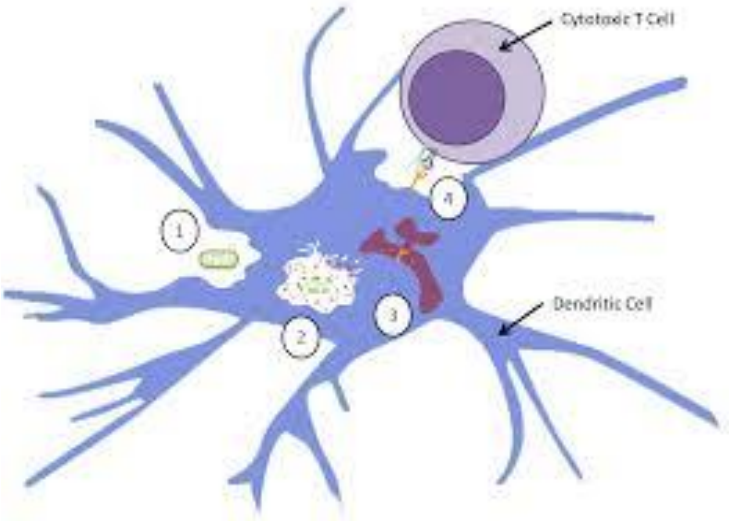
Antigen-Presenting Cells (APCs)

Although B cells are a form of antigen -presenting cell (APC) that we have already discussed with humoral immunity, we will now consider other APCs associated with cellular immunity. These APC's are the dendritic cells and the activated macrophages.

Dendritic Cells

Dendritic cells (DCs) are characterized by long extensions called dendrites because they resemble the dendrites of nerve cells.



They were first identified in anatomical studies of the skin by Langerhans in 1868, and the dendritic cells in the skin and genital tract are still called Langerhans cells, or Langerhans DC.

This represents only one of at least four populations of DCs named for their derivation or location. Other populations are found in the lymph nodes, spleen, thymus, blood, and various tissues, except the brain.

Dendritic cells are the principal APCs to induce immune responses by T cells.

Macrophages

Macrophages (from the Greek for large eaters) are cells usually found in a resting state. They are important for innate immunity and for ridding the body of worn out blood cells and other debris, such as cellular remnants from apoptosis. Their phagocytic capabilities are greatly increased when they are stimulated to become activated macrophages. This activation can be initiated by ingestion of antigenic material.

Other stimuli, such as cytokines produced by an activated helper T cell, can further enhance their capabilities. Once activated, macrophages are more effective as phagocytes and as APCs. Activated macrophages are important factors in the control of cancer cells and such intracellular pathogens as the tubercle bacillus and virus-infected cells.

After taking up an antigen, APCs tend to migrate to lymph nodes or other lymphoid centers on the mucosa, where they present the antigen to T cells located there. T cells carrying receptors that are capable of binding with any specific antigen are present in relatively limited numbers.

Extracellular Killing by the Immune System

We have seen how the action of a cytotoxic T lymphocyte CTL can lead to the destruction of a target cell. A component of the innate immune system that has not yet been discussed can also destroy certain virus-infected cells and tumor cells. These are granular leukocytes (10-15% of circulating lymphocytes) called natural killer (NK) cells. They can also attack parasites, which are normally much larger than bacteria, in contrast to CTLs, NK cells are not immunologically specific; that is, they do not need to be stimulated by an antigen. NK cells cause pores to form in the target cell, which leads to either lysis or apoptosis.

The functions of NK cells and the other principal cells involved in cellular immunity are briefly summarized in Table 17.2.

Cell	Function
T Helper (T_H1) Cell	Activates cells related to cell-mediated immunity: macrophages, T_c cells, and natural killer cells
T Helper (T_H2) Cell	Stimulates production of eosinophils, IgM, and IgE
Cytotoxic T Lymphocyte (CTL)	Destroys target cells on contact; generated from T cytotoxic (T_c) cell
T Regulatory (T_{reg}) cell	Regulates immune response and helps maintain tolerance
Activated Macrophage	Enhanced phagocytic activity; attacks cancer cells
Natural Killer (NK) Cell	Attacks and destroys target cells; participates in antibody-dependent cell-mediated cytotoxicity

Cytokines: Chemical Messengers of Immune Cells

The immune response requires complex interactions between different cells. The communication required for this is mediated by chemical messengers called **cytokines** These are soluble proteins or glycoproteins that are produced by practically all cells of the immune system in response to a stimulus. Many cytokines-there are probably more than 200-have common names that reflect their functions known at the time of their discovery; some are now known to have multiple functions . A cytokine acts only on a cell that has a receptor for it.

Cytokines that serve as communicators between leukocytes (white blood cell s) are now known as **interleukins** (between leukocytes). such as IL- l, and so on, by an international committee.

A family of small cytokines that induces the migration of leukocytes into areas of infection or tissue damage is called **chemokines**, from chemotaxis. They are especially important in inflammation. Certain chemokine receptors are important for infection by HIV.

Another family of cytokines is the **interferons**, originally named for one of their functions, protecting cells from viral infection, such as IFN-α, and so on. A number of these arc available as commercial products in treating disease conditions such as hepatitis and some cancers. A very important cytokine family is that of **tumor necrosis factor**, such as TNF-α, and so on. TNF was originally named because tumor cells were observed to be one of its targets. These cytokines are a strong factor in inflammatory reactions of auto immune diseases such as rheumatoid arthritis. Monoclonal antibodies that block the action of TNF are an available therapy for some of these conditions.

A family of cytokines, **hematopoietic cytokines**, function in controlling the pathways by which stem cells develop into different red or white blood cells. Some of these are interleukins with designations such as IL-3, and so on.

Immunological Memory

The intensity of the antibody-mediated humoral response can be reflected by the antibody titer, the relative amount of antibody in the serum. After the initial contact with an antigen, the exposed person's serum contains no detectable antibodies for 4 to 7 days. Then there is a slow rise in antibody titer: first, IgM class antibodies are produced, followed by IgG peaking in about 10 to 17 days, after which antibody titer gradually declines. This pattern is characteristic of a primary response to an antigen. The antibody-mediated immune responses of the host intensify after a second exposure to an antigen. This secondary response is also called the memory (or anamnestic) response. As shown in Figure 17.16 this response is comparatively more rapid, reaching a peak in only 2 to 7 days, lasts many days, and is considerably greater in magnitude. Some activated B cells do not become antibody-producing plasma cells but persist as long-lived but non proliferating memory cells. Years, or even decades later, if these cells are stimulated by the same antigen, they very rapidly differentiate into antibody-producing plasma cells. A similar response occurs with T cells, which, is necessary for establishing the lifelong memory for distinguishing self from non self.

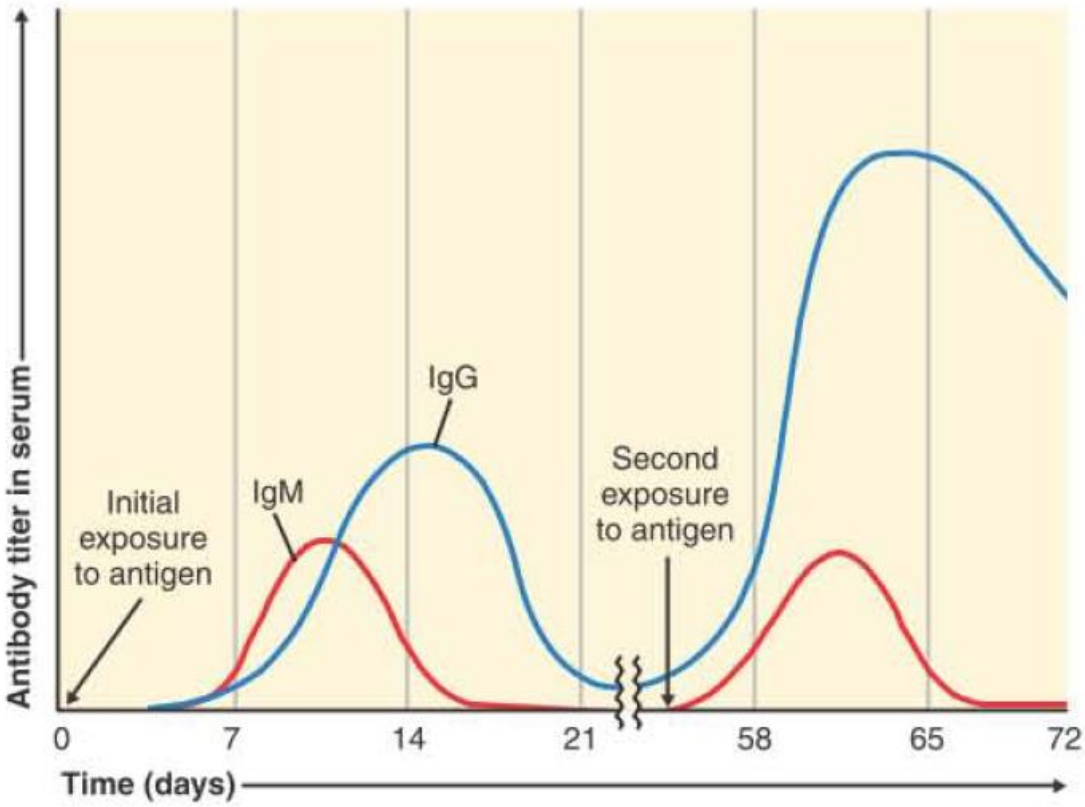


Figure 17.16 The primary and secondary immune responses to an antigen.