

Case Summary

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Version 1; Revised November 2010

The Problem

In early March 2003, a 63 year old man identified only as “Mr. P” went to Scarborough Grace Hospital to get treatment for his chronic heart ailment and acquired an infection from the man in the neighboring bed. Nine days later he went back to the hospital seeking treatment for a high fever and serious cough and died soon after. By the time Mr. P died, Mrs P. had also acquired the infection. In all, 33 others caught the disease from the Ps, making Toronto the site of the worst North American outbreak of severe acute respiratory syndrome (SARS), a disease that had come to Canada via a Chinese-Canadian woman who had been infected in Hong Kong and brought the disease to Toronto. The man from whom Mr. P caught the disease was the woman’s son.

Physicians and nurses, public health workers, and governments have possessed much better understanding of how infectious diseases spread since confirmation of the germ theory of disease in the mid-19th century. Confirmation came as increased speed of travel and larger numbers of travelers meant that outbreaks of infectious diseases could attain epidemic proportions in many countries more quickly than in previous centuries. Limiting the spread of diseases then became a joint effort, with governments taking measures to contain outbreaks at home and warning other governments so they could take action to ward off spread to their countries. Success requires that governments identify outbreaks of an infectious disease soon after the initial cases appear, isolate persons who have the disease or have been in close contact with others having the disease until they are no longer contagious, and minimize the number of non-infected persons who come in contact with the currently infected or any place where germs are likely to be present. Seeking to avert cross-border spread of an infectious disease has long involved quarantining travelers, animals, and shipments of goods that might carry germs from places where outbreaks have occurred until after the incubation period of the disease has passed. Today it may also include vaccination of local residents against the disease or stockpiling remedies. Governments know that quarantine is inconvenient, and are generally under pressure not to impose it unless and until it is clearly necessary. Thus they have

This case was created by the International Dimensions of Ethics Education in Science and Engineering (IDEESE) Project at the University of Massachusetts Amherst with support from the National Science Foundation under grant number 0734887. Any opinions, findings, conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation. More information about the IDEESE and copies of its modules can be found at <http://www.umass.edu/sts/ethics>.

This case should be cited as: M.J. Peterson. 2010. “Reporting Incidence of Severe Acute Respiratory Syndrome.” International Dimensions of Ethics Education in Science and Engineering. Available www.umass.edu/sts/ethics.



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strong motivation to avoid “false positive” (quarantine of uninfected persons) as well as “false negative” (nonquarantine of infected persons) errors.

Governments began formalizing the system of cooperating against the cross-border spread of serious infectious diseases in the mid 1800s through the International Public Health Office. The system was elaborated further after establishment of the World Health Organization (WHO) as a UN specialized agency in 1946. When the new lung infection that killed Mr. and Mrs. P first emerged in late 2002, the relevant international regulations on cooperation against infectious disease were specified in the International Health Regulations of 1969. They did not give the WHO any enforcement powers; it could not, like a national health ministry, order hospitals or others to take particular public health measures. WHO was put in charge of a cooperative system of having national authorities provide warnings about outbreaks of infectious diseases, particularly those likely to spread across national borders, and encouraging mutual cooperation in limiting the spread to as few people as possible. However, the 1969 Regulations only required reporting outbreaks of certain listed diseases, not of any new disease likely to spread. They also established a system of mutual assistance so that states with smaller public health services and lower capacity to identify diseases (especially newly-emerged diseases) could get help from WHO staff or public health agencies in other states and procedures for organizing collaborative work in identifying causes of infection and developing methods of treatment among medical labs around the world. However, states were not obliged to let WHO teams visit disease-stricken areas or have their medical labs participate in collaborative work.

This was the global context within which China revised some of its public health legislation in 1991. A new law specified that the Chinese Ministry of Health (the national-level health department) is the only entity in the country that may report outbreaks of contagious diseases in China to the WHO. The revisions maintained the rule that information about outbreaks of disease is to be treated as “sensitive” and relayed only to officials authorized to receive such information. This gave legislative confirmation to the Chinese Communist Party’s long-running effort to maintain control over the country’s politics even while allowing competition and private ownership of firms in the economy and providing a partial opening of telecommunications, including the internet and e-mail systems.

Meanwhile, the world was beginning to face the problem of newly-emerged diseases: legionella and Ebola hemorrhagic fever in 1976, HIV/AIDS in 1981, Bovine Spongiform Encephalopathy (BSE) (“mad cow disease”) and avian influenza (“bird flu”) and hantavirus in the 1990s. Identifying the source of AIDS infections took 2 years, and another 2 passed before early sequencing techniques revealed its genome.

A New Disease Emerges

In November 2002 the normal seasonal influenza outbreaks in Guangdong Province, the most southeastern part of China with 3,368 km of coast along the South China Sea included cases of what was initially called “atypical pneumonia” – a particularly severe lung infection with other symptoms resembling influenza. Provincial authorities reported those cases to the Ministry of Health in Beijing, but the Ministry did not see any reason to report them on to the WHO since atypical pneumonia was not on the list of diseases for which notification was required and there did not seem to be many cases. The atypical pneumonia was also hard to diagnose because its early symptoms – low-grade fever accompanied after a few days by dry cough and trouble breathing are the same as normal pneumonia’s symptoms. Only a week later do its distinctive symptoms – fever above 100.4° (F), headache and overall body ache, and

more severe trouble breathing set in. Infected persons who will recover start feeling better soon afterward; the 15% of infected who die (mainly those over 60) do so after an additional 4-5 weeks of suffering. Spread is most likely from direct contact, but the virus can survive 16 days on common surfaces like doorknobs and bedding at room temperature.¹

News that the Guangdong flu outbreak included an unusual type of infection was first relayed to WHO's Global Influenza Surveillance Network by the Canadian government at the end of November. The Canadian Global Public Health Intelligence Network (GPHIN), which monitors media and the internet for reports of diseases, had picked up references to the atypical cases in Chinese newspapers. Within a week, the US government's Global Emerging Infections and Surveillance Response System picked up Chinese media reports attributing the new infection to an Influenza B virus, and reported that to WHO. On the basis of the Canadian and US communications, WHO staff asked the Chinese Ministry of Health for information about the outbreaks on December 5th and again on the 11th. On the 12th, the Ministry noted 23 cases of atypical infections, classifying 22 of them as Influenza B infections, and stating that all the cases were consistent with usual seasonal outbreaks.

Information about the actual extent of outbreaks in Guangdong and the significant number of cases with atypical symptoms emerged slowly in January-February 2003. In early January local media reports on panic buying of flu remedies in several Guangdong Province cities elicited an official government statement denying that there was any epidemic. However, a Ministry of Health team from Beijing arrived in Guangzhou, the provincial capital, to assess the situation on January 20th. On the 21st, Canada's GPHIN released its first public report, based on translated Chinese news stories, indicating that cases of "atypical pneumonia" were occurring in Guangdong Province. On the 23rd, Guangdong Province health authorities sent the Ministry of Health an extended report on the cases of "novel atypical pneumonia." As required by Chinese law, this information was transmitted in a document classified as "Top Secret." The report was delivered to the Health Ministry during the Lunar New Year holiday, and no official in the Ministry with clearance to read "Top Secret" documents was available for three days. Even after the report had been read and considered, the Ministry neither made any public statements nor provided information about the outbreak to neighboring provinces.

The first cases of atypical pneumonia in Guangzhou (long known in English as Canton), the capital and largest city of Guangdong Province, were reported on January 31st. The disease spread rapidly, and public health authorities instituted mandatory province-wise reporting of atypical flu cases on February 3rd. A text message saying "There is fatal flu in Guangzhou" began spreading among cell-phone users inside and outside Guangzhou on the 8th. The following day a second inspection team from Beijing, led by the Deputy Health Minister, arrived in town and spurred provincial standardization of hospitalization, treatment, and infection control measures. On the 10th, the WHO Office in Beijing received an e-mail claiming more than 100 people had died of a new influenza in Guangzhou, and asked the Chinese Health Ministry for information. The Ministry response reported on 335 cases of atypical flu, of which 5 had been fatal: 105 cases among healthcare personnel in hospitals or clinics treating the disease and the other 220 in Guangzhou. Meanwhile, the Guangzhou city health bureau issued a press release acknowledging 100 deaths. The Ministry informed WHO that the first cases of the new flu had occurred in November, that the cause of the new flu had not been identified, but that isolation and other measures had brought its spread under control.

¹ Description of symptoms and course of disease from US Center for Disease Control and Prevention, www.cdc.gov.

Chinese Efforts to Identify the Cause of the New Disease

Understanding the physical cause and the severity of an infectious disease is necessary to designing treatments and public health responses. Identifying the cause of infection (bacteria or virus) and understanding whether and how the infection can be transmitted to and among humans are necessary to effective treatments. Estimating what proportion of persons exposed to source of infection get the disease, the time lapse between infection and carrying contagion to others, and understanding the severity of the infection once it sets in are necessary to determining the mix of public health measures to take. A new disease with a low infection rate or low severity will not cause as much worry as one with a high infection rate and great severity. In December 2002, SARS still looked like a fairly low infection rate malady because reported cases were few and isolated; by the end of February 2003 SARS was known to have a high infection rate among those in close contact with infected persons and to be severe. These characteristics led governments to work on limiting its spread even before its physical cause had been identified.

In January 2003 as the disease spread in Guangdong province, the cause was unknown, and identifying it made difficult by the presence of multiple pathogens in the human body. Chinese virologists having access to the few patient samples available from Guangdong Province in early 2003 offered several suggestions. One thought the bacterium *Mycoplasma pneumoniae* was the source. Others suggested that SARS was caused by some form of avian influenza, a suggestion supported by later Hong Kong reports that 2 people there who had recently visited Guangdong Province had been admitted to hospital with infections from the H5N1 avian flu virus. Dr. Hong Tao, a senior researcher in the Institute for Virology at China's Center for Disease Control and Prevention in Beijing, also concluded that the cause was bacterial, either *Chlamydia pneumoniae*, which spreads among humans, or *Chlamydia psittaci*, which spreads from animals to humans. Both are relatives of the *Chlamydia trachomatis* that causes the common sexually-transmitted disease but attack the lungs and can spread through the air. While researchers in Beijing were reluctant to challenge Hong's findings out of deference to his seniority and fame as a leading researcher, members of the Institute for Respiratory Diseases in Guangzhou were skeptical because they knew that attempts to treat the infection with antibiotics had failed. However, there were very few samples from patients. The Health Ministry had forbidden inter-lab transfers on grounds they posed safety risks (some scientists suspected that political and research rivalries were involved) and the ban meant that most Chinese labs, including the Beijing Genomics Institute, which possessed the country's most advanced genome sequencers, had no samples. They were unable to confirm nor challenge the Chlamydia theory. Hong's own team was not able to isolate the bacteria, or even find it in most of the patient samples to which he had access, but this was not clear to other researchers in China until he wrote up his research in April.

SARS spreads outside China

As long as SARS infections and knowledge of their existence were confined to China, the Chinese government could keep quiet without attracting any outside criticism. If it looked likely to spread, or actually did spread, outside China, however, the situation would be very different. Though Canadian and US public health services had picked up and informed WHO about the new atypical pneumonia or flu in late 2002, spread to Hong Kong and beyond are what triggered significant international concern. The January and February media reports on the Guangzhou outbreak were picked up fairly rapidly in Hong Kong since it is about 180 kilometers from down the Pearl River from Guangzhou (express trains reach Hong Kong from

Guangzhou in 2 hours). Though reincorporated into China in 1997 after more than a century of British rule, Hong Kong enjoys considerable autonomy as a “Special Administrative Region” and the government permits more open press and public discussion of many matters than prevails in other parts of China. In anticipation of seeing the new flu there, Hong Kong public health authorities established a citywide reporting system covering patients admitted to hospital with any sort of flu symptoms on February 14th. Within a week hospitals had reported several ordinary flu cases and two cases of humans ill from H5N1 avian flu. Hong Kong authorities reported the 2 human avian flu cases to WHO on the 20th.

H5N1 and other avian flus were already a concern, and these reports led WHO to activate its Global Pandemic Preparedness Plan. This warns governments of likely cross-border spread of highly infectious diseases and includes procedures for requesting and receiving assistance from WHO or a member state in tracing the spread of a disease, developing control measures, and identifying the infectious bacteria or virus causing it. However, the WHO team sent to China was denied permission to travel to Guangdong Province so was unable to observe the situation directly as it would have liked.

Meanwhile, the “atypical pneumonia” or “atypical influenza” did spread to Hong Kong, and then to Hanoi, Singapore, and Toronto after a Chinese physician who had acquired the infection while treating patients in Guangdong Province came to Hong Kong for a wedding, stayed a few days in the Metropole Hotel, and passed the infection to other guests. The first of these cases was identified in Hanoi on the 26th. The Vietnamese reported it to WHO and requested assistance. WHO sent a team of epidemiologists to help Vietnam trace the source and design measures to prevent further spread. Other cases traceable to Hong Kong identified in Singapore and Toronto, as well as a case in Taiwan, were identified during the first week of March and quickly reported to WHO.

Additional cases, amounting to “clusters” because they involved multiple persons in direct contact with the patients falling ill earlier in the month, were soon reported from Hong Kong, Singapore, and Toronto. WHO staff concluded that there was a high risk of further spread, and issued a global alert to warn all member governments of the existence of a new and highly infectious form of “atypical pneumonia” on March 12th. WHO soon had reports covering 150 positively-identified cases outside China, and on the 17th issued an emergency travel advisory covering Guangdong Province, Hong Kong, Hanoi, Singapore, and Toronto. This advisory first used the designation “Severe Acute Respiratory Syndrome,” provided a case definition facilitating identification of infected persons, and recommended measures to minimize its spread.

Parallel, non-communicating research efforts

By late February 2003 labs inside and outside China were trying to identify the cause of the new flu. In mid-February the Chinese Academy of Military Medical Sciences (AMMS) Institute of Microbiology and Epidemiology secured samples from military hospitals and began the work of tracing the pathogen involved. By the end of February they had identified several coronaviruses in the mix of pathogens that seemed likely to be the source of infection. During the first week of March they found that a serum also present in patient samples inhibited growth of the coronavirus. This was an important finding because presence of a serum inhibiting growth of an infectious virus is the first of several standards used to determine what bacterium or virus is causing an unfamiliar infection. However, they did not report this result because they had only a few samples, and wanted to do more work before openly challenging Hong’s Chlamydia theory. As AMMS microbiologist Dr. Yang Ruifu put it, “We wanted to be very sure. Dr.

Hong Tao is very famous in China. We had to show respect.”² This caution meant that AMMS researchers did not report their findings to the Ministry of Health. Nor, given that prohibitions on disclosure of sensitive information included information about infectious diseases, did they contact the coordinator of WHO’s lab network, German virologist Klaus Stöhr. In discussions of likely causes, the Chinese Health Ministry continued to support Hong’s theory.

Members of WHO’s global network of virology labs - all of which were located outside China – had also started working on identifying the cause. On March 17th WHO accelerated their efforts by opening a secure website for data exchange and daily teleconferencing. Unlike in China, where samples were hard to secure, the labs in the network had access to samples from Hong Kong, Singapore, Hanoi, and Toronto, and used overnight air courier services to share materials. Within 24 hours of the first daily teleconference they agreed that a virus was causing SARS, and by March 24th three of the labs had independently isolated one of the coronaviruses isolated by AMMS researchers a month earlier. The network’s follow-up tests showed revealed the distinctive features of the SARS coronavirus, and this allowed the parallel WHO-organized electronic conferences (known as “global grand rounds”) among physicians to supply recommendations for better treatment of the disease.

Shifting context of discussion in China

On April 3rd, after much international and domestic criticism, the Chinese government announced it was giving top priority to containing SARS outbreaks and pledged to cooperate fully in WHO-coordinated efforts to deal with it. The following day the head of China’s Center for Disease Control apologized for his country’s failure to share information about SARS. A newly-sent WHO epidemiological team was allowed into Guangdong Province on the 9th. However, domestic constraints on information dissemination remained in place. Dr. Jiang Yanyong, retired chief of surgery at a Beijing military hospital, accused the government of hiding the extent of SARS infections in Beijing, and Chinese internet sites carried anonymous postings claiming certain hospitals identified by name had entire wards filled with SARS patients. *Time* magazine in the USA ran an article on China’s “mishandling” of SARS repeating these claims together with allegations that Chinese authorities had shifted patients among hospitals when the WHO team visited to disguise the full extent of the outbreak.³ Even after AMMS researchers reported their findings to the Ministry of Health in early April, the Ministry stuck to the Chlamydia theory, formally rebuked Dr. Bi Shengli for announcing to journalists that his work confirmed the coronavirus theory, and set up a team to control publicity about research on SARS on April 12th.

However, the political climate shifted dramatically as news of progress in the WHO lab network spread. Their results became better known after researchers at the British Columbia Cancer Agency’s Michael Smith Genome Sciences Centre in Vancouver posted the full genome of the suspect coronavirus to the internet on April 13th. That day Premier Wen Jiabao publicly admitted that the SARS outbreak is serious and promised that the government will make full disclosures. Soon the mayor of Beijing admitted SARS had spread to Beijing by March 1st, weeks before its presence had been officially acknowledged. On the 14th the Chinese Health Ministry lifted the ban on transferring samples between labs. AMMS immediately

² Quoted in Martin Enserink, “SARS in China: China’s Missed Chance,” *Science* 301, # 5631 (2003).

³ Hannah Beech. “Unmasking A Crisis -- TIME investigates: As SARS rages in China, officials seem more intent on saving face than saving lives.” *Time* 21 April 2003 (v. 161, no. 16), pp. 62-. Similar charges appeared in “China wakes up,” *The Economist* 24 April 2003 and Jonathan Mirsky, “How the Chinese spread SARS,” *New York Review of Books* 30 April 2003, pp. 42- .

sent samples to the Beijing Genomics Institute, which was able to post genomes of four SARS-causing coronaviruses online on the 16th, the same day that WHO released its official statement naming the coronavirus as the source of SARS infections.

Confirmation of the Chinese government's new approach to SARS took many forms. On the 18th, Communist Party members were again instructed, in stronger terms, to make sure local and provincial officials reported fully. To underline the change of direction, Health Minister Zhang Wenkang and Beijing Mayor Meng Xuenong were dismissed for failure to respond adequately to the SARS epidemic. President Hu paid publicized visits to the AMMS lab and the Beijing Genome Institute and praised their work. The government cancelled all large public events scheduled during the weeklong May 1 International Workers' Day holiday because of SARS fears and established an interagency SARS Control and Prevention unit reporting directly to the State Council to coordinate national efforts against the disease. The national government allocated 2 billion yuan (\$240 million) while provincial and local authorities set aside 5 billion yuan (\$602 million) as contingency funds for dealing with SARS and future public health emergencies.

SARS subsides

After China joined the ranks of countries taking SARS seriously, the number of new cases began to fall. By July 5th 2003 WHO felt confident enough about national control measures to announce that all lines of cross-border transmission of SARS had been broken and there was now no danger of an epidemic. Isolated cases did continue to occur, and were reported promptly.

Effects of the Epidemic

The contrast between Chinese responses on one side and Vietnamese, Singapore, and Canadian responses to the outbreak were instructive. When faced with its first case, the Vietnamese government reported it to WHO and asked for assistance in tracing the source of infection. In mid-March, when faced with 62 cases, it also asked the US Center for Disease Prevention and Control for help in designing treatments. Both the WHO and US CDC teams sent to the country were allowed to visit hospitals treating SARS patients immediately and to get samples from patients. Though clearly aware that there were serious and spreading outbreaks in Guangdong Province by the end of January 2003, the Chinese government did not allow any of the WHO teams allowed into the country to go to Guangdong Province until early April. The first cases of atypical flu emerged in Guangdong Province in November 2002, but it was not until March 2003 that provincial authorities issued guidelines to the population about how to limit its spread. In Vietnam, the government moved to isolate the people, mostly hospital staff, exposed to the disease. Singapore was equally vigorous. The disease was brought in by 3 persons returning from Hong Kong. Though Singapore had 205 cases by the end of March, the disease spread no further because of isolation and quarantine. The first SARS case in Toronto was reported on 5 March 2003, and as the total climbed to 100 by the end of the month, Toronto city and Ontario provincial authorities announced and then used emergency powers to isolate people – including two groups numbering more than 100 each – exposed to a probable source of infection. Inter-hospital transfers, a normal part of Canadian medical practice because of specializations among hospitals, were put under special controls. Two hospitals and a public school determined to be seriously contaminated by SARS viruses were closed for decontamination.

Even without the WHO travel advisories tourism to Hong Kong, Singapore, and Toronto would have fallen as individuals aware of the disease changed plans. The Canadian Tourism Commission, a government

agency, later estimated that cancelled trips cost the Canadian economy almost \$519 million between early March and the end of April. Economists estimated that the main SARS outbreaks in November 2002 through June 2003 cost the global economy more than \$40 in lost work time, treatment costs, and lost tourism revenues. The areas most affected were Hong Kong (experiencing an estimated 2.6% drop in GDP from disease-related costs) China (a 1.05% drop in GDP), and Canada (a 0.15% drop in GDP).

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