HHS Public Access

Author manuscript

Birth Defects Res. Author manuscript; available in PMC 2024 August 14.

Published in final edited form as:

Birth Defects Res. 2017 March 15; 109(5): 391–398. doi:10.1002/bdr2.1016.

Preparing for Biological Threats: Addressing the Needs of Pregnant Women

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Abstract

Intentional release of infectious agents and biological weapons to cause illness and death has the potential to greatly impact pregnant women and their fetuses. We review what is known about the maternal and fetal effects of seven biological threats: *Bacillus anthracis* (anthrax); variola virus (smallpox); *Clostridium botulinum* toxin (botulism); *Burkholderia mallei* (glanders) and *Burkholderia pseudomallei* (melioidosis); *Yersinia pestis* (plague); *Francisella tularensis* (tularemia); and *Rickettsia prowazekii* (typhus). Evaluating the potential maternal, fetal, and infant consequences of an intentional release of an infectious agent requires an assessment of several key issues: (1) are pregnant women more susceptible to infection or illness compared to the general population?; (2) are pregnant women at increased risk for severe illness, morbidity, and mortality compared to the general population?; (3) does infection or illness during pregnancy place women, the fetus, or the infant at increased risk for adverse outcomes and how does this affect clinical management?; and (4) are the medical countermeasures recommended for the general population safe and effective during pregnancy? These issues help frame national guidance for the care of pregnant women during an intentional release of a biological threat.

Keywords

biologic; bioterrorism; biowarfare; infectious diseases; pregnant; threats

Introduction

Biological threats, infectious agents released to intentionally cause illness and death, have the potential to greatly impact pregnant women and their fetuses (U.S. Department of Health and Human Services, 2015). Preparation and planning for the possible deliberate release of a biologic agent must take into account the unique considerations of pregnant women. Pregnant women might be more susceptible to infectious agents (e.g., *Listeria monocytogenes*), more likely than nonpregnant women to experience severe disease or greater morbidity (e.g., smallpox and influenza), and might experience a higher rate of mortality (e.g., influenza and hepatitis) (Kourtis et al., 2014; Sappenfield et al., 2013).

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Complications of pregnancy, such as preterm birth, spontaneous abortion, and pregnancy loss, have been associated with maternal exposure to biologic agents (e.g., anthrax and Ebola virus). Fetal exposure to infectious diseases during pregnancy can cause birth defects, growth problems, and neurobehavioral and cognitive delays (e.g., rubella, cytomegalovirus, and Zika). Furthermore, the use of medical interventions (e.g., early diagnosis, vaccines, antimicrobials, antitoxins, and supportive care) for pregnant women may pose risks to the fetuses or infants when used during pregnancy.

In 2016, the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) identified nine biological agents that pose the most serious threat to national security from deliberate, accidental, or naturally occurring causes. We review the implications for pregnant women of several of these biological threat agents: *Bacillus anthracis* (anthrax); variola virus (smallpox); *Clostridium botulinum* toxin (botulism); *Burkholderia mallei* (glanders) and *Burkholderia pseudomallei* (melioidosis); *Yersinia pestis* (plague); *Francisella tularensis* (tularemia); and *Rickettsia prowazekii* (typhus). Although viral hemorrhagic fever and influenza were also identified by the PHEMCE as high priority infectious agents, these are not addressed in this article because it is unclear how they would be used intentionally, and much has already been written about these agents (Siston et al., 2010; Mosby et al., 2011; Jamieson et al., 2014; Meaney–Delman et al., 2015; Fell et al., 2017), including an article on Ebola virus disease in this issue (Bebell et al., 2017).

Evaluating the potential maternal, fetal, and infant consequences of an infectious disease outbreak and the development of recommendations for medical management requires an assessment of several key issues for each biological agent: (1) are pregnant women more susceptible to infection or illness compared to the general population?; (2) are pregnant women at increased risk for severe illness, morbidity, and mortality compared to the general population?; (3) does infection or illness during pregnancy place women, the fetuses, or the infants at increased risk for adverse pregnancy outcomes and how does this affect clinical management?; and (4) are the medical countermeasures (MCMs) recommended for the general population safe and effective during pregnancy?

ANTHRAX

Anthrax is a disease caused by the bacterium *Bacillus anthracis*; many of the specific adverse effects are mediated by one of two toxins produced by this bacterium (Wright et al., 2010). Consequences of anthrax include sepsis, toxin-induced shock, and even death. Weaponized inhalation anthrax is considered one of the most serious biological threats because it is a proven effective bioweapon that causes severe morbidity and mortality (Jernigan et al., 2002; Wright et al., 2010). Although the evidence is limited, it does not seem that pregnant women are at increased risk for acquiring anthrax (Meaney–Delman et al., 2012). It is not clear if pregnant women experience more severe disease or experience a higher rate of adverse outcomes. Anthrax among pregnant women has been associated with maternal and fetal death and preterm labor (Meaney–Delman et al., 2012). Limited evidence to date does not suggest an increased risk of birth defects among infants born to women with anthrax during pregnancy, however, only 17 cases have been reported in the literature and many date back to the early 1900s (Meaney–Delman et al., 2012).

Anthrax medical countermeasures recommended for pregnant women are similar to those recommended for the general population. Pregnant women exposed to inhalation anthrax should receive postexposure prophylaxis (PEP), a regimen that includes a vaccine and an oral antimicrobial (Wright et al., 2010; Meaney–Delman et al., 2014). The PEP regimen is the same regardless of the trimester of exposure (Wright et al., 2010; Meaney–Delman et al., 2014). The Strategic National Stockpile maintains a cache of anthrax vaccine, BioThrax Anthrax Vaccine Adsorbed (Emergent BioSolutions, Rockville, MD) for use during an anthrax emergency response (Wright et al., 2010). In 2010, the Advisory Committee on Immunization Practices considered pregnancy neither a precaution nor contraindication to anthrax vaccine (Wright et al., 2010). In 2014, the Centers for Disease Control and Prevention reaffirmed the recommendation that pregnant women at risk for exposure to aerosolized *B. anthracis* should receive anthrax vaccine adsorbed in conjunction with an antimicrobial agent (Meaney–Delman et al., 2014).

Recommended PEP antimicrobials for adults over 18 years of age include ciprofloxacin, levofloxacin, and doxycycline (Hendricks et al., 2014). Recommendations for pregnant women are similar, with the exception that ciprofloxacin is preferred to doxycycline (Meaney–Delman et al., 2014), because tetracycline has been associated with a possible increased risk for congenital abnormalities (Meaney–Delman et al., 2014). However, if the strain of anthrax is penicillin-sensitive, amoxicillin or penicillin can also be used as the PEP (Meaney–Delman et al., 2014). Antimicrobial agents administered as part of a PEP regimen should be administered for 60 days because anthrax spores may reactivate during this time period (Friedlander et al., 1993; Meaney–Delman et al., 2014).

Treatment of anthrax involves multiagent intravenous antimicrobial therapy in combination with an antitoxin. For pregnant women diagnosed with anthrax in whom meningitis is diagnosed or suspected, a three-drug regimen, including two bactericidal agents and a protein synthesis inhibitor, is recommended. All antimicrobials should be capable of penetrating the central nervous system and achieving adequate antimicrobial levels in the cerebrospinal fluid. The first line intravenous antimicrobial regimen is a combination of ciprofloxacin, meropenem, and linezolid (Hendricks et al., 2014; Meaney–Delman et al., 2014). For pregnant women diagnosed with anthrax in whom meningitis has been excluded, two antimicrobials are recommended, one that is bactericidal and one that inhibits protein synthesis. The first line antimicrobial regimen for nonmeningitis anthrax is a fluoroquinolone and doxycycline. Alternate regimens are recommended but a detailed description is beyond the scope of this review. Ciprofloxacin is the preferred fluoroquinolone for pregnant women because of reports suggesting a higher risk of fetal loss with other quinolones (Meaney–Delman et al., 2013).

An additional component of anthrax treatment is the recommended use of an antitoxin to decrease the toxin-mediated effects of *B. anthracis*. Either raxibacumab or anthrax immune globulin are recommended as adjunctive treatment in combination with antimicrobials (Meaney–Delman et al., 2014). Although evidence is limited to evaluate the safety of anthrax antitoxin during pregnancy, antitoxins have been shown to reduce mortality when used in conjunction with antimicrobials in animal models (Huang et al., 2015). The severe

and potentially fatal nature of inhalation anthrax warrants the use of antitoxin therapy for pregnant women, despite the limited safety data.

Clinical management of pregnant women with inhalation anthrax may require specialty care. Intensive monitoring is needed to continuously assess hemodynamic and respiratory status, as well as to monitor for signs of preterm labor and nonreassuring fetal status. Given the severe nature of the infection and the possibility of preterm delivery, corticosteroids may be considered to promote fetal maturation among women who present with anthrax while preterm (Meaney–Delman et al., 2014).

SMALLPOX

Variola virus causes smallpox, a disease characterized by a distinct rash and high fever. Although the last case of smallpox occurred in 1977, smallpox still poses a threat as a biological weapon (Brilliant and Hodakevic, 1978; Henderson et al., 1999; Petersen et al., 2015). Smallpox has a high case-fatality rate (30% or more) in unvaccinated persons (Henderson et al., 1999). No specific smallpox treatment is currently approved; therefore, supportive care is recommended (Petersen et al., 2015). A vaccination campaign successfully eradicated smallpox in 1980, and this same strategy is the cornerstone of a response to an intentional smallpox event (Henderson et al., 1999; Petersen et al., 2015). Most people living in the United States, including pregnant women, have not been previously vaccinated (Centers for Disease Control and Prevention, 1983). Thus, because population immunity no longer exists, an introduction of smallpox could spread quickly to the now-susceptible population (Henderson et al., 1999). It is not known if pregnant women are more susceptible to the infection.

Pregnant women seem to be at higher risk for severe disease (including hemorrhagic smallpox) than nonpregnant individuals, likely because of their altered immune status (Henderson et al., 1999; Sappenfield et al., 2013; Petersen et al., 2015). Smallpox among pregnant women is associated with an increased risk of perinatal and maternal morbidity and mortality (Suarez and Hankins, 2002). Fetal smallpox has been reported, although the frequency of maternal to fetal transmission is unknown. No specific pattern of birth defects among fetuses exposed to smallpox during pregnancy has been reported, however, given that limited evidence exists, an association cannot be excluded.

Because of the increased risk of maternal and infant morbidity and mortality during an emergency involving smallpox, the Centers for Disease Control and Prevention recommends that pregnant women exposed to smallpox virus or at risk for exposure should be vaccinated (Petersen et al., 2015). Although smallpox vaccination has been associated with a rare complication of fetal vaccinia, the risks of smallpox to both the mother and the fetus likely outweigh this risk of vaccination in women exposed to smallpox virus or at risk for exposure (Cono et al., 2006; Badell et al., 2015). Fetal vaccinia seems to be rare, with less than 50 reported cases in the literature (Badell et al., 2015). Fetal vaccinia has been reported in association with maternal infection in all trimesters. A systematic review of pregnant women who received the smallpox vaccine reported no increased risk of spontaneous abortion, stillbirth, or preterm birth. However, a small increase in the risk of birth defects after the first trimester vaccination was noted, based on a small number of cases (Badell et al., 2015).

Historically, vaccinia immune globulin (VIG) was administered to prevent vaccine-related complications among individuals at high risk for adverse vaccine events (Henderson et al., 1999). Although VIG has been used in the past after smallpox vaccine administration to pregnant women, VIG is not currently licensed for prophylactic use after inadvertent vaccination of pregnant women (Cangene Corporation, 2010). However, if a pregnant woman experiences complications associated with the smallpox vaccine administration, VIG should be considered based on the same criteria as for nonpregnant individuals (Cangene Corporation, 2010).

BOTULISM

Clostridium botulinum and closely-related species are spore-forming, anaerobic organisms that produce botulinum neurotoxin. Botulinum neurotoxin is the most potent known neurotoxin; it binds irreversibly at the neuromuscular junction, causing progressive and potentially profound paralysis that may include respiratory failure (Shukla and Sharma, 2005; Sobel, 2005). Several types of botulism occur including: wound botulism, infant botulism, food-borne botulism, and inhalational botulism (Shukla and Sharma, 2005). Inhalational botulism does not occur naturally, but a single report documents its occurrence in laboratory workers (Middlebrook and Franz, 1997); state-sponsored biowarfare programs have produced stocks of aerosolizable botulinum toxin (Middlebrook and Franz, 1997). Intentional release of aerosolized botulinum toxin has been attempted several times in Japan; however, none of these attempts were successful (Arnon et al., 2001). Use of botulism as a bioterror agent could be perpetrated by foodborne or inhalational routes by contaminating food sources or aerosolization, respectively (Arnon et al., 2001; Shukla and Sharma, 2005; Christian, 2013).

Early recognition, diagnosis, and treatment of botulism are critical (Centers for Disease Control and Prevention, 2006; Centers for Disease Control and Prevention, 1998). The mainstays of treatment are respiratory support and prompt treatment with botulinum antitoxin to prevent further paralysis (Tacket et al., 1984; Arnon et al., 2001; Sobel, 2005; Centers for Disease Control and Prevention, 2006). Early administration of the antitoxin is associated with a lower fatality rate and less extensive paralysis (Tacket et al., 1984; Arnon et al., 2001); however, it does not reverse paralysis present at the time of administration (Arnon et al., 2001).

Little is known about the effects of botulism during pregnancy. Given that ingestion or inhalation of toxin are the potential routes of exposure, susceptibility to illness would not be expected to be greater among pregnant women, as generally, the toxin has a dose-dependent effect. It is not known if pregnant women or infants are more likely to experience adverse outcomes than the general population after botulism; however, pregnant women have been administered equine antitoxin without ill effects (St Clair et al., 1975; Robin et al., 1996). The only recommendations currently published regarding the care of pregnant women with botulism were published over a decade ago. Based on these recommendations, pregnant women should receive treatment with antitoxin, consistent with recommendations for the general population (Arnon et al., 2001).

BURKHOLDERIA

Burkholderia mallei and *Burkholderia pseudomallei* are causes of glanders and melioidosis, respectively, and are considered together, given their many similarities (Gilad et al., 2007). Clinical manifestations of glanders include lesions of the skin and mucosal membranes of the upper respiratory tract, with pulmonary manifestations (pneumonia, pulmonary abscesses, and pleural effusion), and septicemia in some patients (Van Zandt et al., 2013). Melioidosis has highly variable clinical manifestations, including local manifestations (e.g., ulcer and abscess), as well as pulmonary, disseminated, and bloodstream infections (Limmathurotsakul et al., 2016). These organisms are uncommonly found in the United States; however, they have been extensively studied because of their potential for use as bioterror agents (Lipsitz et al., 2012).

Very little is published about these infectious agents during pregnancy. We identified only two case reports of possible or proven melioidosis during pregnancy (Webling, 1980; Abbink et al., 2001); therefore, it is unknown if pregnant women are more susceptible to *Burkholderia pseudomallei* or if they experience more severe disease. In one case, the woman presented at 24 weeks gestation with cystitis, vaginal discharge, and an ulcer on her upper inner thigh, and *Burkholderia pseudomallei* was cultured from urine and vaginal discharge, but not from the ulcer. After receiving partial treatment, the woman was lost to follow-up, but several weeks later she was identified as having a stillborn infant (Webling, 1980). In the other case, the woman was hospitalized for fever and placenta previa at 26 weeks gestation; severe vaginal bleeding at 32 weeks gestation necessitated an emergency Cesarean delivery (Abbink et al., 2001). Her infant presented with sepsis and respiratory distress at 2 days of life; on day 5, a lung abscess was recognized and *Burkholderia pseudomallei* was identified in blood and tracheal aspirate. Ultimately, the infant survived with treatment. Specimens obtained from the mother's cervix postpartum also grew *B. pseudomallei* of the same strain (Abbink et al., 2001). No cases of pregnant women with glanders could be identified in the literature.

There is no vaccine available for melioidosis or glanders (White, 2003; Centers for Disease Control and Prevention, 2012). According to a recent review, recommendations for treatment for *B. pseudomallei* and *B. mallei* for the general population include an initial and minimum of 10 to 14 days intravenous intensive phase (with ceftazidime for uncomplicated patients or meropenem for patients with complications) followed by a 12-week oral eradication phase (with trimethoprim/sulfamethoxazole or amoxicillin/clavulanic acid) (Lipsitz et al., 2012). Intravenous therapy may be extended up to 6 weeks for severe infections. For PEP, recommended drugs are trimethoprim/sulfamethoxazole or amoxicillin/clavulanic acid. The authors noted that trimethoprim/sulfamethoxazole has been associated with adverse pregnancy outcomes (Wen et al., 2008); thus, amoxicillin-clavulanic acid is recommended for pregnant women (Lipsitz et al., 2012). No other pregnancy-specific recommendations are provided.

PLAGUE

Yersinia pestis is the bacterium that causes plague. Plague symptoms depend on the route of exposure. The most common clinical forms of plague are bubonic, septicemic, and

pneumonic. Bubonic plague symptoms include sudden onset of fever, headache, chills, and one or more swollen and painful lymph nodes, called buboes. Septicemic plague symptoms include fever, chills, weakness, and abdominal pain, in the absence of other localizing signs. Pneumonic plague symptoms include fever, headache, weakness, shortness of breath, chest pain, and cough. Hemoptysis occurs once the disease has progressed to fulminant infection. Pneumonic plague is the most severe form of disease and can be spread from person-to-person through infectious droplets, typically from patients with late-stage infection. Aerosolized *Y. pestis* is considered a biological threat, with the potential to cause pneumonic plague (Inglesby et al., 2000).

Plague is a highly virulent disease with case fatality rates of 50 to 95% in the absence of treatment, depending on the clinical form (Kugeler et al., 2015). It is not known if pregnant women are more susceptible to plague, if they experience more severe disease, or if there is an increased risk of adverse maternal or infant outcomes. The literature is limited and difficult to quantify. Although, in several cases, *Y. pestis* was not found in products of conception from plague-infected mothers, one case of intrauterine infection has been reported (Pollitzer, 1954). Pregnant women diagnosed with plague have experienced fetal tachycardia (Welty et al., 1985), fetal distress (Welty et al., 1985), and spontaneous abortion (Jennings, 1903).

No vaccine for plague is currently available (Inglesby et al., 2000; Pechous et al., 2016). Recommendations from the Working Group on Civilian Biodefense distinguish between exposures in a contained casualty setting (in which a modest number of persons are infected) and in a mass casualty event (Inglesby et al., 2000). In a contained casualty scenario, the first-line treatment for the general population is streptomycin or gentamicin, with alternative choices of doxycycline, ciprofloxacin, or chloramphenicol (although streptomycin and chloramphenicol are generally not available in the United States). Treatment recommendations differ for pregnant women: gentamicin is preferred, with alternatives of doxycycline or ciprofloxacin (Inglesby et al., 2000). In a mass casualty event, recommended treatment and PEP for pregnant women are the same as those for nonpregnant adults: either doxycycline or ciprofloxacin, with chloramphenicol as an alternative. Existing recommendations do not indicate a preference for use of doxycycline or ciprofloxacin for treatment or PEP in pregnant women. Treatment is recommended for 10 days or until 2 days after the fever subsides, whereas PEP is recommended for 7 days (Inglesby et al., 2000; Centers for Disease Control and Prevention, 2015a).

TULAREMIA

Francisella tularensis is the causative agent for the zoonotic disease tularemia (Tärnvik, 2007). Research on the use of *F. tularensis* as a biological threat dates back to Japan in the 1930s and 1940s (Dennis et al., 2001). Symptoms of tularemia vary based on the route of exposure, with several different types, including ulceroglandular, glandular, pneumonic, oculoglandular, oropharyngeal, and typhoidal (i.e., without localizing signs). All forms are associated with fever (Centers for Disease Control and Prevention, 2015c).

There is little documentation of *F. tularensis* affecting pregnant women (Ata et al., 2013; Yeşilyurt et al., 2013). Because of the paucity of reported cases, it is unknown if pregnant

women are more susceptible to the infection or at an increased risk of morbidity, mortality, or adverse pregnancy or infant outcomes (Ata et al., 2013).

A recent review identified eight cases of tularemia during pregnancy in the literature (Ata et al., 2013). Two of these were identified from the 1930s, and neither received antibiotic therapy; one ended in pregnancy loss at 21 weeks gestation and, in the other case, the pregnant woman experienced mild illness mid-pregnancy, and then bleeding and anemia near term, but delivered an apparently healthy infant (Bricker, 1931; Bowe and Wakeman, 1936; Ata et al., 2013). The remaining six cases of pregnant women were identified from 2008 to 2012 in Turkey and France; five were treated successfully and delivered healthy infants. The sixth patient presented at 6 weeks gestation with an 18-day history of fever and chills after consuming contaminated water; she was offered antimicrobial therapy but refused. The pregnancy ended with an intrauterine fetal death at 27 weeks (Ata et al., 2013). Although none of the live-born infants were reported to have birth defects, with such a small number of cases, an increased risk of birth defects cannot be excluded. Additional investigations are needed to fully understand the effects of tularemia during pregnancy (Ata et al., 2013).

There is no currently available tularemia vaccine in the United States (Dennis et al., 2001; Centers for Disease Control and Prevention, 2015b). A tularemia vaccine, previously used to protect laboratory workers, is currently under the U.S. Food and Drug Administration review (Dennis et al., 2001; Centers for Disease Control and Prevention, 2015b). The preferred antimicrobials for treatment and PEP include ciprofloxacin or doxycycline (Dennis et al., 2001). No specific recommendations were made for pregnant women, although the recommendations indicate that treatment should be individualized to the patient (Dennis et al., 2001; Tärnvik, 2007). Existing recommendations do not indicate a preference for use of doxycycline or ciprofloxacin for treatment or PEP in pregnant women.

TYPHUS

Rickettsia prowazekii is one of many types of infectious agents that cause typhus. Typhus has already been weaponized and, therefore, could pose a threat as an intentionally used biological agent (Azad, 2007; Bechah et al., 2008). The clinical presentation of typhus varies, however, patients often manifest a rash, high fever (39–40°C), and a headache (Azad, 2007; Bechah et al., 2008). Other commonly associated symptoms include myalgia, arthralgia, abdominal pain, and neurologic symptoms. The case fatality rate for highly virulent strains of *R. prowazekii* is 2 to 30% (Azad, 2007; Dotters-Katz et al., 2013). No cases of *R. prowazekii* were identified in the literature among pregnant women. No vaccine currently exists to protect against *R. prowazekii* (Richards, 2004). In nonpregnant women, the recommended antibiotic regimen is doxycycline or chloramphenicol (Raoult and Drancourt, 1991).

No national recommendations for typhus treatment of pregnant women during an intentional release exist. However, in other rickettsial infections, specifically tick-borne rickettsial disease, as well as with other biological threat agents, tetracyclines are used during pregnancy, specifically in life-threatening situations (Chapman et al., 2006). According to one set of authors, chloramphenicol is considered the preferred treatment for *R. prowazekii*

during pregnancy (Dotters-Katz et al., 2013), however, administration of chloramphenicol during the third trimester of pregnancy can be associated with a risk of grey baby syndrome, an accumulation of toxic metabolites of this drug in newborns (Meaney–Delman et al. 2013).

Discussion

There is a dearth of information on the maternal, fetal, and infant effects of high priority biological threat agents. Of the seven agents reviewed, it is generally unknown whether pregnant women are more susceptible to the offending agent than the general population. Previously, pregnancy was thought to be associated with general immunosuppression; however, emerging evidence suggests that pregnant women are no more susceptible to infections than nonpregnant women, with a few notable exceptions (e.g., *Listeria monocytogenes*) (Sappenfield et al., 2013; Kourtis et al., 2014). Although pregnant women may not be at increased risk for acquiring most infections during a biological attack, there are several examples to suggest that they may experience more severe illness and higher mortality compared with nonpregnant women once infected. For anthrax and smallpox, pregnant women are at risk for mortality. Fetal death and preterm birth have been reported among pregnant women with anthrax, botulism, smallpox, and tularemia. However, these findings are primarily from case reports, and it is unclear if the risk is truly increased; these are not uncommon adverse pregnancy outcomes and without a comparison group, it is simply unknown. Additionally, some of the anthrax cases in pregnant women occurred in the pre-antibiotic era, limiting the generalizability of the findings.

For the majority of the biological threat agents, no specific guidance for pregnant women exists. Despite limited evidence, the needs of pregnant women should be considered during preparedness planning for biological attacks. Special considerations for MCM use can be extrapolated from other infections (e.g., rickettsial infections) as well as from safety data from and animal studies. Although risks to the fetus are a concern, risks of MCM use need to be carefully weighed against the certainty of exposure, the maternal and fetal risks of infection and any long term sequelae. For example, although the smallpox vaccine has been associated with fetal vaccinia and is contraindicated for routine use during pregnancy, in the event of a deliberate release of smallpox, the increased risks of maternal and perinatal morbidity and mortality outweigh the risks of fetal vaccinia and pregnant women should be vaccinated. (Rotz et al., 2001; Badell et al., 2015; Petersen et al., 2015). When multiple MCMs are available, consideration should be given to what is best for the pregnant woman and safest for the fetus. For instance, if multiple antibiotics can be used for PEP or treatment, the teratogenic potential and risks of each regimen should be weighed and balanced with its effectiveness. The safety of each antibiotic should be considered and efforts should be made to ensure that guidelines are consistent when similar antibiotics are used.

Additionally, for many infectious threats, such as botulism and smallpox, pregnant women should receive the same prophylaxis and treatment as the general population (Arnon et al., 2001; Meaney–Delman et al., 2014; Petersen et al., 2015). However, because pregnant women and their healthcare providers often overestimate the harms of medication use

during pregnancy to the fetus, this can lead to reluctance to use necessary and lifesaving MCMs (Sanz et al., 2001; Cono et al., 2006). For this reason, even when guidance for pregnant women is no different than guidance for the general population, it should be clearly communicated that pregnant women receive the same interventions as the general population.

It is essential that preparedness planning for biological threat agents incorporate special considerations for pregnant women. Several interrelated planning components have been proposed in the literature to ensure critical information about the effects of both the threat and the MCMs on pregnant women is captured during a public health emergency. The components proposed are: (1) generic protocols to conduct research with human subjects approval that includes pregnant women; (2) a network of obstetric and pediatric experts; and (3) funding specific to pregnant women (Faherty et al., 2017). As biological threats are increasingly recognized as a public health threat and new MCMs are researched, developed, procured, and stockpiled, the needs of pregnant women must be considered in preparedness planning.

Disclaimer:

The findings and conclusion in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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