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covers and a face shield and/or goggles. If available, N-95 or N-100 respi rators may be used to further limit infection risk. Positive-air-pressure respirators should be considered for high-risk medical procedures, such as intubation or suctioning. Medical equipment used in the care of an infected patient, such as gloves or syringes, should never be reused. Because filovirions are enveloped, disinfecting with detergents (e.g., 1% sodium deoxycholate, diethyl ether, or phenolic compounds) is relatively straightforward. Bleach solutions are recommended at 1:100 for surface disinfection and 1:10 for application to excreta or corpses. Whenever possible, potentially contaminated materials should be auto claved, irradiated, or destroyed. Emerging from research conducted during the 2013–2016 EVD outbreak in Western Africa, a vaccine based on a recombinant vesicu lar stomatitis Indiana virus expressing EBOV GP1,2 (rVSV-ZEBOV/ Ervebo) was the first filovirid vaccine approved for use in the United States and the European Union (EU). It is now widely deployed in both a reactive-ring vaccination strategy, targeting close contacts and their contacts in EVD outbreak settings, and for the preexposure vaccination of health care workers in at-risk regions. More recently, a heterologous dose vaccine candidate incorporating EBOV GP1,2 into an adenovirus vector (Ad26.ZEBOV-GP/Zabdeno) followed by a vaccinia virus vec tor incorporating multiple filovirid antigens (MVA-BN-filo/Mvabea) has been shown to be safe and immunogenic in humans. Though evaluation of efficacy in a clinical trial has not been possible, immu nobridging data gained during nonhuman primate experimentation led to regulatory authorization in the EU under “exceptional circum stances”; the two-dose requirement likely limits current use to proac tive preexposure prevention in “peri-outbreak” settings rather than reactive “in-outbreak” reactive strategies. Development and evaluation of this and other vaccine candidates continue toward complementary preventive approaches for non-outbreak or peri-outbreak settings, with emphasis on the durability of immune responses and increases in preventive breadth toward other filovirids. Even in the absence of high-level evidence, expert consensus informs the targeted use of EBOV-specific vaccine or postexposure prophylaxis (PEP) to prevent infection or disease in health care workers considered to have had a high-risk EBOV exposure (e.g., after needlestick injury). Evidence is needed to inform the use of PEP in high-risk contacts in the field outbreak setting. For male survivors, abstinence from sexual activity with a partner for at least 12 months after disappearance of clinical signs is recommended, unless testing proves semen to be free of filovirid RNA. (The use of condoms is generally recommended for all sexual activities.) Reproductive tract and CNS tissues, including ocular tissues and fluids from survivors, should be

handled with appropriate precautions until demonstrated to be filovirid-RNA free. The role of filovirid-specific therapeutics in the prevention or treatment of filoviral persistence is unclear. ■ ■FURTHER READING Cnops L et al: Essentials of filoviral load quantification. Lancet Infect Dis 16:e134, 2016. Crozier I et al: The evolution of medical countermeasures for Ebola virus disease: Lessons learned and next steps. Vaccines (Basel) 10:1213, 2022. Dudas G et al: Virus genomes reveal factors that spread and sustained the Ebola epidemic. Nature 544:309, 2017. Hoenen T et al: Therapeutic strategies to target the Ebola virus life cycle. Nat Rev Microbiol 17:593, 2019. Jacob ST et al: Ebola virus disease. Nat Rev Dis Primers 6:13, 2020. Kuhn JH et al: Filoviridae, in Fields Virology, Vol 1, 7th ed, PM Howley et al (eds). Philadelphia, Wolters Kluwer/Lippincott Williams & Wilkins, 2020, pp 449–503. Matz KM et al: Ebola vaccine trials: Progress in vaccine safety and immunogenicity. Expert Rev Vaccines 18:1229, 2019. Mulangu S et al: A randomized, controlled trial of Ebola virus disease therapeutics. N Engl J Med 381:2293, 2019. Regules JA et al: A recombinant vesicular stomatitis virus Ebola vaccine. N Engl J Med 376:330, 2017.

Section 16 Fungal Infections Michail S. Lionakis, John E. Edwards, Jr.

Pathogenesis, Diagnosis,

and Treatment of Fungal Infections DEFINITION AND ETIOLOGY In recent decades, human fungal infections have dramatically increased worldwide as a result of the AIDS pandemic, the widespread use of antibacterial agents, and the introduction of cytotoxic agents and precision medicine biologics for the treatment of autoimmune and neoplastic diseases and for use in patients undergoing solid organ transplantation or hematopoietic stem cell transplantation. Moreover, of great concern has been the recent rise in fungal infections caused by drug-resistant species, such as azole- and/or echinocandin-resistant Candida glabrata and Candida auris and azole-resistant Aspergillus fumigatus. Among the ~5 million fungal species, only a few cause human infections (Table 217-1). Fungal infections are classified as mucocutaneous and deep organ infections on the basis of anatomic location and as endemic and opportu nistic infections on the basis of epidemiology. Mucocutaneous infections can cause serious morbidity but are rarely fatal. Deep organ infections cause severe illness and often carry a high mortality rate. The endemic mycoses are caused by fungi that are not part of the normal human microbiota but are environmentally acquired. The opportunistic myco ses are caused by fungi (Candida, Aspergillus) that often are components of the human microbiota and whose ubiquity in nature renders them easily acquired by immunosuppressed hosts (Table 217-1). Opportunis tic fungi cause serious infections when impaired host immune responses allow the organisms to transition from commensals to invasive patho gens. Endemic fungi typically cause self-limited disease in immunocom petent hosts but severe illness in immunosuppressed patients. CHAPTER 217 Pathogenesis, Diagnosis, and Treatment of Fungal Infections Fungi are morphologically classified as yeast, mold, and dimorphic. Yeasts are seen as round single cells or budding organisms. Molds grow as filamentous forms called hyphae both at room temperature and in tissue. Aspergillus, Mucorales, and dermatophytes that infect skin and nails are mold fungi. Variations exist within this classification system. For instance, when Candida infects tissue, both yeasts and filamen tous forms (pseudohyphae) may be present (except in the cases of C. glabrata and C. auris, which form only yeasts in tissue); in contrast, Cryptococcus exists only in yeast form. Dimorphic is the term used to describe fungi that have two forms; they grow as yeasts or large spheri cal structures in tissue but as filamentous forms at room temperature in the environment (Table 217-1). Patients acquire deep organ infection

by molds and endemic dimorphic fungi via inhalation. Skin dermatophytes are primarily environmentally acquired, but human-to-human transmission may also occur. The commensal Candida invades deep tissues from sites of mucocutaneous colonization, usually in the gastrointestinal tract or the skin in the case of C. auris. In this chapter, we outline general principles of immunology, diagno sis, and treatment related to the most common human fungal infections. ■ ■PATHOGENESIS In the past decade, our understanding of fungal recognition pathways and of tissue-specific innate and adaptive antifungal host defense mechanisms has markedly expanded. A major breakthrough has been the discovery and functional characterization of the C-type lectin recep tor/spleen tyrosine kinase/caspase recruitment domain–containing

protein 9 (CLR/SYK/CARD9) signaling pathway, which mediates fungal polysaccharide recognition and orchestrates proinflamma tory mediator production, leukocyte recruitment, inflammasome

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