

The Role of the Obstetrician–Gynecologist in Emerging Infectious Diseases: Monkeypox and Pregnancy

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Early in June 2003, the Centers for Disease Control and Prevention (CDC) announced yet another unique infectious disease outbreak, the first evidence of community-acquired monkeypox in the United States. By July 8, 2003, a total of 71 cases had been reported to CDC from 6 states. When emerging infectious diseases are reported in the United States, particularly when these reports receive widespread media attention, obstetrician–gynecologists may be called upon to rapidly respond to queries from their patients and to address certain infectious disease risks within their clinical practices. In addition, obstetrician–gynecologists may have specific concerns about the implications for an infectious disease outbreak, such as monkeypox, for pregnant women. Therefore, it is important that obstetrician–gynecologists know how to gather up-to-date and accurate information about infectious disease outbreaks and that they be familiar with the public health response system for responding to such outbreaks. (Obstet Gynecol 2004;103:754–6. © 2004 by The American College of Obstetricians and Gynecologists.)

On June 7, 2003, the Centers for Disease Control and Prevention (CDC) announced yet another unique infectious disease outbreak in the United States—monkeypox.¹ Like other recent unusual infectious disease outbreaks such as West Nile virus and severe acute respiratory syndrome (SARS), the initial reports of community-acquired monkeypox generated a lot of attention in the media and interest and concern in the general public.² When emerging infectious diseases are reported in the United States, particularly when these reports receive widespread media attention, obstetrician–gynecologists may be called upon to respond rapidly to queries from their patients and to address certain infectious disease risks within their clinical practice. Therefore, it is important that obstetrician–gynecologists know how to gather up-to-date and accurate information about infectious disease outbreaks and that they be familiar with the public health response system for responding to such outbreaks.

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OUTBREAK OF HUMAN MONKEYPOX

In early June 2003, monkeypox was reported among several residents in the United States who became ill after having contact with sick prairie dogs.¹ By July 8, 2003, a total of 71 cases had been reported to CDC from 6 states (Wisconsin, Indiana, Illinois, Missouri, Kansas, and Ohio).³ This outbreak, which represents the first evidence of community-acquired monkeypox in the United States, resulted from contact with infected prairie dogs that had been housed or transported with African rodents imported from Ghana. Although the illness was generally mild, more serious consequences of disease did occur, including encephalitis in a child under 10 years who was hospitalized and became critically ill.⁴

Monkeypox, which was first discovered in laboratory monkeys in 1958, is a rare zoonotic disease caused by an orthopoxvirus. The first human cases of monkeypox were reported in the Democratic Republic of the Congo in 1970.⁵ After an incubation period of 7–17 days, persons infected with monkeypox typically experience a prodrome consisting of fever, headaches, myalgias, chills, and drenching sweats. This prodromal phase is followed 1–10 days later by the development of a rash that includes macules, papules, vesicles, pustules, and crusts. This rash may be confused with smallpox (variola major) or chickenpox (varicella-zoster). Lymphadenopathy is a prominent feature of monkeypox and may help to differentiate this rash from the rash associated with smallpox or chickenpox. Similar to smallpox, the rash associated with monkeypox typically has lesions that evolve in the same stage over 14–21 days.^{5,6}

Smallpox (vaccinia) vaccine has been reported to reduce the risk of monkeypox among previously vaccinated persons in Africa. Based on this information, CDC recommended that exposed persons be vaccinated.⁷ As of July 11, 2003, 23 people who had been exposed to monkeypox had received smallpox vaccine.³ Although there is currently no proven safe treatment for monkeypox, there are 2 possible treatments that may be consid-



ered in critically ill patients infected with monkeypox—cidofovir and vaccinia immune globulin.⁷

OUTBREAK RESPONSE, REPORTING, AND CONTROL PROCEDURES

In response to the monkeypox outbreak, CDC activated its emergency response system. As part of this response, CDC teams made up of epidemiologists and other personnel were dispatched into the field to assist the state and local health departments in their investigation and control of this outbreak. In addition, the Director's Emergency Operations Center, which is a state-of-the-art secure communications hub at CDC's headquarters in Atlanta, assisted with the agency's response to the outbreak. The Director's Emergency Operations Center is a 7,000-square-foot operations center with 85 workstations, 9 team rooms, and a central command station, as well as high-frequency radio support and geographic information system (disease mapping) capabilities, which is staffed 24 hours a day and 7 days a week. This center is relatively new and designed to more efficiently track and respond to disease outbreaks.

Regarding infection control guidelines, CDC issued written guidance about the handling of possible monkeypox exposures shortly after the first reports of human monkeypox. According to these interim guidelines, clinicians were counseled to ask patients presenting with unexplained fever, rash, or prominent lymphadenopathy about exposure to unusual or exotic pets, especially small mammals such as prairie dogs. If monkeypox was suspected, then standard, contact, and airborne precautions were recommended. These guidelines for precautions are posted on the CDC web site at www.cdc.gov/ncidod/hip/ISOLAT/Isolat.htm. In addition, the guidelines specified that health care providers who suspect monkeypox should report such cases to their state and local health departments. State health departments were then requested to report these cases to CDC.

UNIQUE CONSIDERATIONS IN PREGNANT WOMEN

Most people infected with monkeypox have been relatively young (median age of 28 years), and more than half of the cases (55%) were among women.³ Because a substantial proportion of the cases were women of reproductive age, it is not surprising that some of these women might be pregnant. In addition to pregnancies among the cases, many of the exposed persons were also women of reproductive age and might also be pregnant. Therefore, it is important to consider the implications of this outbreak for pregnant women.

It would be clinically useful to know whether the course of illness among pregnant women would be any

more severe than among nonpregnant persons. Unfortunately, most prior descriptions of monkeypox outbreaks in Africa do not include a description of the natural history of monkeypox among pregnant women.^{8,9} One case of probable congenital monkeypox in Zaire has been described. At approximately 24 weeks of gestation, a pregnant woman developed a febrile illness with a rash; monkeypox virus was subsequently isolated from a vesicular lesion. Six weeks later she delivered a 1,500-g female infant with a generalized skin rash resembling monkeypox. The child died of malnutrition at 6 weeks of age.¹⁰

With smallpox infections, an increased risk of morbidity and mortality among pregnant women compared with nonpregnant persons has been documented.¹¹ It is not known, however, whether a similar increase in disease severity associated with pregnancy would be observed with monkeypox. In terms of potential treatment, the use of cidofovir and vaccinia immune globulin should be considered only in pregnant women who are severely ill. Cidofovir is categorized as pregnancy class C by the Food and Drug Administration because in animal studies embryotoxic and teratogenic effects were noted, including reduced fetal weight and increased incidence of fetal external, soft tissue, and skeletal abnormalities. Regarding immune globulin, although little is known about vaccinia immune globulin in pregnancy, other immune globulins have been studied extensively and generally found to be safe in pregnancy. Although the usefulness and appropriateness of using these 2 treatment modalities in monkeypox is not well established, pregnancy should not be considered a contraindication.¹² Regarding the delivery plan for women with active monkeypox, almost nothing is known about potential genital tract shedding of the virus and the possibility of perinatal monkeypox transmission. Over the past decade or so, much has been learned about genital tract shedding of other viruses such as human immunodeficiency virus and herpes simplex virus and implications for perinatal transmission such as the protective effect of cesarean delivery. However, it is not clear how much of this knowledge might be applicable in the case of monkeypox.

The CDC recommends that persons with close contact to a case of monkeypox be vaccinated with smallpox vaccine, regardless of their pregnancy status. This is consistent with other guidance regarding vaccination for smallpox exposure. Pregnancy is a contraindication to routine nonemergency smallpox vaccination because the vaccine is a live-viral vaccine and cases of fetal vaccinia infection have been reported. However, there are no contraindications to smallpox vaccination after a high-risk exposure such as might occur during a bioterror



attack.^{13,14} There is a CDC-sponsored voluntary registry for pregnant women who receive smallpox vaccine, and vaccinated pregnant women should be asked to participate in this registry.¹⁵ Clinicians can report cases of pregnant women vaccinated with smallpox vaccine through their state health departments or to CDC directly (National Smallpox Vaccine in Pregnancy Registry; telephone: 404-639-8253).

ROLE OF OBSTETRICIAN-GYNECOLOGISTS IN INFECTIOUS DISEASE OUTBREAKS

As international borders blur because of increased travel and transport of both humans and animals and with increasing concern about the potential for bioterror attacks, it is likely that the public health system will continue to face infectious disease threats of new and unusual pathogens. However, it is not just the public health system that will face infectious disease challenges in the coming years. Practicing obstetrician-gynecologists and other clinicians should also expect their patients to ask about these novel infections and to expect current information and reassurance. In addition, clinicians will need to have procedures in place for infection control in both the outpatient and inpatient settings. For example, if a woman presents to her obstetrician-gynecologist's office with a rash illness and her child has a prairie dog for a pet, there should be a system in place for responding appropriately.

The latest information about a variety of outbreaks and other public health issues is posted on the CDC web site (www.cdc.gov), including the *Morbidity and Mortality Weekly Report (MMWR)*; this information summarizes current public health information on a weekly basis. It is also important to understand how the reporting system for infectious diseases is set up. In general, if clinicians are concerned about an unusual clinical presentation or potential outbreak of disease, they should first contact their local or state health departments. The health department staff will then notify CDC as appropriate. In addition, there are several CDC response hotlines that are continuously staffed (24 hours a day, 7 days a week) to respond to queries from physicians. The clinician information line (877-554-4625) provides general information about a variety of public health issues as well as telephone numbers for state and local health departments. The Director's Emergency Operations Center has a hotline (770-488-7100) clinicians can call with concerns about specific patients or clinical situations. As new infections emerge, it will be important for obstetrician-gynecologists and other clinicians to stay up-to-date so that they can help educate and reassure their patients and make reasonably informed clinical decisions.

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Received November 6, 2003. Received in revised form November 19, 2003. Accepted December 9, 2003.

