

# China's Disease Cauldron

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**I**NFLUENZA, OR “the flu”, is a moniker that has come, in the modern vernacular, to represent anything more severe than a cold but less severe than pneumonia. The reality is that a true influenza infection can be extremely debilitating. The influenza virus comes in many forms that continue to circulate in populations of animals, mainly waterfowl such as ducks or geese. The virus readily mutates, and if it mutates in just the right way, it can jump from one species of animal to another. These new hosts, confronted with a virus like none they have seen before, will either survive and develop life-long immunity or succumb to the virus and lose the race to reproduce. This biological dance has occurred throughout recorded history at relatively predictable intervals, when the promiscuous influenza virus has made its way around the world in epidemic waves.

Most recently, a specific strain of the virus, H5N1, has become disturbingly common in poultry populations in Asia. The first recorded appearance of this strain was in the bird flu epidemic that erupted in Hong Kong in 1997, killing six people and resulting in the destruction of almost every chicken on the island, about 1.5 million in all. Efforts to control that epidemic were successful, and the virus is thought to have retreated to its natural host, aquatic waterfowl, in the Guangdong, Hunan and Yunnan provinces in China, where it awaited an opportunity to return.

And return it did in 2001 and 2003, with major outbreaks in Chinese domestic birds that went officially undeclared

to the international community but were unlikely to have been missed by Chinese officials. It was probably during the first of these epidemics that Chinese farmers, seeing their livelihood imperiled and with no government system of compensation for ill animals, began to use the antiviral medication amantadine in bird feed. Preventative use of human medications in otherwise healthy poultry is a common animal husbandry practice that is known to render the drug ineffective over time—and possibly useless for treatment of the human populations for which it was intended. When viral samples of the epidemics were finally obtained, it was determined that the H5N1 strain of influenza circulating in the Asian bird population was amantadine resistant, removing one arrow from a relatively small quiver of defenses against the human form of the disease. By early 2004 the virus had infected flocks in Thailand and Vietnam, resulting in tremendous losses to the Asian poultry sector—\$15 billion by early 2005—and 108 human cases and 55 deaths in the region from December 2003 to July 2005. Each of these human cases, while tragic, can be looked at as a dodged bullet. Most of these individuals became infected from direct contact with poultry, but the virus did not mutate into a form capable of easy human-to-human transmission, a critical element to seeding a human epidemic. In April 2005 it was confirmed that the virus had crossed from poultry into pigs, long considered influenza's middle ground on its way to a sustained human host. This progression, scientifically unsurprising, offers many

ominous signs of a brewing epidemic that could quickly escalate.

This round of influenza is not the first disease to jump out of the Chinese cauldron, nor will it be the last. Conditions in provinces such as Guangdong are the perfect milieu for disease. A dense human population living in close contact with a diverse range of wild and domestic animals creates an ideal opportunity for pathogens to form and propagate. Year-round hot, humid weather and the absence of rigorous hygiene standards further exacerbate the situation. Well-ingrained cultural preferences, such as purchasing food animals live, aggravate these environmental conditions, resulting in a veritable laboratory rife with infectious disease. In 2003 the world learned a painful lesson from the emergence of the Severe Acute Respiratory Syndrome, or SARS, virus that—aided by delayed disclosure by Chinese officials—migrated around the globe before being held at bay. It is with this hindsight that the world is now looking intently at how China deals with the current avian influenza challenge.

### *Looking the Other Way*

TO WHAT extent would a growing influenza epidemic in China be reported swiftly to the international health community? Many postulate that a country with a history of strict information control and refusal of international access to known outbreaks—even threatening harm for deviation from the condoned message—would easily deny the first sign of an erupting influenza epidemic. This assumption was borne out during the SARS outbreak, resulting in tremendous international backlash and, ultimately, the resignation of high-level Chinese officials. However, when dealing with infectious diseases, a delay in disease detection is not always done purposefully, for infrastructural factors can com-

plicate timely and accurate recognition of emerging disease. As such, there are two clear potential impediments to the discovery of an avian influenza outbreak in China: the intentional suppression of information and China's inability or unwillingness to identify and investigate suspicious situations in the first place.

Detection and identification of a disease outbreak require significant effort, especially in a country as large as China. There are costs associated with testing dead animals for disease, culling flocks or quarantining areas may be difficult to justify in a country with high levels of underlying disease. Influenza in particular can be transmitted between wild migratory waterfowl—often not showing ill effect from harboring the disease—to domestic flocks. Emerging illness in this environment requires an astute farmer to notice and report an increase in symptoms among his flock. Notification of this nature could easily lead to the destruction of all animals in the vicinity, a heady disincentive to quick notification of suspicious circumstances. The widespread use of the antiviral medication amantadine to treat and prevent avian influenza was probably a desperate attempt by farmers to protect their livelihoods rather than a practice mandated by government officials, although it likely would not have occurred without government knowledge. In the absence of a reimbursement system for culled animals, the cost of reporting the outbreak will be borne solely by the farmers, creating a significant challenge to detection of avian influenza for even the most transparent of political regimes.<sup>1</sup>

In the post-SARS period, China has indicated a desire to improve disease detection and healthcare infrastructure. Health and disease data are purportedly

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<sup>1</sup>Interestingly, on June 24, 2005, the prime minister of Vietnam declared retroactive compensation for chickens culled in the name of disease prevention and payment for participation in

flowing from medical practitioners and provincial governments upward through fewer political filters to the central government. Focus has been placed on inter-hospital communication in the more densely populated areas along the east coast to increase efficiency in identifying illness trends. On the agricultural front, increased surveillance and disease prevention in animals has been heralded, and improving circumstances surrounding the storage and marketing of live animals has been identified as a critical component of the fight against emerging infectious diseases. While these interventions are not sufficient to address the full scope of the problem, they are indications that some lessons were learned from the SARS epidemic.

Unfortunately, it is unclear in the short term the extent to which improvements are being implemented, or can be implemented, in the most vulnerable areas. Compliance with promulgated regulations affecting long-standing traditions of animal husbandry and cultural etiquette has proven less than complete. The most effective regulations on paper are useless if not actually put into practice, as appears to be the case with some Chinese food-handling practices. Further, the intellectual capacity and infrastructure necessary to build up epidemiological capabilities is difficult to scale up under the best of circumstances, let alone on the eve of an epidemic and under the watchful eye of the international community. Expanding hospital capabilities and infrastructure is a long-term project. Some necessary changes to agricultural policy can be made overnight, such as providing compensation for flocks culled in the line of disease prevention, but convincing an agrarian community to disclose diseased animals will likely take further reassurances. Time will tell the extent to which the trumpeted changes have materialized on the ground. In the meantime, China should be held politically accountable

for not pushing further changes to remedy weaknesses of policy and practice; however, the dynamic nature of public health interventions must also be taken into consideration before attributing political malice.

In the absence of the ability to immediately plug the public health holes, China needs to be willing to engage the international health community for advice without the fear of losing face. A government announcement in mid-June stated that samples of avian influenza-related material couldn't be shipped overseas without prior approval from the Ministry of Agriculture. While not surprising, this effort to stem the dissemination of biological information directly impedes international efforts to understand and prepare for a growing problem. With a virus as feared and potentially costly as avian influenza, there will always be a desire to control the global perception of disease burden. However, effectively shutting down the Chinese scientific community's access to international engagement will greatly hinder their ability to understand and control the problem before it forces itself onto the world stage.

### *Inextricably Linked*

WHILE THE international medical community and WHO will be key to Asia's ability to contain avian influenza, the effects of such an epidemic go beyond simple health threats. Globalization has led to increased interconnectedness of society in many areas—economy, media, travel—resulting in significant structural changes that would have a tremendous impact in the event of a large outbreak of avian influenza. Increased pressure on idle inventories has

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the culling efforts. Vietnam is not the first country to implement such a measure, but it shows the growing appreciation for grassroots participation in disease detection.

developed a global economy that hinges on just-in-time delivery of products assembled on far-off shores. The ease of importing components of manufactured goods, either for assembly or repair, has created a world that takes for granted the great degree of global interdependence required for the functioning of even the most mundane of products. Further, the availability of parts is critically dependent on the free movement of cargo and would be severely affected by any global restriction of the movement of goods. If assembly lines were forced to stop production for lack of inputs, breaking the just-in-time delivery chain, the economic impact would be tremendously magnified.

Even the U.S. Centers for Disease Control and Prevention, which maintains an emergency stockpile of critical childhood vaccines in the event of shortages, requires manufacturers to maintain possession of the vaccines until delivery is requested. This just-in-time stockpile is reasonable for items such as vaccines that require special handling and rotation due to expiration date, but begs the question of how accessible the stockpiles would be in the event of a global transportation emergency.

Why is this relevant to the discussion of avian influenza? During the SARS epidemic in 2003 the World Health Organization (WHO) issued isolated travel advisories designed to discourage travel to impacted regions. Enforcement of these regulations was voluntary, inconsistently applied and not always effective, suggesting that future disease outbreaks might require much more onerous protective barriers. The influenza virus is not only highly contagious but can remain infectious on surfaces long enough that, with modern shipping methods, it could circumnavigate the globe. The declaration of an influenza epidemic would create a strong incentive for border closures to limit the spread to uninfected shores. In the face of an evolving crisis, if a few gov-

ernments were to close their borders, it is likely that many others would follow suit, effectively locking people and products in place. Closing down the world's ability to achieve just-in-time delivery would cause an unprecedented disturbance of the global economy.

A disruption of this nature would quickly become a destabilizing force in countries beyond the regions primarily impacted by the influenza pathogen. The inability to obtain items considered essential by citizens of developed countries would have a significant impact on everyday life. Products necessary for the prevention or treatment of influenza—face masks, respirators, medications—would be difficult if not impossible to construct, making the impact of an influenza outbreak even greater. Further, lifesaving medications or devices unrelated to the treatment of influenza could be in short supply, resulting in casualties even before the virus left foreign shores.

In a scenario such as this, return to normalcy would depend on the deployment of an effective vaccine or on the outbreak running its natural course, which is estimated at six months but could be 18 months or more. And the time frame for vaccine development is dependent on many factors and is therefore highly unpredictable. It is known, however, that expeditious production of a vaccine would be problematic with current global capacity limitations on manufacturing. Presently, about 300 million influenza vaccines are created globally each year, well under what would be needed to vaccinate a world population of over six billion. The infrastructure and techniques used in creating products of this nature are nearly impossible to scale up in the short term, leaving large gaps between demand and supply. As a further example of the many complications in this effort, the development of a vaccine for distribution in the United States would require access to pathogen samples imported from the

affected region. Global transportation of biological materials is usually achieved through contracts with private transport companies. During the SARS outbreak, convincing carriers to move samples of a deadly and unknown pathogen was sometimes a challenge. At present—in non-crisis mode—there is only one global carrier who will accept highly pathogenic samples for international transit, and it is unclear what impact an epidemic would have on their willingness to engage in this activity.

In the face of a growing epidemic and a shortage of the supplies needed to protect against transmission, political officials will need to decide how to allocate valuable resources. There is little doubt that, in a crisis situation with closed borders, governments would hold products made within their borders for their own citizens. Presently, there is a concentration of production capacity for critical interventions in developed countries, leaving most of the developing world without the capacity to create products that might be the front line of defense against an epidemic. There are only nine countries—Australia, Canada, France, Germany, Italy, Japan, the Netherlands, the United Kingdom and the United States—that have existing infrastructure to make an influenza vaccine, and the much touted antiviral treatment Tamiflu is manufactured at a single plant in Switzerland. In a situation where the United States has enough antiviral therapy to treat only 1 percent of its citizens, would it be willing to donate doses to treat the citizens of other countries, even, minimally, foreign heads of state? What would be the political ramifications of denying such a request? Sharing coveted resources with countries experiencing the first wave of infections might be politically difficult to sell domestically, forcing leaders to decide between the appearance of protecting their coveted stocks or assisting neighbors in a crisis.

### *Protect Your Own?*

WITH THE prospect of a global health crisis, can states find a way to cooperate to stem a pandemic? The answer lies in how much preparation is put in place before the onset of a global emergency of this nature and scale. Unlike AIDS, which is crawling around the world leaving a predictable epidemiological footprint on ravaged developing countries, influenza will come as a tidal wave, quickly destroying many lives and economies in its wake. The scientific community now sits poised, waiting for the next mutation that will transform the current virus into a form that can be readily transmitted from human to human, the sign that the human epidemic has begun. However, the impact of an avian flu pandemic for international politics and the economy goes far beyond the health care burden. Global integration, increased reliance on just-in-time production and items sourced from China will make any sustained restrictions on international transportation extremely painful for many economies.

Merely blaming the Chinese for a lack of transparency is not a solution to the challenges faced when dealing with a disease such as avian influenza. China is not unique in needing to confront public health weaknesses, but the size, scope and nature of its domestic agricultural community make the challenge formidable. The avian influenza epidemic among poultry and wildlife in China is already gaining momentum, complicating any radical changes that could be undertaken even if there were the political desire to make them. It is imperative that support and pressure for needed reforms to the public health and agricultural systems be maintained. If the global community demands transparency from China, as it should, there must also be an agreement to help it bear the burden of battling the disease.

The people who sit at the table in any future deliberations surrounding the appropriate response to the threat of emerging infectious diseases such as avian influenza need to include many from beyond the public health community. National trade representatives, transportation representatives and controllers of national money supplies are some of the individuals who should be thinking about what to do in the event of a global influenza pandemic. Familiarizing all segments of society with the possible implications of this type of emergency will greatly aid in the event that tough decisions need to be made in very little

time. Above all, the process needs to be seen as independent of political bias, recognizing that wielding influence will do little to prevent the free movement of the pathogen. Finally, efforts to arrest a developing pandemic demand containment of the virus at the front line—on foreign shores. This strategy may run counter to the perceived short-term national self-interest of developed countries but may also be the only way for the world to counter the power of the ever-agile Mother Nature. □

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