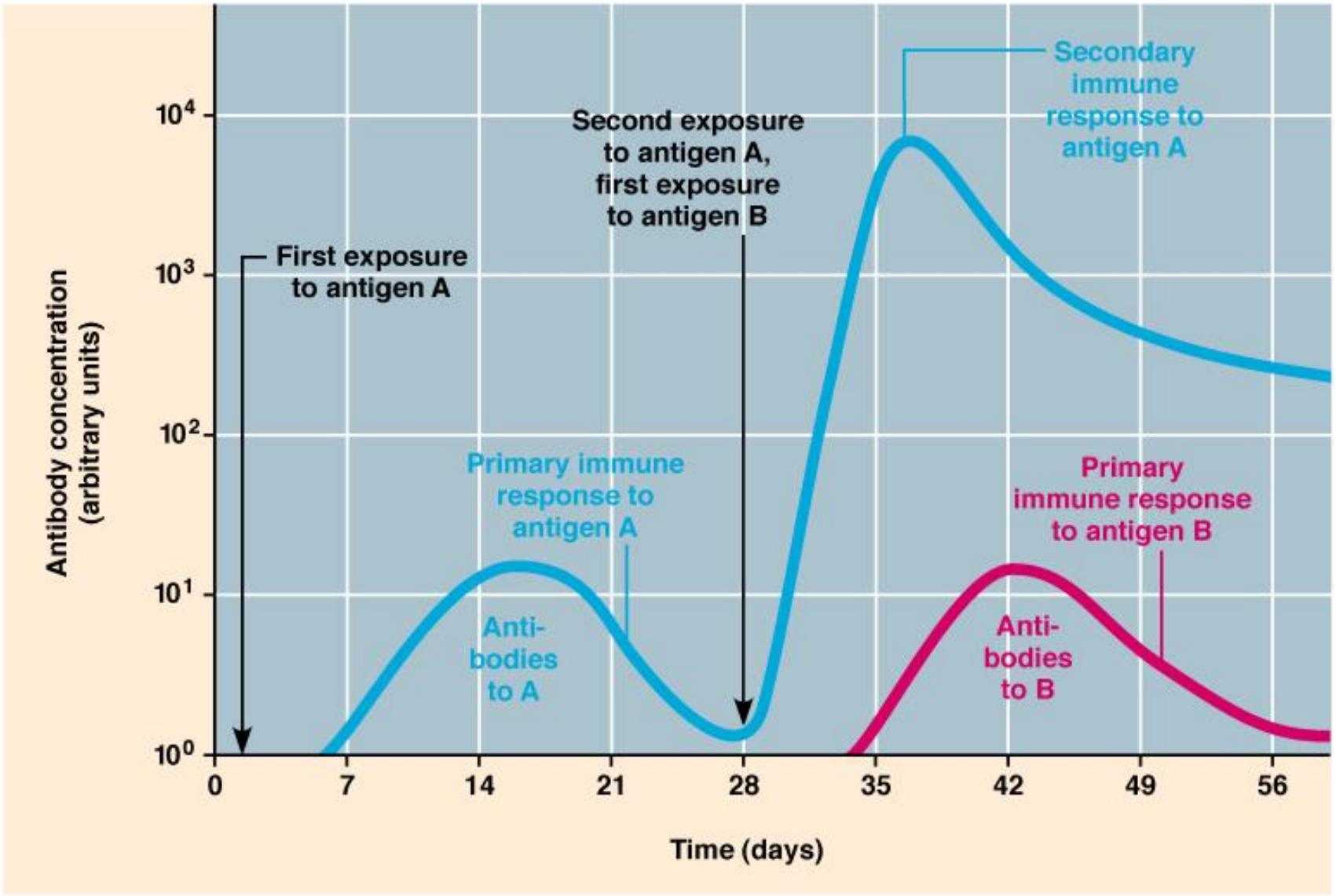
- **After *initial* exposure to antigen, no antibodies are found in serum for several days.**
- **A gradual increase in titer, first of IgM and then of IgG is observed.**
- **Most B cells become plasma cells, but some B cells become long living *memory cells*.**
- **Gradual decline of antibodies follows.**

Immunological Memory (Continued)

Secondary Response:

- Subsequent exposure to the same antigen displays a faster and more intense antibody response.
- Increased antibody response is due to the existence of memory cells, which rapidly produce plasma cells upon antigen stimulation.

Antibody Response After Exposure to Antigen



Primary and Secondary antibody response

Primary antibody response

* first exposure to antigen
* lag period: days or weeks (slow onset)
* Small amount immunogl. low Ab level with gradual increase
- Ab Persist for short duration Weeks then decline rapidly
* Antibody is IgM

Secondary antibody response

* Subsequent exposure
* Lag period: hours (rapid onset)
* large amount immunogl. high Ab with rapid increase
* Persist for long periods (monthes or years)
* Antibody is IgG