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### IN FOCUS

## Preparing for Emerging Infectious Diseases in the Perinatal Population

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#### ABSTRACT

The unprecedented scale of the 2014–2015 Ebola virus outbreak in West Africa and the recent emergence and rapid spread of Zika virus infection and resultant neonatal sequelae show that the geographic range, spread, and effect of emerging infections are unpredictable. Lessons learned from analyzing the response of an academic medical center to care for pregnant women with suspected or confirmed Ebola virus disease can help health care professionals address future threats from emerging infections.

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iral pathogens, such as Ebola and Zika virus, and a wide range of other emerging infectious threats, such as respiratory viruses, foodborne bacteria, and parasites, are associated with adverse maternal and fetal outcomes. In addition, some of these emerging infections are associated with a substantial risk of occupational transmission to health care providers in the obstetric setting, via direct exposure to blood and other body fluids or via airborne transmission of infectious particles. In this article, we briefly review the effect of pregnancy on infection susceptibility and severity, the factors that contribute to the emergence and spread of infectious diseases, and the adverse effects of selected emerging pathogens on pregnant women and fetuses. We summarize our recent experience with Ebola virus disease (EVD) preparedness training in the obstetric setting. In doing so, we aim to highlight some of the risks, training strategies, and control measures to limit the effect of emerging infections in obstetric practice.

Pregnancy is associated with a wide range of immunologic adaptations to allow maternal tolerance of genetically foreign fetal antigens. These events occur at the placental-fetal membranes and systemically, and they result in suppression of maternal cell-mediated responses and the dominance of humoral/antibody-mediated immunity. Maternal cytokines and the hormonal environment are thought to play roles in driving the overall dominance of humoral immunity in pregnancy. Cell-mediated immune tolerance is essential to prevent the rejection of the fetus, but it renders the mother more susceptible to infection with viruses. such as seasonal influenza and the 2009 H1N1 pandemic influenza, and intracellular bacterial pathogens, such as Listeria monocytogenes, that are the specific targets of cytotoxic T lymphocytes (Baud & Greub, 2011; Mertz et al., 2017). The excess risk of influenza in pregnancy may be related not only to the shift away from cellmediated immunity but also to normal physiologic changes that occur in the cardiovascular and pulmonary systems during pregnancy (Jamieson, Theiler, & Rasmussen, 2006).

In addition to host susceptibility, many other factors contribute to the emergence and rapid spread of infectious diseases, including climate and other ecological changes, human behaviors, international travel and commerce, and microbial adaptation. The explosive emergence of Zika virus in South America, Central America, and the Caribbean beginning in 2014 illustrates the contribution of several of these factors. The spread of Zika and other mosquito-borne viral infections in the Americas has been facilitated by the rapidly expanding distribution of several *Aedes* mosquito species that are adapted to a range of climates and prefer to live near and to

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feed on people, as well as by human travel patterns and waning vector control activities (Lambrechts et al., 2012). In adults and children, infection is asymptomatic (~80%) or associated with a mild febrile/rash illness with arthralgia and myalgia (~20%). In pregnant women, maternalfetal transmission results in fetal loss and congenital microcephaly and other neurologic complications in as many as half of live births, especially during the first and second trimesters (Rasmussen, Jamieson, Honein, & Petersen, 2016). Although Zika virus can be transmitted sexually, it does not pose a risk of occupational transmission. Pregnant women should avoid travel to areas where Zika virus transmission is occurring, and recommendations to prevent sexual transmission of Zika virus have been published (Petersen et al., 2016). Dengue virus and chikungunya virus are transmitted by the same mosquito vector in the same geographic distribution as Zika virus. The clinical features of these virus infections are similar, and co-infection can occur (Villamil-Gomez et al., 2016). In contrast to Zika, maternal-fetal infection with dengue or chikungunya virus is not associated with excessive fetal risk.

#### Ebola Virus Disease

Ebola is an emerging hemorrhagic fever virus that was first reported in 1976 in Sudan. Historically, outbreaks of EVD were concentrated in the remote rainforests of Central Africa (Centers for Disease Control and Prevention [CDC], 2017). An outbreak of EVD of unprecedented scope emerged in West Africa in December 2013. Many factors contributed to the undetected spread of Ebola virus and impeded rapid containment, including population mobility, traditional health and burial practices, community resistance, recent civil unrest, and limited health resources and infrastructure. Before the outbreak was finally contained in 2015, there were a total of 28,616 cases of EVD reported in Guinea, Liberia, and Sierra Leone, with 11.310 deaths-more than all prior outbreaks of EVD combined (World Health Organization, 2017).

Ebola virus is a blood-borne pathogen that is likely transmitted to humans from an unknown animal reservoir through hunting and consuming game meat. Human infection is efficiently transferred from person to person through mucosal contact with infected body fluids, including blood (Brainard, Hooper, Pond, Edmunds, & Hunter, 2016). Although there is no current evidence to show that pregnant women are more susceptible to Ebola virus infection than the general population, they appear to be at increased risk for severe illness and death (Muehlenbachs et al., 2017).

Ebola virus infection in pregnancy is associated with greater rates of obstetric complications, including spontaneous abortion, premature rupture of membranes, preterm labor/birth, peripartum hemorrhagic complications, stillbirth, and neonatal death (Black, Caluwaerts, & Achar, 2015). Transplacental EVD infection of the fetus has been documented in stillbirths by reverse transcription polymerase chain reaction (RT-PCR) Q3 of amniotic fluid and fetal blood and tissue (Caluwaerts et al., 2015) but is not universal after maternal infection. Recently, investigators suggested that EVD has placental tropism and that high concentrations of virus can persist in the placenta for months without maternal viremia in pregnant women who survive EVD without fetal loss (Muehlenbachs et al., 2017). Thus, the products of conception of pregnant women with active EVD and those who have survived infection should be assumed to be highly infectious. In these cases, live births and stillbirth fetuses should be treated as potentially infectious for EVD (Black et al., 2015).

Considerable overlap exists among signs and symptoms of suspected EVD and other pregnancy-related complications, especially fever, bleeding, and spontaneous miscarriage (Black et al., 2015). The optimal management of a pregnant woman suspected to have EVD is to isolate her in a special biocontainment facility, to perform a nucleic acid test for EVD, and to manage her conservatively pending the EVD test result (Black et al., 2015). Although obstetric care and invasive procedures can be minimized in stable pregnant women awaiting EVD test results, women who present with obstetric emergencies and suspected EVD pose an enormously high risk of provider exposure to infectious body fluids, especially if the risk of EVD is not immediately recognized and appropriate infection control measures not yet implemented. A case example of staff in the United States exposed to EVD is the symptomatic man with initially unknown EVD who presented to an emergency department in Texas. Two health care staff members contracted EVD after they cared for the man without personal protective equipment. The man died, and the infected staff members were treated in isolation and discharged. This case highlights the need for Download English Version:

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