100 - SECTION 15 Infections Due to RNA Viruses

SECTION 15 Infections Due to RNA Viruses

virus; (2) the fact that the infection can be transmitted by cell-free or cell-associated virus; (3) the fact that the HIV provirus integrates itself into the genome of the target cell and may remain in a latent form unex posed to the immune system; (4) the likely need for the development of effective mucosal immunity; and, importantly, (5) the difficulty that the immune system has in readily mounting broadly neutralizing antibodies in response to natural infection with HIV (see below). Early attempts to develop a vaccine with the envelope protein gp120 aimed at inducing neutralizing antibodies in humans were unsuccess ful; the elicited antisera failed to neutralize primary isolates of HIV. 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. In 2009, a vaccine using a poxvirus vector prime expressing various viral proteins followed by an envelope protein boost was assessed in a 16,000-person clinical trial (RV144) conducted in Thailand among predominantly low-HIV-prevalence heterosexu als. 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 justifi cation for clinical use of the vaccine; however, 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. Three additional similar studies were undertaken in high-HIV-prevalence countries in sub-Saharan Africa as well as in the Americas and certain European countries in attempts to improve on the results of RV144 by a variety of approaches, including increasing the number of vaccine boosts with envelope protein, the use of mosaic antigens, and the addition of adjuvant. Unfortunately, all three of these phase 3 studies of candidate vaccines failed to show efficacy. Another study was terminated early due to lack of efficacy. 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 (Fig. 208-30). It is curious that only about 20% of people with HIV develop broadly neutralizing antibod ies in response to natural infection and they do so only after 2–3 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 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 produc tion of broadly neutralizing antibodies over a reasonable time frame by sequential immunizations. It remains to be seen whether this approach will be feasible. ■ ■FURTHER READING Bekker LG et al: HIV infection. Nat Rev Dis Primers 9:42, 2023. Beyrer C et al: Is HIV epidemic control by 2030 realistic? Lancet HIV 7:e489, 2024. Centers for Disease Control and Prevention (CDC): Clinical Guidance for PrEP. Available at www.cdc.gov/hivnexus/hcp/prep/. Centers for Disease Control and Prevention (CDC): Clinical Guidance for PEP. Available at www.cdc.gov/hivnexus/hcp/pep/. Centers for Disease Control and Prevention (CDC): Clinical Care of HIV. Available at www.cdc.gov/hivnexus/hcp/clinical-care/. Cohn LB et al: Biology of the HIV-1 latent reservoir and implications for cure strategies. Cell Host Microbe 27:519, 2020.

Collins DR et al: CD8+ T cells in HIV control, cure and prevention.

Nat Rev Immunol 20:471, 2020. Eisinger RW et al: HIV viral load and transmissibility of HIV infec tion: Undetectable equals untransmittable. JAMA 321:451, 2019. Fauci AS, Lane HC: Four decades of HIV/AIDS—much accom plished, much to do. N Engl J Med 383:1, 2020. Grosso TM et al: HIV and aging, biological mechanisms, and thera pies: What do we know? AIDS Rev 25:79, 2022. Haynes BF et al: Strategies for HIV-1 vaccines that induce broadly neutralizing antibodies. Nat Rev Immunol 23:142, 2023. Horberg M et al: Primary care guidance for persons with human immunodeficiency virus: 2024 update by the HIV Medicine Associa tion of the Infectious Diseases Society of America. Clin Infect Dis, 2024. [Epub ahead of print.] Kazer SW: Evolution and diversity of immune responses during acute HIV Infection. Immunity 53:908, 2020. Landovitz RJ et al: Prevention, treatment and cure of HIV infection. Nat Rev Microbiol 21:657, 2023. Lisco A et al: Reappraisal of idiopathic CD4 lymphocytopenia at 30 years. N Engl J Med 388:1681, 2023. Moir S, Fauci AS: B-cell responses to HIV infection. Immunol Rev 275:33, 2017. Nkolola JP, Barouch DH: Prophylactic HIV-1 vaccine trials: Past, present, and future. Lancet HIV 11:e117, 2024. Panel on Opportunistic Infections in Adults and Ado lescents with HIV: Guidelines for the Prevention and Treat ment of Opportunistic Infections in Adults and Adolescents with HIV. Available at clinicalinfo.hiv.gov/en/guidelines/hiv-clin ical-guidelines-adult-and-adolescent-opportunistic-infections/ whats-new. Saez-Cirion A, Sereti I: Immunometabolism and HIV-1 pathogen CHAPTER 209 esis: Food for thought. Nat Rev Immunol 21:5, 2021. UN Joint Programme On HIV/AIDS (UNAIDS): 2024 global AIDS report — The Urgency of Now: AIDS at a Crossroads. Available at www

.unaids.org/en/resources/documents/2024/global-aids-update-2024. U.S. Department of Health and Human Services Panel on Viral Gastroenteritis Antiretroviral Guidelines for Adults and Adolescents: Guidelines for the use of antiretroviral agents in adults and adoles cents living with HIV. Available at clinicalinfo.hiv.gov/en/guidelines/ hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new. Venter WDF et al: The long wait for long-acting HIV prevention and treatment formulations. Lancet

HIV 11:e711, 2024. Section 15 Infections Due to RNA Viruses Umesh D. Parashar, Roger I. Glass

Viral Gastroenteritis Acute infectious gastroenteritis is a common illness that affects persons of all ages worldwide. It is a leading cause of death among children in developing countries, accounting for an estimated 0.5 million deaths each year, and is responsible for up to 6–8% of all hospitalizations among children in industrialized countries, including the United States. Elderly persons, especially those with debilitating health conditions, also are at risk of severe complications and death from acute gastroen teritis. Among healthy young adults, acute gastroenteritis is rarely fatal but incurs substantial medical and social costs, including those of time lost from work. Several enteric viruses have been recognized as important etiologic agents of acute infectious gastroenteritis (Table 209-1, Fig. 209-1).

Revision #1
Created 2026-01-06 16:32:33 UTC by Omar Ayman
Updated 2026-01-06 16:32:33 UTC by Omar Ayman