Emerging Infectious Diseases: Zika Virus

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Conditions leading to emerging infectious diseases (EIDs):

-definition of EID — could be infection caused by entirely new microorganism starting to spread, re-emergence of pathogen poorly controlled, or antibiotic resistance on major scale; societal disruption — caused by, eg, massive famine or flooding, war; can result in re-emergence of diseases; changes in health care — hospital-acquired infections leading cause of complications within health care system; although significant progress made in control, risk still increasing due to number of invasive procedures performed; widespread use of implanted medical devices has led to more infection (although devices increasingly becoming safer); changes in food production — risk for food-borne diseases higher now than in previous generation, but progress has been made in controlling them; changes in human behavior — sexual revolution of 1960s resulted in pandemic of sexually acquired infections; environmental changes — urbanization of Africa has resulted in massive spread of AIDS, Lassa virus, and Ebola virus throughout continent; in North America, living closer to nature results in proximity to animals that carry pathogenic agents; risk for tick-borne diseases significantly increased; almost two-thirds of EIDs have animal reservoir (zoonsosis); changes in public health infrastructure — in Soviet Union, implication of economy resulted in widespread failure to immunize children; changes in microorganisms — influenza viruses changes structure and cause pandemic disease with new strains every 10 to 30 yr; international travel — increases capacity for spread of diseases

Preparing for EIDs: plans must be implementable nationally and locally; terrorist attack of September 2001 led to major commitment of resources; preparing for bioterrorism synonymous with preparing for EIDs

History of Zika virus (ZIKV): outbreak of febrile illness occurred in northeastern Brazil in August 2014; quickly determined that it was not dengue, but ZIKV; ZIKV is flavivirus (RNA virus), same class of virus that causes hepatitis C, yellow fever, Japanese B encephalitis, St. Louis encephalitis, tick-borne encephalitis, and dengue; first identified in 1947 in Uganda (isolated from primate); at first uncertain whether able to cause human disease; until 2000, only few well-documented cases; serologic screening in Asia determined that virus French Polynesian strain with additional mutations; within 10 mo of introduction to Brazil, massive epidemic underway

Epidemiology: seen throughout South and Central America; 31 countries in Western hemisphere have had documented cases, most caused by mosquito transmission; microcephaly — in Brazil, 10-fold increase in newborns with severe microcephaly seen coincident with ZIKV outbreak; children with microcephaly severely developmentally delayed, and most require total care for rest of lives; estimated 5000 cases of microcephaly in Brazil; study in New England Journal of Medicine — found 72 pregnant Brazilian women with active polymerase chain reaction (PCR)-positive ZIKV infection; serial ultrasonography (US) throughout pregnancy and examination of infant at birth performed; found that 29% of women had abnormal fetal US; 2 infants died in pregnancy, 5 had severe growth retardation, and 7 had major neurologic abnormalities (5 cases of microcephaly); evidence of placental ischemia seen; study — showed that ZIKV triggers toll-like receptor 3 (TLR3; TLRs inform body that “invader” coming and turn on immune system); if TLR3 turned on at high level in pregnancy, causes apoptosis of neural progenitor cells in developing fetus (probable mechanism of neuroteratogeny); number of women were infected late in pregnancy (6th to 7th mo of gestation) and had severely impaired children; also noted marked upsurge in GBS; almost all GBS cases in Brazil immunoglobulin (Ig)M-positive for ZIKV; estimated incidence ranges from 1 in 500 to 1 in 10,000; deemed international public health emergency by World Health Organization in February 2016; by May 2016, 61 countries had documented ZIKV, and >500 introduced cases seen in United States, all sexually transmitted

Pathophysiology: reservoir — infected humans and primates (primates probably major reservoir); transmitted in nature by bites from infected Aedes mosquitoes (classically Aedes aegypti). Aedes mosquitoes — daytime feeders that also transmit dengue and Chikungunya virus; A aegypti found throughout southern part of United States, while A albopictus found as far north as Great Lakes areas; widely disseminated throughout southern, eastern, and central part of United States; other transmission — transfusion of blood and blood products, organ transplantation, sexual (particularly man to woman), and vertical (to fetus)

Clinical features: 80% of infections asymptomatic; of those asymptomatic, often have mild rash, low-grade fever, slight headache, and characteristic conjunctivitis

Management: no special precautions needed, unless potential exposure to blood present; standard precautions indicated; aspirin not recommended for treatment (infection possibly dengue and could precipitate hemorrhagic dengue); symptomatic treatment; if woman infected, determine whether pregnant; if not pregnant, should have contraception for ≥3 mo (ideally, 6 mo); women clear virus more rapidly than men (can carry ZIKV in semen for ≤2 mo); if pregnant woman infected, immediately perform US and consider
amniocentesis (decision about whether to terminate pregnancy needed if infection with teratogenic effects present); infected men should use condoms for ≥2 mo after infection if sexual partner attempting to become pregnant, and if partner pregnant, should use condoms throughout pregnancy.

**Diagnosis:** easy to diagnose with PCR; serologic test has significant cross-reactivity with other flaviviruses; plaque-reduction neutralization test needed to confirm that infection true ZIKV, not other flavivirus; serum positive by PCR first (usually within 3–4 days); urine positive longer (after 7 days); cerebrospinal fluid positive if headache and neurologic symptoms present; amniotic fluid likely positive if infant infected.

**Controlling ZIKV globally:** avoiding travel to hyperendemic countries; mosquito eradication (priority in Central and South America); in Puerto Rico, limited spraying being done with pyrethrin; protection against mosquito bites (wearing long-sleeved clothing when outside, sleeping under screens and nettings with air conditioning or fan; impregnating clothing with permethrin); study found that full-strength 25% N,N-Diethyl-meta-toluamide (DEET) resulted in almost total protection for 5 hr; natural agents ineffective or unreliable; picaridin safe and effective repellent; Puerto Rican study showed that mosquito traps markedly reduced incidence of Chikungunya; screening pregnant women in endemic areas; delaying pregnancy until epidemic controlled; screening blood and organ donors; experimental dengue vaccine recently approved, and similar vaccine effective for ZIKV “desperately” needed.

**Suggested Reading**