

Selection and activation of B cells

When antigen is introduced into an individual, B cells with receptors for that antigen bind and internalize it into an endosomal compartment, and process and present it on MHC class II molecules to helper T cells (Topics H2 and H4). These B cells are triggered to proliferate, giving rise to clones of large numbers of daughter cells. Some of the cells of these expanding clones serve as memory cells, others differentiate and become plasma cells (Topic E3) which make and secrete

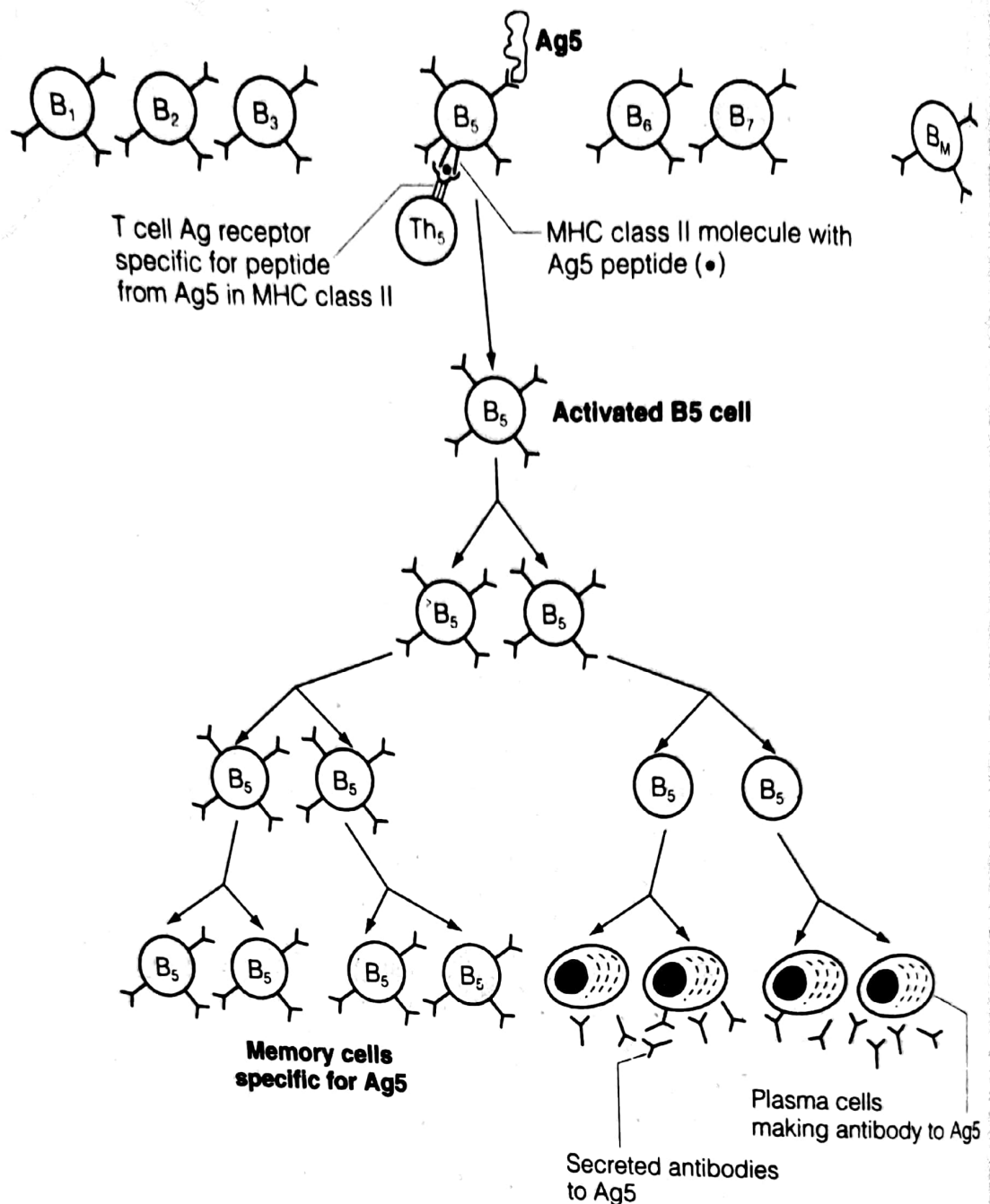


Fig.1. Clonal selection, memory cells and plasma cells.

large quantities of specific antibody. For example, on introduction of antigen 5 (Ag5) into a person (Fig. 1), more than 10^6 B cells have the opportunity to interact with it. Only a very few B cells (e.g. B5) have receptors specific for this antigen. B5 binds Ag5, internalizes, and processes and presents it on MHC class II molecules on the surface of this B cell. T helper cells with specific receptors for a peptide from Ag5 in MHC class II bind to this complex and stimulate this B cell to clonally expand and differentiate into memory B cells and plasma cells which produce soluble antibody to Ag5. In addition, direct T cell interaction with the B cell induces class switching, which depending on the type of helper cell (Th1 vs Th2) and the cytokines it secretes, will result in production of antibody of the IgG, IgA or IgE classes (Topic F2).

Primary and memory responses

When introduced into an individual who has not previously encountered the antigen (e.g. microbe), a **primary** immune response will develop within 4-5 days (Fig. 2). This response results initially in the production of IgM and then IgG or other antibody isotypes directed toward the antigen, and has a duration and

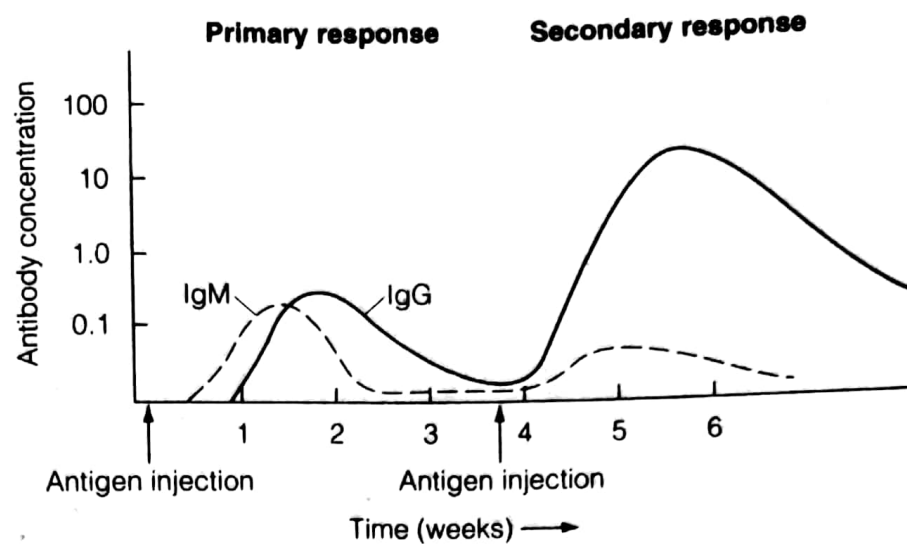


Fig. 2. Kinetics of the immune response.

antibody isotype profile which depends on the quantity of antigen introduced and its mode of entry. The antibody produced reacts with remaining antigen, forming complexes and/or precipitates which are eliminated by phagocytes. Antibody is continually made by plasma cells during their short life span (3–4 days). If enough antigen is introduced initially, there could be restimulation of antigen specific B cells, subsequent development of more plasma cells and thus increased production of antibody. Eventually, when all of the antigen has been removed and none remains to stimulate B cells, the antibody response will reach its peak and the concentration of antibody in the circulation will begin to decrease as a result of the normal rate of catabolism of the antibody.

At the time antigen is reintroduced, more antigen specific B cells exist in the individual compared with the period before primary introduction of antigen. Moreover, these cells have differentiated to more responsive memory B cells. Thus, a secondary (memory or anamnestic) antibody response occurs which is characterized by a much shorter lag period before significant levels of antibody are found in the serum, by the presence of many more plasma cells, by a higher rate of antibody production, and thus a much higher serum concentration of antibody, usually of the IgG class.

Responses are usually multiclonal

Although antibodies produced by a single cell and its daughter cells are identical (homogeneous or monoclonal), the response to a given antigen involves many different clones of cells and thus, overall, is very heterogeneous (multiclonal). Considering the size of an antigenic determinant, the number of determinants on a molecule, and the number of different molecules on a microorganism, the response to a microorganism results in a large number of different antibodies (Fig. 3). Even antibodies against a single antigenic determinant are heterogeneous, indicating that the immune system is capable of producing many different antibodies, even to a single well-defined antigenic determinant. This heterogeneity is essential for many of the protective functions of antibodies (Topic F5).

Cross-reactive responses

Occasionally, a similar or identical antigenic determinant is found in association with widely different molecules or cells. This is termed cross-reactivity. Thus, the presence in most individuals of antibodies directed toward blood group carbohydrates other than their own is a result of the presence on certain

microorganisms of carbohydrate antigens which are very similar, if not identical, with the blood group antigens. Infection with such an organism causes the production of antibodies directed toward the antigenic determinants of the microorganism including these carbohydrate antigens (Table 1).

The development of immunity to one organism could, in some instances, protect against infection by another organism with cross-reactive antigens. Many vaccines are effective because of similar or identical determinants expressed by: (a) both virulent and avirulent strains of the organism; or (b) toxic molecules and their non-toxic derivative (Topic R4). Natural or innate antibody to a wide variety of molecules is probably a result of the same phenomenon. In addition, certain kinds of autoimmune disease may be due to infection by organisms bearing antigens that are cross-reactive with normal self antigens. Group A β -hemolytic streptococcal infections may lead to rheumatic fever as a result of the development of antibodies to the streptococcal determinants. Because of the similarity of the streptococcal antigens to molecules in heart tissue, the antibodies may then react with and damage not only the microorganism but also heart muscle cells (Topic U3).

Table 1. Examples of clinically relevant cross-reactivity

Immunogen	Cross-reactive antigen	Importance
Tetanus toxoid	Tetanus toxin	Protection vs bacterial toxin
Sabin attenuated strain of polio virus	Poliomyelitis	Protection vs pathogenic polio virus
Various microorganisms	Type A and type B RBC carbohydrates	Transfusions
β -hemolytic <i>Streptococcus</i>	Heart tissue antigens	Rheumatic fever