

April 15, 2005

Pandemic waiting in the wings

Terrorist attack scenarios expose nation's vulnerabilities to natural public health threats

While the thought of a terrorist attack involving the release of smallpox continues to linger in many minds, experts warn that the dreaded virus poses much less of a risk to public health than a global epidemic, or pandemic, of influenza, considered by experts to be the "single greatest acute threat the world faces."

Health-care professionals believe the world is long overdue for the next major epidemic. A likely contender could surface within the next 12 to 18 months — avian influenza, or "bird flu," which is currently spreading through much of Southeast Asia.

Prior to the September 11, 2001, terrorist attacks, a group of prominent scientists and government leaders in Washington, D.C., conducted a two-day bioterrorism exercise known as Dark Winter, which simulated a smallpox attack in the United States. The findings of this scenario revealed that U.S. preparedness to respond to such a catastrophe was woefully inadequate. Avian flu would pose a far more contagious and difficult-to-control threat. In the post-9/11 world, experts warn that — while some steps have been taken to improve this situation — much more progress is needed. Numerous tabletop exercises have continued to test the U.S. public health system in response to a bioterrorist attack or naturally occurring disease outbreak. In each case, glaring vulnerabilities have indicated a dire need to adopt a sense of urgency in upgrading the nation's ability to protect society from death and mayhem in the event of an actual act of bioterrorism or the next global pandemic: possibly in the form of avian flu.

Only a matter of time

The U.S. Centers for Disease Control and Prevention (CDC) currently views avian flu as the "most important threat we are facing right now." Avian flu occurs naturally all over the world among wild birds, which usually do not get sick from the virus. The virus is very contagious, however, and domesticated birds that come in contact with it can get quite sick and die. Humans do not usually acquire avian influenza directly from birds, but outbreaks caused by certain strains of the virus have been documented since 1997.

There are many subtypes of avian influenza type A that are differentiated by the proteins found on the surface of the type A virus — hemagglutinin

(HA) and neuraminidase (NA) proteins. There are 16 HA subtypes and 9 NA subtypes, and each combination of the two proteins is a different flu subtype. Potentially, there are 144 subtypes of avian influenza type A that could occur in birds.

Currently there are only three known subtypes of human influenza type A — H1N1, H1N2 and H3N2. H1N1 is the virus that caused the 1918 "Spanish flu" pandemic, killing more than 500,000 people in the United States and as many as 50 million worldwide. More than half of the deaths were of young, healthy adults. H1N2 is the "Asian flu" virus that killed about 70,000 people in the United States. It was first identified in China in late February 1957 and spread to the United States by June 1957. H3N2 is the virus that caused the "Hong Kong" flu of 1968-1969, which resulted in 34,000 deaths among the U.S. population.

The specific avian flu virus currently found in Asian birds, H5N1, killed 23 people in Thailand and Vietnam from December 2003 to March 2004. The virus resurfaced in poultry in several Asian countries in June 2004 and began infecting humans in December, with 74 documented cases causing 49 deaths so far, although experts believe the number of cases may have been significantly underreported. No human cases of this strain of avian flu have yet been reported in the United States.

This particular strain of avian flu has been especially hard on humans, with a fatality rate of 70 percent. However, officials believe that rate may be extreme because the only cases authorities are seeing are seriously ill patients, and there are likely other cases that have been less severe. The avian flu currently spreading throughout Southeast Asia has been deadly in all age groups, as was the 1918 flu.

In most instances, human infections are attributed to contact with infected poultry or contaminated surfaces. A 1997 outbreak of H5N1 in Hong Kong was stopped by destroying that city's entire poultry population, but not before six people died.

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Symptoms of avian flu in humans range from typical flu-like symptoms—fever, cough, sore throat and muscle aches—to conjunctivitis, or “pink eye,” pneumonia, acute respiratory distress and other severe and life-threatening complications.

So far, there are no confirmed cases of human-to-human transmission of H5N1, but given the propensity for the type A bird flu to mutate, experts warn it is likely to happen. The influenza virus reproduces rapidly, mutating into new forms as well as building resistance to drugs. Influenza's ability to mutate is what makes it impossible to eradicate. Each year's vaccine is based on a recommendation by the World Health Organization (WHO), which determines which flu viruses are likely to be most common in different parts of the world. Whether or not it will be successful against the prevailing influenza is a gamble, but usually the vaccine is effective.

The CDC recently began a series of experiments in an effort to assess the likelihood of a pandemic virus mutating from the H5N1 strain. The rapidly mutating nature of H5N1, plus lessons learned from the previous three pandemics cause health officials and scientists grave concern about the virus. Both the Asian flu and Hong Kong flu viruses were found to contain a combination of genes from a human flu virus and an avian flu virus. This occurs when a virus “reassorts,” – two flu viruses infect the same cell in a human or in some intermediary organism. An avian flu virus and human flu virus can combine, or reassort, into a new, more lethal virus that can be transmitted directly from human to human.

The increased mobility of the population due to World War I contributed to the spread of the 1918 influenza, just as the ease of international travel facilitated the 2003 spread of severe acute respiratory syndrome (SARS). When SARS first appeared, it spread from China to Canada and around the world within a matter of weeks, infecting more than 8,000 people and killing 774

of them in 27 countries before it was finally contained. SARS also originated in a non-human host and mutated until it was able to spread by human-to-human contact. Should avian flu mutate into a virus with human-to-human transmission, no national borders will contain the spread of the disease.

Evidence now suggests that the H5N1 virus has found a permanent haven among the poultry population in parts of Asia. Health experts facing a recurrence of avian flu fear that measures introduced during last year's outbreak, such as disinfection and vaccines, will no longer control the disease. Studies that compare the virus over time show that it is becoming more pathogenic among poultry and survives for longer periods in the environment. Scientists say that it is only a matter of time until H5N1 evolves to the point that it can be transmitted directly from one person to another.

Are we ready?

Whether the result of terrorism or caused by Mother Nature, a public health crisis can create the same spiral of chaos. By affecting the masses, a pandemic could cripple essential services such as police and fire protection, utilities and communications services. While the vast majority of SARS cases occurred in China, the outbreak produced worldwide economic losses of an estimated \$30 billion. Yet most businesses fail to consider the potential cost of an avian flu pandemic, both in terms of employee absenteeism and disruptions to the global economy.

In a report listing possible terrorist strikes perceived by the U.S. Department of Homeland Security to be the most plausible and devastating, one scenario described the potential release of pneumonic plague into an airport, sports arena or train station. The report included estimated casualties and economic damage resulting from such an attack, recommending that federal, state and local governments prepare a plan of response. While avian flu poses a more likely threat from natural causes, the similarities in the

results demonstrate the need for heightened concern and attention to preparing for the next flu pandemic.

Many experts are encouraged by the fact that researchers are already working on an avian flu vaccine and closely monitoring the situation, thereby improving the world's chances of containing a mutated strain of the virus. If a new virus strikes soon, however, defensive measures such as an experimental vaccine would not yet be ready.

After the 1997 and 2003 avian flu outbreaks in Hong Kong, doctors affiliated with the WHO's influenza network began work on a vaccine. When the virus resurfaced in a new form in January 2004, laboratories determined that the virus had mutated. Because of this, work that had been underway to produce a vaccine against an H5N1-like pandemic virus had to start over. The National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, recently began recruitment of healthy adults for a study to test the safety and effectiveness of a trial vaccine against H5N1.

When one of only two manufacturers for the U.S. flu vaccine supply was shut down last year due to contamination, it obliterated half the nation's stockpile and created chaos in state and local influenza immunization programs. Under present circumstances, experts predict that even in the event of a human influenza pandemic for which a vaccine already exists, it would take at least six months from the start of a pandemic to distribute vaccine to the public.

In the absence of a vaccine for avian flu, the antiviral drug oseltamivir, (Tamiflu®), has shown promise in preventing and treating avian flu in humans. The Infectious Diseases Society of America recommends that the United States stockpile enough of the drug to treat 50 percent of the population, or about 150 million doses. Current U.S. supplies contain only 2 million doses. Faced with a lethal contagion such as

avian flu, the lack of adequate medical supplies could lead to panic, with people fleeing infected areas and attempting to cross into states with available medication.

An avian flu outbreak would stretch the public health systems of all countries to their limits. Because there is a massive global shortage of health-care workers, no country has the hospital capacity or resources to adequately respond to an epidemic. The influx of patients during a normal flu season strains many U.S. emergency rooms; a pandemic could send up to 10 million people to hospitals nationwide. Victims would exceed hospital capacity, requiring schools, armories and other public facilities to be turned into ad hoc hospitals. The lack of hospital beds and health-care workers would only accelerate the spread of the virus.

Much like the "Dark Winter" exercise in 2001, this month's "Topoff 3" drill in Connecticut and New Jersey raised questions regarding America's readiness for a biological attack. In January 2005, "Atlantic Storm" in Washington, D.C., simulated the release of smallpox by terrorists in Europe and the United States. That scenario predicted riots on the border between two European countries, one of which closed its borders to protect its supply of smallpox vaccine.

Experts say that there would be similar problems if H5N1 becomes transmittable between humans. Ninety percent of the world's population lives in countries that have no vaccine production. Therefore, a handful of countries would control the delivery of lifesaving products to millions, which could create foreign policy problems with lasting repercussions. As in the tabletop exercises, borders would close, segments of the population would be quarantined and the economic impact would be catastrophic. Already, President George W. Bush has added pandemic influenza to the list of communicable diseases for which passengers arriving via U.S. international flights may be quarantined.

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What can be done?

According to the Food and Agriculture Organization of the United Nations, avian flu is now considered endemic in Southeast Asia. Rather than discussing how to eradicate the disease, the focus has shifted to containing it before a mutation sparks a pandemic. While the disease has not yet spread worldwide, precautionary measures should be implemented now, before a health emergency develops.

Fortunately, the same steps that can improve detection and treatment of emerging epidemics could also mitigate the effects of a biological attack. Corporate leaders should support and actively call for a greater focus on strengthening the U.S. public health system. Improved communication systems are needed to effectively monitor and update national and local health-care professionals regarding epidemiological changes. Sharing such information can help to identify and respond to potential pandemics or bioterrorist attacks more quickly, a critical component to controlling the situation and minimizing the impact.

In Oregon, state officials, the Oregon Department of Agriculture and the Department of Human Services developed plans for disposing of infected poultry, using protective gear to prevent poultry workers from contracting the virus and distributing antiviral drugs in the most effective manner. Businesses should also play a role in prevention efforts and response planning.

Coordination among public and private sectors can raise awareness of avian flu developments and enhance communication, which would be vital in a global health crisis. Companies should establish relationships with emergency response agencies and develop local response plans, which could benefit the community in a flu pandemic, terrorist attack or natural disaster. Facilities' physical security programs should also be considered during the planning, since effective access control could help to prevent unauthorized individuals

from spreading disease intentionally or releasing biological agents of terror.

Employers with interests abroad should carefully consider non-essential travel to areas affected by the H5N1 outbreaks (Cambodia, China, Indonesia, Malaysia, Thailand and Vietnam). Individuals traveling to Asia within the next nine months should consult their physicians about possibly getting a prescription for a supply of Tamiflu® to take with them. In such cases, the individual should take care to learn warning signs of the flu and know when and how to properly take medication. Travelers to countries with avian flu cases should avoid eating any food from poultry or visiting areas with live poultry, such as markets and farms.

At the individual level, people need to practice basic good hygiene, such as handwashing, as well as taking advantage of available flu vaccinations. Being vaccinated against human influenza could reduce the possibility of becoming infected with avian and human flu strains simultaneously, which could produce a form of avian flu that could be transmitted from person to person.

The threat is undeniable: Whether from terrorists launching a successful biological attack or from a naturally occurring influenza pandemic, future public health crises are inevitable. The far-reaching scope of such events could have unimaginable consequences for global trade and economies. The public and the business community must demand and support measures to strengthen the U.S. public health system — at both the state and local levels — before an avian flu pandemic ravages the world.



The Lipman Report Editors