CHAPTER 11

THE IMMUNE RESPONSE
B cells

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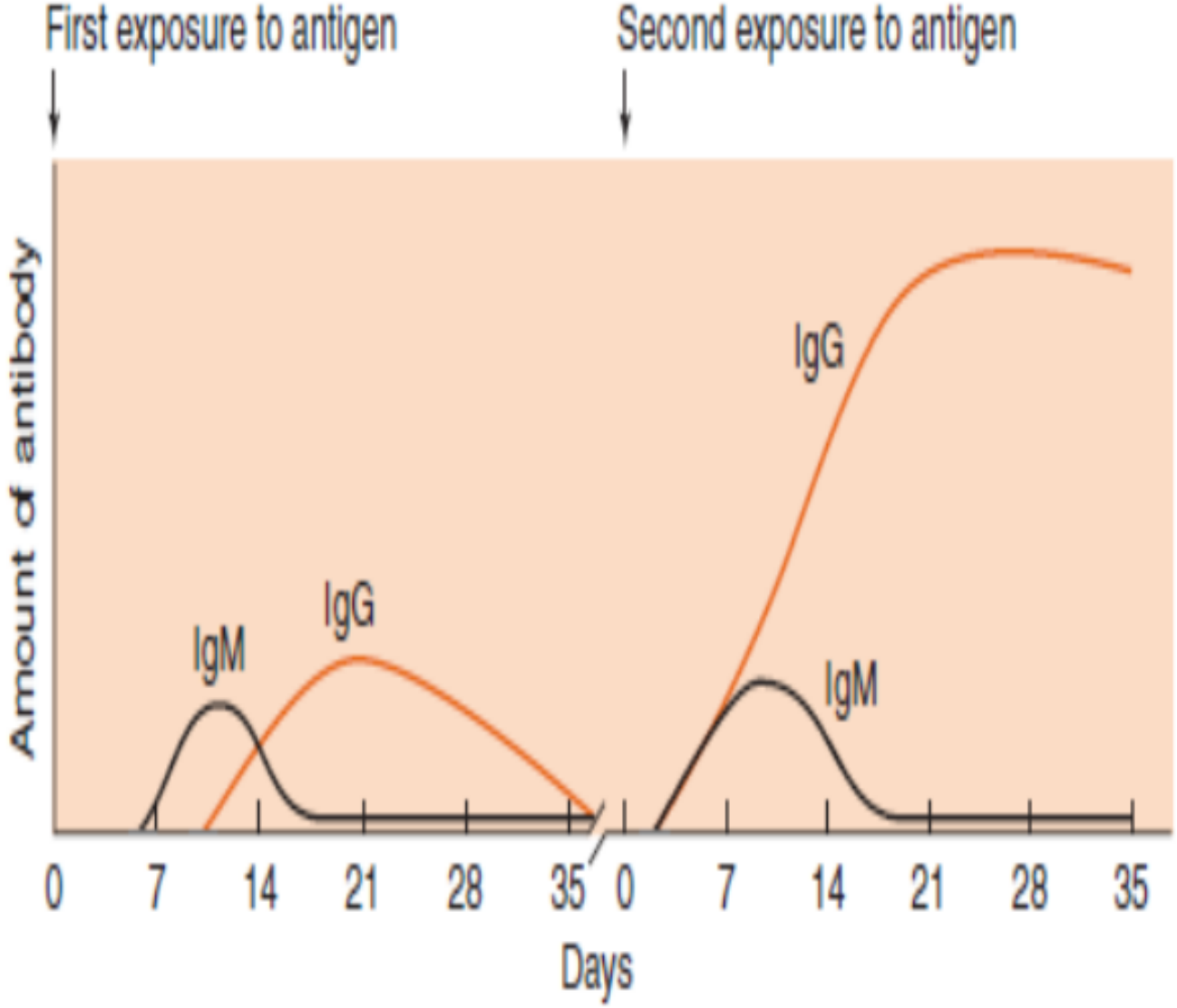

First exposure to antigen
Second exposure to antigen
Amount of antibody
IgM
IgG
IgG
IgM
0
7
14
21
28
35
0
7
14
21
28
35
Days

THE PRIMARY ANTIBODY RESPONSE

- The primary antibody response is characterized by the initial production of IgM.
- As the response matures, IgG antibodies rapidly increase in concentration.
- IgM antibodies appear in the blood within 3 days to 2 weeks after exposure to a novel immunogen.

- The first antibodies that are produced react with residual antigen and therefore are rapidly cleared.
- After the initial lag phase, however, the antibody titer increases logarithmically to reach a plateau.

- Reexposure to an immunogen, a **secondary response**, induces a heightened antibody response (also termed **anamnestic response**).

- The antibodies develop more rapidly, last longer, and reach a higher titer.

- The antibodies in a secondary response are principally of the IgG class

THE SECONDARY RESPONSE

- When there is a second encounter with the same antigen months or years after the primary response, there is a **rapid antibody response** (the lag period is typically only **3–5 days**)
- to **higher** levels than the primary response.

- This is attributed to the **persistence of antigen-specific "memory cells"** after the first contact.

THE SECONDARY RESPONSE

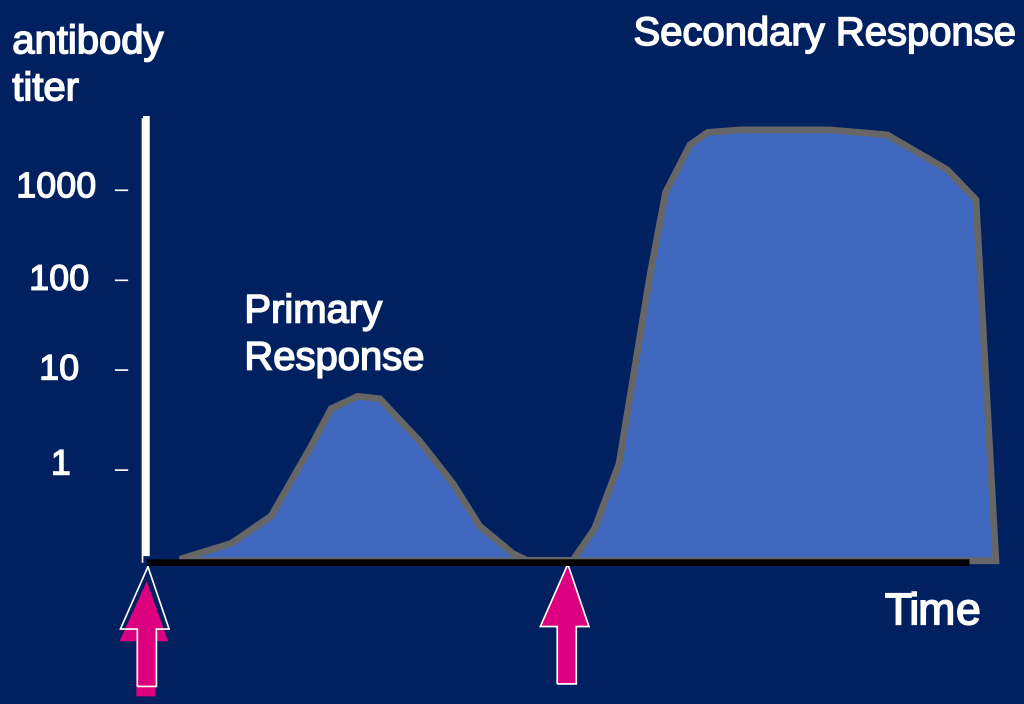
- These memory cells proliferate to form a large clone of specific B cells and plasma cells, which mediate the secondary antibody response.
- During the secondary response, the amount of IgM produced is similar to that after the first contact with antigen.

- However, a much **larger** amount of **IgG** antibody is produced,
- and the levels tend to persist much **longer** than in the primary response.

- With each succeeding exposure to the antigen, the antibodies tend to bind antigen more firmly.

- **Antibody binding improves** because mutations occur in the DNA that encodes the antigen-binding site, a process called **somatic hypermutation.**

The Anamnestic Immune Response



- Some mutations result in the insertion of different amino acids in the hypervariable region that result in a better fit and cause the antigen to be bound more strongly.

- The subset of plasma cells with these improved hypervariable regions are more strongly (and more frequently) selected by antigen and therefore constitute an increasingly larger part of the population of antibody-producing cells.

- This process is called **affinity maturation.** One important effect of booster doses of vaccines is to improve antibody binding by enhancing the affinity maturation process.

- Affinity maturation occurs in the germinal centers of the follicles in the spleen and lymph nodes.

- Follicle dendritic cells capture antigen–antibody complexes on their surface via Fc receptors.

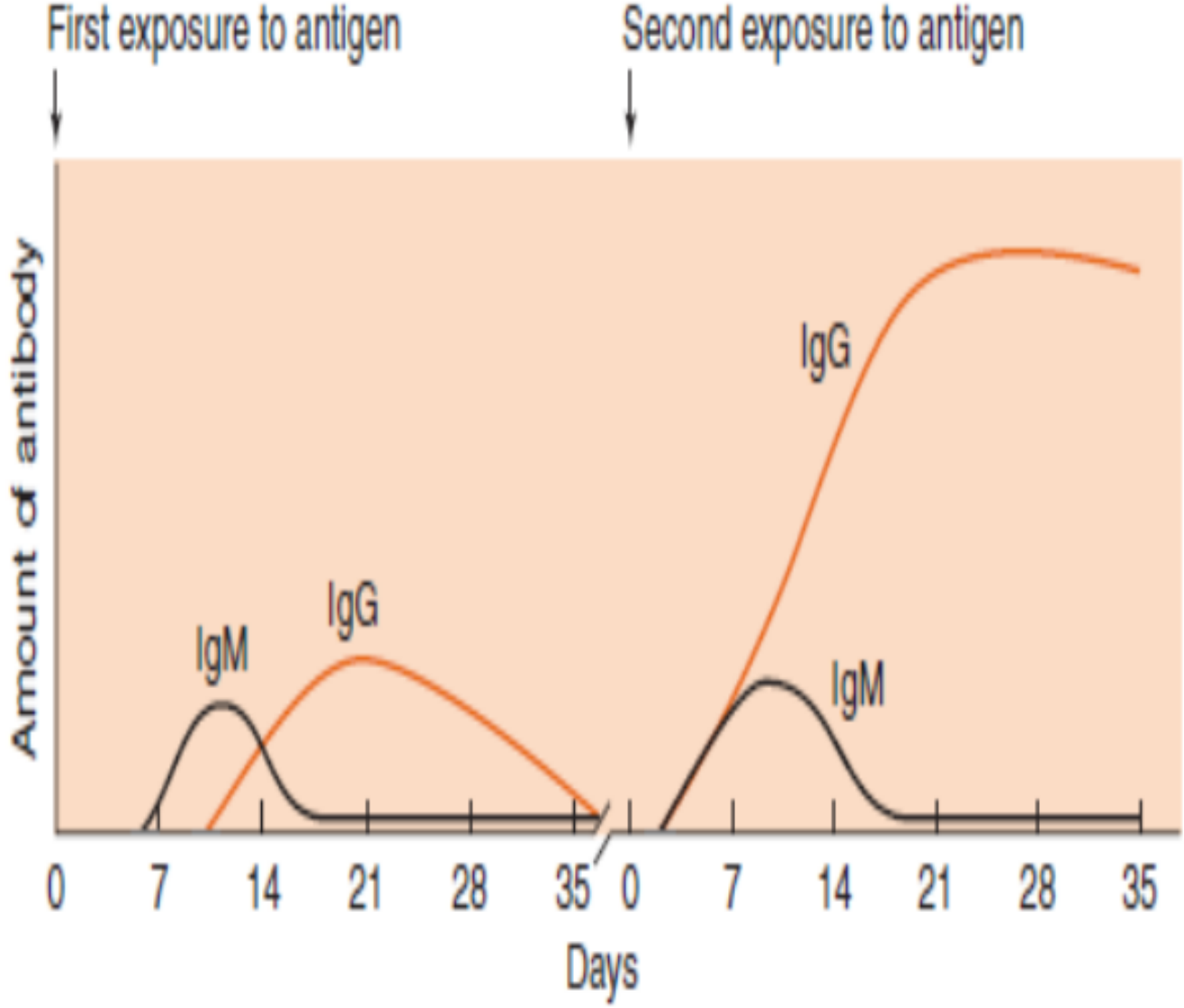
- The complexes interact with an activated B cell bearing the immunoglobulin that best fits the antigen, and it is that B cell that is stimulated to form a clone of many B cells capable of synthesizing the improved antibody.

RESPONSE TO MULTIPLE ANTIGENS ADMINISTERED SIMULTANEOUSLY

- When two or more antigens are administered at the same time, the host reacts by producing antibodies to all of them.

- Competition of antigens for antibody-producing mechanisms occurs experimentally but appears to be of little significance in medicine.

- Combined immunization is widely used (e.g., the diphtheria, tetanus, and pertussis [DTP] vaccine or the measles, mumps, rubella [MMR] vaccine).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Protective Functions of Antibodies

Antibodies can produce resistance to infection by five major mechanisms.

1. **Enhanced Phagocytosis** —Antibodies produce resistance by opsonizing (coating) organisms, which make them more readily ingested by phagocytes. directed against microbial infections in which virulence is related to polysaccharide capsules (eg, pneumococcus, *Haemophilus* spp., *Neisseria* spp.).

In such infections, antibodies complex with the capsular antigens and make the organisms susceptible to ingestion by phagocytic cells and destruction within the cells.

- **2. Virus Neutralization** —Antibodies directed against specific viral proteins can bind to the virus and block the ability of the virus particle to attach to its cellular receptor. Since the virus cannot invade the cell, it cannot replicate.

- **3. Neutralization of Toxins** —Antibodies can neutralize toxins of microorganisms (eg, diphtheria, tetanus, and botulism) and inactivate their harmful effects.

- **4. Complement-Mediated Lysis —**The attachment of antibodies to viral proteins on virus infected cells or to a microbial cell can activate the complement system leading to cell lysis.

- **5. Antibody-Dependent Cell Cytotoxicity (ADCC) —** The attachment of antibodies to viral proteins on the virus infected cell can lead to the interaction of the antibody-coated cells with a killer cell, leading to lysis.

- Since antibodies are protective, strategies have been developed to induce their production (Active Immunity) or to administer preformed antibodies to the host (Passive Immunity).