Biotechnology and Molecular Biology Review Vol. 6(2), pp. 21-30, February 2011
Available online at http://www.academicjournals.org/BMBR
ISSN 1538-2273 ©2011 Academic Journals

Standard Review

Emerging infections and bioterrorism emergencies: Where do we go from here?

I. O. Okonko[1]*, M. O. Ojezele[2], E. T. Babalola[3], J. C. Nwanze[4], O. K. Mejeha[5] and T. A. Amusan[6]

[1]Department of Biochemistry and Microbiology, Lead City University, Ibadan, Nigeria.
[2]Department of Nursing Science and Public Health, Lead City University, Ibadan, Nigeria.
[3]Department of Microbiology, Crawford University, Igbesa, Ogun State, Nigeria.
[4]Department of Pharmacology and Therapeutics, Igbinedion University, Okada, Edo State, Nigeria.
[5]Department of Microbiology, Federal University of Technology, Owerri, Imo State, Nigeria.
[6]Medical Laboratory Unit, Department of Health Services, University of Agriculture, Abeokuta, Ogun State, Nigeria.

Accepted 18 November, 2010

Emerging infectious disease outbreaks and bioterrorism attacks warrant urgent public health and medical responses. Response plans for these events may include use of medications and vaccines for which the effects on pregnant women and fetuses are unknown. Recent experiences with outbreaks of severe acute respiratory syndrome, monkey pox and anthrax, as well as response planning for bioterrorism and pandemic influenza, illustrate the challenges of making recommendations about medical interventions for victims. Experience with bioterrorism attacks (anthrax), viroterrorism attacks (arena viruses) and emergency response preparedness (smallpox vaccination) has been gained. Understanding the physiology of the body, the factors that influence the teratogenic potential of medications and vaccines and the infection control measures that may stop an outbreak will aid planners in making recommendations for care during large-scale infectious disease emergencies.

Key words: Bioterrorism, emerging infections, emergence preparedness, pathogens, viroterrorism.

INTRODUCTION

Emerging infectious diseases defined as infectious diseases whose incidence in humans have increased during the past two decades or threatens to increase in the near future, are increasingly recognized by physicians as an important threat to pregnant women. Emerging infectious diseases include novel pathogens that have newly emerged, such as severe acute respiratory syndrome (SARS), as well as pathogens that could potentially be used as biologic weapons (Jamieson et al., 2006).

Bioterrorism and viroterrorism threats include plague, glanders, Q fever, filoviruses, anthrax, smallpox, brucellosis, botulism, and ricin. Indeed, the world is like a and the use of genomics for the agents of tularemia, brucellosis, and clostridial gas gangrene (Lindler et al., 2004; information on genetic fingerprinting for forensic studies). The threat of emerging infections and bioterrorist swarm with viral zoonoses. There are also genetically-engineered protein toxins. Some authors also provided attacks has heightened the need to make disease surveillance more sensitive, specific, and timely (Henderson, 1999; Fine and Layton, 2001). The primary purpose of reporting diseases is to trigger an appropriate public health response so that further illness can be prevented and public fears allayed (M'ikanatha et al., 2003). The concept of continual virus movement has prevailed over the past years in part because of the failure to identify a vertebrate reservoir (Monath, 1989),

*Corresponding author. E-mail: mac2finney@yahoo.com.

and in part because of the dearth of ecologic data to support or refute alternative modes of transmission (Carrion et al., 2007).

Challenges

The challenges facing issues of emerging infectious disease as bioterrorism agents is that unfortunately, information about how pregnant women are affected by many of these novel and emerging infections is limited (Jamieson et al., 2006). For example in the case of pregnant women during an outbreak; whether the use of a medication or vaccine is harmful to the embryo or fetus depends on multiple factors, including the nature of the agent e.g., live versus killed vaccine, its dose and route of administration, timing of use during gestation, concomitant use of other agents, nature of the infection being treated or prevented, and genetic susceptibility of the pregnant woman and of the embryo or fetus (Cono et al., 2006). Another challenge facing disease surveillance and emergency preparedness is to shorten the time of the entire process so; useful epidemiologic and viroterrorism response data can be rapidly obtained (Anderson et al., 2003). The problem of developing new antiviral agents, especially those specific for one or only a few viral diseases, is circular and is of great concern too. Without such treatments rapid agent identification is not necessary, but without such identification no pressing commercial justification for developing specific antiviral agents exists, except for HIV; because they will not be widely used. To be successful, diagnosis and therapy must be linked. Also, containment of infectious disease agents is also of great concern when dealing with radiologic hazards and to contain infectious agents (Gargan et al., 1988).

Identification of viral sources

To routinely detect new and potentially lethal viruses, researchers may need to create completely automated and contained laboratories that continually search for and sequence viruses from a wide variety of sources to hone skills, demonstrate efficiency and develop improved systems, methods and reagents (Anderson et al., 2003). Two approaches can be used, if necessary, to link viruses to patients. In the first approach, viruses would be tracked geographically, first in terms of large regions, and then, sequentially, in terms of smaller areas. Detecting a new agent in large pooled samples would thus be repeated in smaller, localized pools that had been combined hierarchically to generate the larger pool (Lee et al., 2001). According to Anderson et al. (2003) several key questions remain to be addressed in a practical project: (1) Can this process be carried out rapidly enough to support a timely therapeutic or prophylactic response to a new agent-natural or engineered? (2) Will the novel virions that originated from one or a very few infected persons be recovered and detected? (3) Can the affected persons be located? (4) Will the presence of antibodies in the starting samples against most known viruses affect the separations?

NOVEL PATHOGENS

Severe acute respiratory syndrome (SARS)

During the worldwide outbreak of SARS in 2003, several countries reported cases of SARS both in children and adults even in pregnant women. In a case-control study conducted in Hong Kong, pregnant women with SARS had more severe disease than nonpregnant women and an increased risk for admission to the intensive care unit, development of renal failure, development of disseminated intravascular coagulopathy and death (Lam et al., 2004). Of 8 cases of laboratory-confirmed SARS reported in the United States, 2 were in pregnant women; the small number of cases precludes definitive conclusions about the severity of the disease (Stockman et al., 2004).

Prions

Prions are believed to be the causative agents of a group of rapidly progressive neurodegenerative diseases called transmissible spongiform encephalopathies, or prion diseases. They are infectious isoforms of a host-encoded cellular protein known as the prion protein. Prion diseases affect humans and animals and are uniformly fatal. The most common prion disease in humans is Creutzfeldt-Jakob disease (CJD), which occurs as a sporadic disease in most patients and as a familial or iatrogenic disease in some patients (Claudio, 2007).

Avian influenza-H5N1

Avian influenza-H5N1 has caused the greatest number of human cases and death. It may develop the characteristics needed to start influenza pandemic by improving its transmissibility among humans through reassortment or through a more gradual process of adaptive mutation.

CONVENTIONAL INFECTIOUS DISEASE THREATS

Malaria

People in malaria-endemic regions are at risk of becoming infected with *Plasmodium falciparum*; 1 of 4 parasites that cause malaria in humans (Loebstein et al.,

1997).

Typhoid

Typhoid (enteric) fever is a global infection caused by *Salmonella typhi* with a fatality rate of 10%. The disease is a cause for concern and a major public health problem in developing countries (Asia and Africa), especially in Nigeria due to poor sanitary conditions and lack of or inadequate potable water. The World Health Organization (WHO) estimated an annual infectious rate of 21.6 million and approximate death rate of 600 000 with the highest percentage in Africa and Asia. An estimated 22 million cases of typhoid fever and 200,000 related deaths occur worldwide each year (Crump et al., 2004). Approximately, 400 cases of typhoid fever among persons with onset of illness in the United States, most of whom are recent travelers, are reported to CDC each year (Center for Disease Control and Prevention (CDC), 2008).

Toxoplasma gondii

T. gondii is a parasite that infects humans primarily through ingestion of infected raw or undercooked meat and, less frequently, by exposure to infected cat feces.

Hansen disease or leprosy

Hansen disease or leprosy is caused by *Mycobacterium leprae*, which can multiply and cause symptomatic disease, particularly in hosts with decreased immunity (Brent, 2004).

Listeriosis

In 2000, an outbreak of listeriosis among Hispanic persons in North Carolina was reported as a result of ingestion of contaminated homemade Mexican-style cheese (Doering et al., 2002). *Listeria monocytogenes*, a foodborne pathogen, is responsible for approximately 2,500 cases of serious illness in the United States each year (Lo and Friedman, 2002; Food and Drug Administration, 1979). There are still more of these conventional pathogens which have caused outbreaks in recent times.

POTENTIAL EFFECTS OF BIOTERRORISM

The working group on civilian biodefense has identified a limited number of biologic agents that are of particular concern (Borio et al., 2002). Evidence exist that infection with some of these pathogens, including smallpox virus and some of the hemorrhagic fever viruses, are very severe on their victims and may be more severe on women during pregnancy (Jamieson et al., 2006). Although, pregnant women are not immunosuppressed in the classic sense, immunologic changes of pregnancy may induce a state of increased susceptibility to certain intracellular pathogens, including viruses, intracellular bacteria and parasites (Cono et al., 2006).

Measles (Rubeola)

Evidence also indicates that measles (Rubeola) is more common and severe in pregnant women. Accounts of measles outbreaks before an effective vaccine was available indicate that pregnant women may be more severely affected.

Smallpox (Variola virus)

Clinical experience with smallpox (Variola virus) before vaccination and disease eradication indicates that pregnant women are more susceptible to variola infection and have more severe disease. Pregnant women are more likely than nonpregnant women to have hemorrhagic smallpox (purpura variolosa), a severe variety of the disease (Jamieson et al., 2006).

VIRAL HEMORRHAGIC FEVERS (VHFS)

The viral hemorrhagic fevers, including Lassa fever and Ebola, may be more severe during pregnancy.

Lassa virus

Lassa virus causes thousands of deaths annually in western Africa and is considered a potential biological weapon (Centers for Disease Control and Prevention (CDC), 2004). Lassa fever is a viral hemorrhagic fever caused by a rodentborne arenavirus that is endemic in West Africa. The first reported case of Lassa fever, caused by infection with an arenavirus, was described in a pregnant patient. In this initial outbreak, 11 patients and staff members who were exposed to the index patient died (White et al., 2002). One study found that after pregnancy ended, whether by abortion or normal delivery, women rapidly improved (Price et al., 1988). In 2004, the Centers for Disease Control (CDC) and prevention reported a fatal case of Lassa fever in New Jersey (Fisher-Hoch et al., 1995). Auditory or vestibular dysfunction may develop in patients with Lassa fever, and tinnitus, autophony, hearing loss, dizziness, vertigo, nystagmus and ataxia have been reported (Rybak, 1990). In their review of a 1989 nosocomial Lassa fever

outbreak in a Nigerian hospital, Fisher-Hoch et al. (1995) noted a high fever in the index patient, who was taken to surgery on February 25. Solbrig and McCormick (1991) reported that neuropsychiatric sequelae of Lassa fever have included sleep disorders (insomnia), asthenia, multiple somatic complaints, psychosis, hallucinations, personality disorders, severe adjustment reactions, dementia, mania, depression and finally, induced damage to the brain stem with resultant autonomic dysfunction.

Ebola virus

Ebola virus, a member of the Filoviridae group, is transmitted by direct contact with blood, secretions, or contaminated objects and is associated with high case-fatality rates. Unlike risk for death from Lassa fever, which is highest during the third trimester of pregnancy, risk for death from Ebola is similar during all trimesters (Mupapa et al., 1999).

Yellow fever

Yellow fever (YF) is an important reemerging arboviral disease and a cause of severe illness and death in South America and Africa. The prevailing paradigm of yellow fever virus (YFV) ecology in South America is that of wandering epizootics. The virus is believed to move from place to place in epizootic waves involving monkeys and mosquitoes, rather than persistently circulating within particular locales (Monath, 1989).

OTHER EMERGING INFECTIONS

Pneumocystis jiroveci

P. jiroveci (formerly *P. carinii*) has long been identified as a cause of pneumonia in immunocompromised persons. *Pneumocytis* pneumonia was first identified in malnourished children in European orphanages during World War II and was later associated with severe immunosuppression in HIV-infected persons (McNally et al., 2005). However, this agent is increasingly causing infection among immunocompetent persons. Evidence also indicates that *Pneumocytis* pneumonia may be more severe during pregnancy and that *Pneumocystis* may be perinatally transmitted by HIV-infected women to their children (McNally et al., 2005).

Psittacosis

Psittacosis is primarily a flulike illness characterized by fever, headache, and atypical pneumonia. *Chlamydophila psittaci* (formerly *Chlamydia psittaci*), the causative agent, is transmitted by inhalation of material from infected birds or by exposure to infected amniotic fluid or placentas of sheep or goats. Illness during pregnancy can be quite severe, mimicking HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome but without hypertension. Most women rapidly recover after pregnancy (McNally et al., 2005).

THE GROWING FIELD OF COUNTER-BIOTERRORISM

In recent years, the CDC and prevention have been funding several states to develop electronic laboratory reporting (Jorgensen, 1997). A more thorough understanding of the pitfalls of such existing systems can provide insights to improve the development and implementation of new media in infectious disease surveillance. With recent funding for activities to defend the public's health against terrorism and naturally occurring diseases, development of automated reporting systems has been accelerated (Centers for Disease Control and Prevention (CDC), 2002).

Counter bioterrorism measures include the following: Identification of viral sources, surveillance system, disease reporting system, early detection and management of a biological terrorism attack. As the popular saying to be forewarned is to be forearmed, given advance notice, even by weeks, of an impending viral outbreak, the hope exists that the tools and imaginations of molecular biology will find the means to prepare some effective biological defense (Centers for Disease Control and Prevention, 2001).

Automated surveillance and disease reporting system

Recent advances in provider and laboratory information management have facilitated one step towards the modernization of surveillance which is the development of automated reporting systems (Anderson et al., 2003). Evidence from deployed systems shows promise in the ability of electronic laboratory reporting to deliver more timely and complete notifications than paper-based methods (Henderson, 1999).

WHO global outbreak alert and response network (GOARN)

Beginning in March, 2003, after WHO recognized, through its GOARN, an outbreak of severe respiratory illness with high transmissibility in healthcare settings and international spread through airline travel, WHO issued a series of global alerts, travel advisories, and recommendations for diagnosis, clinical management,

and prevention of transmission (Centers for Disease Control and Prevention (CDC), 1997).

Global emerging infections system (GEIS)

The GEIS of the US Department of Defense (DOD) as it applies to biodefense was reported by Bell et al. (2003). Surveillance systems used by US DOD-GEIS were described by Linder (2004), from the electronic surveillance system for the early notification of community-based epidemics to newer systems, along with ways to integrate DOD and civilian surveillance systems (Lindler et al., 2004).

The national electronic disease surveillance system (NEDSS)

The NEDSS and bioterrorism preparedness initiatives are expected to further enhance disease surveillance by supporting integration of electronic data from various sources (Lucey, 2006).

Aerosol pathogenesis and biological weapons defense

Effect levels are particularly relevant given by the US Cities Readiness Initiative that involves planning for an aerosol attack with anthrax or another agent in US metropolitan areas (Doyle et al., 2002). Anderson (2003) proposes a system for continuing surveillance of viral pathogens circulating in large human populations. Given this existing technology base, an integrated, automated, and contained system for surveillance of the human “virome” can be implemented within 1 to 2 years. While these newly available electronic transmission methods can increase timeliness and completeness of infectious disease reports, limitations of this technology may unintentionally compromise detection of, and response to, bioterrorism and other outbreaks (Anderson et al., 2003). Current federal funding for emergency preparedness surveillance and epidemiology capacity is expected to stimulate widespread use of automated systems in infectious disease reporting (Anderson et al., 2003).

Furthermore, the requirement that providers and laboratories report immediately by telephone when they detect organisms indicating an outbreak or an unusual occurrence of potential public health importance is expected to continue even when automated reporting systems are implemented. Modern technology can translate into better public health preparedness by enhancing and complementing existing reporting systems (Anderson et al., 2003). Such a system could monitor the levels of known viruses in human populations, rapidly detect outbreaks, and systematically discover novel or variant human viruses.

MEDICAL CONTRIBUTIONS OF GLOBAL SURVEILLANCE

There is a possibility of linking rapid detection to rapid responses, including vaccine and therapeutic antibody development, in an attempt to abort epidemics caused by new viruses while they are in progress. In the atmosphere of an actual terrorist attack with a biological agent, the consequences of false outcomes place an enormous strain on public services, as demonstrated by the recent anthrax episodes as reported by Anderson (2003).

Medical countermeasures for emerging infection and bioterrorism emergencies

Decisions about the treatment or prophylaxis of emerging infections must take into account the effect on the patients’ health and the potential risks such as a mother's health and that of the embryo or fetus. In preparation for potential bioterrorism emergencies, the US government has stockpiled medications and vaccines, most of which are rated by FDA as one of the categories B through X, which indicates that they could pose a risk to the unborn fetus or that insufficient information exists to evaluate their potential fetal risk. Some of these products are commonly used in routine healthcare such as ciprofloxacin, gentamicin, and doxycycline, but others are reserved for emergency preparedness and response activities and for deployed military personnel such as smallpox and anthrax vaccines (Anderson et al., 2003).

Some emergency response medications and vaccines fall outside of the FDA labeling system because they are not licensed by FDA. Some are newly developed and still in pre-licensure clinical trials; others are no longer licensed and predate the classification system (Anderson et al., 2003). In an emergency setting with a high risk for life-threatening exposure to an infectious pathogen, recommendations likely will call for the use of vaccination and prophylactic medications, when they are available for pregnant women, despite unknown risks to the fetus. Other measures that can protect persons who are unable or choose not to receive vaccination or prophylactic medications include limiting exposure to persons who may be infectious, avoiding public gatherings and restricting travels to affected area.

Issues in medical countermeasures

In recent years, the public health and medical communities have faced several emerging infectious disease

outbreaks, including SARS and monkey pox, and much consideration has been given to preparation for a future influenza pandemic. In addition, experience with bioterrorism attacks (anthrax) and emergency response preparedness (smallpox vaccination) has been gained. These events required careful consideration of recommendations for the care of patients, especially pregnant women (Cono et al., 2006).

The SARS outbreak of 2003, caused by a newly identified coronavirus, affected >8,000 persons worldwide (Jamieson et al., 2006). Reports suggest that the clinical course and outcomes of SARS might be more severe for pregnant than for non pregnant women (Ng et al., 2004). Identifying appropriate treatment modalities during the SARS outbreak was challenging, due to the lack of information about the newly identified disease (Lam et al., 2004). Ribavirin was initially chosen because of its broad antiviral spectrum. Corticosteroids were used in an attempt to limit the tissue damage caused by the inflammatory response (Anderson et al., 2003). However, issues regarding the teratogenicity of these medications have been raised, further complicating decisions about their use during pregnancy. Some animal studies have suggested that ribavirin is teratogenic, but limited experience is available regarding its effects on human pregnancies. On the basis of more recent data, the efficacy of ribavirin and corticosteroids in the treatment of patients with SARS has been questioned (Anderson et al., 2003). Other medications, such as interferons, have been proposed for use in future SARS outbreaks, but use of these medications in pregnant women may also be of concern.

In June 2003, the first outbreak of monkey pox in the Western hemisphere occurred in the United States (Lai, 2005). Because of the high death rate associated with monkey pox on the African continent and lack of experience with monkey pox in the United States, CDC recommended smallpox (vaccinia) vaccination approximately 85% effective against monkeypox (Centers for Disease Control and Prevention, 2003a). The outbreak was traced to importation of infected rodents that infected pet prairie dogs and other small mammals kept as pets. Smallpox vaccination during pregnancy poses a low risk for fetal vaccinia, which can lead to preterm birth, fetal and neonatal death (Centers for Disease Control and Prevention, 2003a).

Planning for a future influenza pandemic must include specific considerations for pregnant women (Centers for Disease Control and Prevention, 2003). Because pregnancy has been shown to increase the risk for influenza-associated complications, pregnant women are considered a high-risk group and are recommended to receive influenza vaccination during interpandemic years (Wharton et al., 2003). This vaccine is inactivated and is considered safe for pregnant women. It is reformulated each year to include the anticipated viral strains of the upcoming influenza season. During a pandemic, an effective vaccine may initially be unavailable or in limited supply. In such a situation, chemoprophylaxis will be an important option for pregnant women. Unfortunately, no information is available regarding the effects on the fetus of neuraminidase inhibitors (oseltamivir and zanamvir) and the medications likely to be useful in an H5N1 pandemic (Rasmussen and Hayes, 2005). Thus, weighing the risks associated with infectious exposure in a pregnant woman and risks associated with medication exposure to her unborn child is difficult.

The anthrax attacks of 2001 prompted the first, large-scale recommendations for use of prophylactic medications in response to bioterrorism. The recommended medication for initial antimicrobial drug prophylaxis of asymptomatic exposed adults was ciprofloxacin, doxycycline and amoxicillin as alternative therapies if the strain was susceptible (Laibl and Sheffield, 2005). Because of an observed association between fluoroquinolones and joint and cartilage toxicity in juvenile animals (Harper et al., 2005), ciprofloxacin was generally not recommended during pregnancy if efficacious alternatives are available. Although, information on the safety of ciprofloxacin in pregnant women was lacking, the available limited information suggested that its use during pregnancy was unlikely to be associated with a high risk for structural birth defects. In addition, maternal exposure to tetracyclines, which include doxycyline, carries the known risks of staining the primary teeth, concern about bone growth and abnormal tooth enamel in the fetus, and rare instances of hepatic necrosis in pregnant women (Dolin, 2005).

Although, penicillins are considered safe during pregnancy, the fact that *Bacillus anthracis* strains may have penicillinase activity led to the recommendation that amoxicillin be used for prophylaxis only if the specific strain was shown to be penicillin sensitive. On the basis of these considerations, CDC recommended that ciprofloxacin be the antimicrobial drug of choice for initial prophylactic therapy of asymptomatic pregnant women exposed to *B. anthracis* during the 2001 anthrax attacks (Inglesby et al., 2002). The American College of Obstetricians and Gynecologists Committee on Obstetric practice endorsed these recommendations and emphasized that prophylaxis be limited to women exposed to a confirmed environmental contamination or a high-risk source, as determined by local public health officials (Grady, 2003).

In 2003, the United States embarked on an effort to vaccinate public health and medical bioterrorism response teams against smallpox. In the absence of circulating smallpox virus, vaccination in pregnant women or women who desire to become pregnant within 28 days of the vaccination was contraindicated because of the risk for fetal vaccinia (Billings et al., 2004). However, after an intentional attack, pregnancy should not be considered an absolute contraindication to vaccination (Billings et al., 2004). In the event of exposure or high risk

for exposure to smallpox, pregnant women are advised to receive the vaccine because the risk for death and serious illness from smallpox-particularly during pregnancy outweighs the risk for fetal vaccinia.

These examples demonstrate some of the challenges facing healthcare providers when considering prophylaxis and treatment in response to emerging infections or bioterrorism attacks. Decisions regarding appropriate prophylaxis and treatment must take into account the risks associated with specific medications or vaccines versus the risk for illness and death from a possible infectious exposure (Ng et al., 2004). Information on the effectiveness and safety of some medical countermeasures is limited for the general population, and even less information is available for pregnant women (Anderson et al., 2003).

SENTINELS OF BIOTERRORISM AGENTS

A number of biological terrorism agents have little potential for secondary spread in either animal or human populations, including *B. anthracis* and *Clostridium botulinum*. For other agents, however, evidence that their introduction into an animal population could cause an epizootic that would then place additional human populations at risk has been found. For example, studies of mosquitoes native to the United States have demonstrated their potential to spread a disease such as Rift Valley fever through livestock and other animal populations (White et al., 2002), even though person-to-person transmission does not occur. Agents such as *Coxiella burnetii* and *Brucella* spp. spread easily in animal populations through direct contact and can then pose a wider risk to humans, even though human-to-human transmission does not occur. Agents such as alphaviruses that are prevalent in wild bird populations can spread over a wide area in a short time (Gargan et al., 1988). For a numwetin ber of biological terrorism agents, there is evidence that animals could provide early warning of an acute attack. Most priority bioterrorism agents are zoonotic in origin. As a result, an attack on human populations with a bioterrorism agent would likely pose a health risk to animal populations in the target area; therefore, integrating veterinary and human public health surveillance efforts is essential. The potential use of animals as "sentinels" of a human bioterrorism attack can be differentiated from the possibility of a direct attack on animals of agricultural importance (agroterrorism) (Howard et al., 1996).

The CDC and prevention, in planning for the early detection and management of a biological terrorism attack, has recommended the "prompt diagnosis of unusual or suspicious health problems in animals," as well as establishing "criteria for investigating and evaluating suspicious clusters of human and animal disease or injury and triggers for notifying law enforcement of suspected acts of biological or chemical terrorism" (Rabinowitz et al., 2006). Similarly, an indicator of a biological terrorism attack would be "increased numbers of sick or dead animals, often of different species. Some biological warfare (BW) agents are capable of infecting/intoxicating a wide range of hosts" (Centers for Disease Control and Prevention, 2000). In part because of such recommendations, calls have been made for enhanced veterinary surveillance for outbreaks of animal disease caused by bioterrorism agents and better communication between animal health and human health professionals. For such efforts to succeed, the relevance to human health of disease events in animals must be established. The public health infrastructure must look beyond passive surveillance of acute animal disease events to build capacity for active surveillance and intervention efforts to detect and control ongoing outbreaks of disease in domestic and wild animal populations.

Animals could provide an early warning to humans if clinical signs could be detected before human illness emerged or soon enough to allow preventive measures to be initiated. This early detection could occur because an animal species had increased susceptibility to a particular agent, because the disease caused by the agent had a shorter incubation period, or because animals were exposed sooner (or at more intense and continuous levels) than the human population (Centers for Disease Control and Prevention, 2000). The simultaneous appearance of disease signs and symptoms in animals may contribute to the more rapid identification of a biological warfare agent that was produced nonspecific effects in nearby persons. If a released biological agent persists in the environment (such as soil, water, or air), active surveillance for sporadic illness in animals could help detect ongoing exposure risks. Additionally, the geographic pattern of sick or dead animals could indicate the persistence of a biological threat (Centers for Disease Control and Prevention (CDC), 2000). Animal populations such as wild birds, commercially shipped livestock, and animals involved in the local or international pet trade, could play a role in the maintenance and spread of an epidemic attributable to an intentional release of a biological agent.

STEPS IN PREPAREDNESS FOR BIOLOGICAL AGENT ATTACKS

The above findings suggest the need for certain steps related to preparedness for biological agent attacks and this include

1. Improved communication is needed between animal health and human health professionals, so that sentinel events could be rapidly detected. Such improvement would mean overcoming existing barriers to communication; a recent survey found that physicians and veterinarians communicate little about zoonotic issues (Cottrell and Morgan, 2003).
2. Also, an adequate surveillance network should be

developed to detect unusual health events in animal populations. Data on usual trends is missing for most animal species that could be potential sentinels. Whether public health resources can be committed to gathering such baseline data remains an open question.
3. Active surveillance of animal populations, including wildlife and companion animals, could fill a critical need in the aftermath of an attack involving certain bioterrorism agents by helping identify persistent sources of infection in the environment.
4. Better approaches for intervention are needed to be able to stem the propagation and amplification of an introduced biological warfare agent into a wild or domestic animal population. The US experience with West Nile virus reflects the difficulties of controlling an emerging zoonotic threat as it spreads through animal populations (Grant and Olsen, 1999).
5. There is need for additional research to fill knowledge gaps about animals as sentinels of human disease threats, including data on relative susceptibilities and exposure pathways for animal species living near human populations (Rabinowitz et al., 2006).

Concrete approaches

According to Rabinowitz (2006) concrete steps could include:

1. Establishment of surveillance veterinary clinics in strategic areas with incentives for practitioners to report unusual events.
2. Another approach would be to make greater use of electronic databases of animal diseases.
3. Common links or web-based interfaces should be developed to integrate human and animal disease surveillance information. Reporting systems for wildlife professionals and the public should be created, and their use should be encouraged to document unusual disease events and die-offs.
4. Another constructive step would be to improve the capacity of existing veterinary rapid-response teams, which exist in many states, to carry out active surveillance with animal populations as well as to improve the coordination of veterinary diagnostic laboratories.
5. Again, barriers to funding and cooperation between animal and human health agencies need to be addressed. In the past, these have hampered efforts to have a coordinated approach to the collection of animal surveillance data.
6. In addition, state-based efforts would need to be coordinated on a regional and national scale.

CONCLUSIONS AND RECOMMENDATIONS

Developing recommendations for prophylaxis and treatment of emerging and bioterrorism pathogens can be especially difficult. Data on the effects of some emergency response countermeasure treatments are limited especially on pregnant women and fetuses. Emergency response planners should include recommendations for treatment in pre-event response plans, rather than creating them during an emergency. Clinicians should become familiar with recommendations for prophylaxis and treatment of persons with emerging and bioterrorism pathogens so that they will be prepared to discuss risks and benefits of recommended treatments with their patients. Long-term goals should include evaluation of the effects of emergency response treatments, research and development of safer and effective medications when warranted.

Compared with what is known about conventional disease threats, knowledge about currently recognized emerging infectious diseases is quite limited. Soon we will likely be faced with novel pathogens about which little or nothing is known. Because the effects of emerging infections in some patients such as pregnant women might differ from those in the general population, it therefore become necessary that pregnancy must be considered a potential risk factor for disease susceptibility as well as for illness and death. Unfortunately, pregnancy issues are often not well addressed in outbreak investigations, ongoing prospective studies, or emergency preparedness planning. Future scientific inquiry and medical investigations must include pregnancy-related issues as a vital component.

The above listed steps in preparedness for biological agent attacks and bioterrorism emergencies would foster ongoing communication between community practitioners and regional public and private diagnostic laboratories (veterinary and medical inclusive) to establish baseline disease incidence trends and algorithms to identify outbreaks (Dauphin et al., 2004). The growing awareness that animal health and human health are inextricably linked, however, makes cooperation between human and animal health professionals imperative to strengthen the evidence base that will allow for rational use of animal data in public health decision-making. More so, detecting the agent in mobile animal populations could therefore signal the ongoing spread of the agent and provide an opportunity for interventions to prevent further spread. From all the issues discussed above it becomes imperative that the primary goal of public health response to emerging infections and bioterrorism attacks is to limit illness and death by providing the safest and most effective medical countermeasures in a timely manner to persons at greatest risk.

REFERENCES

Anderson NG, Gerin JL, Anderson NL (2003). Global screening for human viral pathogens. Emerging Infect. Dis. J., 9 (7): 768-773.
Bell D, Jenkins P, Hall J (2003). World Health Organization (WHO) Conference on Severe acute respiratory syndrome: where do we go from here? Emerging Infect. Dis. J., 9 (9):1091-1092.
Billings RJ, Berkowitz RJ, Watson G (2004). Teeth. Pediatrics, 113 (4): 1120-1127.

Borio L, Inglesby T, Peters CJ, Schmaljohn AL, Hughes JM, Jahrling PB, Ksiazek T, Johnson KM, Meyerhoff A, O'Toole T, Ascher MS, Bartlett J, Breman JG, Eitzen EM Jr, Hamburg M, Hauer J, Henderson DA, Johnson RT, Kwik G, Layton M, Lillibridge S, Nabel GJ, Osterholm MT, Perl TM, Russell P, Tonat K; Working Group on Civilian Biodefense. (2002). Hemorrhagic fever viruses as biological weapons: medical and public health management. J. Ame. Me. Assoc. (JAMA), 287: 2391-2405.

Brent RL (2004). Utilization of animal studies to determine the effects and human risks of environmental toxicants (drugs, chemicals, and physical agents). Pediatrics, 113*:* (4): 984-995.

Carrion Jr. R, Brasky K, Mansfield K, Johnson C, Gonzales M, Ticer A, Lukashevich I, Tardif S, Patterson J (2007). Lassa Virus Infection in Experimentally Infected Marmosets: Liver Pathology and Immunophenotypic Alterations in Target Tissues. J. Virolo., 81(12): 6482-6490

Center for Disease Control and Prevention (CDC, 2008). Prevention of Specific Infectious Diseases. CDC Health Information for International Travel 2008 available at: http://www.cdc.gov/travel/index.htm. (Accessed 20/06/2008)

Centers for Disease Control and Prevention (2001). Guidance for fiscal year 2001 supplemental funds for epidemiology and laboratory capacity for infectious diseases (ELC) cooperative agreement [ELC supplement A- NEDSSS FY2001: New activities]: National electronic disease surveillance system (NEDSS) activities. [Accessed June 20, 2008.] http://www.cdc.gov/nedss/About/NEDSS_RFA_2001.pdf

Centers for Disease Control and Prevention (CDC) (1997). Electronic reporting of laboratory data for public health. [Accessed June 12, 2008]. http://www.cdc.gov/od/hissb/docs/elr-1997.pdf

Centers for Disease Control and Prevention (CDC). (2000). Biological and chemical terrorism: strategic plan for preparedness and response. Recommendations of the CDC Strategic Planning Workgroup. *Morbidity and Mortality Weekly Report (MMWR) 49*:1–14.

Centers for Disease Control and Prevention (CDC). (2002). Electronic reporting of laboratory data for public health. 1997. (Accessed June 12, 2008). http://www.cdc.gov/od/hissb/docs/elr-1997.pdf

Centers for Disease Control and Prevention (CDC). 2004. Imported Lassa fever—New Jersey, 2004. *Morbidity and Mortality Weekly Report* (*MMWR*) *53*:894–897.

Centers for Disease Control and Prevention. (2003). Updated interim CDC guidance for use of smallpox vaccine, cidofovir, and vaccinia immune globulin (VIG) for prevention and treatment in the setting of an outbreak of monkeypox infections. http://www.cdc.gov/ncidod/monkeypox/treatmentguidelines.htm [Accessed July 13, 2008].

Centers for Disease Control and Prevention. (2003). Update: multistate outbreak of monkeypox—*Illinois, Indiana, Kansas, Missouri, Ohio, Wisconsin, Intials(2003). Morbidity and Mortality Weekly Report, (MMWR) *52*: 642-646.

Claudio Soto (2007). Prions: The New Biology of Proteins. CRC Press, Taylor and Francis Group, Boca Raton, Florida, USA, p.184.

Cono J, Cragan JD, Jamieson DJ, Rasmussen SA (2006). Prophylaxis and Treatment of Pregnant Women for Emerging Infections and Bioterrorism Emergencies. Emerging Infect. Dis. J. 12(11): 1631-1637

Cottrell TS, Morgan ER (2003). Animal surveillance in NBC defensive operations. J. Royal Army Med. Corps, 149: 225-230.

Crump JA, Luby SP, Mintz ED (2004). The global burden of typhoid fever. Bull. World Health Organ., 82(5): 346-353.

Dauphin G, Zientara S, Zeller H, Murgue B (2004). West Nile: worldwide current situation in animals and humans. Comprehensive Immunol. Microbiol. Infect. Dis., 27: 343-355.

Doering PL, Boothby LA, Cheok M (2002). Review of pregnancy labeling of prescription drugs: is the current system adequate to inform of risks? Am. J. Obstetrics and Gynecol, 187: 333-339.

Dolin R (2005). Influenza: interpandemic as well as pandemic disease. N. Engl. J. Med., *353*: 2535-2537.

Doyle TJ, Glynn KM, Groseclose SL (2002). Completeness of notifiable infectious disease reporting in the United States: an analytical literature review. Am. J. Epidemiol., 155: 866-874.

Fine A, Layton M (2001). Lessons from West Nile encephalitis outbreak in New York City, 1999: implications for bioterrorism preparedness. Clin. Infect. Dis., 32: 277-282.

Fisher-Hoch SP, Tomori O, Nasidi A, Perez-Oronoz GI, Fakile Y, Hutwagner L, McCormick JB. (1995). Review of cases of nosocomial Lassa fever in Nigeria: the high price of poor medical practice. British Med. J., 311: 857-859.

Food and Drug Administration (1979). 21 CFR 201.57 Use-in pregnancy ratingsystem.http://a257.g.akamaitech.net/7/257/2422/04nov20031500/edocket.access.gpo. gov/cfr_2001/aprqtr/21cfr201.57.htm (Accessed June 2008)

Gargan TP 2nd, Clark GG, Dohm DJ, Turell MJ, Bailey CL (1988). Vector potential of selected North American mosquito species for Rift Valley fever virus. Am. J. Trop. Med. Hygiene *38*:440–446.

Grady R (2003). Safety profile of quinolone antibiotics in the pediatric population. Pediatrics Infect. Dis. J., *22*:1128–1132.

Grant S, Olsen CW (1999). Preventing zoonotic diseases in immunocompromised persons: the role of physicians and veterinarians. Emerging Infect. Dis. J., *5*:159-163.

Harper SA, Fukuda K, Uyeki TM, Cox NJ, Bridges CB (2005). Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report (MMWR) Recommendation Report, 54: 1-40.

Henderson DA (1999). The looming threat of bioterrorism. Science, *283*: 1279-12782.

Howard JJ, Grayson MA, White DJ, Oliver J (1996). Evidence for multiple foci of eastern equine encephalitis virus (Togaviridae:Alphavirus) in central New York State. J. Med. Entomol., *33*: 421-432.

Inglesby TV, O'Toole T, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Friedlander AM, Gerberding J, Hauer J, Hughes J, McDade J, Osterholm MT, Parker G, Perl TM, Russell PK, Tonat K. (2002). Anthrax as a biological weapon, 2002: updated recommendations for management. JAMA, 287: 2236-2252.

Jamieson DJ, Theiler RN, Rasmussen SA (2006). Emerging Infections and Pregnancy. Emerging Infect. Dis. J., *12(11)*: 1638-1643

Jorgensen DM (1997). Gestational psittacosis in a Montana sheep rancher. Emerging Infect. Dis., 3: 191-194.

Lai ST (2005). Treatment of severe acute respiratory syndrome. Eur. J. Clin. Microbiol. Infect. Dis., 24: 583-591.

Laibl VR, Sheffield JS (2005). Influenza and pneumonia in pregnancy. Clin. Perinatol., 32: 727-738.

Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, Wong TY, Lai ST, Ho LC (2004). A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. Br. J. Gynecol (BJOG), 111: 771-774.

Lee TH, Montalvo L, Chrebtow V, Busch MP (2001). Quantitation of genomic DNA in plasma and serum samples: higher concentrations of genomic DNA found in serum than in plasma. Transfusion, 41: 276-282.

Lindler LE, Lebeda FJ, Korch GW (2004). Book Review on Biological Weapons Defense: Infectious Diseases and Counterbioterrorism. Humana Press, Totowa, New Jersey, pp. 597.

Lo WY, Friedman JM (2002). Teratogenicity of recently introduced medications in human pregnancy. Obstetrics and Gynecol, 100: 465-473.

Loebstein R, Lalkin A, Koren G (1997). Pharmacokinetic changes during pregnancy and their clinical relevance. *Clinical Pharmacokinetics 33*: 328–343.

Lucey DR (2006). Book Review on Biological Weapons Defense: Infectious Diseases and Counterbioterrorism. *Emerging Infectious Diseases J. 12(4)*: 713-714

M'ikanatha NM, Southwell B, Lautenbach E (2003). Automated laboratory reporting of infectious diseases in a climate of bioterrorism. *Emerging Infectious Diseases J. 9(9)*:1053-1057

McNally LM, Jeena PM, Lalloo U, Nyamande K, Gajee K, Sturm AW (2005). Probable mother to infant transmission of *Pneumocystis jiroveci* from an HIV-infected woman to her HIV-uninfected infant. AIDS, 19: 1548-1549.

Monath TP (1989). Yellow fever. Boca Raton (FL): CRC Press, pp. 139-231.

Mupapa K, Mukundu W, Bwaka MA, Kipasa M, De Roo A, Kuvula K, Kibadi K, Massamba M, Ndaberey D, Colebunders R, Muyembe-

Tamfum JJ (1999). Ebola hemorrhagic fever and pregnancy. J. Infect. Dis., 179(1): 11-12.
Ng PC, Leung CW, Chiu WK, Wong SF, Hon EK (2004). SARS in newborns and children. Biol. Neonate, 85: 293-298.
Price ME, Fisher-Hoch SP, Craven RB, McCormick JB (1988). A prospective study of maternal and fetal outcome in acute Lassa fever infection during pregnancy. Br. Med. J., 297: 584-587.
Rabinowitz P, Gordon Z, Chudnov D, Wilcox M, Odofin L, Liu A, Dein **J** (2006). Animals as sentinels of bioterrorism agents. Emerging Infect. Dis. J. 12(4): 647-652.
Rasmussen SA, Hayes EB (2005). Public health approach to emerging infections among pregnant women. Am. J. Public Health, 95: 1942-1944.
Rybak LP (1990). Deafness associated with Lassa fever. J. Am. Med. Assoc.(JAMA), 264: 2119.
Solbrig MV, McCormick JB (1991). Lassa fever: central nervous system manifestations. J. Trop. Geographical Neurol., 1: 23-30.
Stockman LJ, Lowther SA, Coy K, Saw J, Parashar UD (2004). SARS during pregnancy, United States. Emerging Infect. Dis. J., 10: 1689-1690.
Wharton M, Strikas RA, Harpaz R, Rotz LD, Schwartz B, Casey CG, PearsonML, Anderson LJ (2003). Recommendations for using smallpox vaccine in a pre-event vaccination program: supplemental recommendations of the Advisory Committee on Immunization Practices and the Healthcare Infection Control Practices Advisory Committee. Morbidity and Mortality Weekly Report (MMWR) Recommendation Report, 52: 1-16.
White SR, Henretig FM, Dukes RG (2002). Medical management of vulnerable populations and co-morbid conditions of victims of bioterrorism. Emerging Med. Clin. North Am., 20: 365-392.