THE PRELUDE: EVENTS BEFORE THE SARS EPIDEMIC

Outbreak in Guangdong

3.1 The SARS epidemic in Hong Kong was preceded by a similar epidemic in the neighbouring Guangdong Province. It came to light when news media in Hong Kong began reporting on 10.2.03 an unusual epidemic of fatal pneumonia-like illness in the Province. The reports described the epidemic as spreading rapidly and that people were gripped by fear, with scenes of panic buying of antibiotics and masks.

3.2 Acting on the media reports, the DH in Hong Kong telephoned on 10.2.03 health officials in the Municipal Health and Antiepidemic Station of Guangzhou and the Director General of Department of Health, Guangdong, but was unable to establish contact. A letter enquiring about the reported outbreak was subsequently faxed to both offices. This and follow-up phone calls went unanswered. The Director of Health eventually approached the Ministry of Health in Beijing for assistance.

3.3 On the next day, 11.2.03, the Guangzhou Bureau of Health conducted a press conference at 10:30am, in which officials announced the following –

Rumour mills fuel panic

Propelled by text messages on mobile phones and the internet of a worsening epidemic in the Guangdong Province, public fear intensified in Hong Kong on Tuesday 11.2.03. Scenes of panic buying crossed the boundary and spread to Hong Kong. Supermarkets and grocery stores reported they had run out of white vinegar, following claims that fumigating a room with boiling vinegar could kill germs and help prevent the spread of pneumonia. Local herbalists also reported brisk trade on items of herbal medicine reputed to enhance the body immune system, particularly against pneumonia.

- Guangzhou, capital city of Guangdong Province, had been affected by an infectious atypical pneumonia for more than a month
- There were more than 100 cases, many of whom were healthcare workers
- All patients were under effective treatment and their conditions were under control
- A biological attack or plague was dismissed as rumour
- The public was urged not to panic or believe in rumours, and to avoid unnecessary worry.

Forewarned is forearmed: a critical consideration

The first cases of what came to be called SARS probably occurred in Guangdong Province in November 2002. The Committee learnt that on 23.1.03 the relevant health authority in the Province produced an expert investigation report on the cases of atypical pneumonia. The report was apparently circulated to a limited audience. The Hong Kong authority was not a recipient of the report, neither was WHO.

The report provided an initial consensus amongst the experts on the atypical pneumonia cases, covering the following –

- Diagnosis: Atypical pneumonia of unknown aetiology, probably viral in origin
- Epidemiological characteristics: Age and sex distribution described, with epidemic curve plotted. Clustering in place and persons also noted. Possibly transmitted by respiratory droplets, with a certain degree of infectivity
- Clinical features: Incubation period about 4 days, with a range of 1–11 days. Symptoms comprised fever, headache, arthralgia, myalgia, malaise and non-productive cough. No elevated white cell count, a few had lymphopenia. Chest x-ray showed varying degrees of patchy shadows
- Treatment principles: A range of options were described for reference, including use of corticosteroids, antiviral therapy, Chinese medicine, etc
- Preventive measures: Isolation of patients in single rooms; environmental decontamination; staff protection (wearing of masks and hands washing); prompt notification and investigation, and measures to prevent spread
- Suggestions: Health Department in the Province should advise all provincial areas of the need to monitor the situation closely. All new cases should be notified and investigated promptly. Emphasis was made of the importance of intensive care facilities and of the need to enhance the strength and management of these services.

The expert report therefore contained information of significant value to decision makers for disease control and prevention. Owing to the limited circulation of the report, others were not forewarned, and therefore forearmed.

3.4 On the same day, 11.2.03, WHO announced that it had received reports from the Chinese Ministry of Health in Beijing "of an epidemic of acute respiratory syndrome with 300 cases and 5 deaths in the Guangdong Province". It further reported that a team from the Ministry of Health was working with health officials in the Province to investigate the epidemic and collect samples for laboratory analysis.

Update on Guangdong epidemic

On 14.2.03, WHO provided further information on the Guangdong epidemic in its Weekly Epidemiological Record. It stated that cases had been reported from 6 municipalities in Guangdong Province: Foshan, Heyuan, Guangzhou, Jiangmen, Shenzhen and Zhongshan. Without elaborating, it went on to say, "todate, virus isolation for influenza has been negative".

On 18.2.03, the Chinese Centre for Disease Control and Prevention in Beijing reported that *Chlamydia Pneumoniae* had been identified as the probable cause of the epidemic in Guangdong Province.

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Response from Hong Kong

3.5 In Hong Kong, two key events happened on 11.2.03. First, in the late afternoon, the Director of Health, with the information from Guangzhou and enquiry results in Hong Kong, conducted a media briefing. She reassured the community that Hong Kong had not identified any unusual pattern of influenza-like illness and respiratory tract infection, including pneumonia, but that DH would be monitoring the situation closely because of the pneumonia cases in Guangdong Province. She also reminded the public to take steps to prevent influenza during its peak season between January and March.

3.6 Second. HA head office established a working group to step up surveillance of cases of pneumonia in public hospitals. The purpose was to provide early warning to the system. As pneumonia cases in HA hospitals could (based on historical data) reach up to 1,400 cases per month at that time of the year, the working group decided to focus on the more severe type of pneumonia, namely those patients with pneumonia who required assisted ventilation, or treatment in intensive care / high dependency care units. Hence, the group was named the HA Working Group on Severe Community-Acquired Pneumonia. Membership comprised experts in microbiology, internal medicine and intensive care medicine. DH was represented by a senior consultant in community medicine (communicable disease). A set of procedures was agreed by the Working Group for the HA to make notification of severe community-acquired pneumonia cases to DH for epidemiological investigation and action. Private hospitals were

subsequently requested by DH on 13.2.03 to make similar notification of severe communityacquired pneumonia cases upon admission.

Surveillance Findings: Avian Flu Cases

3.7 On 13.2.03, Princess Margaret Hospital of HA notified DH of a case of severe communityacquired pneumonia involving a 33-year-old man. He had a history of travel to Fujian, China with his wife, two young daughters, and son (aged 9). The youngest daughter developed pneumonia on 28.1.03 in Fujian, was admitted to a local hospital but eventually died on 4.2.03 in Fujian. The family returned to Hong Kong and three members were subsequently admitted to hospital –

- 33-year-old man: admitted on 11.2.03, eventually died on 17.2.03
- 9-year-old boy: admitted on 12.2.03, eventually recovered
- The wife: admitted on 13.2.03, eventually recovered.

On 19.2.03, the Government Virus Unit of DH confirmed Avian Flu (H5N1) infection in the 9-year-old boy, and a day later the same infection was confirmed in the 33-year-old man.

3.8 Apart from initiating a series of public health measures locally to prevent a resurgence of Avian Flu (H5N1) infection in the human population in Hong Kong, DH also alerted WHO and the Ministry of Health in Beijing. It was this that led WHO to issue a global alert on Avian Flu on the same day.

Past trend of pneumonia cases

The HA Working Group on Severe Community-Acquired Pneumonia undertook a study to ascertain past trends of cases of pneumonia in Hong Kong. The results are illustrated graphically below –



The conclusion was that there was no unusual increase in the number of pneumonia cases in Hong Kong during this period.

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Surveillance Findings: Other Severe Community-Acquired Pneumonia Cases

3.9 On 27.2.03, the HA Working Group on Severe Community-Acquired Pneumonia convened a meeting to review all reported cases in February. A total of 39 severe community-acquired pneumonia cases were identified as at 26.2.03. Key findings are summarised below –

Figure 3.3 Summary findings of severe community-acquired pneumonia cases 1-26 February 2003

| Male:Female ratio | 1.4:1 | |
|--|-------|--------|
| Age > 50 years old | 72% | (n=28) |
| Recent travel to China | 36% | (n=14) |
| Outcome as at 26.2.03 | | |
| o died | 31% | (n=12) |
| discharged | 13% | (n=5) |
| Laboratory results - causative agents | | |
| Adenovirus | 5.1% | (n=2) |
| Avian Flu (H5N1)* | 2.6% | (n=1) |
| Bacterial | 5.1% | (n=2) |
| o Influenza A | 5.1% | (n=2) |
| Influenza B | 7.7% | (n=3) |
| o Parainfluenza | 5.1% | (n=2) |
| Psittacosis | 5.1% | (n=2) |
| Rickettsia | 2.6% | (n=1) |
| Unknown | 61.5% | (n=24) |
| Total | 100% | (n=39) |

* Only the 33-year-old man with Avian Flu was included as severe community-acquired pneumonia. His 9-year-old boy did not have severe pneumonia.

The shadow of Avian Flu (H5N1) virus

The first outbreak of Avian Flu (H5N1) virus in humans was reported in 1997 in Hong Kong. The infection affected 18 individuals, 6 of whom died. The outbreak was eventually halted by a territory-wide slaughter of more than 1.5 million chickens. Studies revealed that the main mode of viral transmission was from bird to man; man-to-man transmission was rather inefficient. However, genetic mutation of the H5N1 virus in future outbreak, altering its transmission efficiency from manto-man, could not be ruled out.

Two months before the Guangdong outbreak became known, Hong Kong announced on 10.12.02 that a number of dead waterfowl in Penfold Park in Shatin were found to have been infected with the H5N1 virus, necessitating park closure for a month. About a fortnight later, a similar announcement was made about the dead waterfowl in Kowloon Park.

Inevitably this was linked to the two human cases of Avian Flu infection in February 2003. There was also considerable speculation at the time that H5N1 virus was the prime suspect for the Guangdong outbreak. Unfortunately, this proved a false trail to many investigators, both locally and internationally.

3.10 The most eye-catching result was that no causative agent could be detected in 61.5% of the severe community-acquired pneumonia cases. This finding was consistent with past experience that approximately two-third of atypical pneumonia cases in Hong Kong were of unknown aetiology.

The Case of the Guangzhou Professor

3.11 Amongst the severe communityacquired pneumonia cases of unknown aetiology in February was a professor from Guangzhou, China. The professor, *AA*, was admitted to HA's Kwong Wah Hospital with severe pneumonia on Saturday 22.2.03, a day after arriving in Hong Kong to attend the wedding of his relative. He died on 4.3.03 in the hospital. Subsequent epidemiological

The index patient's clinical course

A medical doctor from a Guangzhou hospital, *AA* walked in to attend the accident and emergency department of Kwong Wah Hospital on 22.2.03. He was triaged as an "urgent" case. He gave a history of having been in contact with patients suspected to have atypical pneumonia during 11-13 February. He developed flu-like symptoms on 15.2.03. He self-treated with antibiotics and improved. He claimed to have fully recovered before making the trip to Hong Kong. There was no evidence in the case notes that he indicated to staff that he was infectious.

His presenting symptoms at the accident and emergency department were that of fever and shortness of breath. The diagnosis was that of severe pneumonia. He was admitted directly to the intensive care unit, where he was intubated because of his rapidly deteriorating clinical condition. The patient was jointly managed by specialist physicians and clinical microbiologists from Kwong Wah Hospital and Queen Mary Hospital, the latter also a teaching hospital of the University of Hong Kong. *AA* did not respond to active treatment, and finally succumbed on 4.3.03. He was only confirmed to have SARS in mid-April, after the diagnostic test became available.

Management of severe community-acquired pneumonia

The HA Working Group on Severe Community-Acquired Pneumonia held a total of 7 meetings between 11 February and 18 March 2003. On 21.2.03, the Working Group issued a document on the management of severe Community-Acquired Pneumonia in the form of "Frequently Asked Questions" to all HA hospitals through the hospitals' infection control officers. The document, also posted on the HA website accessible by HA staff, covered the following topics –

- case definition and background incidence of severe communityacquired pneumonia
- procedures of notification
- arrangement for laboratory testing
- infection control measures with emphasis on droplet precautions: cohorting of patients; distance of 3 feet; gloves and gowns; masks; hands washing and disinfection of the environment and equipment
- use of antiviral drugs.

investigations in mid-March identified AA as the index case of the outbreak in *Hotel M* in Hong Kong where he stayed for only one night. *Hotel M* was later identified as the source of spread internationally through infected hotel guests and visitors who unknowingly carried the SARS infection to other countries.

Hospital Infection Control

3.12 After being seen by a medical officer, *AA* was re-assessed by a consultant in the accident and emergency department. Upon admission to the intensive care unit, the patient was placed in an isolation room. All staff caring for him wore N95 masks, cotton gowns and implemented droplet precaution and universal precaution measures. This was consistent with the advice promulgated on 21.2.03 by the HA Working Group on Severe Community-Acquired Pneumonia.

3.13 The infection control measures implemented by Kwong Wah Hospital were evidently effective in protecting staff from infection. Epidemiological investigation revealed that only one healthcare worker, a registered nurse in the accident and emergency department, was probably infected by AA during the episode. Although she had not had any direct contact with AA, she had nursed a patient in the cubicle next to his while he was at the accident and emergency department. The registered nurse was admitted to hospital on 28.2.03, recovered well and was discharged on 18.3.03. She was subsequently confirmed as a SARS case.

Case investigation of professor AA : chronology

On 21.2.03, *AA* (aged 64) and his wife arrived in Hong Kong and checked into room 911 of *Hotel M*, where they stayed for one night. They spent the afternoon shopping with the brother-in-law of professor *AA*, also husband of sister *CC*.

On 22.2.03, *AA*'s son and daughter arrived in Hong Kong from Guangzhou. *AA* was admitted to Kwong Wah Hospital. His wife checked out of *Hotel M*, and moved to stay at the home of sister *CC* with her son and daughter.

On 23.2.03, *AA*'s son, asymptomatic throughout, returned to Guangzhou.

On 24.2.03, *AA*'s wife reported at the time of interview that she had developed fever (temperature: 38.4°C). She was advised to seek treatment at the accident and emergency department. However, she indicated that she wanted to receive treatment in Guangzhou. Later that evening, she returned to Guangzhou with her daughter, who was asymptomatic at the time.

Case Investigation and Contact Tracing

3.14 Upon receipt of the severe community-acquired pneumonia notification on 24.2.03, DH's Kowloon Regional Office sent a public health nurse to undertake case investigation and contact tracing. As *AA* was already intubated at the time, no direct interview with the patient was made. The nurse, however, made copies of his clinical notes. She also interviewed by telephone the patient's wife, daughter and sister *CC*. A significant negative contact history was that *AA* had not been

exposed to any poultry in the two weeks prior to the onset of symptoms. Neither did he keep any chickens, ducks or birds, nor go to any market where live poultry was kept.

3.15 The case investigation revealed that there were five family contacts: the patient's wife, daughter and son, all residents of Guangzhou, as well as his sister *CC* and her husband, both residents of Hong Kong. All family contacts were advised to watch out for symptoms of respiratory tract infection, and personal hygiene was emphasised.

Further Development – Brother-in-law of AA

3.16 On 28.2.03, the brother-in-law (aged 53) of professor *AA*, also husband of sister *CC*, was admitted to the medical ward of Kwong Wah Hospital via the accident and emergency

department. Clinical presentation features included that of high fever and shortness of breath. Chest x-ray showed pneumonia features. His clinical condition ran a downhill course, and he was intubated and transferred to the intensive care unit on 4.3.03. He succumbed two weeks later on 19.3.03.

3.17 Subsequent epidemiological investigation by DH's Kowloon Regional Office revealed that the brother-in-law of *AA* was the probable infection source of a healthcare assistant who worked in the same ward where the patient was hospitalised. This was the only person, also the only hospital staff, infected by the patient. The healthcare assistant was admitted to the medical ward of Kwong Wah Hospital on 7.3.03. She was intubated and transferred to the intensive care unit on 12.3.03. She eventually recovered and was discharged on 27.3.03.



Ground-breaking discovery

The 53-year-old brother-in-law of professor *AA*, also husband of sister *CC*, had a lung biopsy (removal of lung tissue) while in Kwong Wah Hospital. It was from this specimen that the microbiology team of the University of Hong Kong made their ground-breaking scientific discovery: the identification of a novel coronavirus as the causative agent of the SARS infection on 22.3.03. The team was the first in the world to grow the virus in isolation.



SARS coronavirus

The discovery was made at an unprecedented pace, a week after the term SARS was coined by WHO. It was the first important victory in the human battle against SARS. It paved the way for the development of a rapid diagnostic test and laboratory experimentation with therapeutic regimens. It also furthered human understanding of the virus through the work on genome sequencing and molecular studies.

Further Development – Sister CC

3.18 On 1.3.03, sister *CC* attended the accident and emergency department and was admitted to the medical ward of Kwong Wah Hospital. Diagnosed to have chest infection, she was stable clinically. She was discharged on 6.3.03 with antibiotics. She was never a case of SARS.

The Case from Union Hospital

3.19 On 22.2.03, the day the Guangzhou professor, AA, was admitted to Kwong Wah Hospital, another patient with severe community-acquired pneumonia was transferred from the private Union Hospital in Shatin to Prince of Wales Hospital. The patient, a 49-year-old female, went to Henan, Guangzhou to visit her mother on 31.1.03. While there, she developed fever, chills and cough with sputum. She decided to come to Hong Kong on 17.2.03 and was admitted to Union Hospital on the same day. Her chest x-ray showed pneumonia features. She was nursed initially in a twin room in the medical ward, but moved to a single isolation room with negative pressure two days later when she became more short of breath. The nursing staff wore surgical masks only, and nebuliser treatment was prescribed to relieve her shortness of breath. However, her clinical condition continued to deteriorate and she developed respiratory failure. She was transferred and admitted directly to the intensive care unit of Prince of Wales Hospital on 22.2.03.

3.20 The patient made progressive improvement in Prince of Wales Hospital. Ten days after admission, on 4.3.03, she was well enough to discharge herself from Prince of Wales Hospital against medical advice. She was last reviewed in Union Hospital on 8.3.03. The patient was diagnosed to have SARS in April 2003 using paired serum samples.

Case investigation and contact tracing

3.21 Upon receipt of the severe community-acquired pneumonia notification from HA on 22.2.03, DH's New Territories East Regional Office carried out epidemiological investigation and contact tracing. Four relatives, who joined the patient in Guangzhou, were identified as contacts and were placed under medical surveillance. Only one, a 42-year-old female, was eventually found to have developed SARS.

3.22 In addition, a nurse who took care of the patient in Union Hospital developed symptom of malaise on 22.2.03, followed by myalgia, cough, fever and chills two days later. She was admitted to Princess Margaret Hospital on 27.2.03. She made a full recovery and was discharged on 5.3.03. Using paired serum samples, she was later diagnosed to have SARS in April 2003. 3.23 A second nurse from Union Hospital, also with a history of looking after a patient with atypical pneumonia, was admitted to Princess Margaret Hospital around the same time. However, she presented with gastrointestinal symptoms, had a normal chest x-ray, and was clinically not a pneumonia case. She was discharged on 5.3.03, and was never diagnosed as having SARS.

3.24 For Prince of Wales Hospital, infection control measures including droplet precautions were implemented because the patient was a severe community-acquired pneumonia case on admission. As a consequence, no healthcare staff became infected during this episode of care of what eventually turned out to be a SARS patient.

The Case Transferred from Hanoi

3.25 On Wednesday 5.3.03, DH was informed by WHO that *DD* would be transferred from the French Hospital in Hanoi, Vietnam for further management. Investigation at the time suggested the patient was suffering from Influenza B, complicated by Adult Respiratory Distress Syndrome. DH contacted HA head office and Princess Margaret Hospital to discuss the arrangement for receiving the patient. On 6.3.03, *DD* was transferred to Hong Kong via International SOS, with an accompanying message that there was an outbreak of unknown infection amongst healthcare workers who had looked after him in Hanoi. Their symptoms were that of fever, malaise and headache. Princess Margaret Hospital therefore arranged for *DD* to be admitted directly to its intensive care unit. Despite active treatment, *DD*'s condition continued to deteriorate and he succumbed on 13.3.03. *DD* was subsequently identified as a contact of professor *AA* in *Hotel M*, and went on to become the source of the SARS outbreak in Hanoi.

Hospital Infection Control

3.26 During the period of *DD*'s treatment, Princess Margaret Hospital implemented strict infection control measures. The patient was admitted to a single bed cubicle of the intensive care unit, with negative pressure facility. All healthcare staff working in the cubicle were required to put on surgical/N95 masks, gloves and eye/face shields. Universal precaution measures were also introduced. In addition, the number of staff taking care of the patient was kept to a minimum.

3.27 The result was that no healthcare workers in Princess Margaret Hospital were infected during this episode.

Case Investigation and Contact Tracing

3.28 As DD was too ill to be interviewed. DH tried to obtain information from DD's wife on 7.3.03, but she was not ready to be interviewed. She was approached again the next day. However, she was unable to provide full details of her husband's travel history. Eventually, the picture put together was that DD travelled from the USA to Shanghai, China in mid-January 2003. He came to Hong Kong in early February, then flew back to Shanghai before returning to Hong Kong again. He had already developed flu-like symptoms before travelling to Hanoi on 25.2.03. On the next day, 26.2.03, he was admitted to the French Hospital in Hanoi. His condition deteriorated rapidly after admission, requiring mechanical ventilation since 2.3.03.

3.29 DH's investigation identified *DD*'s wife and four relatives as contacts of the case, two of whom were living in Shanghai. *DD*'s wife and the two relatives in Hong Kong were placed under medical surveillance with health advice on personal hygiene and measures to prevent respiratory tract infection. All three remained asymptomatic at the end of the surveillance period.