

1284 The premise of universal precautions is that every specimen should be handled as if it came from someone infected with a bloodborne pathogen. All samples should be double-bagged, gloves should be worn when drawing blood, and spills should be immediately disinfected with bleach.

In attempting to put this small but definite risk to the health care worker in perspective, it is important to point out that ~200 health care workers die each year as a result of occupationally acquired hepatitis B infection. The tragedy in this instance is that these infections and deaths due to HBV could be greatly decreased by more extended use of the HBV vaccine. The risk of HBV infection following a needle-stick injury from a hepatitis antigen-positive patient is much higher than the risk of HIV infection (see “Transmission,” above). There are multiple examples of needle-stick injuries where the patient was positive for both HBV and HIV and the health care worker became infected only with HBV. For these reasons, it is advisable, given the high prevalence of HBV infection in HIV-infected individuals, that all health care workers dealing with HIV-infected patients be immunized with the HBV vaccine.

TB is another infection common to HIV-infected patients that can be transmitted to the health care worker. For this reason, all health care workers should know their PPD status, have it checked yearly, and receive 6 months of isoniazid treatment if their skin test converts to positive. In addition, all patients in whom a diagnosis of TB is being entertained should be placed immediately in respiratory isolation, pending results of the diagnostic evaluation. The emergence of drug-resistant organisms, including the extensively drug-resistant TB strains that have been identified in Africa, has made TB an increasing problem for health care workers. This is particularly true for the health care worker with preexisting HIV infection.

One of the most charged issues ever to come between health care workers and patients is that of transmission of infection from HIV-infected health care workers to their patients. This is discussed in “Occupational Transmission of HIV: Health Care Workers, Laboratory Workers, and the Health Care Setting,” above. Theoretically, the same universal precautions that are used to protect the health care worker from the HIV-infected patient will also protect the patient from the HIV-infected health care worker.

▲ PREVENTIVE VACCINE AGAINST HIV INFECTION

Given that human behavior, especially human sexual behavior, is extremely difficult to change, a critical modality for preventing the spread of HIV infection is the development of a safe and effective vaccine. Historically, vaccines have provided a safe, cost-effective, and efficient means of preventing illness, disability, and death from infectious diseases. Successful vaccines for the most part are predicated on the assumptions that the body can mount an adequate immune response to the microbe or virus in question during natural infection and that the vaccine will mimic the natural response to infection. Even with serious diseases, such as smallpox, poliomyelitis, measles, and influenza among others, the body in the vast majority of cases clears the infectious agent and provides protection, which is usually life-long against future exposure. Unfortunately, this is not the case with HIV infection since the natural immune response to HIV infection is unable to clear the virus from the body and cases of superinfection are not uncommon. Some of the factors that contribute to the problematic nature of development of a preventive HIV vaccine are the high mutability of the virus, the fact that the infection can be transmitted by cell-free or cell-associated virus, the fact that the HIV provirus integrates itself into the genome of the target cell and may remain in a latent form unexposed to the immune system, the likely need for the development of effective mucosal immunity, and the fact that it has been difficult to establish the precise correlates of protective immunity to HIV infection. A fraction of a percent of HIV-infected individuals are “elite controllers” in that they maintain extremely low and even undetectable levels of viremia in the absence of cART, and a number of individuals have been exposed to HIV multiple times but remain uninfected; these facts suggest that there are elements

of host defense or an HIV-specific immune response that have the potential to be protective. Early attempts to develop a vaccine with the envelope protein gp120 aimed at inducing neutralizing antibodies in humans were unsuccessful in that the elicited antisera failed to neutralize primary isolates of HIV cultured and tested in fresh peripheral blood mononuclear cells. In this regard, two phase 3 trials were undertaken in the United States and Thailand using soluble gp120, and the vaccines failed to protect human volunteers from HIV infection. In addition, two separate vaccine trials aimed at eliciting CD8+ T cell responses to prevent infection and, if unsuccessful in preventing infection to control postinfection viremia, also failed at both goals. Recently, a vaccine using a poxvirus vector prime expressing various viral proteins followed by an envelope protein boost was tested in a 16,000-person clinical trial (RV144) conducted in Thailand among predominantly low-prevalence heterosexuals. The vaccine provided the first positive, albeit very modest, signal ever reported in an HIV vaccine trial, showing 31% protection against acquisition of infection. Such a result is certainly not sufficient justification for clinical use of the vaccine, but it served as an important first step in the direction of the development of a safe and effective vaccine against HIV infection. Follow-up studies of RV144 indicate that nonneutralizing or weakly neutralizing antibody responses against certain constant epitopes in the otherwise highly variable V1-V2 region of the HIV envelope may be associated with the modest degree of protection observed in that clinical trial. Additional studies are planned in attempts to improve on the results of RV144 by a variety of approaches, including increasing the number of vaccine boosts with envelope protein.

An area of HIV vaccine research that is currently being actively pursued is the attempt to induce broadly neutralizing antibodies by developing as immunogens for vaccination certain epitopes on the HIV envelope that are the targets of naturally occurring broadly neutralizing antibodies during HIV infection. It is curious that only about 20% of HIV-infected individuals develop broadly neutralizing antibodies in response to natural infection and they do so only after 2 to 3 years of ongoing infection. By the time these antibodies appear, they can neutralize a broad range of primary HIV isolates, but they appear to be ineffective against the autologous virus in the infected subject. Upon close examination, these broadly neutralizing antibodies manifest a high degree of somatic mutations that were accumulated over time and are responsible for their affinity maturation and broadly neutralizing capacity. The goal of current efforts is to develop the conformationally correct HIV envelope epitopes that, when used as immunogens, would direct the immune response of an uninfected individual to the production of broadly neutralizing antibodies over a reasonable time frame by sequential immunizations. It remains to be seen whether this approach will be feasible.

PREVENTION

Education, counseling, and behavior modification are the cornerstones of any HIV prevention strategy. A major problem in the United States and elsewhere is that many infections are passed on by those who do not know that they are infected. Of the ~1.1 million persons in the United States who are HIV-infected, it is estimated that ~16–18% do not know their HIV status and approximately 49% of all new infections are transmitted by those people who are not aware that they are infected. In this regard, the CDC has recommended that HIV testing become part of routine medical care and that all individuals between the ages of 13 and 64 years be tested at least one time. These individuals should be informed of the testing and be tested without the need for written informed consent. Each individual could “opt out” of testing, but testing would otherwise be routinely administered. Individuals who are practicing high-risk behavior should be tested more often. In addition to identifying individuals who might benefit from cART, information gathered from such an approach should serve as the basis for behavior-modification programs, both for infected individuals who may be unaware of their HIV status and who could infect others and for uninfected individuals practicing high-risk behavior. The practice of “safer sex” is the most effective way for sexually active uninfected