The H5N1 Virus: Global Health Implications and a Need for Chinese Preparedness

In three decades of economic development since adopting economic reforms, the costs and benefits of China's emergence as a global market become increasingly evident. The wealth generated by the economic interdependence that characterizes growing trade relations in East Asia, and around the world, has allowed for greater mobility and frequency in physical transactions across borders. This fluidity as allowed by economic transformation, however, has exacerbated the transmission of disease as well. Fast-mutating and fast-traveling pathogenic illnesses such as the H5N1, or bird flu, virus offer particularly difficult global health concerns. Outbreaks of this highly pathogenic avian influenza virus were reported nearly simultaneously in eight Asian countries neighboring China between December 2003 and January 2004, with a ninth reporting in August 2004, implying that the viruses spread quickly and recently (Sims et al, 2005). China, as a hub for trade and interaction, is strategically located as one of the most effective exporters of the disease. In looking at the historical and environmental attributes of the H5N1 virus, the mechanisms that have facilitated its spread across the world, and the measures needed to combat the possibility of a pandemic outbreak, it becomes clear that China is and will continue to be a necessary player in vaccine administration and containment measures.

Profiling the H5N1 Virus

Influenza-A virus subtype H5N1, also known as A(H5N1) or simply H5N1, is a subtype of the Influenza A virus that can cause illness in humans and many other animal species (WOAH, 2005). According to the International Committee on Taxonomy of Viruses, a bird-adapted strain of H5N1, called HPAI A (H5N1) for "highly pathogenic avian influenza virus of type A of subtype H5N1," is the causative agent of H5N1 flu, commonly known as avian influenza or the bird flu (ICTVdB, 2002). It is endemic in many bird populations, especially in Southeast Asia. One strain of HPAI A(H5N1) is spreading globally after first appearing in Asia. It is epizootic, an epidemic in nonhumans, and panzootic, affecting animals of many species over a wide area, killing tens of millions of birds. Most mentions of "bird flu" and H5N1 in the media refer to this strain (Kou, 2005).

The H5N1 virus occurs naturally among birds in the same manner influenza occurs among humans during cold season (Ungchusak, 2005). Wild birds from around the world can carry the viruses in their intestines, but usually do not get sick from them. H5N1 viruses are very contagious among birds, however, and can make some domesticated birds very ill, killing them. Infected birds transmit the influenza virus through their saliva, nasal secretions and feces (Monto, 2005). Susceptible birds become infected when they have direct contact with contaminated secretions or excretions, or through indirect contact such as with surfaces that are contaminated by infected birds. For example, domesticated birds may become infected with avian influenza virus through contact with infected waterfowl or other infected poultry. Free-ranging birds, in particular, are susceptible to this manner of transmission (Institute of Medicine, 2004). Domestic birds can also be infected if they come into contact with surfaces, objects or materials—such as cages, and even dirt or feed—that have been contaminated with the virus.

Infection with the avian influenza viruses in domestic poultry can cause two primary forms of disease that are classified by low and high extremes of virulence: the “low-pathogenic” and “high pathogenic” forms. The low-pathogenic type may often go undetected and usually just causes mild symptoms, such as ruffled feathers and decreased egg production (Sodhi and Sharp, 140). However, the high-pathogenic type spreads much more rapidly through flocks of poultry, affecting numerous internal organs and having a mortality rate that can reach up to 90-100%

within just 48 hours (ibid). The most susceptible to fowl to human infections are those who have frequent and direct contact with poultry, such as farmers. Scientists have found, however, that two mutations are necessary for the virus to infect humans, enabling the pathogens to bind to human proteins which are significantly different from bird proteins (Kou, 2005). To investigate how the virus might do this, the researchers looked at samples of H5N1 that had been taken from birds and also from infected humans.

Spreading H5N1: from Birds to Birds and to Humans

China's southern Guangdong Province has been identified as the source of the H5N1 virus, according to a genetic analysis of the virus (Wallace et al, 2007). Eventually, it spread to domestic ducks by 2000 which played a key role in the 2003 and 2004 outbreaks (Sims et al, 2005). The secretion of the viruses by domestic ducks increased by early 2004, and there is some evidence that they can also be transmitted by wild birds. The migratory birds from which viruses have been isolated were usually sick or dead, however, suggesting that they would have had limited potential for carrying the viruses over long distances unless sub-clinical infections were prevalent (Sodhi and Sharp, 141). Only low pathogenic viruses were isolated from fecal matter of migratory birds as tested in the Mai Po Marshes of Guangdong in November 2004 (Chen et al, 2006). As wild birds may not be the primary hosts, most scientists look to domestic poultry as the primary hosts spreading the virus.

That the virus exists in birds naturally but has not caused significant damage until lately is rather perplexing. Some possible explanations include limited virus secretion by domestic waterfowl infected with the H5N1 virus more recently, the confusion of avian influenza with other serious diseases, unsanctioned use of vaccines, and limited surveillance that results in under-reporting of disease (Sims et al, 2005). In fact, a decision by China's poultry producers to vaccinate birds after an outbreak in Hong Kong in 1997 may have been a mistake and could have contributed to the problem (ChinaDaily, 2004). Studies suggest that vaccination may have facilitated the selection of the Fujian-like sub-lineage (Roos, 2006). Although this sub-lineage is not more virulent or mobile, the mutations need to be contained and limited if an effective vaccine is to be developed. Incomplete administration of a full round of the vaccine can result in vaccine resistance in which the virus survives the abbreviated treatment and these resistant stains can then go on to infect more organisms. The race to find more effective drug treatments is exacerbated by vaccine misuse (Fauci, 2005).

The increased amount of international travel and trade has also contributed to the spread of disease. The newly-appointed Senior United Nations System Coordinator for Avian and Human Influenza David Nbarro said that his researchers "suspect that one of the reasons for the current spread has more to do with trade in live birds than to do with the movement of the virus through wild birds" and that in addition to trade, "we should also add the possibility of chance infection: trade plus rather than just trade (Associated Press, 2007)." In tracking the flow of trade in general from China to the rest of the world and comparing it to the amount of poultry traded illustrates just how fast and far the disease can spread (Kimball, 2/7/2007). World exports of poultry increased dramatically and accounted for over 10 percent of world consumption in 2002 (Orden et al., 2002). Predicting a 63-percent increase in global demand for meat through 2020, a report on Animal Agriculture and Global Food Supply, the Council for Agricultural Science and Technology attributed 88- percent of the projected increase to developing countries, with China accounting for half of that increase (CAST, 1999).

Furthermore, over half of China's poultry meat imports are transshipped through Hong Kong instead of directly to Chinese ports in the mainland, although local companies are struggling to change this measure (USA, 2001). Starting from November 1, 2004, all meat re-exported from China through Hong Kong's port was required to comply with a pre-inspection requirement by China Inspection Co. in Hong Kong (FSIS, 2007). The inspections in Hong Kong are hoped to greatly decrease the smuggling, re-labeling or repackaging of products in an effort to improve the food safety and quarantine system in China. The large amount of goods traveling through a given location makes Hong Kong a H5N1 hotspot. In contrast, Indochina appears to be a regional sinkhole, while also demonstrating bidirectional dispersal between localities within the region (Reuters, 2007). An evolutionary trace of a protein called haemaggluttinin, which sits on the surface of the H5N1 molecule, across the geographical distribution of the virus' phylogeny or family tree suggests a mechanism by which H5N1 is able to infect repeated cycles of host species across localities, regardless of the host species first infected at each locale (Wallace et al, 2007). In other words, researchers found that Indochina—Thailand, Cambodia and Vietnam—appears to provide a sustainable atmosphere for proliferation of the virus and to absorb different strains, so H5N1 tends to spread in local areas but does not travel from the locality to anywhere else.

It is in these areas that the H5N1 seems to be incubating, causing more human cases. Interestingly, China has had significantly fewer human cases of the avian flu despite being the origin of the virus whereas there are far more cases in Indochina. Overall, there have been a total of 277 cases of H5N1 in humans, causing 167 deaths (WHO, 2007). Flu viruses, however, mutate and evolve extremely easily and scientists believe the virus could soon acquire the ability to pass between humans. A human-to-human strain could trigger a repeat devastation that scientists worry will be similar to what was experienced during the 1918 flu pandemic. The 1918 flu pandemic was thought to have killed between 20 and 40 million people worldwide and infected over 22 percent of the world's population (Reid et al, 2003). As of now, the virus is still bird-based and human infections are relatively difficult.

Figure 1: Cumulative Number of Confirmed Human Cases of Avian Influenza A (H5N1)

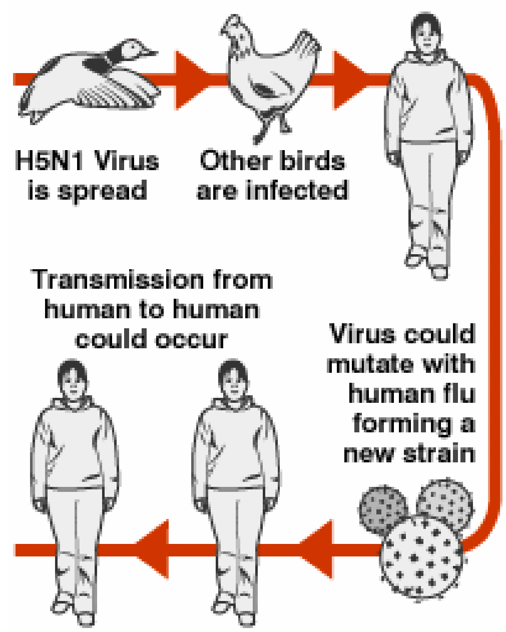
Country	2003		2004		2005		2006		2007		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	0	0	6	6
China	1	1	0	0	8	5	13	8	1	0	23	14
Djibouti	0	0	0	0	0	0	1	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	5	3	23	13
Indonesia	0	0	0	0	19	12	56	46	6	5	81	63
Iraq	0	0	0	0	0	0	3	2	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	1	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	1	1
Thailand	0	0	17	12	5	2	3	3	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	0	0	93	42
Total	4	4	46	32	97	42	116	80	14	9	277	167

Total number of cases includes number of deaths; WHO reports only laboratory-confirmed cases. All dates refer to onset of illness.
Source: WHO, March 1, 2007
http://www.who.int/csr/disease/avian_influenza/country/cases_table_2007_03_01/en/index.html

Despite difficulty of transfer, human transfers may still exceed reports. Dr. Henry L. Niman, a biochemist in Pittsburgh, has argued that there have been 20 to 30 human-to-human infections (McNeil, 2006). He argues that it is rather unlikely that seven infections among six relatives and a neighbor in Indonesia, with onset dates stretching from Feb. 15 to March 4 2005, had all been acquired from feathers that the family had plucked from diseased wild swans in early February (ibid). In addition, most clusters are hard to investigate because they may not even be noticed until a victim is hospitalized, and are often in remote villages where people fear talking about disease (Olsen, 2005).

In the small number of the human samples, scientists have found that the virus acquired some minor changes to the haemagglutinin protein. The flu virus spreads when the protein binds to the receptors on cells, which act as docking stations, which allows the virus to invade and infect the cells (CDC, 2007). In the majority of the samples, the haemagglutinin could only bind to bird cell receptors, but the researchers found that in limited human samples, the haemagglutinin could bind to both bird and human cell receptors (Chen et al, 2006). It is thought this is a key step needed for H5N1 to be able to spread from human to human. Further analysis revealed two separate mutations at different positions on the protein had enabled H5N1 to recognize human receptors (ibid). The researchers believe that discovering the location of the mutations would help them identify H5N1 strains that could develop pandemic potential. Dr Wendy Barclay, a molecular virologist from Reading University, UK, said "This work shows that at least two changes in the haemagglutinin protein are needed for H5N1 to transform to strain that could infect humans, and knowing what these are will help to inform surveillance." (BBC, 2006).

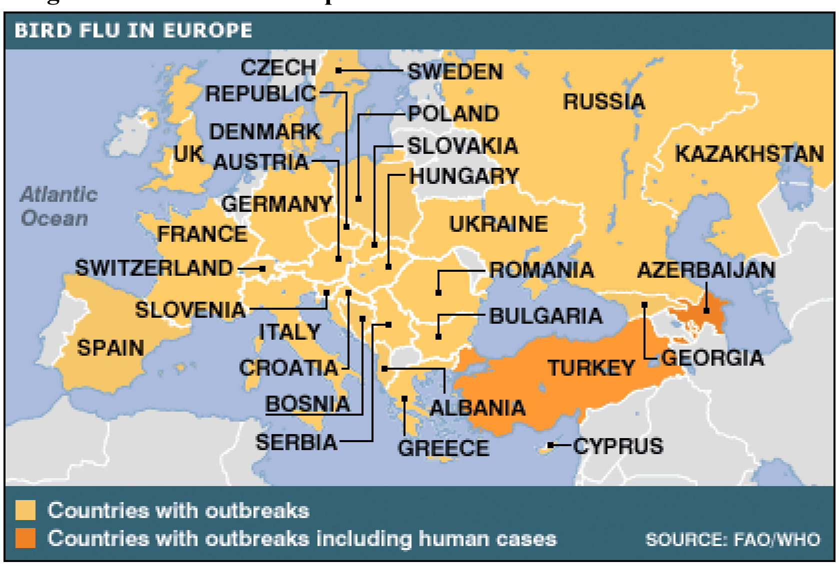
Figure 2: Bird to Human Transfer of H5N1



Source: BBC, June 29, 2006
http://news.bbc.co.uk/2/hi/science/nature/4947454.stm

Despite the possibility for human-to-human transfers, a uniquely human form of the H5N1 virus does not yet exist, so the humans who have caught the virus so far have caught the avian H5N1 virus. In general, people who catch it have symptoms that include fever, cough, sore throat, vomiting, muscle aches, conjunctivitis and, in severe cases, breathing problems and even pneumonia that can be fatal (Ungchusak, 2005). The severity of the infection, however, depends in large part on the infected person's immune system and whether the victim has been exposed to the strain before, in which case they would have developed partial immunity (FAO, 2005). Symptoms for a humanized version of the H5N1 are still unknown, and they could be different from the avian type. With the mortality rate of the H5N1 avian flu in humans being so high, it would be necessary to track a potential spread between humans in order to effectively combat it. The variances in symptoms, however, make it more difficult. For example, a boy who had contracted the H5N1 virus experienced diarrhea, rapidly falling into a coma without developing any flu- like symptoms or the respiratory complications associated with the disease (NIAID, 2005).

Figure 3: Bird Flu in Europe



Source: BBC, March 8, 2007
http://news.bbc.co.uk/2/hi/health/4531500.stm

In September of 2005, David Nabarro warned the global community that a real outbreak of avian influenza could kill somewhere between 5 million and 150 million people (UN, 2005). With the fatality rate at approximately 60-percent, many scientists are requesting adequate resources to fight what is often seen as a major world threat to possibly billions of lives (Webster, 122). In fact, experts have identified key events—such as creating new clades, infecting new species, or spreading to new areas—that mark the progression of an avian flu virus towards becoming pandemic and many of those key events have occurred more rapidly than expected (Schwartz, 2005).

The mutation rate of the virus is crucial in understanding how to combat it should an outbreak occur. Researching how it evolves and which proteins in the body it targets will also draw a clearer picture as to how to create a base vaccine. For instance, there have been studies of the levels of cytokines, or groups of proteins and peptides that are used in organisms as signaling compounds to help cells communicate with each other, in humans who contracted the H5N1 virus (BWH, 2007). These cytokines are essential in mobilizing the immune system and producing inflammation (ibid). This increase in cytokines is also associated with the flu symptoms. A protein that concentrates in sites of infection and increases production of other cytokines, tumor necrosis factor alpha, is signaled by the cytokines to destroy cells; damage to the tissue associated with an infection by the flu virus is what can make the virus fatal (Spector, 2005). The spread of inflammation triggered by the H5N1 virus is dramatic, as illustrated through the positive feedback process resulting from stimulation of the immune system. The H5N1 strain induces higher levels of cytokines than more common flu virus types, causing more extensive damage by triggering “cell destruction” by the increased amounts of the tumor necrosis factor alpha protein (Webby et al, 2004).

Several sub-lineages of the H5N1 have emerged, causing concern about the ability to respond to various strains when even the first is still a cause of great uncertainty. The different sub-lineages of the H5N1 viruses isolated from China between 1999 and 2004 had a range of genotypes and even had considerable variability within genotypes. The epidemic was not caused by the introduction and spread of a single virus but was caused by multiple viruses that were traced to the original H5N1 virus through the haemagglutinin gene (Sims et al, 2005). Dealing with the problems of mutation is particularly difficult in nations that lack the financial resources to buy the vaccines, mostly produced in private sectors, as well as in convincing poorer people to buy preventative shots. Among the difficulties preparation measures face is creating a vaccine in time, but also distributing it and administering it correctly.

Current Research

Due to the high lethality and virulence of the virus, its endemic presence, its increasingly large host reservoir and its ongoing mutations, the H5N1 virus is very possibly the world's largest current pandemic threat. Billions of dollars are being spent researching H5N1 and preparing for a potential influenza pandemic. Yet, as Dr. Daniel Lucey, co-director of the Biohazardous Threats and Emerging Diseases graduate program at Georgetown University argues, "There is no H5N1 pandemic so there can be no pandemic vaccine (NCBI, 2005)." There are, however, "pre-pandemic vaccines" that have been created and are currently being tested and refined (Walker, 2006). These "pre-pandemic vaccines" offer a sort of primer for the mass production of a vaccine more specific to a new pandemic strain of the virus. Private companies that manufacture vaccines are also being encouraged to increase their capacity so that if a pandemic vaccine is needed, facilities will be available for rapid production.

There is no highly effective treatment for the H5N1 virus but oseltamivir, commercially marketed by Roche AG as *Tamiflu*, can inhibit the influenza virus from spreading inside the user's body, although tests have not proven consistency (Ward, 2005). Some countries and organizations are focusing on this drug to make preparations for a possible H5N1 pandemic (La Montagne, 2004). In April of 2006, Roche AG announced that a stockpile of three million courses of Tamiflu treatment was at the disposal of the World Health Organization to be used in case of a pandemic; separately the company donated two million courses to the WHO to give to developing nations that may be affected by such a pandemic but cannot purchase sufficient doses of the drug (Associate Press, 2006). Once these drugs are purchased, however, there are still greater problems that developing nations face. China, among these developing nations, can exacerbate the issue.

The Problem and China more Specifically

Southern China. “It is probably still originating there and spreading,” says Walter Fitch, a professor of ecology and evolutionary biology, who goes further to say that “if you can control the virus at its source, you can control it more efficiently (Reuters, 2007).” Furthermore, scientists at Shantou University, in addition to scientists in Xiamen and Hong Kong, say that the “only way to stop the virus is to control it in southeast China, but the Chinese authorities have denied the country is the epicenter of the virus and opposed independent flu research (ibid).” China is crucial not only to an emergency response, but also in a general response to the H5N1 virus. Without government support, it may be difficult to address the issues as efficiently. The Chinese government claims that it is taking the threat seriously and offering support to generate vaccines by encouraging research projects; yet, little concrete action has been taken.

In responding to studies that point to China’s mishandling of vaccine implementation, for instance, the Chinese government has shown great resistance to criticism. The Agriculture Ministry said that a Chinese conducted gene sequence analysis found high uniformity in all the variants of the virus found in southern China, which means that they belong to the same gene type (Roos, 2006). There are contradictions between what international researchers have found and what the Ministry of Agriculture says, so unless the Ministry shares viruses and specific information on a regular basis, diagnostics will be done on strains that are old and the results may be less applicable (ibid). The Ministry of Health, however, has urged regional bureaus to strengthen measures against SARS, human cases of bird flu and even plague, placing SARS, human cases of bird flu and plague as top priorities for efforts to prevent and handle major public health emergencies (Xinhua, 2007). Yet, that plague is still a priority may speak to the various healthcare concerns that China's Ministry of Health faces.

China has, however, published a contingency plan to respond to an outbreak that outlines the structure of a national pandemic preparedness system tailored to address influenza, as well as emergency reaction responses and goals:

> The Ministry of Health urged all localities to also draft their own contingency plans, while taking into account local conditions so as to be better prepared for a possible flu pandemic.
>
> The national plan will have four levels of alert -red, orange, yellow and blue - which will indicate the seriousness of the outbreak. The most serious level, "red," will be announced in case of the consistent and rapid spread of new sub-type flu virus, or if the World Health Organization (WHO) announces the outbreak of a flu pandemic. If a "red alert" is issued, health authorities above the county level must mobilize all medical resources and set up temporary clinics, while the Ministry of Health will issue daily reports on the surveillance and control of the pandemic. The plan also says that the Ministry of Health is responsible for organizing and coordinating epidemic preparedness work and, if needed, suggesting to the State Council the establishment of a national public health contingency headquarters.
>
> In addition, the China Center for Disease Control and Prevention (CDC) will administer the national avian influenza surveillance system and require health authorities above the county level to ensure the collection, registration and delivery of flu virus samples for testing.
>
> (EAP, 2006)

Limitations with China's contingency plan still exist, however, as the number of doses estimated to effectively combat the virus is not available to stockpile and China is ill-equipped to distribute the drugs should they be stockpiled. China's biggest drug maker contacted Tamiflu maker Roche about producing the antiviral drug in China in 2005, and now bird flu patients in China are being treated with Tamiflu, Amantadine, and Rimantadine according to their symptoms (DNC, 2005). Yet, the existent drugs are not extensively tested as of now. Any mass production will still have to follow extreme cautions so as not to exacerbate misuse of vaccines or creation of resistant flu strains. After an effective vaccine is created, stockpiling adequate amounts of it is the next challenge. Robert Webster of St Jude Children's Research Hospital in Memphis, Tennessee argues that "Stockpiling pre-pandemic vaccines is more valuable than people realize," whereas "it may not necessarily protect you from infection, but it will probably stop you dying (MacKenzie, 2006)."

China Center for Disease Control is responsible for the surveillance of influenza incidence, molecular epidemiology study of the virus strain, establishment of a development strategy for avian flu vaccines, participation vaccine research and development, and the design of the technical roadmap (China CDC, 2007). It provides support for companies such as Sinovac in the realms of surveillance, virus isolation and constructing prototype strains using the Chinese strain (Lin, 2006). China has made significant improvements in its biopharmaceutical industry. However, Chinese biopharmaceutical enterprises are largely distributed in the economically developed provinces, municipalities, and regions such as Beijing, Shanghai, Shenzhen, and Changchun in East, Central, and North China, where nearly 75% of Chinese biopharmaceutical enterprises are located (Langer, 2006). The difficulty will be supplying drugs and vaccines for rural populations in areas where infrastructure does not exist and more live poultry is present.

Given an environment where making an adequate return is uncertain and where implementing regulations lack clarity, the relatively small number of newly opened hospitals and clinics in rural China is no surprise (Lipson, 2004). Also, of the 29,000 medical facilities of all types registered in China in 2003, only 45 have foreign investment and another 15 have investment from Hong Kong, Taiwan, and Macao; among these there is still a lack of quality of services and health practitioner training (Mao, 2006). The vast majority of these would not qualify as hospitals; most can only act as primary care and dental clinics, emergency evacuation centers, and research facilities (Lipson, 2004). Adequately equipped hospitals are primarily located in urban areas and it would be more difficult in the chaos of a pandemic to address concerns in the countryside.

Measures Needed to Combat the Virus

While China is still making limited improvements in providing adequate facility infrastructure and reforming the health system in China, vaccine research has been rather successful although somewhat hurried. In 2004, lead emerging Chinese biotechnology company Sinovac and the China CDC signed an avian flu vaccine co-development agreement (Medical News Today, 2004). In 2006, Sinovac announced positive preliminary results of its Panflu vaccine and the Chinese government publicly announced plans for mass production (Nuzzo, 2006). Overly optimistic production and distribution, however, is dangerous and there are suggestions that the completed vaccine should be approached with more caution and undergo more testing before mass producing it (Lin J et al, 2006).

China lacks transparency in regards to the virus origins, as well as research findings and data. More transparency is necessary to ensure a unified and organized global response. Also, supplying vaccines for a fast mutating virus will be increasingly difficult as strains become more varied. It would require at least three months after the virus emerges to begin a full-scale production of a vaccine that could prevent detectable illness caused by the strain but it is hoped that, by one year after the foremost recognition of the virus, vaccine production could increase until one billion doses were produced (SDN, 2006). Greater health reforms are also necessary in China to provide basic safety nets and access to treatment should an outbreak occur.

Problems with distribution of the vaccine will be paramount in the case of an outbreak. The health and productivity of workers that make up China's manufacturing power is critical to the country's interest. In the long term, as China becomes a market on which Western companies increasingly depend, the health of over a billion consumers will play a very important role in the world economy. These concerns speak to a series of questions regarding the abilities of China's public health system. In regards to the role of China's population as both manufacturers and consumers, the answers to those questions will help ascertain the effects that a pandemic flu outbreak within China could have on the global economy (Carlson, 2007). China lacks the infrastructure to effectively do so, but it is not the only country that will face this problem. Even the most developed countries, such as the US, face extreme lack of preparedness in this regard. Simply having the facilities will not ensure successful vaccine distribution. In fact, Japan's Asahi Shimbun newspaper reported that the country's prefectures, or states, had enough stockpiles of the anti-flu drug Tamiflu for only 37,400 people in 2005 — less than 1 percent of the Health Ministry's recommended amount (Associated Press, 2005).

Numerous factors converge to cause shortages in vaccine availability in localities, such as production problems, reduction in the number of vaccine manufacturers, and overwhelming demand for certain vaccines for which distributors are unprepared (Sloan, 2004). In an outbreak, it would be necessary to overcome these factors quickly for most efficient distribution. The present shortage in the US influenza vaccine supply, for example, has placed more public attention on the recurrent troubles faced by public health officials in ensuring the availability of vaccines. In fact, vaccine spending across the globe is rather limited. The world pharmaceutical market is estimated at 340 billion dollars annually, whereas the total global vaccine market is estimated to be only six billion dollars a year, which is a smaller market than for just one drug such as Lipitor (Poland, 2005). About one billion dollars of this amount is ascribed to a single pediatric vaccine, and approximately two billion is for other pediatric vaccines, which leaves only three billion dollars for all other remaining vaccines (Batson, 2003). Producing the funds to mass-distribute a vaccine for H5N1 would be a scramble; measures are necessary to gradually stockpile a baseline drug to respond to an outbreak in a more efficient manner.

Affecting more than Health Issues

Beyond even health issues, there are significant damages than a pandemic can have on the economy. Even a limited outbreak strains the livelihood of poultry farmers and other people in the agricultural sector. Munir Akram, president of the UN Economic and Social Council, said that the H5N1 virus is a call for cooperative action, more investment in vaccines and commitment from the entire world to share the costs (ECOSOC, 2005). Quarantines and mass culling of poultry has, in the past, had some resistance from local farmers who hid birds in the house or did not allow government officials full access to their poultry. This was due in large part to either inadequate or complete lack of financial compensation for the birds killed. To address these concerns, international financial institutions should consider creating a fund to establish preparedness plans that compensate farmers for losses incurred by a mass culling of their poultry (ibid). Concerns about the flu affect not only trade with China, but poultry trade in general. The total value of U.S. poultry exports slipped by 12 percent to 1.9 billion dollars; this drop was caused by widespread consumption declines in light of fears about the avian flu (USAPEEC, 2007).

Beyond some dips in trade and criticisms of the Chinese government to be more forthcoming with information, however, bilateral relations do not seem to be strained by epidemic outbreaks. Reports do not highlight any discontent that Indonesia may have with

China, particularly as the H5N1 has hit Indonesia the hardest and originated from China. Yet, in the case of a pandemic, China will have to prove able and willing to address outbreaks. In the case of a higher death toll, especially on a global level, a sensible reaction from China will play a large role in allowing for greater cooperation and effective response to the pandemic. Its role in the spread of the virus will also place more responsibility on China as a status quo power.

Conclusion

Despite a proactive approach to supporting vaccine research and development, the biggest challenges that China faces is transparency in information sharing, ability to distribute vaccines and responsible administration of the drug. In regards to transparency, China needs to respond better to criticism whereas it may fear its connection with the H5N1 virus damages its image; further denial of this connection could hurt vaccine research and production. Studies illustrate the importance of looking at the alpha strain, as produced in Southern China. Researching this strain and developing vaccines around its properties can help contain the exportation of more of this virus. Furthermore, simply sharing new virus information with the international community would help in global pandemic response and preparedness. A lack of exchange, however, speaks to a lack of responsible action on the part of China.

The production of a vaccine is difficult and should proceed with great caution. The ability to stockpile and distribute the drug, however, is also of great concern. Without the hospitals and trained personnel in relative proximity of those who are afflicted, China will have difficulty in distributing the drugs to more rural provinces. A lack of equipped hospitals and clinics, even in cities, is a great challenge in responding to any health crisis. Working more closely with NGOs or the World Health Organization may help but, once again, a lack of transparency makes it more difficult to share information, decreasing efficiency and effectiveness.

Responsible administration of the drugs, once they are safely and consistently tested as well as distributed to the necessary locations, is also important. The partial vaccination of poultry in the past could have led to the emergence of new strains. Education is necessary for local administration to understand the implications of an incomplete or partial administration of vaccines. Furthermore, a Chinese NGO alliance could help grass-roots administration and distribution as well as awareness. As illustrated in greater cooperation with the HIV epidemic, an alliance can integrate the resources of China's NGOs and coordinate their participation in domestic and international viral control projects to enable them to play a more important role in fighting disease (China CDC, 2007).

That China lacks the infrastructure of many developed countries, and that many developed countries are also significantly unprepared to effectively handle a potential outbreak, is cause of great concern and indicative of the need for a more organized global health program. China has taken significant steps in vaccine production and research in regards to the H5N1 virus. China has tried to be relatively more aggressive and open in dealing with bird flu after it was criticized for being reticent during the 2003 outbreak of SARS. Yet, it must work more closely with international organizations and provide greater access to information so that a pandemic can be prevented. That there is considerable evidence pointing to China’s Guangdong Province as the source of the H5N1 virus, and that the Chinese government refuses to acknowledge its role in the exportation of the disease, speaks to China’s important role as a stakeholder in the international community. While there are indicators that China seeks to address its lack of preparedness, it is still a far cry from being a responsible and active player in preventing a potential global outbreak.