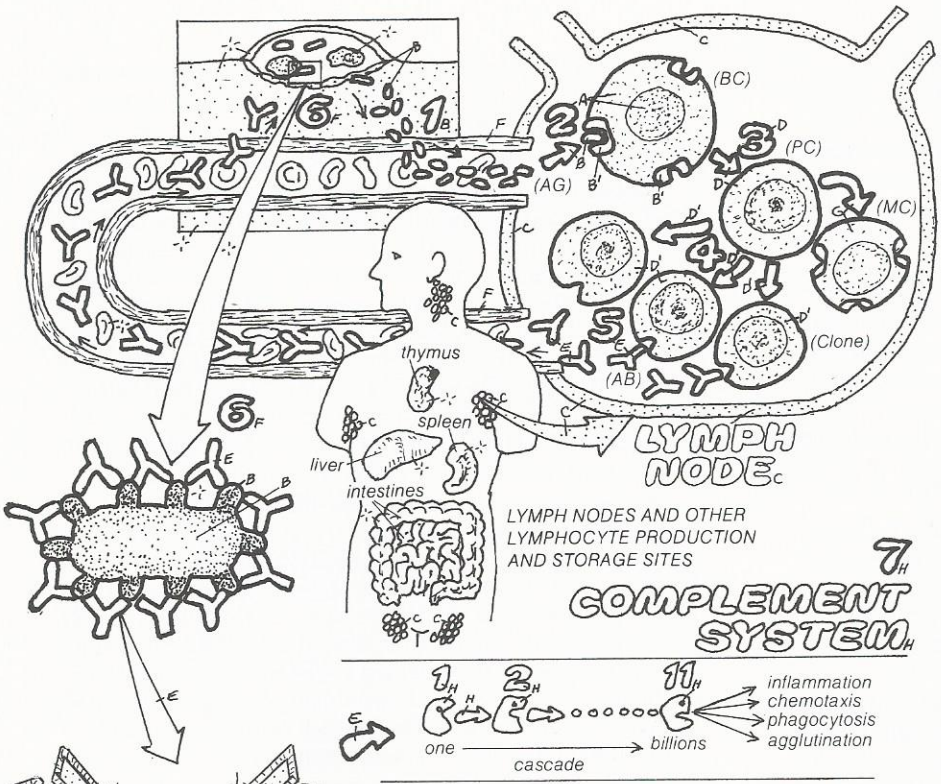
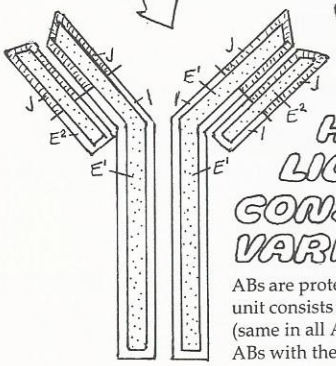
ACQUIRED IMMUNITY: SPECIFIC ANTIBODY RESPONSE



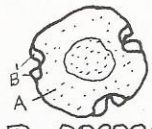
LYMPH NODES AND OTHER LYMPHOCYTE PRODUCTION AND STORAGE SITES

COMPLEMENT SYSTEM H

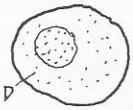


ANTIBODY E (IMMUNOGLOBULINS)
HEAVY CHAIN E'
LIGHT CHAIN E2
CONSTANT PART I
VARIABLE PART J

ABs are protein molecules (immunoglobulin, Ig) with two or more subunits. Each subunit consists of a heavy and a light polypeptide chain. Each chain has a constant part (same in all ABs) and a variable part (different in each AB). The variable part endows ABs with the ability to recognize the various AGs (i.e., selectivity and specificity).



RECOGNIZES ANTIGENS
B-LYMPHOCYTE A



FORMS CLONES, SECRETES ANTIBODIES
PLASMA CELL D

MAKES ANTIBODIES FOR FUTURE USE
MEMORY CELL G

Antigens (AGs) are foreign protein or polysaccharide substances on the surface of microbes entering the body (1). In the lymph nodes, AGs are detected by receptors on B-lymphocytes (BCs) (2). Each BC is genetically programmed to respond to one particular AG. Sensitized BCs transform into plasma cells (PCs) (3). PCs divide, forming a clone (4); the clone produces antibodies (ABs) (5) rapidly and profusely. Each AB is specific for an AG. The ABs circulate in the lymph and blood, binding to and deactivating AG (6). ABs can inactivate AG either directly or indirectly by activating the complement system (7), a cascade of enzyme reactions in the plasma that facilitates direct actions of ABs and promotes chemotaxis and inflammatory responses, causing lysis or phagocytosis of AG cells.

MICROBE/ANTIGEN B
B-LYMPHOCYTE A
AG-RECEPTOR B'
PLASMA CELL D
CLONE D'
ANTIBODY E
BLOOD CIRCULATION F
MEMORY CELL G

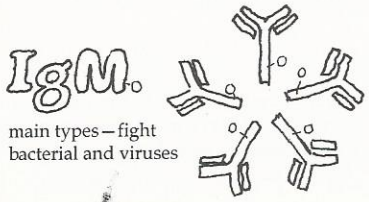
CLASSES OF ANTIBODIES E

(*secretory immunoglobulins*) in milk, gastric and respiratory mucosal fluids

B-cells surface, recognize antigens

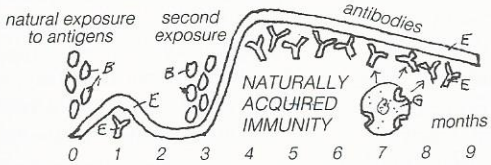
participate in allergic reactions

(*g-globulins*) main types—fight bacterial and viruses

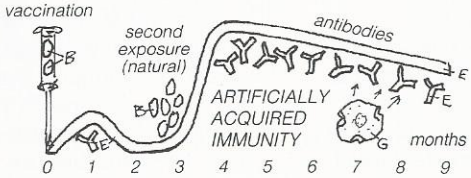


main types—fight bacterial and viruses

MEMORY CELL FUNCTION G

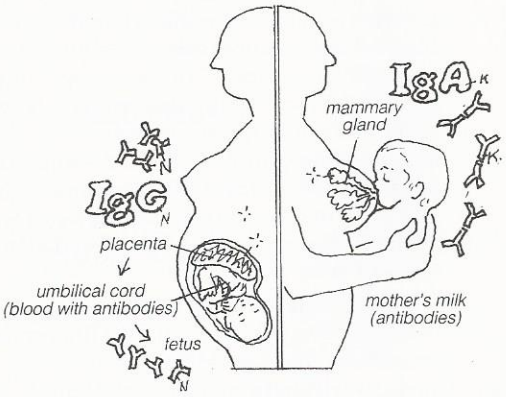


After exposure to AG and during sensitization, some PCs transform to memory cells (MCs). These remain dormant in the lymph nodes for long periods. Upon further exposures to the AG, MCs will evoke a pronounced, exaggerated response (AB production) that will rapidly deactivate AGs. The MC response is the basis of natural and long-term immunity against bacteria and some viruses.



The MCs response is also the basis of the practice of immunization and vaccination practices. Small amounts of AG (dead or live) is given by injection. B-cells detect the AG and form PCs to make ABs and also MCs. These remain dormant until a natural invasion of the same antigen or microbe when MCs will evoke a pronounced, exaggerated response (specific AB production) that will rapidly deactivate the natural AGs.

PASSIVE IMMUNITY E



Some ABs (IgG type) transfer from mother to fetus across placenta to supply the fetus with natural immunity. Antibodies (type IgA) also are secreted in the milk for transfer to newborn via suckling. Newborn's intestinal mucosa can absorb whole IgA antibody proteins intact. This ability lasts for the first few weeks of life, showing the value of breast feeding in early weeks of life. The colostrum (first milk) is specially enriched in antibodies.

ACQUIRED IMMUNITY: B-LYMPHOCYTES & ANTIBODY-MEDIATED RESPONSES

Two types of acquired immunity – The *lymphocytes* participate in immune responses that develop *slowly* and *specifically* against particular foreign substances (*antigens*). This response is genetically programmed but occurs only *after* exposure to the antigen (*acquired immunity*). Two types of acquired immune responses are: *humoral-* or *antibody-mediated responses*, carried out by the *B-lymphocytes* (this plate) and *cell-mediated responses*, carried out by the *T-lymphocytes* (next plate, 148).

ACTIVE ANTIBODY-MEDIATED IMMUNITY

Antigens are usually foreign proteins (e.g., toxins), either free-floating or on the surface of infectious organisms – The presence of antigens is sensed by special receptor molecules on the surface of *B-lymphocytes* in the *lymph nodes*. The early precursor B-cells are in the bone marrow but migrate into bursa-like organs – e.g., lymph nodes – to mature. The numerous B-cells are specialized to detect a certain type of antigen. The B-cells are genetically programmed to express the receptors that recognize specific antigens. These surface receptors are a type of antibodies (see below).

Antibodies are produced by clones of plasma cells – The detection of an antigen sensitizes the B-cells; they transform into larger secretory cells called *plasma cells*. These proliferate, forming a *clone*, which synthesizes and secretes, for export to the plasma and tissues, a large amount of a specific protein called an *antibody*, whose function is to bind and neutralize the antigens (see below) of mainly bacterial origin. The formation and proliferation of plasma cells are controlled by the release of *cytokines* from the *helper T-lymphocytes* (plate 148). Antibody production against foreign antigens is a form of *active immunity* and takes from *days* to *weeks* to fully develop.

Several classes of antibodies – All the varieties of antibodies produced against the many different antigens are protein molecules (*immunoglobulins, Ig*). IgG (*γ-globulins*) and IgM are the most abundant types and function against bacterial and viral infections. The IgD type exists on the surface of B-cells for recognizing antigens, and the IgE-type antibodies participate in allergic reactions. The IgA-type antibodies are *secretory immunoglobulins* produced by a type of resident plasma cells and released into the secretions of the gastrointestinal and respiratory mucosa and milk.

Antibody molecules have variable & constant segments – Each antibody is roughly Y-shaped, consisting of *heavy chains* (peptide chains) and two *light chains*. The heavy chains provide the *constant* part of the antibody molecule, which is the same in all antibodies; the light chains, located in the arms of the Y (attached to the heavy chains), constitute the *variable* and functionally significant part of the molecule. Thus, each antibody has two sites, one on each of the variable arms, for interaction with the antigen. The extreme diversity of antibodies is largely based on structural variation (amino acid composition) in the variable protein chains.

Antigen-antibody binding deactivates microbes & their toxins – Upon encountering an antigen in the blood or tissue fluids, the antibodies bind with the antigen molecules in order to neutralize and deactivate them. Deactivation occurs by *direct* combination, causing *precipitation* (agglutination) or by *masking* the active sites of the antigens. If antigen is a free toxin molecule, the antigen-antibody complexes tie together, forming clumps to be engulfed by phagocytes. Binding of antibodies to surface antigens of microbes causes the microbes to be recognized, attacked, and destroyed by the phagocytes.

The complement system helps antibodies destroy microbes – Antibodies can also achieve the same goals *indirectly* by activating the *complement system*, which consists of a series of enzymes arranged to catalyze a cascade of chemical events. The combination of a single antibody molecule with the antigen activates this cascade, which rapidly mobilizes millions of enzymes that quickly lyse the microorganism to which the antigen is attached or cause agglutination and similar defensive reactions.

Memory cells learn to make antibodies for future encounters with antigens – After antigens are removed, the antibodies diminish in number. Upon second exposure to the same antigen, a large amount of the same appropriate antibody is produced. This enhanced response is due to a type of plasma cell called the *memory cell*. B-cells produce memory cells upon their first exposure to the antigen. Memory cells "learn" how to produce the antibody but rest until the second exposure to the same antigen, when they are activated and form clones that produce large amounts of the antibody. This is the basis of long-term immunity against infections.

PASSIVE IMMUNITY, VACCINATION, & AUTOIMMUNE REACTIONS

Passive immunity refers to antibody transfer across placenta & via milk – Embryos and younger fetuses are essentially devoid of antibodies, as they live in a protected environment. Some maternal antibodies (IgG antibodies) can transfer across the placenta. Maternal antibodies are also provided after birth in the form of milk IgA immunoglobulins. The newborn intestinal mucosa can engulf and absorb whole IgA antibody proteins intact. This ability lasts for the first few weeks of life and is one reason breast feeding is encouraged even if for a short duration. The colostrum (first milk) is specially enriched in antibodies (plate 159).

Vaccination involves artificial activation of memory cells – The memory cells are involved in the phenomenon of immunization by *vaccination*, in which the body is intentionally exposed to a small amount of dead or transformed antigen (e.g., dead smallpox virus) in order to sensitize the immune system and form memory cells. When the body is exposed to the same antigen later (e.g., during a real smallpox infection), antibody production will be quick and intense and usually effective.

Therapeutic use of antibodies – Monoclonal antibodies produced in the laboratory by culturing B cells can be given to patients suffering from specific diseases. The results are effective but short lasting. The use of antibodies to find and kill tumor and cancer cells is now under investigation.

Autoantibodies are the cause of autoimmune diseases – Occasionally, antibodies are mistakenly produced against certain normal surface proteins of the body's own cells. Also, antibodies produced against a foreign protein may mistakenly attack a normal cell surface protein that resembles the antigen (cross-reaction). These attacks of *autoimmune antibodies* cause damage to or death of the invaded cell and produce a wide variety of diseases (*autoimmune diseases*), such as Grave's disease (hyperthyroidism), Type-I diabetes, myasthenia gravis, rheumatoid arthritis, and multiple sclerosis.

CN: Use the same colors as on previous page for antigen (A) and blood circulation (F).
1. Follow the numbered sequence above, beginning in the upper left rectangle.
2. Color the lymph node sites in the body.
3. Complete antibodies and the complement system.
4. Give a separate color to each class of antibodies.
5. Color acquired and passive immunity material below.