# Public Health Approach to Emerging Infections Among Pregnant Women

Sonja A. Rasmussen, MD, MS and Edward B. Hayes, MD

As public health professionals respond to emerging infections, particular attention needs to be paid to pregnant women and their offspring. Pregnant women might be more susceptible to, or more severely affected by, emerging infections. The effects of a new maternal infection on the embryo or fetus are difficult to predict. Some medications recommended for prophylaxis or treatment could harm the embryo or fetus. We discuss the challenges of responding to emerging infections among pregnant women, and we propose strategies for overcoming these challenges. (*Am J Public Health*. 2005;95:1942–1945. doi:10.2105/AJPH.2004.054957)

Recent outbreaks of West Nile virus disease,[1] severe acute respiratory syndrome,[2] monkeypox,[3] and anthrax,[4] and concern over pandemic influenza[5] and bioterrorism,[6] highlight the importance of responding to emerging infections[7] (defined as those for which the incidence has risen in the past 2 decades or threatens to rise in the near future).[8] In developing response strategies, public health practitioners must consider the impact of strategies on pregnant women and their offspring,[7,9–14] so that exposed women are appropriately advised and treated. We outlined challenges that public health professionals

**TABLE 1—Emerging Infections Among Pregnant Women: Challenges and Proposed Public Health Response**

| Challenges | Response |
|---|---|
| Pregnant women could be more susceptible to infection or have increased morbidity and mortality from infection, because of altered immune response or physiological changes of pregnancy | • Evaluate pregnancy as a potential risk factor for susceptibility to infection and for increased morbidity and mortality<br>• Develop specific recommendations to prevent and treat infection of pregnant women |
| Emerging infection in pregnant women could cause adverse effects in embryo or fetus, even when maternal infection is mild or asymptomatic | • Educate health care providers about emerging infections, available diagnostic studies, preventive measures, and treatment<br>• Encourage health care providers to maintain a high index of suspicion for emerging infections when evaluating even mild symptoms in pregnant women; in some cases, screening of asymptomatic women may be indicated so that prophylaxis or early treatment can be provided |
| Prophylaxis and treatment of emerging infections may be contraindicated in pregnant women, because of potential adverse effects of vaccine or medication on embryo or fetus | • Carefully weigh the benefits of prophylaxis and treatment of pregnant women against the potential risks to the embryo or fetus |
| Effects of emerging infection on embryo or fetus are often unknown and difficult to predict, based on previous experience with maternal infections, and can present long after birth | • Consider a wide range of effects of emerging infection on embryo or fetus<br>• Initiate surveillance for effects of infections during pregnancy and continue well beyond the newborn period; consider a wide range of possible sequelae |
| Diagnosis of emerging infections in embryo, fetus, or infant is often difficult and is often dependent on obtaining appropriate specimens at critical time periods | • Educate health care providers about appropriate diagnostic specimens and timing of collection |

face regarding emerging infections in pregnant women and propose strategies for response (Table 1).

Increased susceptibility and risk for relapse or exacerbation of infections during pregnancy have been reported for several infections.[15–18] Pregnant women are also known to have increased morbidity and mortality from certain infections.[19–23] Thus, when risk factors for disease susceptibility and severity (e.g., age and presence of chronic conditions) are examined, pregnancy should be considered a potential factor. The development of recommendations for treatment and prophylaxis specific to pregnant women may need to be considered (e.g., influenza vaccination is recommended for women who will be pregnant during the influenza season because of increased morbidity and mortality during pregnancy).[22]

Because seemingly benign maternal infections can have serious consequences on the health of the embryo or fetus (hereafter referred to as "fetus"),[24,25] potential manifestations of infection in pregnant women should be carefully evaluated. Public health professionals should educate health care providers about emerging infections occurring in their area, available diagnostic testing, preventive measures, and treatment. Providers should be encouraged to have a high index of suspicion for emerging infections when evaluating symptoms in pregnant women. For some infections (e.g., HIV),[26,27] screening of asymptomatic women might be indicated to prevent or provide early treatment of congenital infection.

Certain vaccinations or medications are contraindicated during pregnancy because of their potential fetal effects.[28] Fetal effects of most medications are not known.[29] Benefits of the vaccine or medication to be used for prophylaxis or treatment need to be weighed against the potential risk to the fetus. For example, information on ciprofloxacin, the recommended antimicrobial for adult postexposure prophylaxis against *Bacillus anthracis,* during pregnancy is limited.[30] However, given the high morbidity and mortality known to be associated with anthrax, the benefits of ciprofloxacin prophylaxis have been deemed to outweigh the potential risks in women with high-risk exposure.[31]

The effects of some infections are well known;[25] however, for an emerging infection, diverse fetal effects of infection need to be considered. The risk for transmission from mother to fetus and the likelihood of adverse fetal effects can vary with the gestational timing of infection.[32,33] Fetal effects can vary depending on the infectious agent and include spontaneous abortions, preterm birth, intrauterine growth retardation, neonatal sepsis, birth defects, and developmental disabilities. Some congenital infections can cause later manifestations (e.g., hearing loss) in infants appearing normal at birth.[33] Careful physical and developmental examination of infants born to infected women is essential, but it can be difficult to determine additional studies to be performed. Cardiac echocardiography, ophthalmologic examination, brain imaging, and hearing evaluation all could be considered, and surveillance for effects of congenital infections needs to continue beyond the newborn period.

Diagnosis of a new congenital infection can be difficult. New diagnostic assays developed for adults may need to be applied without data regarding their sensitivity and specificity for congenital infection. Microbial culture, nucleic acid amplification, and immunohistochemical staining can document infection, but sensitivity of these tests is limited. Detection of specific IgM in infant serum provides strong evidence of congenital infection.[34] However, false-positive IgM results have been reported,[35,36] and infection early in pregnancy might not elicit a fetal IgM response.[35,37] Because maternal IgG in the infant's circulation disappears by age 12 months, documenting increasing or persistent microbial-specific IgG several months after

birth may indicate congenital infection.[34,35] Because health care providers might not be familiar with difficulties associated with diagnosis of congenital infection, public health professionals should provide training about appropriate diagnostic specimens and timing of specimen collection to diagnose an emerging infection.

As public health professionals deal with emerging infections, they must consider the impact of infectious agents on pregnant women and their offspring. A carefully planned public health approach, which includes input from individuals with expertise in pediatrics, obstetrics, and infectious diseases, will improve our ability to protect women and their offspring from adverse consequences associated with emerging infections. ■

## About the Authors

*Sonja A Rasmussen is with the Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention. Edward B. Hayes is with the Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention.*

*Requests for reprints should be sent to Sonja A. Rasmussen, 1600 Clifton Road NE, Centers for Disease Control and Prevention, MS E-86, Atlanta, GA 30333 (e-mail: skr9@cdc.gov).*

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## Contributors

S.A. Rasmussen and E.B. Hayes formulated the concepts, reviewed the pertinent literature, and wrote the paper.

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## References

1. Hayes EB, O'Leary DR. West Nile virus infection: a pediatric perspective. *Pediatrics.* 2004;113:1375–1381.

2. Svoboda T, Henry B, Shulman L, et al. Public health measures to control the spread of the severe acute respiratory syndrome during the outbreak in Toronto. *N Englå J Med.* 2004;350:2352–2361.

3. Reed KD, Melski JW, Graham MB, et al. The detection of monkeypox in humans in the Western Hemisphere. *N Engl J Med.* 2004;350:342–350.

4. Inglesby TV, O'Toole T, Henderson DA, et al. Anthrax as a biological weapon, 2002: updated recommendations for management. *JAMA.* 2002;287:2236–2252.

5. Webby RJ, Webster RG. Are we ready for pandemic influenza? *Science.* 2003;302:1519–1522.

6. Mortimer PP. Anticipating smallpox as a bioterrorist weapon. *Clin Med.* 2003;3:255–259.

7. Centers for Disease Control and Prevention. Preventing emerging infectious diseases: A strategy for the 21st century. Overview of the updated CDC plan. *MMWR Recomm Rep.* 1998;47:1–14.

8. Emerging Infectious Diseases Journal website. Centers for Disease Control and Prevention. Available at: http://www.cdc.gov/ncidod/eid/about/background.htm. Accessed November 27, 2004.

9. Emerging Infectious Diseases: Addressing the Problem of Diseases of Pregnant Women and Newborns. Centers for Disease Control and Prevention. Available at: http://www.cdc.gov/ncidod/emergplan/pregnant_and_newbornes/pregnant_and_newborn.pdf. Accessed December 5, 2004.

10. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol.* 2004;191:292–297.

11. Stockman LJ, Lowther SA, Coy K, Saw J, Parashar UD. SARS during pregnancy, United States. *Emerg Infect Dis.* 2004;10:1689–1690.

12. Centers for Disease Control and Prevention. Interim guidelines for the evaluation of infants born to mothers infected with West Nile virus during pregnancy. *MMWR Morb Mortal Wkly Rep.* 2004;53:154–157.

13. Centers for Disease Control and Prevention. Intrauterine West Nile virus infection—New York, 2002. *MMWR Morb Mortal Wkly Rep.* 2002;51:1135–1136.

14. Kadanali A, Tasyaran MA, Kadanali S. Anthrax during pregnancy: case reports and review. *Clin Infect Dis.* 2003;36:1343–1346.

15. Okoko BJ, Enwere G, Ota MO. The epidemiology and consequences of maternal malaria: a review of immunological basis. *Acta Trop.* 2003;87:193–205.

16. Avelino MM, Campos D, Jr., do Carmo Barbosa de Parada J, de Castro AM. Pregnancy as a risk factor for acute toxoplasmosis seroconversion. *Eur J Obstet Gynecol Reprod Biol.* 2003;108:19–24.

17. Lyde CB. Pregnancy in patients with Hansen disease. *Arch Dermatol.* 1997;133:623–627.

18. Snider D Pregnancy and tuberculosis. *Chest.* 1984;86:10S–13S.

19. Harris JW. Influenza occurring in pregnant women. *JAMA.* 1919;14:978–980.

20. Freeman DW, Barno A. Deaths from Asian influenza associated with pregnancy. *Am J Obstet Gynecol.* 1959;78:1172–1175.

21. Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol.* 1998;148:1094–1102.

22. Harper SA, Fukuda K, Uyeki TM, Cox NJ, Bridges CB. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2004;53:1–40.

23. Lam CM, Wong SF, Leung TN, et al. A case-controlled study comparing clinical course and outcomes of pregnant and nonpregnant women with severe acute respiratory syndrome. *Bjog.* 2004;111:771–774.

24. Jongen VH, van Roosmalen J, Tiems J, Van Holten J, Wetsteyn JC. Tick-borne relapsing fever and pregnancy outcome in rural Tanzania. *Acta Obstet Gynecol Scand.* 1997;76:834–838.

25. Bale JF, Jr. Congenital infections. *Neurol Clin.* 2002;20:1039–1060.

26. Centers for Disease Control and Prevention. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46:1–25.

27. Rutstein RM. Prevention of perinatal HIV infection. *Curr Opin Pediatr.* 2001;13:408–416.

28. Centers for Disease Control and Prevention. Supplemental recommendations on adverse events following smallpox vaccine in the pre-event vaccination program: recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2003;52:282–284.

29. Lo WY, Friedman JM. Teratogenicity of recently introduced medications in human pregnancy. *Obstet Gynecol.* 2002;100:465–473.

30. Centers for Disease Control and Prevention. Updated recommendations for antimicrobial prophylaxis among asymptomatic pregnant women after exposure to Bacillus anthracis. *MMWR Morb Mortal Wkly Rep.* 2001;50:960.

31. Management of asymptomatic pregnant or lactating women exposed to anthrax. *Int J Gynaecol Obstet.* 2002;77:293–295.

32. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet.* 1982;2:781–784.

33. Stagno S, Whitley RJ. Herpesvirus infections of pregnancy. Part I: Cytomegalovirus and Epstein-Barr virus infections. *N Engl J Med.* 1985;313:1270–1274.

34. Lewis DB, Wilson CB. Developmental immunology and role of host defenses in fetal and neonatal susceptibility to infection. In: Remington JS, Klein JO, eds. *Infectious Diseases of the Fetus and Newborn Infant.* 5th ed. Philadelphia: W.B. Saunders Company; 2001:25–138.

35. Alford CA. Immunoglobulin determinations in the diagnosis of fetal infection. *Pediatr Clin North Am.* 1971;18:99–113.

36. Pinon JM, Dumon H, Chemla C, et al. Strategy for diagnosis of congenital toxoplasmosis: evaluation of methods comparing mothers and newborns and standard methods for postnatal detection of immunoglobulin G, M, and A antibodies. *J Clin Microbiol.* 2001;39:2267–2271.

37. Alford CA, Foft JW, Blankenship WJ, Cassady G, Benton JW. Subclinical central nervous system disease of neonates: A prospective study of infants born with increased levels of IgM. *J Pediatr.* 1969;75:1167–1178.