

Emerging Infectious Diseases in Pregnancy

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It has been recognized for centuries that pregnant women have unique susceptibilities to many infectious diseases that predispose them to untoward outcomes compared with the general adult population. It is thought a combination of adaptive alterations in immunity to allow for the fetal allograft combined with changes in anatomy and physiology accompanying pregnancy underlie these susceptibilities. Emerging infectious diseases are defined as those whose incidence in humans has increased in the past two decades or threaten to increase in the near future. The past decade alone has witnessed many such outbreaks, each with its own unique implications for pregnant women and their unborn fetuses as well as lessons for the health care community regarding response and mitigation. Examples of such outbreaks include, but are not limited to, severe acute respiratory syndrome, the 2009 H1N1 pandemic influenza, Ebola virus, and, most recently, the Zika virus. Although each emerging pathogen has unique features requiring specific considerations, there are many underlying principles that are shared in the recognition, communication, and mitigation of such infectious outbreaks. Some of these key principles include disease-specific delineation of transmission dynamics, understanding of pathogen-specific effects on both mothers and fetuses, and advance planning and contemporaneous management that prioritize communication among public health experts, clinicians, and patients. The productive and effective working collaboration among the Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine has been a key partnership in the successful communication and management of such outbreaks for women's health care providers and patients alike. Going forward, the knowledge gained over the past decade will undoubtedly continue to inform future responses and will serve to optimize the education and care given to pregnant women in the face of current and future emerging infectious disease outbreaks.

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Emerging infectious diseases are defined as pathogenic outbreaks whose incidence in humans has increased in the past two decades or threaten to increase in the near future.¹ The importance of emerging infec-

tious diseases has been recognized for at least 20 years and continues to increase in importance and scope for many societal and ecologic reasons.^{2,3} Such outbreaks of novel pathogens frequently cross national and territorial boundaries (in part as a result of the robust travel of modern life) and include recently highlighted and severe pathogens such as severe acute respiratory syndrome (SARS), the 2009 H1N1 pandemic influenza, Ebola virus, and, most recently, the Zika virus. In addition to these highly publicized outbreaks of recent times, emerging pathogen terminology also includes less dramatic, but often no less menacing, considerations such as 1) new infections resulting from changes or evolution of existing organisms, 2) known infections spreading to new geographic areas or populations, 3) previously unrecognized infections appearing in areas undergoing ecologic transformation, and 4) old infectious reemerging as a result of the development of antimicrobial resistance to known standard agents or

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breakdowns in public health measures.¹⁻³ Commonly cited emerging infectious diseases of interest and some pathogen specifics are compiled in Box 1.

It has been appreciated for centuries that pregnant women have unique immunologic and physiologic characteristics that predispose them to heightened rates of serious and sometimes fatal outcomes from varied infectious diseases. This observation is mostly attrib-

uted to the combination of somewhat altered cellular immunity capabilities (presumably to allow for the fetal allograft) combined with changing anatomic specifics that can challenge primarily cardiovascular and respiratory systems with advancing gestational age.⁴⁻⁹ More recent research has focused on relative concentrations and potencies of various immunoglobulins (immunoglobulin G) during pregnancy as part of the explanation for altered pregnancy immunity.¹⁰ Additionally, ongoing investigations are assessing the role of the placenta and its inherent ability to block some viral pathogens from access to the fetus.¹¹ Ongoing research will continue to delineate the specifics of the immunology of pregnancy and its effect on disease transmission and pathogenesis.

The heightened susceptibility to adverse outcomes is most often noted for viral pathogens, with bacterial and parasitic infections occasionally also having this predilection. In addition, pregnant women also have unique characteristics worthy of attention with regard to infectious diseases (and their countermeasures) from clinicians including, but not limited to, the teratogenic potential of an infecting pathogen, differing transmission susceptibilities and specific implications for fetal infection during different stages of pregnancy, and the effect of an in utero infection on subsequent neonatal and infant development. Importantly, despite a predilection for worse outcomes, it does not appear (for the majority of pathogens) that pregnancy makes women more susceptible to acquiring an infection with the possible exceptions of human immunodeficiency virus, malaria, and potentially listeriosis.¹²

In addition to the inherent risks posed by emerging infectious diseases to pregnant women, the concept of the medical establishment's preparedness and response in the face of novel outbreaks has also recently received considerable attention. Much of the early focus toward preparedness was centered on the likelihood of an impending influenza pandemic.^{13,14} However, the concepts and collaborations have now matured to include guidance and directives that are simultaneously relevant for a broad range of pathogens as well as specific outbreaks.¹⁵⁻¹⁷ This is most recently evidenced by the appropriate attention received by, and prioritization given to, the ongoing Zika virus outbreak. A robust collaboration among the Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (the College), and the Society for Maternal-Fetal Medicine has also been paramount in highlighting important up-to-date knowledge, thereby enabling practice that is based on the best available data during the evolution of Zika and others. The

Box 1. Commonly Noted Emerging and Reemerging Pathogens of Interest

Pandemic influenza viruses

Novel influenza strains, emerging from antigenic shift in the influenza virus, causing occasional severe influenza pandemics

SARS-associated coronavirus

Highly pathogenic, novel severe respiratory virus that emerged and rapidly spread globally from a small location in China

Ebola virus

Previously recognized serious pathogen associated with modest-sized outbreaks before 2014 (largest outbreak); strikingly high mortality rate

Zika virus

Previously underappreciated pathogen until ongoing outbreak with its association with fetal malformations (most notably microcephaly); its unique characteristics put this outbreak at the intersection of emerging infectious diseases, reproductive rights, and global health security

West Nile virus

The most common mosquito-borne infection in the United States; no documented direct fetal effect

Chikungunya virus

Mosquito-borne virus that was previously found in Asia, Africa, and Europe that has recently been detected in the Americas; no documented direct fetal effect

Methicillin-resistant *Staphylococcus aureus*

Well-known reemerging pathogen given its aggressive clinical nature and relatively limited antimicrobial treatment options

Vancomycin-resistant enterococci

Classic reemerging pathogen that serves as an ongoing reminder of the ever present and evolving epidemic of antimicrobial resistance

SARS, severe acute respiratory syndrome.

women's health field has successfully aligned in response to these recent outbreaks in a manner that will undoubtedly serve pregnant women optimally. This article highlights a series of recent high-profile, specific emerging pathogens of significant maternal-fetal importance given their important lessons to the obstetric and public health community. In addition, the pathogens chosen for discussion have some unique and challenging features and provided unique foundations for progress in the area of health care provider, facility, national, and international preparedness planning and disease mitigation.

SEVERE ACUTE RESPIRATORY SYNDROME

Severe acute respiratory syndrome is a previously unrecognized emerging infectious disease caused by a novel pathogen that challenged the global health community's ability to effectively communicate and cooperate toward a goal of eventual containment. Believed to have originated in China's Guangdong Province late in 2002, it appears to have been spread internationally in the winter of 2003 by a physician who had traveled to the region to provide care against a new mysterious respiratory pathogen. Traveling home from China, he stayed one night at what later came to be referred to as Hotel M (from the epidemiologic perspective) in Hong Kong and was noted to have been ill for approximately 7 days prior with the same respiratory symptoms as his patients. Subsequent to his short, 24-hour stay, approximately 12 additional guests fell ill from this same unknown pathogen (the majority of whom were staying on the same floor as him in the hotel, yet without significant close contact) and then proceeded to travel abroad and perpetuate the global spread of what is now known as SARS. Involved countries included Canada, Vietnam, Singapore, Ireland, and the United States. In total, the World Health Organization (WHO) recognized at least 8,400 associated cases, with more than 800 deaths in greater than 32 countries recorded over roughly 6 months.^{5,18} It was accordingly dubbed the first 21st century pandemic.

The infection was characterized by a rapid onset of fever plus other nonspecific symptoms (headache, malaise, and myalgia) followed by a nonproductive cough that progressed to shortness of breath and respiratory failure in a subset of patients. Characteristic laboratory aberrations include lymphopenia and elevated lactate dehydrogenase levels. The causative agent was later noted to be a novel coronavirus likely present in animals being sold in local markets and subsequently infecting those handling the animals (zoonotic spread). Importantly, the subsequent human-to-human

spread was through respiratory droplets, yet early on, given the many unknowns, infection control practices included all phases of precautions: respiratory, contact, and droplet.

Cohorting (grouping of persons [patients or health care workers] who have been exposed to a disease, a form of isolating groups to minimize disease spread within in a location) and isolating of patients in facilities as well as widespread public education, contact tracing, quarantine practices, border surveillance, and travel advisories were instituted and successfully contributed to the eventual global control within approximately 5 months of first notification.^{5,18} In the few affected obstetric hospitals, close attention was paid to minimizing exposure to unaffected patients and staff by way of cohorting exposed and infected patients, visitor limitations, vigilance toward the use of personal protective equipment (such as masks and gowns), clinical flexibility, facility temporary closure, working collectively to establish coordinated and regionalized care, and a willingness to consider and establish care models that minimized mixing of patients and obstetric health care providers.^{18,19} All of these nonpharmaceutical interventions are important for all facilities providing care to pregnant women to consider and plan for in advance. This is a key lesson from the SARS epidemic; traditional nonpharmaceutical countermeasures are very effective for curbing disease spread, even in the absence of pharmaceutical interventions.

Understanding the effects of SARS on pregnancy is more challenging given the relatively low numbers of women infected. The few small available case series suggest that pregnant women had at least equal, and likely higher, rates of severe illness, intensive care unit admission, and death (similar to other serious respiratory pathogens in pregnancy).^{18,20} As noted in other severe respiratory infections, some women underwent preterm cesarean delivery presumably for maternal respiratory benefit. No documented cases of perinatal transmission were noted despite relatively rigorous methods of investigation for viral particles, serologic responses, or both in neonates born to infected mothers. The low numbers of infected pregnant women were also attributable in part to the critically important and rigorous infection control practices noted (cohorting, regionalization of care, minimizing patient and health care worker mixing, use of personal protective equipment) used in hospitals that were successful in interrupting disease transmission.¹⁸⁻²⁰ The importance of the traditional infection control measures in and of themselves cannot be overemphasized. Important lessons for obstetric health care providers,

Box 2. Important Lessons Learned for Health Care Providers and Facilities From Select Recent Emerging Infectious Disease Outbreaks

SARS virus

- Novel emerging pathogens originating abroad can become local problems quickly given international travel patterns and methods of transmission
- Globally coordinated nonpharmaceutical responses to infectious disease outbreaks are critically important for disease mitigation and control
- Nonpharmaceutical efforts to minimize nosocomial spread of infectious diseases are critically important, especially in busy labor and delivery units with its inherent risks of exposure to numerous body fluids
- Clinical flexibility for facilities management is an important principle when dealing with a serious infectious disease with high potential for local spread among patients and health care providers

Influenza virus

- Even when predicted, expected, or both, emerging and reemerging infectious diseases (pandemic influenza) can cause significant morbidity and mortality in pregnancy
- Timely availability and use of influenza vaccine in pregnancy is a major priority for obstetric providers to recommend both in seasonal and pandemic outbreaks
- Influenza can be a severe respiratory disease that can be transmitted person to person before symptom onset, complicating mitigation efforts
- Early use of anti-influenza antivirals are very important and may lessen the severity of infection for mothers and their offspring
- Immediately postpartum women (2 weeks) are at similar heightened risk of morbidity and mortality as pregnant women from influenza

Ebola virus

- Pregnant women are susceptible to serious illness and death from Ebola infection
- Very high associated pregnancy wastage rates, and no infant has survived long-term after being born to an Ebola-infected mother
- Transmission of Ebola is very permissive making screening, recognition, and sequestering or cohorting* critically important interventions to undertake in the management of this infection to minimize spread
- Numerous body fluids have been found to carry Ebola infectious particles challenging infection control practices, including amniotic fluid
- Labor and delivery with its high risk of exposure to bodily fluids is a highly vulnerable area for inadvertent transmission and should be managed accordingly

Zika virus

- Unexpected new or reemerging infections can arise at any time, from any location, and can threaten the entire global health community
- The combination of the exact nature of transmission and the effect of an emerging infectious disease drives the societal attention and medical establishment's response in real time
- When little substantiated data are available at the onset of outbreaks, more conservative public health guidance is appropriately delivered
- Public health guidance must be appropriately updated, altered, or both as the nature and understanding of a novel outbreak evolves
- The true and full effect of outbreaks with teratogenic potential is not known for many years after the outbreak ensues

SARS, severe acute respiratory syndrome.

*Cohorting is grouping of persons (patients or health care workers) who have been exposed to a disease—a form of isolating groups to minimize disease spread within a location.