Emergency pathogens as a threat for future pandemics

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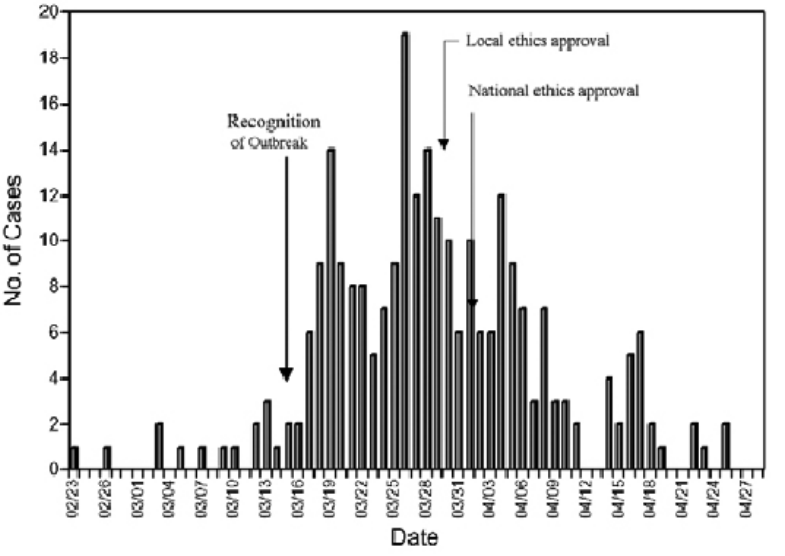
Up until the late 1990s we often spoke of the potential of new emerging diseases, the eventuality of pandemics and the threat of bioterrorism, but we had little real time experience to impress upon us the potential gravity of such events and how to best be able to prepare and respond. There was a widespread belief that we had closed the book on infectious diseases, an attitude that resulted in cutbacks on spending on public health and infection control worldwide. Since then we have experienced each of these events: each has demonstrated gaps in our systems, but has provided teachings that hopefully will make us better prepared for future events.

The fears and predictions of attacks with biological weapons, which were increasing at the close of the twentieth century, were transformed into reality not long after September 11, 2001, when several anthrax-laden letters were sent through the U.S. postal system. The attack challenged our medical preparedness and scientific understanding of the epidemiology of biothreat agents. It is fortunate that this was not a massive aerosol release that could have exposed hundreds of thousands. Rapid diagnoses and medical treatments limited casualties and increased survival rates, but tragically some individuals died of inhalational anthrax. Even as physicians tested new treatment regimes and scientists employed new ways of detecting anthrax and decontaminating the mail, new predictions were made for potentially even more devastating attacks with anthrax, smallpox, plague, tularemia, botulism, or hemorrhagic fever viruses. Fear gripped the nation. This event resulted in the development of a universal incident management system across all of government in the United States of America called the National Incident Management System. This model has enhances effectiveness in a wide range of emergencies, including natural disasters (e.g. earthquakes, floods, hurricanes, pest and disease outbreaks, and wilderness and other types of fires), nuclear and conventional events, or the accidental or deliberate introduction of a biological, chemical or radiological agent.

The cases of anthrax emphasize that in the event of serious outbreaks of infectious diseases, rapid communication of epidemiologic data to front-line medical care providers (especially emergency physicians and primary care clinicians) is essential so that they may initiate appropriate diagnostic procedures and therapies. To prevent similar deaths and cases of anthrax, more than 30,000 people received antibiotics as a consequence of possible exposure preventing an estimated 10–28 case of inhalational anthrax. The need for continual re-evaluation of conventional wisdom regarding this disease as well as other potential bioterrorist threats has been made clear from these recent experiences.

On March 12, 2003, the World Health Organization issued a global health alert stating that a new, unrecognizable, flulike disease may spread to health care workers. We now know this illness as severe acute respiratory syndrome (SARS). By August 2003, there were 8422 SARS cases and 916 deaths reported from 29 countries. SARS galvanized the world to the threat of emerging infectious diseases and provided a dress rehearsal for subsequent challenges such as H5N1 and H1N1 influenza. During SARS, thousands of patients received treatments such as ribavirin and corticosteroids. Despite this, no controlled clinical trials assessing the efficacy of these agents were conducted. In view of its broad-spectrum antiviral activity, treatment with ribavirin was initiated empirically very early after the recognition of the SARS outbreak. A large Canadian cohort of patients with suspected or probable SARS treated with ribavirin despite no evidence that it was of any benefit, nor was it ever subsequently shown that it was of any benefit. Sixty-one percent of the patients had evidence of haemolytic anaemia, and hypocalcaemia and hypomagnemia were reported in 58% and 46% of patients, respectively. A total of 28% of patients required a blood transfusion. Muller and colleagues demonstrated the difficulty in designing, getting approval and carrying out a clinical study to answer important questions regarding safety and efficacy of a form of therapy.



As a result of this failure, faced with a second global SARS outbreak, clinicians would not have controlled data on which to base therapeutic decisions. The ability to launch a trial quickly in the face of an outbreak is dependent on the speed of protocol development and the time required for obtaining ethics approval and study funding. Strategies that could be developed before the next outbreak of an unknown or novel pathogen to facilitate the rapid initiation of trials include the establishment of a collaborative multicenter research network, the creation of a contingency fund for urgent therapeutic trials, and the development of new processes for emergency expedited ethics review.

In late April 2009, Mexico became the epicenter of the first pandemic since 1968. Within a few days, the virus that was causing the epidemic in Mexico was identified in many other countries worldwide, and on June 11, 2009, the World Health Organization raised the status from epidemic to pandemic. Thus, the first influenza pandemic of the new millennium was officially declared. Since then, and through December 5, 2009, 208 countries have reported cases and over 10,000 deaths have occurred as a consequence of the pandemic. All of these events have revealed gaps in ability to respond, but have also taught us important lessons that will help us prepare for future threats. Although the rate of death was lower than initially predicted, the numbers of cases of H1N1 influenza, of hospitalizations and of years of life lost were substantial. Although the prepandemic investment may have improved our ability to respond to an outbreak, major gaps clearly remain, and the experience of this outbreak raised new questions. The majority of pandemic H1N1 influenza vaccine ordered has not, and will not, be used, leading some to worry that the whole immunization campaign was a waste of taxpayers' money. However, at least some economic analysis suggests that the pandemic vaccination program was actually cost-effective. Most of us also recognize that pandemic vaccine contracts and programs are a form of insurance — not always needed, but still a wise investment. Despite our best intentions, the vaccination program arrived too late in most countries. While Canadian vaccination rates compared favourably with those in the US (about 24%) and some European countries (both France and Germany vaccinated between 6% and 10% of their populations), they remained lower than those of other countries (e.g., Norway, which vaccinated 45% of its population, and Sweden, which vaccinated 75%). Last year's events clearly show that our current methods of vaccine production are too slow for an adequate response to a pandemic, that much of our planning for pandemic-related vaccination was incomplete, and that even the best-intentioned program can be undermined by unanticipated internal and external events. As always during

outbreaks, communication was the area that posed the greatest challenges. A report from the Harvard School of Public Health found that people who didn't get vaccinated didn't believe pandemic H1N1 influenza was dangerous and were also concerned about the safety of the vaccine. Learning how to deliver the right message to the public and how to educate ourselves about responding to "moderate risk" should be at the top of the list of gaps we need to fill before the next pandemic.

References:

- Stephens MB, Marvin B. Recognition of community-acquired anthrax: has anything changed since 2001? Mil Med. 2010 Sep;175(9):671-5.
- Rubin GJ, Dickmann P. How to reduce the impact of "low-risk patients" following a bioterrorist incident: lessons from SARS, anthrax, and pneumonic plague. Biosecur Bioterror. 2010 Mar;8(1):37-43.
- Annelli JF. The national incident management system: a multi-agency approach to emergency response in the United States of America. Rev Sci Tech. 2006 Apr;25(1):223-31.
- Atlas RM. BIOTERRORISM: From Threat to Reality. Annu. Rev. Microbiol. 2002. 56:167–85.
- Muller MP et al. Clinical Trials and Novel Pathogens: Lessons Learned from SARS. Emerging Infectious Diseases Vol. 10, No. 3, March 2004
- Low DE and McGeer A Pandemic (H1N1) 2009: assessing the response. CMAJ. 2010 Nov 23;182(17):1874-8.
- Knowles SR, Phillips EJ, Dresser L, Matukas L. Common adverse events associated with the use of ribavirin for severe acute respiratory syndrome in Canada. Clin Infect Dis. 2003 Oct 15;37(8):1139-42.