From: Manipulating the immune response to fight infection

Immunobiology: The Immune System in Health and Disease. 5th edition.

Janeway CA Jr, Travers P, Walport M, et al.

New York: Garland Science; 2001.

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There are several requirements for an effective vaccine. The particular requirements for successful vaccination vary according to the nature of the infecting organism. For extracellular organisms, antibody provides the most important adaptive mechanism of host defense, whereas for control of intracellular organisms, an effective CD8 T-lymphocyte response is also essential. The ideal vaccination provides host defense at the point of entry of the infectious agent; stimulation of mucosal immunity is therefore an important goal of vaccination against those many organisms that enter through mucosal surfaces. Effective protective immunity against some microorganisms requires the presence of preexisting antibody at the time of exposure to the infection. For example, the clinical manifestations of tetanus and diphtheria are entirely due to the effects of extremely powerful exotoxins (see Fig. 9.23). Preexisting antibody against the bacterial exotoxin is necessary to provide a defense against these diseases. Preexisting antibodies are also required to protect against some intracellular pathogens, such as the poliomyelitis virus, which infect critical host cells within a short period after entering the body and are not easily controlled by T lymphocytes once intracellular infection is established. Immune responses to infectious agents usually involve antibodies directed at multiple epitopes and only some of these antibodies confer protection. The particular T-cell epitopes recognized can also affect the nature of the response. For example, as we saw in Chapter 11, the predominant epitope recognized by T cells after vaccination with respiratory syncytial virus induces a vigorous inflammatory response but fails to elicit neutralizing antibodies and thus causes pathology without protection. Thus, an effective vaccine must lead to the generation of antibodies and T cells directed at the correct epitopes of the infectious agent. For some of the modern vaccine techniques, in which only one or a few epitopes are used, this consideration is particularly important. A number of very important additional constraints need to be satisified by a successful vaccine (Fig. 14.23). First, it must be

safe. Vaccines must be given to huge numbers of people, relatively few of whom are likely to die of, or sometimes even catch, the disease that the vaccine is designed to prevent. This means that even a low level of toxicity is unacceptable. Second, the vaccine must be able to produce protective immunity in a very high proportion of the people to whom it is given. Third, because it is impracticable to give large or dispersed rural populations regular 'booster' vaccinations, a successful vaccine must generate long-lived immunological memory. This means that both B and T lymphocytes must be primed by the vaccine. Fourth, vaccines must be very cheap if they are to be administered to large populations. Vaccines are one of the most cost-effective measures in health care, but this benefit is eroded as the cost-per-dose rises.