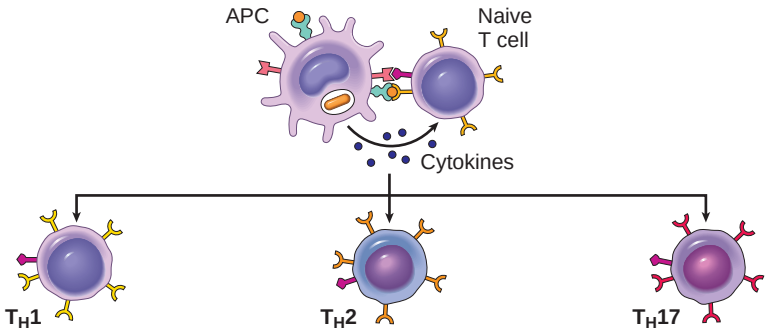

	T_H1	T_H2	T_H17
Major cytokines produced	IFN-γ	IL-4, IL-5, IL-13	IL-17, IL-22
Cytokines that induce this subset	IFN-γ, IL-12	IL-4	TGF-β, IL-6, IL-1, IL-23
Immunological reactions triggered	Macrophage activation, stimulation of IgG antibody production	Stimulation of IgE production, activation of mast cells and eosinophils	Recruitment of neutrophils, monocytes
Host defense against	Intracellular microbes	Helminthic parasites	Extracellular bacteria, fungi
Role in disease	Autoimmune and other chronic inflammatory diseases (such as IBD, psoriasis, granulomatous inflammation)	Allergies	Autoimmune and other chronic inflammatory diseases (such as IBD, psoriasis, MS)

Figure 6-11 Subsets of helper T (T_H) cells. In response to stimuli (mainly cytokines) present at the time of antigen recognition, naive CD4+ T cells may differentiate into populations of effector cells that produce distinct sets of cytokines and perform different functions. The dominant immune reactions elicited by each subset, and its role in host defense and immunologic diseases, are summarized. These populations may be capable of converting from one to another. Some activated T cells produce multiple cytokines and do not fall into a distinct subset. IBD, inflammatory bowel disease; MS, multiple sclerosis.

perform different functions (Fig. 6-11). Cells of the T_H1 subset secrete the cytokine IFN-γ, which is a potent macrophage activator. The combination of CD40- and IFN-γ-mediated activation results in "classical" macrophage activation (Chapter 3), leading to the induction of microbicidal substances in macrophages and the destruction of ingested microbes. T_H2 cells produce IL-4, which stimulates B cells to differentiate into IgE-secreting plasma cells, and IL-5, which activates eosinophils. Eosinophils and mast cells bind to IgE-coated microbes such as helminthic parasites, and function to eliminate helminths. T_H2 cells also induce the "alternative" pathway of macrophage activation, which is associated with tissue repair and fibrosis (Chapter 3). T_H17 cells, so called because the signature cytokine of these cells is IL-17, recruit neutrophils and monocytes, which destroy some extracellular bacteria and fungi and are involved in some inflammatory diseases.

Activated CD8+ T lymphocytes differentiate into CTLs that kill cells harboring microbes in the cytoplasm. By destroying the infected cells, CTLs eliminate the reservoirs of infection.

Humoral Immunity: Activation of B Lymphocytes and Elimination of Extracellular Microbes

Upon activation, B lymphocytes proliferate and then differentiate into plasma cells that secrete different classes of antibodies with distinct functions (Fig. 6-12). Antibody responses to most protein antigens require T cell help and are said to be *T-dependent*. In these responses, B cells ingest protein antigens into vesicles, degrade them, and display peptides bound to class II MHC molecules for recognition by helper T cells. The helper T cells are activated and express CD40L and secrete cytokines, which work together to stimulate the B cells. Many polysaccharide and lipid antigens cannot be recognized by T cells but have multiple identical antigenic determinants (epitopes) that are able to engage many antigen receptor molecules on each B cell and initiate the process of B-cell activation; these responses are said to be *T-independent*. T-independent responses are relatively simple, whereas T-dependent responses show features such as immunoglobulin isotype switching and affinity maturation (described below), which require T cell help and make the responses more varied and sophisticated.

Each plasma cell is derived from an antigen-stimulated B cell and secretes antibodies that recognize the same antigen that was bound to the BCR and initiated the response. Polysaccharides and lipids stimulate secretion mainly of IgM antibody. Protein antigens, by virtue of CD40L- and cytokine-mediated helper T-cell actions, induce the production of antibodies of different classes, or isotypes (IgG, IgA, IgE). *Isotype switching* is induced by cytokines including IFN-γ and IL-4. Helper T cells also stimulate the production of antibodies with high affinities for the antigen. This process, called *affinity maturation*, improves the quality of the humoral immune response. Isotype switching and affinity maturation occur mainly in germinal centers, which are formed by proliferating B cells, especially in helper T cell-dependent responses to protein antigens. Some activated B cells migrate into follicles and form germinal centers, which are the major sites of isotype switching and affinity maturation. The helper T-cells that stimulate these processes in B lymphocytes migrate to and reside in the germinal centers and are called *follicular helper T cells* (T_{FH}).

The humoral immune response combats microbes in many ways (Fig. 6-12). Antibodies bind to microbes and prevent them from infecting cells, thus neutralizing the

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