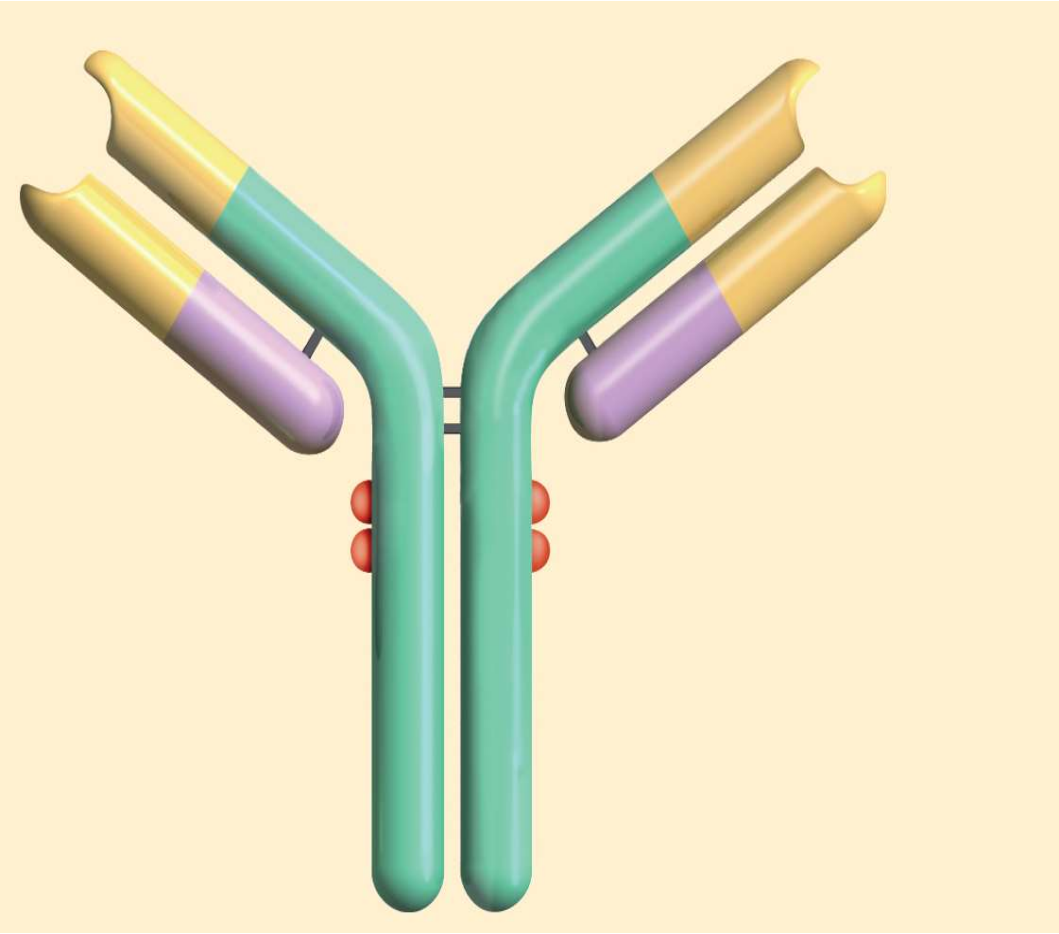
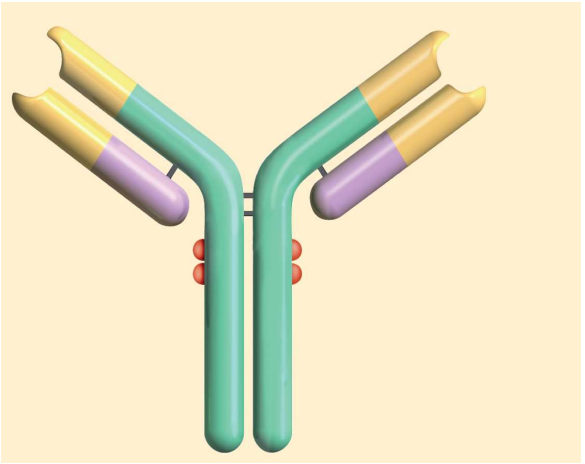
C22.6

Antibodies
Structure & Function



Antibodies

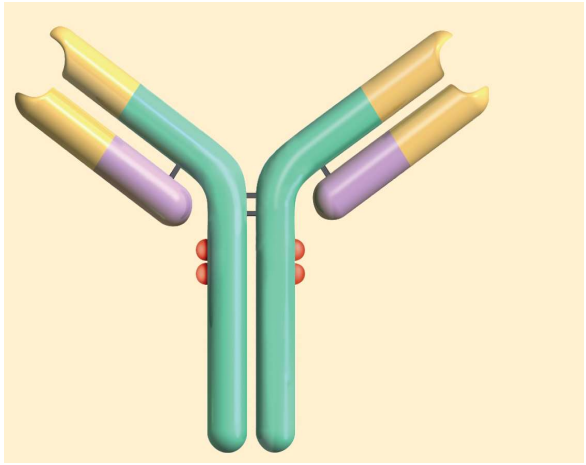
Immunoglobulin (Ig) – an antibody is a defensive gamma globulin (i.e. protein) found in the blood plasma, tissue fluids, body secretions, and on some leukocyte membranes /// (but not inside our cells!)



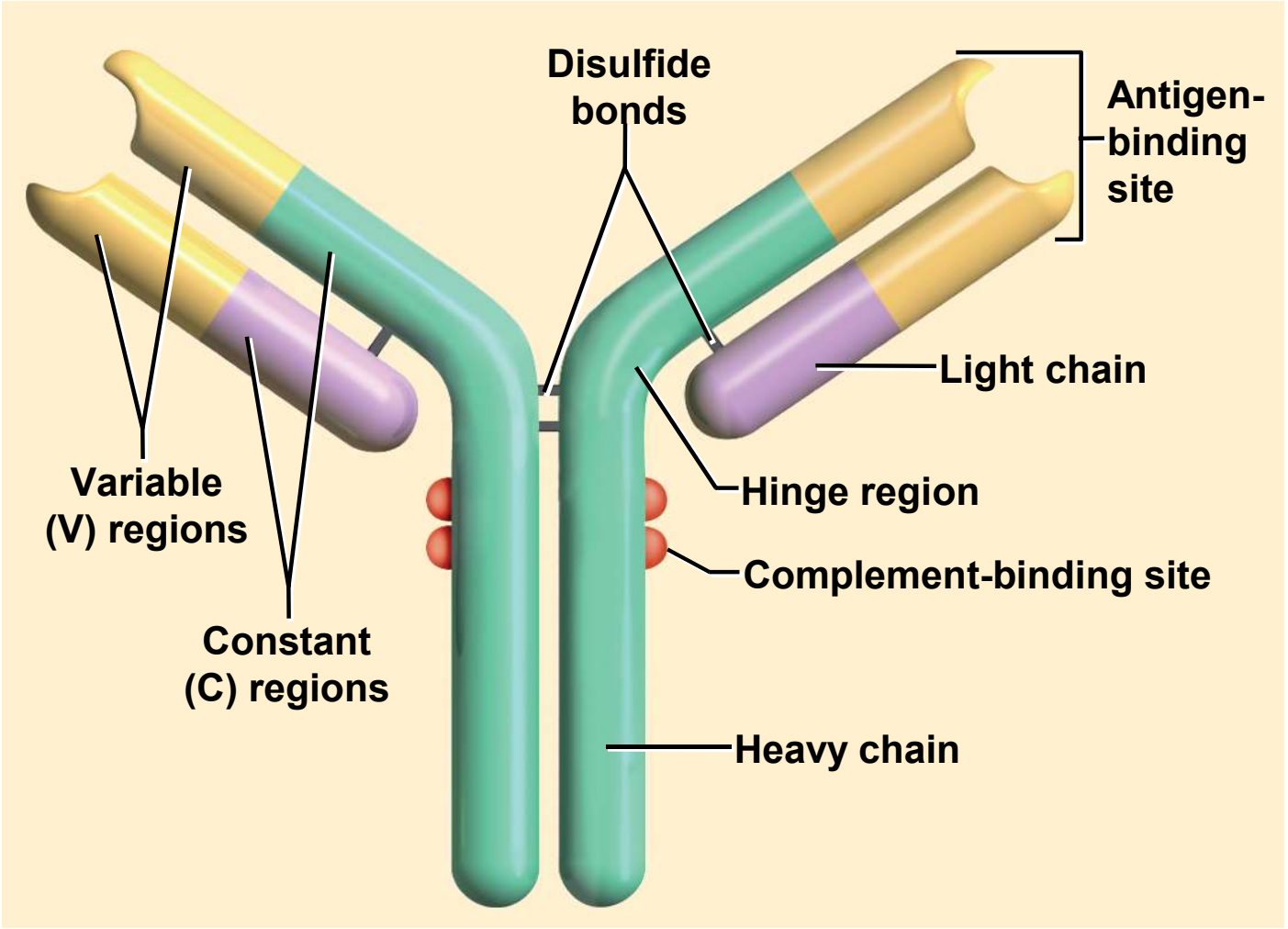
- the basic structural unit of an antibody.....
- composed of four polypeptide chains linked by **disulfide (-S-S-) bonds**
- two larger **heavy chains** about 400 amino acids long // heavy chains have a hinge region where antibody is bent
- two **light chains** about half as long
- **variable (V) region** in all four chains // gives the antibody its uniqueness

Antibodies

- **antigen binding site** – formed from the V regions of the heavy and light chain on each arm // attaches to the epitope of an antigen molecule
  - Each monomer can bind to two epitopes
  - Epitopes can be on same cell or on two different cells (e.g. aglutination)
- **constant (C) region** has the same amino acid sequence within one person and determines mechanism of antibody action



Antibody Structure



Antibody Structure

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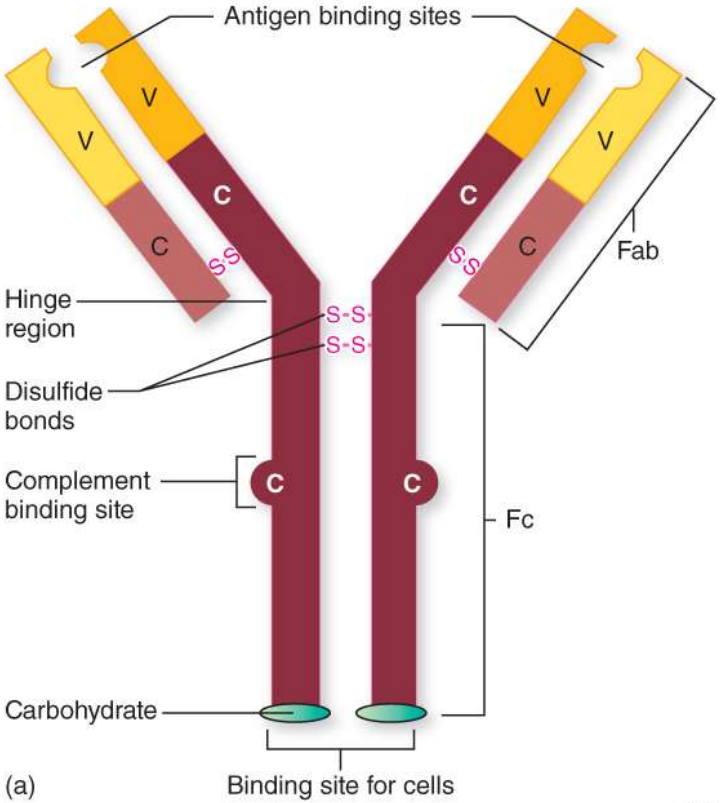
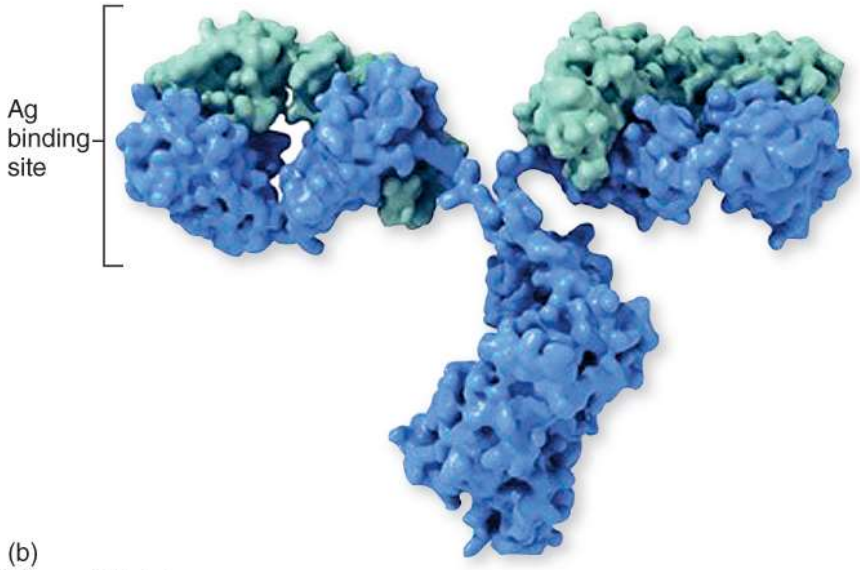
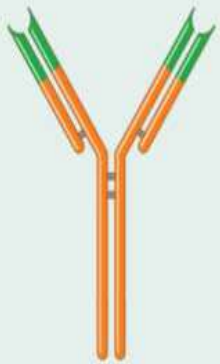
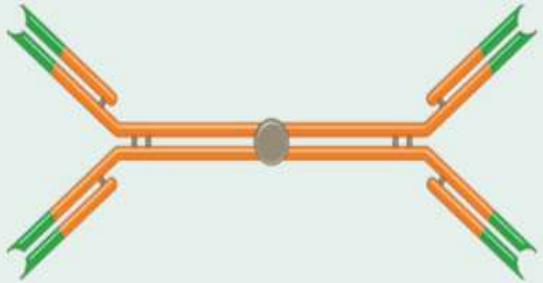


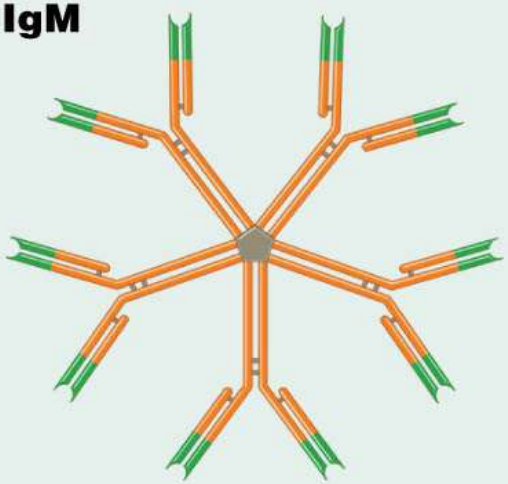
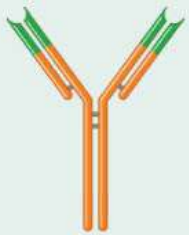
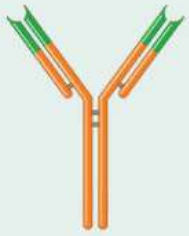


(b): U.S. National Library of Medicine

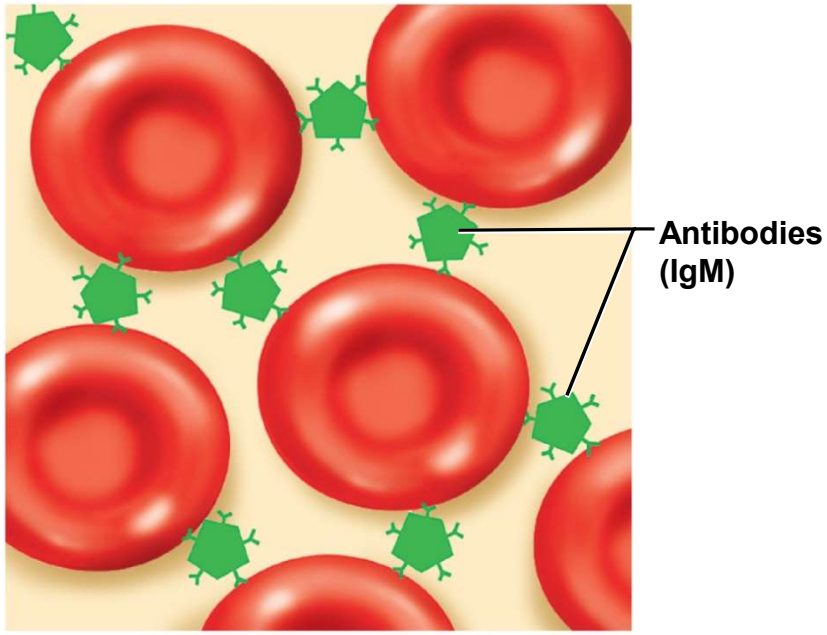
Five Classes of Antibodies

- Remember **"MADGE"** (IgM – IgA – IgD – IgG – IgE)
  - Note: a single plasma cell is able to produce all four classes of antibodies – with same antigen binding site
  - Single plasma cells makes 2,000 antibodies per second for 7 days – clonal selection produces millions of active plasma cells
  - A single plasma cells may start to produce IgM antibodies and then produce IgG later in the infection

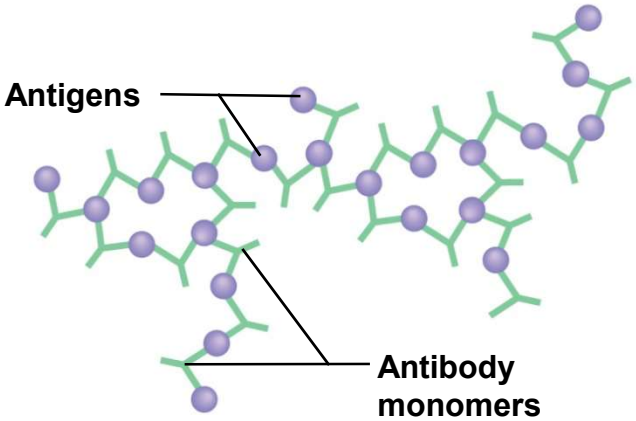
CLASS	FUNCTION
IgG 	• Makes up the majority of antibodies in serum • The only antibody that can cross the placenta from mother to fetus • Functions in opsonization, neutralization, and complement fixation
IgA 	• Found in secretions such as breast milk and saliva • Functions in agglutination and neutralization

CLASS	FUNCTION
IgM 	• The first antibody secreted on exposure to an antigen • Potent agglutinating and precipitating agent • Functions in complement fixation
IgE 	• Binds mast cells and basophils and triggers their degranulation, facilitating inflammation, particularly in the allergic response
IgD 	• Antibody found exclusively on the surface of B cells • Has a role in B cell sensitization and activation

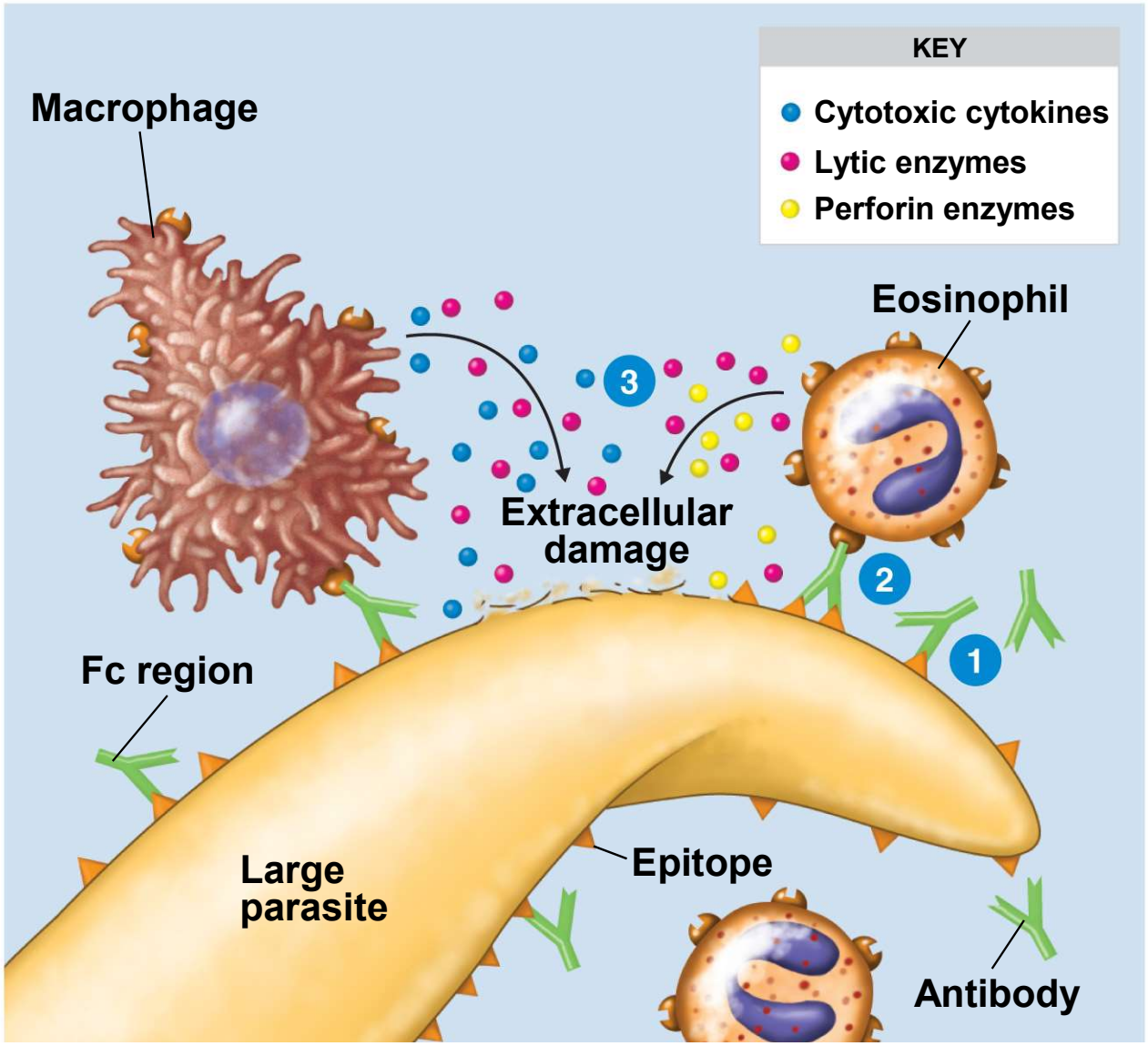
Agglutination



(a)



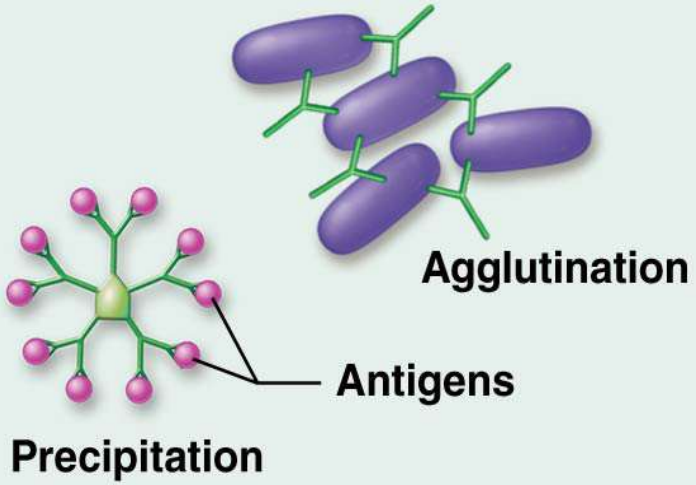
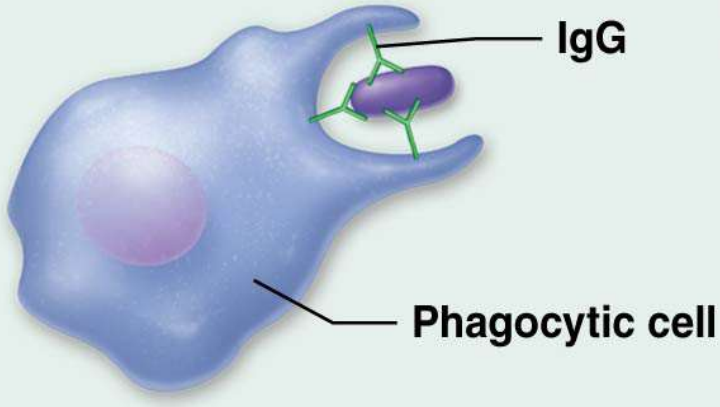
Antibody-dependent cell-mediated cytotoxicity (ADCC).

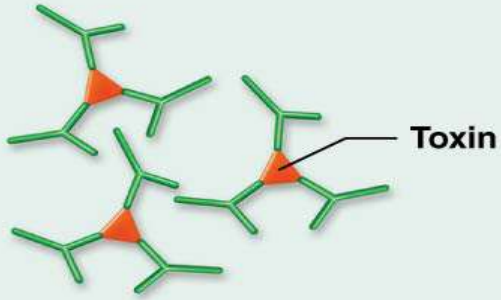
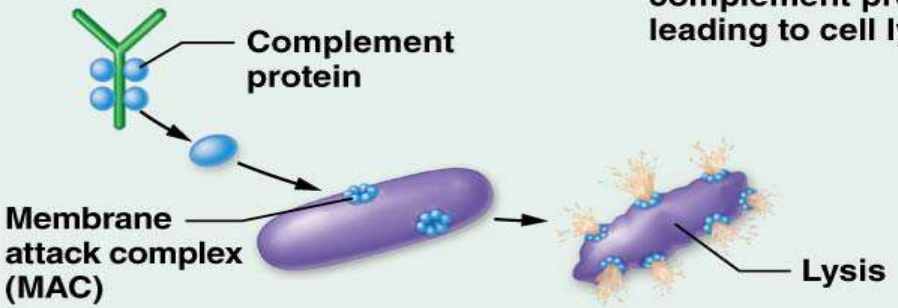
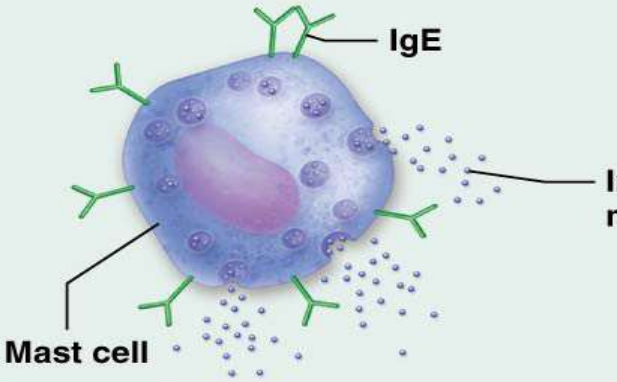


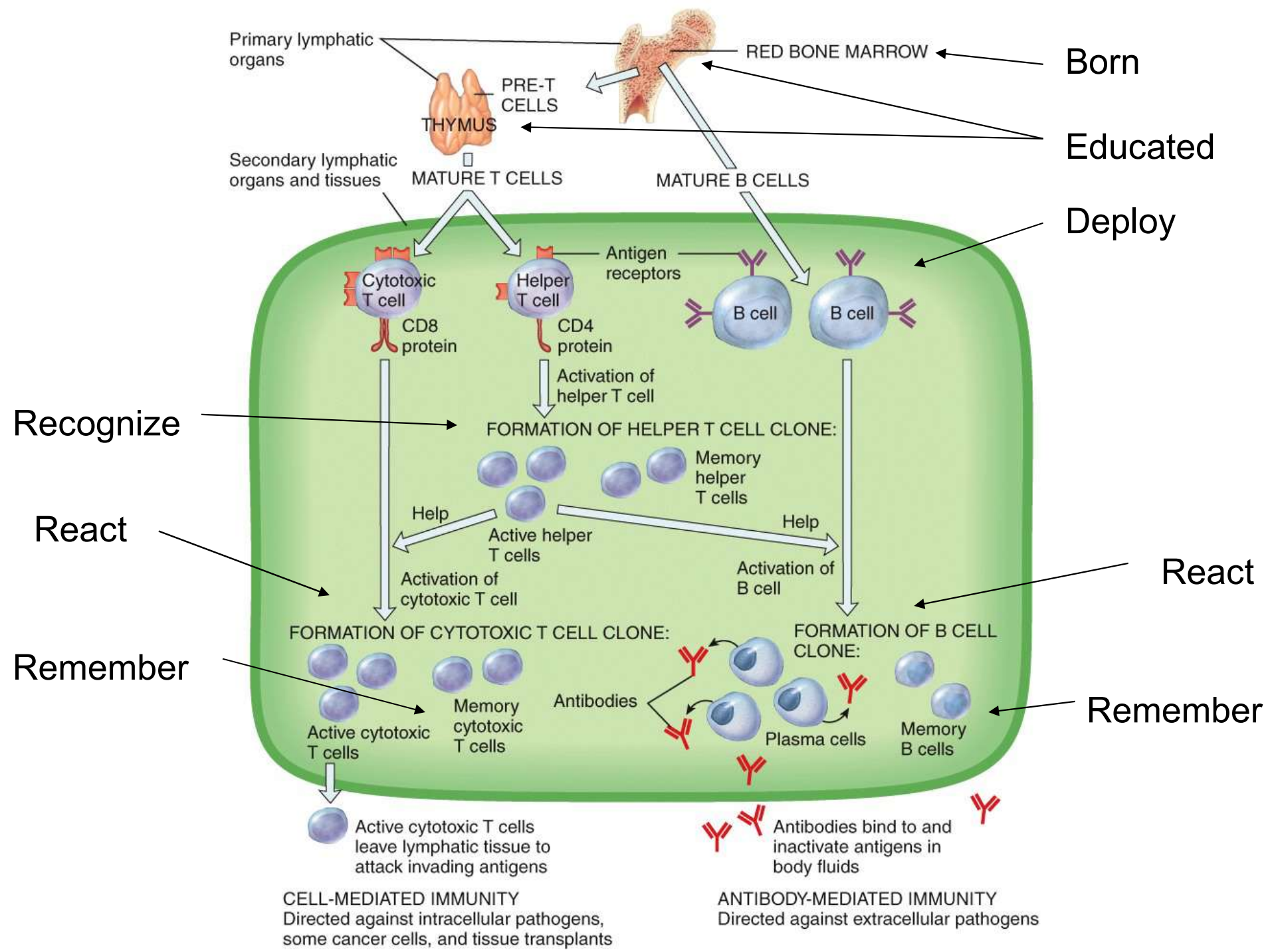
(a) Organisms, such as many parasites, that are too large for ingestion by phagocytic cells must be attacked externally.

Functions of Antibodies.

- Agglutination/Percipitation
- Opsonization
- Neutralization
- Complement Activation
- Stimulation of Inflammation

FUNCTION	DESCRIPTION
Agglutination/precipitation  	Antibodies clump antigens together to enhance phagocytosis.
Opsonization  	IgG coats antigens and binds phagocytes, enhancing phagocytosis.

FUNCTION	DESCRIPTION
Neutralization 	Antibodies bind pathogenic components of toxins and block toxic effects.
Complement activation 	Antibodies activate complement proteins, leading to cell lysis.
Stimulation of inflammation 	IgE binds mast cells and basophils, and triggers release of inflammatory mediators.


Primary lymphatic organs
RED BONE MARROW
Born
PRE-T CELLS
THYMUS
Educated
Secondary lymphatic organs and tissues
MATURE T CELLS
MATURE B CELLS
Deploy
Antigen receptors
Cytotoxic T cell
Helper T cell
B cell
B cell
CD8 protein
CD4 protein
Activation of helper T cell
Recognize
FORMATION OF HELPER T CELL CLONE:
Memory helper T cells
React
Help
Help
Active helper T cells
Activation of cytotoxic T cell
Activation of B cell
React
FORMATION OF CYTOTOXIC T CELL CLONE:
FORMATION OF B CELL CLONE:
Remember
Antibodies
Memory cytotoxic T cells
Active cytotoxic T cells
Plasma cells
Memory B cells
Remember
Active cytotoxic T cells leave lymphatic tissue to attack invading antigens
Antibodies bind to and inactivate antigens in body fluids
CELL-MEDIATED IMMUNITY
Directed against intracellular pathogens, some cancer cells, and tissue transplants
ANTIBODY-MEDIATED IMMUNITY
Directed against extracellular pathogens

What is the difference between a primary & secondary humoral response?

- Primary immune response – immune reaction brought about by the first exposure to an antigen
  - appearance of protective antibodies delayed for 3 to 6 days while naïve B cells multiply and differentiate into plasma cells
  - as plasma cells produce antibodies, the **antibody titer** (level in the blood plasma) rises
    - IgM appears first, peaks in about 10 days, soon declines
    - IgG levels rise as IgM declines, but IgG titer drops to a low level within a month

What is the difference between a primary & secondary humoral response?

- primary response kills pathogen and leaves one with an immune memory to the patogen's antigen
  - during clonal selection, some of the clonal cells becomes memory B cells
  - found mainly in germinal centers of the lymph nodes
  - memory cells able to mount a very quick secondary response // memory cells respond in a matter of minutes or hours to foreign antingen /// not days!

What is secondary humoral immunity?

- Occurs when re-exposed to the same antigen
- New plasma cells from memory B cells form within hours
- IgG titer rises sharply and peaks in a few days
- response is so rapid that the antigen has little chance to exert a noticeable effect on the body
- no illness results – not even a fever!
- low levels of IgM also secreted and quickly declines
- IgG remain elevated for weeks to years // conferring long lasting protection
- The “memory function” does not last as long in humoral immunity as it does in cellular immunity

Humoral Immunity Responses

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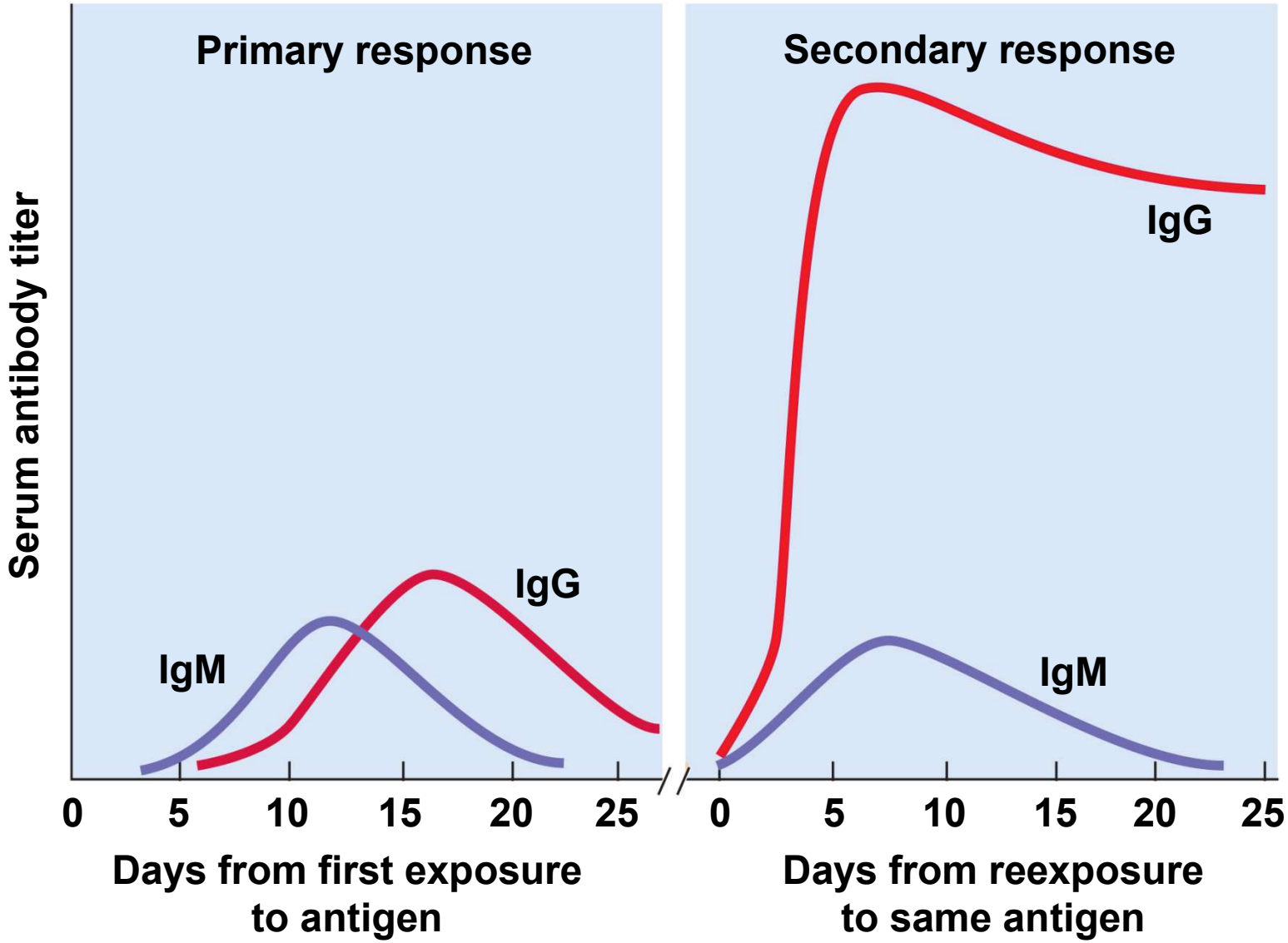

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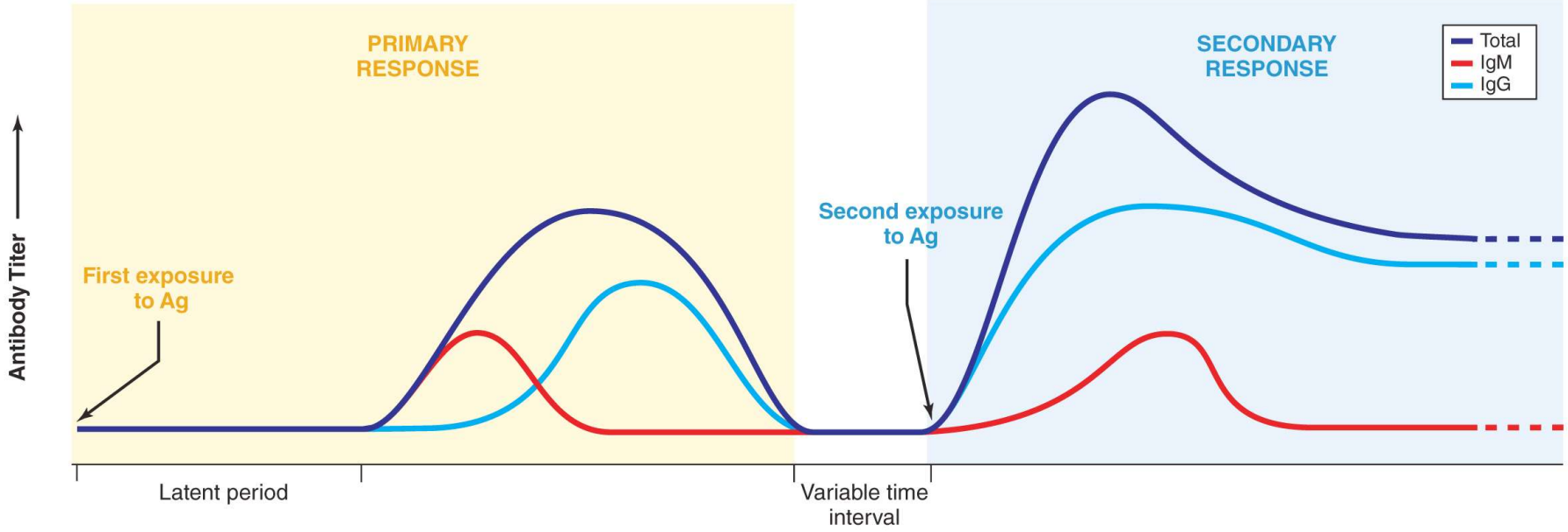
Table 13.9 Primary and Secondary Response to Antigens



Upon the first exposure to an antigen, the system undergoes a **primary response.** The earliest part of this response, the *latent period,* is marked by a lack of antibodies for that antigen, but much activity is occurring. During this time, the antigen is being concentrated in lymphoid tissue and is being processed by the correct clones of B lymphocytes. As plasma cells synthesize antibodies, the serum titer increases to a certain plateau and then tapers off to a low level over a few weeks or months. Early in the primary response, most of the antibodies are the IgM type, which is the first class to be secreted by plasma cells. Later, the class of the antibodies (but not their specificity) is switched to IgG or some other class (IgA or IgE).

After the initial response, there is no activity, but memory cells of the same specificity are seeded throughout the lymphatic system.

When the immune system is exposed again to the same immunogen within weeks, months, or even years, a **secondary response** occurs. The rate of antibody synthesis, the peak titer, and the length of antibody persistence are greatly increased over the primary response. The speed and intensity seen in this response are attributable to the memory B cells that were formed during the primary response. The secondary response is also called the **anamnestic response.** The advantage of this response is evident: It provides a quick and potent strike against subsequent exposures to infectious agents.

How may the response to adaptive immunity vary between different people?

- Immune responses may be:
  - Just right / maintains healthy state
  - Too vigorous = hypersensitivity (e.g. Anaphylactic shock)
  - Too weak = immunodeficiency disease (e.g. AIDS)
  - Misdirected against wrong target cells = autoimmune diseases (i.e. Type 1 diabetes)