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FESS Issue Brief

September 2005

ENVIRONMENTAL FACTORS AFFECTING THE SPREAD OF BIRD FLU

Josh Rothstein
Foundation for Environmental Security and Sustainability

Key Points

For nearly two years, conditions in Asia have set the stage for a global avian influenza pandemic. Developed countries are strengthening their own defenses by rehearsing scenarios, stockpiling drugs and vaccines, and improving public health systems. However, many nations, including those home to avian influenza or threatened by its immediate spread, are far behind in preparedness measures. The mobility of today's global economy and society makes prevention of avian influenza in every country an international concern.

Addressing environmental links to the spread of avian influenza may provide essential information to delay, minimize, or even prevent a costly pandemic. Possible environmental links that should be addressed include:

◊ Deforestation and other methods of habitat destruction affecting the routes of migratory birds.

◊ Farming environments that facilitate the spread of bird flu to other animals or humans.

◊ The human utilization of water sources that contact infected birds or animals.

◊ Market environments that facilitate the spread of avian influenza to other animals and humans.

International cooperation in addressing these issues is essential. Once a pandemic begins, nations likely will devote their resources to the protection of their own population. It is, therefore, necessary to commence immediately international programs identifying environmental links contributing to the spread of avian influenza and developing effective and appropriate countermeasures.

Addressing the Threat

Avian influenza (bird flu) has the potential to cause a healthcare crisis of unprecedented global dimensions. Many predict a global pandemic far worse than the 1918 Spanish Flu, which killed 40 million to 50 million people. A larger, denser global population, coupled with modern transportation systems of both goods and people, could result in a pandemic killing far more people worldwide. The consequences of such a pandemic would stretch beyond just public health. International relations, commerce, politics, travel, medicine, and economic and social infrastructures would be affected due to widespread infection and worldwide mitigation efforts.

The world is dangerously unprepared for such a pandemic. A recently developed vaccine shows promise in providing immunity to the disease, but further planning for mass production and distribution is necessary. The virus has also shown susceptibility to the anti-viral treatments, Oseltamivir (Tamiflu) and Zanamivir (Relenza); however, exact dosages and efficacy remain unclear. The current lack of international healthcare strategies, planning, and cooperation will pose a problem as well. Even if developed countries, such as the United States, prevent the disease from spreading within its borders, they will likely be affected by the collapse in the global economy resulting from the millions of infected people worldwide. In the developing world, where the capacity to respond will be significantly less, the results could be catastrophic.

Recently, knowledge of the potential devastation caused by widespread infection has caused the issue to become a significant political and economic concern in the United States and internationally. Advances such as the establishment of antiviral therapy stockpiles, vaccine production, bird surveillance programs, and poultry import bans are encouraging signs that the world is heading in the right direction. However, to fully address and prevent the possibility of a pandemic, the root causes of the spread of the disease must be explored. Research regarding the links between environment and the disease may assist in the prevention and mitigation of a potentially catastrophic pandemic.

The Virus and its Spread

Influenza viruses are divided into three categories—A, B, and C. Influenza A strains are of the highest concern as they can cause large epidemics and pandem-

Note: The author would like to express his gratitude to Dr. Daniel Lucey of the Georgetown University School of Medicine for his comments on an earlier draft of this *Issue Brief*.

ics; type B influenza usually causes less severe outbreaks; and type C is known to cause only mild symptoms in people. Influenza A can infect a wide range of animals, including humans, birds, pigs, seals, and whales.

Influenza A viruses are further divided into subtypes based on the surface proteins hemagglutinin (HA) and neuraminidase (NA). There are 16 variations of hemagglutinin and nine variations of neuraminidase, combining to form the numerous subtypes of the virus. Many of these subtypes infect only a certain species. Only a few subtypes, H1N1, H1N2, and H1N3 currently occur widely in humans. Out of the avian subtypes, H5N1 is the one of the most virulent. It has killed large numbers of poultry, tigers, leopards, and more humans than any other avian strain.

Waterfowl, especially ducks, are the reservoir host for bird flu viruses. Many of these species remain virtually unaffected by the disease, and may carry the virus extremely long distances along their migratory routes. Infected birds spread the disease through their saliva, nasal secretions, and feces. Vulnerability to the disease is varied throughout bird species, with domestic birds generally having the highest level. The disease can be spread between wild and domestic birds in the migratory birds' search for food, water, and shelter. Migratory birds are believed to have played a part in the spread of the disease throughout Asia, and to have the capability to spread it throughout the world.

There are two types of avian influenza, low pathogenic (LPAI), and highly pathogenic (HPAI). HPAI is usually characterized by a high rate of spread and mortality in poultry. Many times, wild birds may pass the low pathogenic phenotype of avian influenza to domestic poultry. LPAI may then mutate to the highly pathogenic phenotype within the domestic bird population. Domestic ducks and other waterfowl have been found to be asymptomatic to the 2004 H5N1 strain, yet can shed the virus for at least 11 days. Highly pathogenic H5N1 has a mortality rate in domestic poultry approaching 100 percent. Aside from transmission via migratory birds, the disease may be spread inadvertently among farms through the transport of infected poultry or contaminated materials.

Influenza viruses are constantly undergoing a process called antigenic *drift*. This process leads to virus mutation and the emergence of new strains. Existing antibodies may not protect against new flu strains resulting from this process. Viruses also may undergo a process known as antigenic *shift*. This occurs when two viruses mix or reassort genetic material within a host. Antigenic shift may result in a completely new flu strain, to which humans have no prior immunity.

Currently, sustained person to person transmission of H5N1 has not occurred. However, if the avian H5N1 strain were to mix with a human strain inside a host, it could gain the dangerous ability to sustain person to person spread. Pigs serve as viable hosts for this reassortment as a result of their susceptibility to both avian and human flu viruses. They also often live in close proximity to both bird and human populations on farms. In fact, pigs are usually a necessary intermediary for avian flu viruses to be able to infect humans. However, in 1997, H5N1 became the first avian flu virus to gain the ability to infect humans directly from birds. Humans have little pre-existing immunity to H5 flu viruses, as they have never circulated among people. Consequently, H5N1 with the ability to sustain efficient person-to-person spread could result in a pandemic with high rates of morbidity and mortality.

From January 2004 through August 2005, at least 61 human deaths occurred in Asia as a result of bird flu. Hundreds of millions of birds in Asia have died as a result of culling or the disease itself. Until recently, the disease was primarily restricted to the southeastern parts of Asia, but, in the summer of 2005,

As a result of the virus's known association with both migratory and domestic bird populations, it is likely that environmental factors do and will play a significant role in the spread of the disease.

H5N1 spread to birds in Kazakhstan, Mongolia, and Russia. On August 16, 2005, H5N1 birds were confirmed as far west as Chelyabinsk in the Ural mountains. Russia has warned of the possibility of the disease continuing to spread westward and throughout the world.

It is possible that these birds will carry the virus to Europe, Africa, and the Middle East as they begin to migrate to warmer climates. As the disease becomes more widespread, its chances of reassorting within a host (genetic shift) or mutating over time (genetic drift) to gain the ability to spread from person to person are increasing.

Additional information is required regarding the actual mechanism of spread thus far. It is plausible that the main sources of spread have not been migratory birds, but solely the transportation of domestic poultry, illicit smuggling of poultry for "cock fighting," and the movement of people and farming equipment. Although migratory birds have not been confirmed to be responsible for the spread of the disease so far, it is likely that they have played at least some part. More importantly, they have the ability to contribute immensely to the spread of the disease in the future.

As a result of the virus's known association with both migratory and domestic bird populations, it is likely that environmental factors do and will play a significant role in the spread of the disease. Effects on habitats through urbanization and deforestation may cause alternate migratory routes, resulting in increased contact between wild and domestic birds. Certain farming and market practices, especially in Asia, cause unnecessary contact between birds, pigs, and humans, increasing the chances of a dangerous reassortment taking place. Lastly, the proximity of and contact between farms and human populations or a water source can facilitate the spread of the disease from birds to humans, thus providing more opportunities for the virus to gain the ability to spread from person to person.

A Growing Population and a Growing Threat

Asia provides a great variety of water bird habitats including rivers, tundra, estuaries, lakes, marshes, coastal marshes, beaches, mudflats, atolls, mangroves, and coral reefs. According to Wetlands International, the largest threat to the long-term conservation of water birds in Asia is changes in habitat due to human land utilization practices.

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Drainage of wetlands and land claiming takes place in most countries throughout the continent, especially in coastal temperate and tropical regions with high levels of urbanization. An increase in human activities throughout the continent, especially in agriculture, has resulted in a large decrease in the natural wetland and forest habitats of migratory birds.

Deforestation and urbanization may contribute to the spread of bird flu in multiple ways. Increased urbanization in previously undeveloped areas will increase contact between wild birds and humans. As a result, bird-to-human transmitted avian influenza cases may increase. As urbanization increases, contact between humans and animal vectors of diseases increases, and zoonotic diseases have more opportunity to infect humans. The destruction of forests in new regions has been linked to numerous previous disease epidemics. Many tick-borne zoonoses are transmitted to people through deforestation and urbanization, along with diseases such as plague and malaria, vectored by fleas and Anopheles mosquitoes, respectively.

Deforestation and urbanization may play a larger role in the spread of bird flu through habitat destruction. Migratory birds usually are extremely loyal to their annual migratory destinations, as well as their "stopover" points en route. These stopover points are used to replenish fat storages, and are vital to a bird's survival along its journey. As forests and wetlands are destroyed, the stopover points are destroyed as well. The birds are forced to look for other places to rest and refuel. Farms and cities are often the alternative, as they can provide shelter and food.

The utilization of farms as stopover points for migratory birds increases the contact between wild and domestic birds, allowing more opportunity for the disease to infect poultry and other domestic bird populations. Furthermore, the increase in human or pig exposure to the virus allows more opportunity for the

disease to mix with a human flu virus within the host.

Asia is expected to have the highest rate of urbanization in the world over the next 25 years. According to the Urban Land Institute, the urban population of Asia is expected to nearly double from its 2000 numbers to 2.7 billion people in 2030. The need for expanded housing and farmland in Asia is causing high rates of deforestation. The increase in farmland not only destroys the usual stopover points for birds, but also produces alternative stopping points that provide an environment that facilitates interaction between wild and domestic birds. Russia is experiencing high rates of deforestation east and west of the Ural Mountains. This may contribute to the subsequent spread of avian influenza over the Ural Mountains and into Europe. The same trends in deforestation are occurring elsewhere, and eventually may contribute to the global spread of the disease.

Urbanization may more directly affect the spread of bird flu by simply providing more densely populated areas. The virus's ability to spread through respiratory droplets will allow it to spread rapidly throughout densely populated urban areas.

Improved documentation of migratory bird routes in Asia would provide essential knowledge for the establishment of bird and human surveillance programs in potentially vulnerable urban areas. This also would provide information as to where to screen forests or wetlands for infected birds prior to clearing the land for farms or housing. Deforestation and urbanization in areas found to be in proximity to migration paths of avian influenza-carrying birds should be minimized when possible.

Mixing Bowls on Farms

Many farms in Asia rival the large-scale poultry establishments in the United States, but lack the hygenic standards present in the West. Extremely large numbers of chickens live in tight quarters, sharing food and space. These farms provide a nearly perfect environment for avian influenza to spread throughout the entire chicken population. The virus may be subsequently spread to other farms on tractors, shoes, cages, and clothing.

Pigs are susceptible to both avian influenza and human influenza strains, making them a possible host for viral reassortment should they become infected with the two strains simultaneously. Many Asian farms keep pigs and poultry relatively close to each other. This practice greatly increases the chances of a pig acting as a "mixing bowl" for H5N1 and a human virus. The feces or saliva of an infected bird also may be carried unknowingly to a pig on farming equipment or materials.

Farming environments that allow for close interaction among humans, pigs, ducks, and birds pose a large threat for the spread of the disease. Segregation of these animals is vital in minimizing the possibility of spread. Additionally, wild bird-proof chicken houses, decontamination of all incoming people and equipment, and the proper sterilization of farmers' hands, clothes, and equipment after working with birds would greatly assist in the prevention of bird flu. However, the implementation of these safe farming environments and practices is extremely difficult. There are innumerable farms throughout Asia, many of which are small-scale or backyard farms with limited money and space available. As a result of their lack of money, size, and previous outbreak control experience, sanitary farming environment measures are difficult to install on these farms.

In July 2005, an international conference sponsored by the World Organization for Animal Health, The World Health Organization, and the Food and Agriculture Organization in Kuala Lumpur discussed strategies of avian influenza prevention. Emphasis was placed on the education of these small-scale farmers, and compensating them for reporting outbreaks. As suggested in the conference, the cost of implementing such programs may exceed the financial capacity of certain countries; therefore, international assistance likely will be necessary. The United States Agency for International Development (USAID) has launched campaigns to help educate the public in affected Southeast Asian countries and minimize disease transmission from wild to domestic birds on farms. These measures need to be continued on small and large scale farms and surrounding populations throughout the world, as farming environments may play a large role in the transmission of avian influenza to humans.

Survival and Spread in Water

Avian influenza also may be spread to birds and humans through contaminated water. Migratory ducks can shed the virus into lakes, ponds, or other bodies of water that are used as drinking or bathing water for the surrounding community. According to Poultry Health Services the virus can survive water at 22 degrees Celsius for 4 days, and at 0 degrees Celsius for 30 days.

People also may unknowingly spread the virus to a common water source after coming into contact with an infected bird or surface.

This possibility is increased if the water source is in close proximity to a farm. Similarly, animals or birds may transport the virus on their fur or feathers to a body of water if they have recently come into contact with an infected animal or contaminated surface on a farm or other location.

Currently, no documented human cases of avian influenza have occurred through contact with a water source. However, the possibility certainly exists. Populations using a water source frequented by birds or animals or in close proximity to a farm are in danger of getting infected. Increased surveillance and education campaigns in these areas would help in preventing future human cases.

Market Hot Zones

Open live animal markets (wet markets) in Asia are known for spreading zoonotic diseases to people. Customers inspect live animals and have them killed on the spot to ensure freshness. Many people, particularly in China and Southeast Asia, believe that eating fresh, wild animals will promote vitality and health. These animals are often transported long distances from their natural habitats, bringing with them microorganisms endemic to their regions. Unsanitary, crowded conditions in these markets provide an ideal environment for these microorganisms to infect new species, including humans. SARS, for example, is believed to have jumped to humans from civet cats sold in open markets.

Often, birds and animals are caged on top of each other, providing an easy environment for avian influenza to infect animals. This, coupled with close human contact, allows for increased probability of a human and avian strain simultaneously infecting a host animal. Similarly, these markets provide environments that make it easy for humans to become infected with avian flu through contact with an infected bird or animal, again increasing the probability of simultaneous infection and the emergence of a new strain.

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As a result of the dangers posed by wet markets, many groups and scientists have suggested the permanent closing of these open markets. However, closing these markets may cause more problems than it would solve. Closing down wet markets would put thousands of people out of work, many of whom would resort to selling these live birds and animals on the black market. This would make regulation of these sales even more difficult. Additionally, closing down markets is extremely unrealistic given low enforcement capacity and popular dissent among citizens.

As opposed to shutting down the markets, education campaigns for wet market employees, customers, and hunters focused on hygenic standards and sanitation should be continued and improved. Currently, education and sanitation campaigns have been implemented throughout Asia, and are showing signs of success. Supermarkets are gaining prominence, and younger consumers are buying frozen packaged meat as a result of the disease potential in live markets.

The Kuala Lumpur conference also issued a list of suggestions for preventing the spread of bird flu in wet markets. These suggestions include constant monitoring for dead or sick birds, centralized location of waterfowl slaughtering, separate storage of different species of live and slaughtered birds, and mandatory rest days for the premises to be inspected and cleaned.

It is essential for a similar trend to continue worldwide as the threat of the disease increases. Governments should have plans to shut down wet markets if the disease becomes widespread. In 1997, Hong Kong quickly banned quails, aquatic birds, ducks, and geese from its markets, and the Guangdong province in China was able to decrease the number of live civet cats sold in animal markets during the SARS crisis in 2003. Countries must continue to coordinate plans to control wet markets immediately in an emergency outbreak situation

Flyways to the Middle East

The major migratory flyways in Asia encompass Siberia, the Caspian Sea, the Arabian Gulf, the former Soviet republics, and extend to Alaska, Australia, and the island countries of the Pacific. In addition to spreading west of the Ural Mountains, it appears likely that

migratory birds will carry avian influenza through Central Asia to the Caspian Sea area from its current position in the Ural Mountains. There are extensive wetlands in the surrounding Caspian states, such as the Volga deltas, the Ural and the Kura rivers, and the Kara Bogaz Gol.

These areas should be monitored closely, especially now that many of these states are beginning to discover and tap oil reserves throughout their respective countries. If this new oil exploration is not properly managed, it may inflict damage on the wetlands of the area. This damage may cause alternate migratory routes, resulting in increased stopover points on proximate farms and towns.

Worldwide Collaboration

Individual nations should begin to prepare for pandemic situations specific to their own country, such as quarantine procedures, rotation of military personnel, priorities in vaccination and medication distribution, and the maintenance of productive capability in the face of widespread disease. However, the most effective approach to defeating a pandemic will entail global cooperation and oversight.

Diseases do not respect international borders. This is especially true now, with modern transportation allowing disease translocation throughout the world literally overnight. Nations must accept this reality, and begin to strategize accordingly. In the event of rapid global spread, cooperation among countries will prove essential. Even if a few countries are somehow able to prevent the spread of the disease within their borders, they still will be affected by global economic and political spin-off effects. It is, therefore, in every nation's best interest to work in coordination with an international governing body to oversee research, surveillance, the production of medicine, and public communication. Further collaboration will be needed to establish quarantines, culling campaigns, border closings, and other mandatory disease control measures.

The World Health Organization may be a good choice for the international oversight of avian influenza preparedness and response. The WHO serves as the main international body overseeing health, and would be effective in coordinating global efforts. The U.S. CDC, and similar agencies of other countries, whose primary mission is to protect the health of their country's own citizens, should continue to work closely with the WHO.

The WHO currently conducts worldwide surveillance of the flu, arbitrates international disputes revolving around diseases, oversees laboratories, and acts as a global voice to refute or confirm rumors. Additionally, the WHO works closely with the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE). Through these networks, a necessary and effective multidisciplinary approach toward diseases is established. This cooperation will prove extremely beneficial during any global pandemic, including avian influenza. However, in order for the WHO to be truly effective in preventing and responding to such a global pandemic, its abilities need to be strengthened through international investments of both money and trust.

The WHO, FAO, and OIE already have taken steps in addressing some environmental issues. However, further research into environmentally altered migratory bird routes, increased bird and disease surveillance in areas of urbanization, and public education campaigns in highly threatened areas is required. In addition to the WHO, individual countries should be encouraged to initiate and continue their own research and development in environmental and other contributors to bird flu. Collaboration among multiple countries with the financial and research capabilities to perform multidisciplinary research would expedite the addition of vital information to prevention planning.

> Enacting countermeasures to address environmental issues that facilitate and contribute to the spread of bird flu is essential to stopping the disease at its source.

An Opportunity for the United States

The Bush administration has invested large mounts of money in bioterrorism and epidemic prevention and response. Recently, the United States has come to recognize

the threat of avian influenza as a top priority in this field. Since fiscal year 2001, the funding for the CDC and National Institutes of Health (NIH) flu programs was increased by 242 percent and 320 percent, respectively. The United States has stockpiled 2.3 million doses of Tamiflu with plans to reach eventually 20 million doses, and Congress has appropriated $3.7 billion to improve the domestic public health infrastructure in preparation for bird flu or another outbreak. On September 15, 2005, U.S. Health and Human Services (HHS) announced a $100 million contract to Sanofi-Pasteur to make H5N1 vaccine and awarded a $2.8 million contract to GlaxoSmithKline for 84,300 treatment courses of Zanamivir. On a local level, USAID is addressing the disease by strengthening the capacity of local and regional organizations to prevent and respond to a crisis, and is allocating personal protective equipment to highly threatened countries. USAID also set aside money for the WHO to improve global coordination and surveillance systems.

U.S. agencies such as the USDA, CDC, and NIH currently conduct research on vaccine and medication production, surveillance, epidemiology, and pathogenesis of avian influenza. The United States and other countries developing similar prevention and response methods may benefit greatly by further utilizing their resources to explore environmental and other issues relating to the initial spread of the disease. Many American wildlife and conservation organizations study migratory patterns and environmental issues, but limit their research to North American birds. An increase in the understanding of how deforestation, urbanization, and other environmental issues have affected stopover points in Asia has the potential to assist greatly in the development of future international policy and actions to limit further spread. Similarly, aid in the forms of money and expertise to help in the establishment of safe farming and marketing practices can help prevent the unnecessary spread of flu epidemics.

Enacting countermeasures to address environmental issues that facilitate and contribute to the spread of bird flu is essential to stopping the disease at its source. In a speech at the United Nations on September 14, 2005, President Bush announced an international partnership that requires countries that face an outbreak to immediately share information and provide samples to the World Health Organization. On September 16, 2005 HHS Secretary Mike Leavitt announced plans to lead a delegation to Southeast Asia to meet with health officials and heads of state. The United States is taking a leadership role in developing such a partnership, and may find it beneficial to continue its leadership on this issue by devoting public health funds and expertise to further develop international environmental programs linked to research on the potential origins and effects of a bird flu pandemic.■

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Foundation For Environmental Security and Sustainability
8110 Gatehouse Rd, Suite 625W
Falls Church, VA 22042
703.560.8290

www.fess-global.org

Darci Glass-Royal, Co-Executive Director
Ray Simmons, Co-Executive Director
Jeffrey Stark, Director of Research and Studies

This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID). The contents are the responsibility of the Foundation for Environmental Security and Sustainability and do not necessarily reflect the views of USAID or the United States Government.