

SARS Epidemic: SARS Outbreaks in Inner-land of China

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Overview

Severe Acute Respiratory Syndrome (SARS), also known in China as Infectious Atypical Pneumonia (IAP), is the 21st century's first infectious disease to severely threaten the public health of the human population (WHO, 2003a). A respiratory transmitted disease caused by a virus, SARS is highly infectious and is rapidly transmitted, inflicting severe complications and a high case fatality rate. The first round of the SARS pandemic led to global panic and billions of dollars economic losses, for due to lack of effective SARS drugs, governments throughout the world had to take rigid steps toward prevention and treatment of the disease.

The SARS epidemic began with the first reported case in Guangzhou, China (Wang et al., 2004), on 16 November 2002. Eight months later, the disease had spread to 26 countries in Asia, America, and Europe, resulting in a reported 8,096 cases and 774 deaths (WHO, 2004). In this global epidemic, China, with 7,429 cases and 685 deaths, accounted for 91.8% of the world's reported cases and 88.5% of the deaths (5,327 SARS cases and 349 deaths were reported in 24 provinces in the inner-land of China – mostly in Beijing and Guangzhou, which, with a combined 4,033 cases, accounted for 75.7% of the total number in the inner-land of China; Hong Kong had 1,755 cases, 299 deaths; Taiwan: 346 cases, 37 deaths; Macao: 1 case, 0 deaths) (He et al., 2003; Peng et al., 2003; Yang et al., 2003; Leadership Group of SARS Prevention and Control in Beijing, 2003; Chinese Center for Disease Control and Prevention, 2003).

The second round of the SARS epidemic broke out locally in various areas of Guangdong province where, from December 2003 until February 2004, four laboratory-confirmed cases were reported but did not result in death (Liang et al., 2004). Singapore (WHO, 2003c), Taiwan (WHO, 2003d), and inner-land of China (Ministry of Health, People's Republic of China, 2004) each had one laboratory infection (total three lab infection events). The laboratory infections from inner-land of China resulted in the third round of the SARS outbreak, infecting nine patients and resulting in one death. These outbreaks, having forced the realization that the prevention of laboratory infections is an important component to avoid a SARS

outbreak, soon came under effective control after firm measures of prevention and treatment were taken.

During the first round of the SARS pandemic, Chinese scientists excluded many common causes of the disease and focused on the exploration of a “new pathogen.” The WHO established a global laboratory network on 17 March 2003, and scientists from China and other nations began to work together on finding the causative pathogen of SARS. They conducted research through approaches of viral morphology, molecular biology, serology, and animal studies in 13 network laboratories throughout nine countries (five were in China). On April 16th, the WHO declared that a new coronavirus, dubbed “SARS-CoV,” was the pathogen causing SARS (WHO, 2003b). Although epidemiology and experimental results have shown that SARS-CoV comes from animals, further research is necessary to determine the major animal reservoir from which the pathogen derives.

Research has made it clear that SARS is an acute infectious pneumonia caused by SARS-CoV (Drosten et al., 2003; Hong et al., 2003; Zhu et al., 2003; Rota et al., 2003). SARS cases have tended to cluster by family and hospital, mainly transmitted by close contact via droplet transmission. Clinically manifested as fever, pulmonary progressive inflammation, and dyspnea, SARS is characterized by symptomatic infection and there is no transmissibility within the incubation period of 1–12 days (Ministry of Health, People’s Republic of China, 2005). Studies show that bodily fluids, such as blood, saliva, and feces, as well as pathological anatomical tissues of patients, contain SARS viruses (Lau et al., 2005).

There are currently no effective therapeutic drugs for SARS. Epidemiological data showing that reinfections have not occurred in recovered patients reveal that SARS patients can have strong immunity after recovery, thus suggesting that an effective vaccine, which is still in clinical study, would be able to prevent SARS infection (Weidong et al., 2006). There has also been significant progress in developing SARS diagnostic reagents. Combining the application of approved reagents, including the detection of viral nucleic acid, protein antigen, and serum viral antibody, the SARS infection could be detected in its early stages (i.e., within approximately 1 week of infection) (Ministry of Health, People’s Republic of China, 2005; Che et al., 2004). Until effective vaccine and therapeutic drug research have reached fruition, the comprehensive prevention and treatment remain the basic principle to control the SARS infection.

Epidemiological Features

Current Status of Epidemic

Since 2002, SARS has broken out three times: the first epidemic spread worldwide from November 2002 to July 2003 (WHO, 2004); the second spread locally in Guangdong province between December 2003 and February 2004 (Liang et al.,

2004); and the third developed on a small scale from laboratory infection in the inner-land of China from March to April 2004 (Ministry of Health, People's Republic of China, 2004). Furthermore, two other laboratory infections occurred in Singapore (WHO, 2003c) and Taiwan (WHO, 2003d), although they did not result in an epidemic.

Features of the First Epidemic

Geographic Distribution

The first case of SARS was discovered in Fushan city, Guangdong province, with onset date of 16 November 2002 (Wang et al., 2004). The last case occurred in Taiwan on 15 June 2003 (WHO, 2004). After starting in Guangdong, the epidemic in China then spread to Shanxi, Xichuan, and Beijing, followed by further expansion to other regions of China. Altogether, in accordance with the outbreak and transmission, China can be divided into the following four regional categories (He et al., 2003; Peng et al., 2003; Yang et al., 2003; Leadership Group of SARS Prevention and Control in Beijing 2003; Chinese Center for Disease Control and Prevention, 2003):

- Regions with a localized epidemic (Guangdong)
- Regions where an introduced case induced a localized epidemic (Beijing, Inner Mongolia, Shanxi, Hebei, Tianjin, et al.)
- Regions where a case was introduced but did not lead to a localized epidemic (Shanghai, Shandong, Hunan, Liaoning, Ningxia, et al.)
- Regions without reported cases (Hainan, Yunnan, Guizhou, Qinghai, Tibet, Xinjiang, Hei Longjiang et al.)

Time Distribution

SARS had caused worldwide epidemic as SARS cases were reported in China (including Hong Kong), Vietnam, Singapore, and Canada from November 2002 to February 2003. The disease was effectively under control by June 2003. During these 7 months, the period from mid-March to mid-May of 2003 witnessed the highest number of reported cases.

The localized outbreak in China's Guangdong province lasted from January to February of 2003, and then rapidly expanded to other regions in China until the last case of disease was reported on June 11. The incidence of SARS in Guangdong province peaked in February, while in other regions it peaked between early April and mid-May, reflecting the earlier appearance of cases in Guangdong. Although primary cases appeared in the cities of Fushan and Heyuan in Guangdong province and in Hechi city in Guangxi province, there is no evidence of intertransmission of these primary cases among the different cities (He et al.,

2003; Peng et al., 2003; Yang et al., 2003; Leadership Group of SARS Prevention and Control in Beijing, 2003; Chinese Center for Disease Control and Prevention, 2003).

Population Distribution

Youths and those in the prime age group make up the majority of SARS patients. According to data collected from 5,327 SARS cases in China, the main age group for onset infection ranges from 20 to 60 years old, accounting for 85% of the total cases. While those aged 20–29 years account for 30% of the total number of cases, those under the age of 15 show a low incidence of SARS; children under the age of 9 show an even lower incidence (He et al., 2003; Peng et al., 2003; Yang et al., 2003; Leadership Group of SARS Prevention and Control in Beijing, Epidemiological features of severe acute respiratory syndrome in Beijing, 2003; Chinese Center for Disease Control and Prevention, 2003; Liang et al., 2004).

No significant differences have been found between men and women with regards to SARS infection. A comparison of incidence rates in different professions shows that, as one might assume, medical personnel have a higher incidence of SARS. Up to 20% of SARS cases were in medical staff (in some provinces, up to 50%); the number of cases in medical staff declined in the later stages of the epidemic, largely due to effective preventive measures of medical staffs. Students made up 8.6% of the total number of cases; however, the cases were sporadic, with no cases occurring as school clusters. A study in Guangdong found SARS cases among people, such as restaurant cooks and meat animal's vendors or purchasers, who had no history of contact with SARS patients but had been in contact with wild animals (He et al., 2003; Peng et al., 2003; Yang et al., 2003; Leadership Group of SARS Prevention and Control in Beijing, Epidemiological features of severe acute respiratory syndrome in Beijing, 2003; Chinese Center for Disease Control and Prevention, 2003).

Distribution Features of Death Cases

The WHO reported that in the epidemic of 2002–2003, the case-fatality rate of SARS ranged from 0%–50%, with different age groups with different fatality rates. The case-fatality rate of those under the age of 24 is lower than 1%; that of those between 24 and 44 years-old is 6%; 45–66 years-old is 15%; 65 years and older is over 50% (WHO, 2004). In China, the case-fatality rate of SARS is 6.6% (He et al., 2003; Peng et al., 2003; Yang et al., 2003; Leadership Group of SARS Prevention and Control in Beijing, 2003; Chinese Center for Disease Control and Prevention, 2003) and the death rate of SARS in whole population is 0.024/100,000; elderly patients account for a higher proportion of SARS fatalities (approximately 44% of all SARS deaths), with the fatality rate of patients who are above 60 years of age being 11%–14%. Generally, the fatality rate increases with age. SARS

patients who also have other diseases such as high blood pressure, diabetes, heart disease, emphysema, or tumors have a high fatality rate.

Features of the Second Outbreak

From 5 January to 2 February of 2004, Guangzhou city in Guangdong province reported four mild SARS cases with confirmed laboratory tests (Liang et al., 2004). The four patients did not experience severe clinical conditions and no clear sources of infection were found. They did not infect others and had no history of travel or activities in the wild, although two of them may have had contact history with wild animals.

Features of the Third Outbreak

From 25 March to 17 April of 2004, Anhui and Beijing reported a total of nine cases, which were later confirmed to have derived from research laboratories conducting SARS research (Ministry of Health, People's Republic of China, 2004). Anhui reported two cases and one death; Beijing reported seven cases, none of which resulted in death. Two of the nine cases resulted from direct contact with the infectious virus in the research laboratory, while the remaining seven were secondary infections of one laboratory infection.

Other Infections

Since the WHO declared on 5 July 2003 that the first global SARS epidemic had ended, two other research laboratory-related infections later occurred in addition to the aforementioned outbreaks. Both of these later infections (one in Singapore (WHO, 2003c) on 8 September 2003; the other in Taiwan (WHO, 2003d) on 17 December 2003) were confirmed to have resulted from laboratory accidents; neither of these infections brought about a SARS epidemic.

Source of Infection, Routes of Transmission, Population Susceptibility

Sources of Infection

SARS patients are the main source of infection, because the disease is communicable as soon as patients exhibit symptoms of the disease, growing more infectious as the disease manifests itself through apparent symptoms such as fever and coughing, and even more so when patients develop acute respiratory distress syndrome (ARDS). The disease likewise becomes less infectious as fever declines (Ministry of Health, People's Republic of China, 2005).

Although SARS patients compose the main source of infection, patients in the incubation period (1–12 days after the time of infection) and patients released from hospitals have not been found to be infectious to others (Ministry of Health, People's Republic of China, 2005).

SARS-CoV infection is characterized by symptomatic infection; however, mild cases, such as the cases in the second outbreak, and nonsymptomatic infection may exist. For instance, people who breed or sell wild animals in Guangdong province show a significant number of SARS-CoV infection with no apparent clinical symptoms. These subclinical cases have not been found to be infectious (Ministry of Health, People's Republic of China, 2005).

Polymerase chain reactions (PCR) or serological tests of various animal species, such as the civet cat, wild pig, rabbit, snake, badger, bat, and jungle fowl, have shown positive results, which suggest that the SARS virus may come from animals (Chinese SARS Molecular Epidemiology Consortium, 2004; Song et al., 2005; Kan et al., 2005; Li et al., 2005); however, further evidence is needed to confirm this hypothesis.

In addition to SARS patients and various animal species, research institutes that conduct SARS research, testing, and production of diagnostic reagents and vaccines may become sources of SARS infection under certain circumstances, depending on these institutes' safety regulations, management, staff quality, health monitoring, and whether they have designated health care centers (WHO, 2003c,d; Ministry of Health, People's Republic of China, 2004).

Routes of Transmission

The major and most important route of SARS transmission is respiratory droplet transmission through close contact (short distance transmission) with a patient (Yang et al., 2003; Ministry of Health, People's Republic of China, 2005). The recipient then inhales droplets containing viral particles coughed out by the patient. However, transmission via aerosol without close contact is also reported as the route of SARS transmission, which led to the outbreaks in hospitals in severely-infected areas and in certain communities. Direct contact such as hand-to-hand contact is another important route of SARS transmission. There have also been reports of the viral isolation from bodily fluid – like teardrops. There is no epidemiological proof for blood, sex, and vertical transmissions, but the possibility of intestinal transmission can not be excluded.

Population Susceptibility

Although the general population is susceptible to SARS infection, infection rates differ among population subgroups. For reasons yet unknown, children have a lower infection rate than the rest of the population. Those in close contact with SARS symptomatic patients and those without effective protection in a SARS treatment environment (i.e., medical staff, patients' relatives and friends) form a

high-risk population, as do SARS laboratory researchers and those who work with wild animals such as civet cats.

It has been proven that the human body can generate a protective antibody after SARS infection, and maintain the antibody at a high level for 2 years after the onset of the disease (Li et al., 2006). Consequently, no SARS patients have been reported to become reinfected after recovery. These data indicate the possibility of generating an effective immunity after infection with SARS; however, since SARS is chiefly a symptomatic infection, those who have not yet been infected are still susceptible after a SARS epidemic.

Clinical Manifestations, Diagnostic Criteria, and Treatment Principles of SARS

Major Clinical Manifestations of SARS (Ministry of Health, People's Republic of China, 2005)

Major clinical manifestations of SARS include fever, progressive pulmonary inflammation, and dyspnea. The disease may be classified as occurring in five successive periods.

1. Incubation period: The first 1–12 days (usually 1–7 days) after infection; not infectious to others in this period.
2. Initial period: The first 1–3 days of the onset of the disease. Most patients show clinical manifestations such as fever, a nonreceding body temperature, and increased pulse rate. The disease progresses very quickly in some patients, manifesting itself in dry coughing, short breaths or obstruction of breathing, and abnormal chest X-rays.

Fever is the first symptom, with body temperature reaching over 38°C. More than half of the patient population exhibit other symptoms such as headache, joint and muscular soreness and debilitation, dry coughing, chest pain, and diarrhea. Few cases have symptoms of upper respiratory catarrh with unclear pulmonary signs, and moist rale can be heard in some of them.

3. Progression period: The period usually occurring between the 4th and 7th days of the course of disease, during which the disease further progresses in most patients. Fever and toxic symptoms of infection continue; pulmonary affliction, usually manifested as a progressive development of chest distress, tachypnea, and dyspnea, worsens – particularly after physical movement; saturation of blood oxygen declines; and chest X-rays show more abnormalities.
4. Acme period: The period between the 8th and 14th days after the onset of disease. Patients continue showing the aforementioned symptoms, although body temperatures further reach unusual levels. Most patients keep this high temperature if they are not hospitalized; however, even with hospitalization,

some severe patients are unable to return to a normal body temperature. Patients show acute lung injury and even ARDS, with chest X-rays demonstrating leafy pulmonary infiltration or severe hypoxemia. Some show impairment of multi-organs, with severe cases showing multi-organ functional defects.

5. Convalescence period: The period between the 15th and 28th days after the onset of disease. Body temperature gradually declines, clinical manifestations lessen, pulmonary pathological damages begin to be absorbed, fever and toxic symptoms disappear prior to other symptoms, followed by a gradual decline and ultimate disappearance of such anoxia symptoms as chest distress, shortness of breath, and breath obstruction; saturation of blood oxygen of lymphocytes, and X-rays of the chest return to normal. Most patients can meet the standards of hospital release after 2 weeks of recovery; however, absorption of lung shadow (lung damage shown in X-ray) requires further recovery time. A few severe cases may retain restrictive ventilatory disorder and declining pulmonary diffusion for a short period, but most usually convalesce within 2–3 months after leaving the hospital.

Diagnostic Criteria of SARS (Ministry of Health, People's Republic of China, 2005)

Diagnosis of SARS

Suspected Cases

Those who have clinical manifestation of the disease and pathological changes in their pulmonary X-rays but show no history of being in close contact with SARS patients or other epidemiological evidence can be regarded as suspected cases. For them, further epidemiological investigation and etiological and serological tests are needed. Those who are suspected of being infected based on epidemiological evidence and certain clinical manifestations, but without pathological changes in their pulmonary X-rays, are also considered suspected cases.

Clinically Diagnosed Cases

If the possible diagnoses of other diseases have been excluded, clinical diagnoses of SARS may be given to those with SARS epidemiological connection, related clinical manifestations, and pathological changes in pulmonary X-rays.

Confirmed Diagnosis

On the basis of suspected and clinical diagnosis, confirmed SARS diagnosis may be given if any of the following conditions is met:

- SARS-CoV RNA testing of secretion or serum is positive
- SARS-CoV-specific nucleocapsid antigen testing of serum (or blood plasma) is positive
- Anti-SARS-CoV antibody conversion test is positive
- Antibody titer in recovery period is four times higher than that in early period.

Laboratory Diagnosis

The available laboratory detection techniques and studies of the etiological and serological features of SARS patients now make it possible to conduct tests at different periods in the course of the SARS disease. When supplemented with clinical manifestations, these tests can positively diagnose SARS.

Early Diagnosis

Within 5 days of the onset of disease, serum and a nasopharynx swab of a patient need to be collected to test the nucleocapsid protein (protein N) and nucleate of SARS virus in serum, and then the viral nucleates in patients' nasopharynx to assist the serum test. If the serum protein N and nucleates in the serum or nasopharynx are positive, the patient may be diagnosed with SARS.

Routinely taking SARS-CoV protein N testing with serum sample of causative-agent uncleared pneumonia patients in early period may enable early detection of SARS in this particular group.

Metaphase Diagnosis

Conducted 6–10 days after the onset of disease. Patients' nasopharynx swab, feces, anal swab, blood, and urine are collected and tested first for SARS viral nucleates. Meanwhile, a patient's serum is tested for viral nucleocapsid protein, nucleic acid, and antibodies of IgG and IgM as supporting proof. Positive test results or antibody conversion warrant the diagnosis of SARS.

Late Stage Diagnosis

Conducted anytime after the tenth day since the onset of disease. Patients' serum, nasopharynx swab, anal swab, feces, and urine are collected and SARS IgG and IgM are tested with serum samples first and then viral nucleocapsid protein in serum and viral nucleates in the other samples as supporting proofs. If antibodies become positive or increase fourfold, or if viral nucleates and nucleocapsid protein tests are positive, then the patient can be diagnosed with SARS.

Thus far, China has had ELISA testing reagents for serum nucleocapsid protein of the SARS virus, IgM and IgG antibody testing reagents (ELISA and fluorescence) on the serum of SARS patients, and real-time PCR reagents to SARS viral nucleic acid in various samples. All of these reagents have obtained approval from the government. Isolation of viral samples which are etiologically positive (nucleocapsid protein and nucleates) and SARS viral neutralization experiments on samples which are antibody positive are useful for further clarified diagnosis. Regarding the use and interpretation of other testing methods for blood-lymphocytes and X-rays, “Consensus of the management of Severe Acute Respiratory Syndrome” published by MOH of China can be referenced (Ministry of Health, People’s Republic of China, 2005).

Differential Diagnosis

Early SARS diagnosis, to a certain extent, is an exclusive diagnosis. Prior to SARS diagnosis, other diseases that cause similar clinical manifestations must be excluded. Especially, some manifestations being negative in SARS can help differentiate the diseases. For instance, SARS does not cause lung necrosis; therefore, emphysema of the chest or cavity will not occur if the disease is, indeed, SARS. Moreover, although SARS is a viral infection, it rarely leads to rash (excluding drug rash) or lymphadenectasis. Symptoms of upper respiratory catarrh are scarcely seen in SARS. All that has mentioned can be considered as criteria to rule out other diseases. The many other pneumonias with fever, low WBC, and pulmonary infiltration, which are caused by non-SARS pathogens such as atypical pathogen, virus, fungus, and common bacteria, and so on, need to be carefully differentiated. However, in addition, some other diseases, such as TB, tumor, pulmonary vasculitis, allergic pneumonia, and acute interstitial pneumonia, also need to be considered in an exclusive diagnosis.

Treatment Principles of SARS

Although the pathogen of SARS has been identified, the mechanism by which the virus causes disease is not clear. Thus far, no effective anti-viral treatment has been scientifically and clinically approved. Consequently, symptomatic supportive treatment and treatment targeting various disease complications remain the main treatment of the disease, including the use of glucocorticoids. It is necessary to correctly implement mechanical ventilation, treat complications positively, and actively develop a combination therapy of Western and traditional Chinese medicine. Large doses of long-term blind drug therapy – especially the combination of multiple drugs such as antibiotics, antiviral drugs, immunomodulators, and glucocorticoids – must be rejected as a form of treatment. Detailed treatment regimens may be

consulted in “Consensus of the management of Severe Acute Respiratory Syndrome” published by MOH of China (Ministry of Health, People’s Republic of China, 2005).

Lessons Learned from SARS Epidemic and Experiences Based on Successful Control of SARS in Inner-Land of China

Lessons Learned from SARS Epidemic

Characteristics of the Spread of SARS (Chinese Center for Disease Control, 2003)

During the SARS epidemic in the inner-land of China, 24 provinces, autonomous regions, and municipalities submitted SARS case reports, while seven provinces and autonomous regions (Hainan, Guizhou, Yunnan, Hei Longjiang, Tibet, Qinghai, and Xinjiang) did not. The epidemic was concentrated in six areas, including Beijing (2,521 cases), Guangdong (1,512 cases), Shanxi (448 cases), Inner Mongolia (282 cases), Hebei (215 cases), and Tianjin (175 cases), making up 96.7% (5,153 cases) of the nation’s cases and 94.3% (329 deaths) of the nation’s deaths from SARS. Of the other regions of China, six provinces had between 10 and 35 cases and 12 provinces had less than 10 cases.

The epidemiological investigation showed that SARS outbreaks in 24 provinces of inner-land of China have apparent applications. The survey study indicated that Guangdong and Beijing were the most important sources of transmission for China’s SARS epidemic. From Guangdong, the disease spread to Xichuan, Hunan, Inner Mongolia, Shanxi, Beijing, Anhui, Shanghai, and Fujian; then from Beijing, it spread to Gansu, Jilin, Liaoning, Shanxi, Chongqing, Hubei, Zhejiang, Tianjin, and Hebei.

Lessons Drawn from the SARS Spread

Two months after the first case was reported on 16 November 2002, Guangdong had a SARS outbreak. During the 2-month period of the outbreak, medical staffs and local government officials in Guangdong had learned of the severity of the disease and had acquired a basic knowledge of the clinical manifestations, major routes of transmission, and response measures to the disease.

By early February 2003, Guangdong province had managed to contain the outbreak by formulating and implementing a series of effective public health measures. Unfortunately, Guangdong’s experience did not help the rest of China to control the further spread of SARS. What happened in Guangdong between December 2002 and January 2003 recurred many times in a worse manner in many

other provinces. There are disputes about whether Guangdong's efforts to contain the SARS epidemic in February were strong enough. Objectively, one can offer the explanation that a new infectious disease necessitates a learning process such as Guangdong's; however, this explanation fails with regard to Beijing's repetition of Guangdong's process, which resulted in a high number of infections among medical staffs in March 2003 – 2 months after the outbreak in Guangdong. The consequences of this mistake have resulted in an important lesson worthy of reflection.

1. The consideration that should accord severe infectious diseases the top priority in emergency public health events was inadequate. Nowadays, infectious diseases – especially acute and severe ones transmitted via respiratory and intestinal tracts – may appear as either newly emerged infectious diseases or weapons in biological terrorism. Since such diseases usually emerge in an explosive and indiscriminate manner and have wide spread impact, they often lead to panic, social disorder, and economic trauma. Historically, severe epidemics had sometime changed war outcomes, wreaked social disorder, and altered political regimes. Considering these grave potential impacts, the establishment of a response system to severe infectious diseases should be given significant priority in the response system of sudden public health incidents. Acute and severe viral infectious diseases generally do not have specific and effective prevention and treatment measures; therefore, emergency response, prevention, and control need to be given the top priority.
2. The most significant revelation from the SARS outbreaks is that the response system to emergency public health events is inadequate. In the epidemics, weaknesses in China's command system, information system, prevention and treatment teams, and corresponding material storages were completely exposed. For the past two decades, the public health service in China has lagged behind, primarily due to inadequate funding. To solve these problems is an essential step for China to build a harmonious modern society with long-term lasting and equilibrating economic development. The establishment of China's CDC-centered nationwide laboratory monitor network, epidemic information network, emergency teams, and material storage is an essential component in building up the national response to public health emergencies.
3. No consummate public reporting institution of epidemic is observed. In the beginning of the epidemic, the policy of "strict inward while loose outward" concerning SARS blocked the epidemic information. The mystery of epidemic disease hovered among the public. Information was not transparent and blocked between related CDCs and researchers, even among departments of government including China and international organizations. This delayed the timely control of the epidemic and even initiated a confidence crisis among the public. It is essential to develop a complete system to announce and report epidemics – a scientific system to analyze and explain epidemics so that various departments can coordinate control of the epidemic and so that the public can correctly understand the epidemic and positively support the measures that the government takes to contain the epidemic.

4. The cognition needed to promptly tackle key problems in science and technology when a new infectious disease occurs is deficient. In early February 2003, common belief held that SARS was caused by a “new etiological agent.” So as to “keep the outbreak confidential,” only a few research institutions independently began to organize teams to try to identify the new etiological agent. (National Institute for Viral Disease Control and Prevention, 2003a) Unclear about the details of the outbreak and the lack of a mechanism of collaborative research, each research institute worked independently, making the much-needed national cooperation impossible. At the end of February and beginning of March, a national program proposal requesting collaboration in etiology, epidemiology, and clinical remedy finally reached the related departments of government (National Institute for Viral Disease Control and Prevention, 2003). However, collaborative research, organized by the government, did not start until mid-April of 2003. In this regard, it is understandable that, although scientists in inner-land of China had observed “coronavirus” in autopsies of SARS patients by the end of February, which was one month earlier than the discovery made by a group of Hong Kong scientists, their work was never publicly released. Scientific and technological sectors in China learn from this lesson the importance of establishing a systematic scientific and research response to emergencies when threatened by a new disease.

Experiences Based on Successful Control of SARS

China has a responsible government, which took timely and effectively measures nationwide in the face of severe SARS outbreaks. Without reliable diagnostic reagents, effective drugs, or vaccines, “four early” steps stressing “early detection, early report, early quarantine, early treatment” were adopted in early-April of 2003 according to basic principles of containing infectious diseases and targeting major clinical manifestations and transmission features of SARS. Within the 2 months following “four early” steps, SARS transmission was controlled and blocked nationwide. To offer scientific support for the implementation of the “Four Early Steps,” the experiences could be summarized as follows:

- Publicize the epidemic to get understanding, support, and cooperation from the public to facilitate government efforts to contain the epidemic
- Disseminate knowledge of SARS to promote the public’s ability of self-protection
- Establish a network system of reporting the epidemic to actively monitor the epidemic so that prevention and control measures can be most effectively focused
- Develop designated hospitals with strict quarantines of patients and medical monitors on those in close Contact with patients and improve the preventive and protective condition and ability of doctors and nurses
- Strengthen aid and treatment to patients to minimize the number of deaths

- Promptly launch scientific and technological research and intensify studies on etiology, epidemiology, and medical treatment

Drawing lessons and experiences from the SARS outbreaks, the Chinese government, and its health workers have further acknowledged the important position of prevention and control infectious diseases in the public health cause. In May of 2003, the Chinese government formulated the “Regulations on Preparedness for and Response to Emergent Public Health Hazards” (People’s Republic of China, 2003) and revised the “Law of the People’s Republic of China on the Prevention and Treatment of Infectious Diseases” (People’s Republic of China, 2004). All provincial governments activated components of the “Emergency Preparedness Plan for Emergent Public Health Hazards” and prepared the needed personnel, materials, technology, and grounds. China’s capacity to respond to emergency public health events has improved significantly with a broad variety of improvements for such keynote infectious diseases as SARS during the past few years, including the following:

- Establishment of a nationwide direct report network of epidemic diseases,
- An epidemic-publicizing institution
- Identification of fever clinics in designated infectious disease hospitals
- Operation of monitor networks on severe infectious diseases
- Cooperative efforts in handling problems of diagnostic techniques, prevention and control measures.

The experiences in controlling the first SARS outbreak played a crucial role in the response to four mild SARS cases that appeared in Guangdong in early 2004. The diagnoses of these four cases were fast and accurate, conforming to check result from WHO network laboratories (Liang et al., 2004). No epidemic formed, largely due to the developed firm means of preventing the outbreak. The same prevention and control measures were applied in nine laboratory SARS infections in Beijing. Upon learning that two suspected SARS cases in Anhui came from a certain research institute in Beijing, related experts were quickly sent to Anhui on 21st April. Beijing also found SARS suspected cases at the same day. That afternoon, Beijing SARS network laboratory test results confirmed the clinical diagnosis of SARS. Meanwhile, epidemiological analyses suggested connections between Anhui and Beijing cases, and additionally circled the potential range of those who had come into close contact with the infected patients. The Beijing government publicized the outbreak according to emergency preparedness planning on 23rd April and followed up with decisive measures to close up the epidemic sites, quarantine close contact persons with patients, and give quick treatments to patients (Government of Xuan Wu Qu, Beijing, 2004). The firm reactions blocked successfully the transmission of SARS. The experience showed that China had remarkably improved its response to acute and severe infectious diseases after its previous “SARS accident,” and its response measures to the emergency proved efficient. The same improvement was later evident in the prevention and control of avian flu and pig streptococcal infection in China (Yu et al., 2006).

Why, then, did a SARS laboratory infection transmit to the public in April of 2004? If the world's largest epidemic of streptococcal infection in pigs (Yu et al., 2006) could be spread among the public, what would the result be? Evidently, there is still much to be done to develop prevention and control response systems to outbreak emergencies.

Main Factors Contributing to SARS Epidemic in China and China's Prevention and Control Strategies

It may not be an accident that SARS first broke out in China. Hong Kong (China) reported in 1997 for the first time that humans could be infected by avian flu (H5N1). Of flu viruses that caused worldwide pandemic four times, two originated in China – H2N2 in Guizhou in 1957 and H3N2 in Hong Kong in 1968. In recent years, avian flu has broken out in Asia (including China) and spread. Not long ago, the world's largest epidemic of streptococcal infection in pigs was seen in Sichuan, China (Yu et al., 2006). Furthermore, in the past two decades, new diseases have emerged in other countries of Asia. It seems that Asia has become a significant origin for new infectious diseases – but why? Perhaps this issue must be placed in the context of China – even, to a larger extent, of Asia – for a solution.

Main Factors Contributing to SARS Epidemic in China

1. For the past 30 years, Asia, particularly China, has experienced rapid social and economic development. A large population on weak foundations, in combination with rapid progress, has severely polluted the environment and damaged ecological balance. This has enhanced the opportunities for pathogenic microorganisms that had been previously blocked and limited to hit larger populations, and also augmented the risk of a trans-genus spread of microorganisms, thereby presenting social and economic surroundings advantageous for new diseases.

Studies illustrate that SARS-CoV derives from animals, showing that during long periods of frequent contact with people, the virus evolves from nonpathogenic to pathogenic. An unregulated breeding industry of wild animals in Guangdong provided the womb to the evolution of this microorganism.

2. Rapid economic development has caused significant changes in human communication and lifestyles, which have consequently accelerated the rapid transmission of infectious diseases via respiratory and intestinal tracts. This accelerated transmission was witnessed in the rapid spread of the SARS epidemic from the original outbreak in Guangdong (in China) to cases in 26 countries in Asia, North America, and Europe within the course of 2 months. Although, from this

data, it may seem that the infectivity of SARS is very high, it is still far weaker than that of influenza. At present, if no effective measures are taken with the emergence of an influenza pandemic, its coverage might greatly surpass that of the devastating flu pandemic of 1918.

Moreover, the cognition of the negative impacts of infectious diseases on social development is far from enough. The initial position of infectious diseases, especially highly pathogenic ones, in emergency public health hazards has been neglected. The funds invested in laboratory test networks and networks monitoring infectious diseases are ultimately inadequate. Confronted with the epidemic, its related information is unclear and responses are not powerful. These factors facilitate chaos and loss of control in epidemic situations.

China's Prevention and Control Strategies

1. To practice the “concept of scientific development” in all around and prioritize the public health within social and economic development. The development of public health services is a critical standard by which to measure social and economic progress. In China, while the national economy had doubled in the two decades before 2002, the investments in public health services had conversely dropped by approximately 45% compared with that in 1980s, nearly destroying the already weak disease prevention and control network. Therefore, it is no wonder that SARS could so easily penetrate the hospital defense lines and rapidly spread throughout the nation. The lessons learned from the SARS outbreaks are not exclusively related to SARS, but are rather far-reaching and applicable to future scientific endeavors.

To strategically practice the “concept of scientific development,” one must make the development of public health services, which is directly related to public life and health, a significant standard by which to measure social and economic progress. To effectively and tactfully respond to new infectious diseases such as SARS, the prevention and control of infectious diseases need to be accorded top priority in the development of a response system to public health emergencies. Therefore, one must build and improve upon a response commanding system, a monitoring network, an information-reporting network, a technical platform, prevention and treatment teams, and a storage system of materials for infectious disease emergencies.

2. To keep ecological balance and protect the environment are important measures to reduce the emergence of new diseases and prevent their further expansion. In analyzing human social development, it is apparent that the occurrence of new diseases is always accompanied by ecological imbalance and environmental damages caused by social and economic development. For example, the infamous infectious disease smallpox appeared after humans shifted from a nomadic lifestyle to live in agricultural settlements that made the original ecology and

environment obvious change. In monitoring ecological balance, a society must practice strict regulations in handling wild animals, for many diseases may be transmitted from animals to humans. Livestock and poultry, for instance, live in close contact with human beings and thereby create multiple areas for the transmission of common diseases such as the flu and Japanese B encephalitis. The casual capture and breeding of wild animals also offer grounds for the occurrence of the SARS virus. To ensure sustainable stability and development in a society in which the economy progresses at a high rate, it is critical to establish a harmony between humans and nature so as to protect the environment, maintain an ecological balance, decrease the occurrence of new diseases, and create enjoyable surroundings for human life and health.

Strategies and Measures of SARS Prevention and Treatment (Wang et al., 2003)

General Principles of Prevention and Treatment

SARS has been included in the “Law of the PRC on the Prevention and Treatment of Infectious Diseases” (People’s Republic of China, 2004) as one of the severe infectious diseases that require key prevention and treatment for management. Although there have been no effective therapeutic and preventative drugs for SARS thus far, there are satisfactory diagnostic reagents. Thus, the general principle of SARS prevention and treatment may be defined as a system of comprehensive prevention and treatment measures aimed at three key points of infectious sources, transmission routes, and susceptible populations, which focus mainly on managing and containing infectious sources, and preventing and controlling transmissions within hospitals. Efforts must be made to implement the “Four Early” policy that calls for “early detection, early report, early quarantine, early treatment,” especially during the period of SARS epidemic, and to emphasize local quarantine and local treatment to avoid a long-distance transmission.

Measures of Prevention and Treatment

Avoid or Reduce Viral Infections of Humans from the External Environment

Prevent and Control Animals from Contracting the SARS Viral Infection

We are still unclear about animals’ infection of SARS-CoV, infection components, and the impacts. Monitoring studies need to be strengthened on animal hosts in high risk areas such as Guangdong province, followed by steps to reduce or avoid animal infections or spread SARS virus.

Prevent SARS-CoV Infections Transmitted from Animals to Humans

According to a study on the economic values of infected animals, the procedures requiring the management of infectious animal sources to kill or quarantine wild animal species should be adapted to dwindle their chances of contact with humans instead of terminating the infection among the animals. Thus, when the management should have eliminated the sources of infection and consequently eliminate the possibility of transmission to humans, it instead only reduced the chances of animal-to-human transmission.

Strengthen the Safety of Laboratories

Strengthen the biological safety management of all institutions concerning SARS research, testing, and reagent and vaccine manufacturing. In the condition that possible profits and risks were fully demonstrated, the topics and contents of SARS-related pathogenic studies were carefully selected and only the qualified laboratories and researchers could be authorized to launch studies. To prevent the spread of laboratory infection to the public, it was needed to improve the management organization for severe infectious diseases, formulate and improve technique operation standards of biological safety in severe infectious disease labs, strengthen the biological safety training of related professionals who may be exposed to the SARS virus or potential infectious materials, and establish a system to report suspect symptoms, such as fever, among laboratory staff to ensure they can get treatment in designated hospitals in time.

Prevent and Control Human-to-Human Transmission

Management of Infectious Sources

- Management of patients: Try to detect early, report early, quarantine early, and treat early. It is extremely important to establish precautionary measures and a SARS protective and clinical treatment system.
- Management of those in close contact with patients: Establish systems of medical monitoring and follow-up investigation for people in close contact with SARS patients.

Cut-Off Routes of Transmission

- Strengthen the control of in-hospital infections: A prerequisite of avoiding in-hospital infections is choosing hospitals and wards that meet standards to receive SARS patients. During an outbreak, designated hospitals and fever clinics must be set up in accordance with standardized requirements – equipped with

essential preventative and disinfection facilities, and with utilities bearing obvious, eye-catching labels. Specialized patient areas, wards, elevators, and passages must be established specifically to receive SARS patients.

- Practice good self-protection: Individual precautionary equipment includes a shielding face mask, gloves, protective clothing, eyewear or veil, and shoe covers. Of these precautions, the shielding face mask and gloves are the most important.

Protection of Susceptible Population

Research for a SARS vaccine is now underway. China started the first trial of a SARS inactivated vaccine on humans in May of 2004 (Jiang-Tao Lin et al., 2007). Although global research on a SARS vaccine has seen great progress, it still has a long way to go before it can produce a vaccine for real practice on humans. Studies show that the correct use of interferon has certain preventive effects for SARS infection; however, there have been no effective vaccines or drugs for prevention, leaving the strengthening of self-protection as the main measure to protect susceptible populations.

Other Prevention and Treatment Measures

1. Collaborate multi-departmentally for good prevention and treatment of SARS in joint efforts; it is vital for the control of a SARS outbreak to establish a powerful organizing and commanding system supported by the coordination and collaboration of multiple departments.
2. Disinfection and management of infectious sources: Abide by the principle of “early, exact, strict, and real” in the management of epidemic foci or epidemic areas, i.e., take early steps with exact targets, execute measures strictly and put them into real practice, and disinfect epidemic foci seriously. In most cases, it is not necessary to disinfect the extended surrounding areas of the foci of an epidemic.
3. Quarantine and manage public places: If SARS breaks out or spreads with a trend of further expansion, emergency steps should be taken according to either “Frontier Health and Quarantine Law of People’s Republic of China” and “Regulations on Domestic Communications Health Quarantine” or the 25th and 26th rules in “Law of the PRC on the Prevention and Treatment of Infectious Diseases.”
4. Intensify health education, social care, and psychological intervention: Publicize knowledge of SARS prevention and treatment in a wide range and through various media. Educate the public so as to raise awareness of self-protection and support the current prevention and treatment work; adjust the education focus to cater to the changes of the epidemic; take full advantage of the role and function of the media and direct public opinion by utilizing the media to focus on

disseminating knowledge of prevention and treatment; make the public understand the measures of mass prevention and mass treatment; and clarify the public's responsibilities and obligations. The reports must adhere to the truth, and try to reduce any reports that may lead to a sense of panic among the public.

Priority on SARS Prevention and Treatment in China

1. Intensify the development of SARS testing laboratories: To provide reliable and powerful technique back-ups to the "Four Early" policy, we need to put into serious practice the hardware construction and management of laboratories, testing plans, storage of reagents, and working staff. As well, we have to ensure biological safety and reliable test result.
2. Intensify the management of key susceptible animals: Set up monitoring and testing systems of the SARS virus in susceptible animals in high risk regions to allow the issuance of a prompt precaution warning of the possibility of a SARS outbreak.
3. Intensify the management of SARS laboratories to ensure that laboratories are not sources of SARS infections.
4. Upgrade early precautionary systems that report SARS cases so as to detect SARS patients as soon as possible and take immediate actions of prevention and control in cases of detected infections.
5. Improve the clinical treatment and prevention system so as to raise the recovery rate, reduce the fatality rate, and block inter-hospital infections and transmission to the public.
6. Update medical quarantine and observation systems so that a SARS outbreak can be blocked and controlled on a smallest scale in the shortest time.

This article was finished in 2005. During the 3 years from 2004, no SARS cases have been reported. Since SARS is featured by symptomatic infection (Ministry of Health, People's Republic of China, 2005), it is impossible that SARS-CoV could be hidden in population without disease. The results from monitoring of SARS-CoV of animals in recent 2 years in different provinces, especially in Guangdong province, did not show that SARS-CoV existed. These results indicated the SARS-CoV causing the epidemic in 2003 might disappear in nature and reemergence of SARS seems to be depended on a new SARS virus derived from mutation. However, the four confirmed SARS cases with mild manifestations and caused by a SARS-CoV differentiated from the SARS-CoV in 2003 (Liang et al., 2004) told us the "mild" SARS-CoV may be still hidden in animal hosts. Since the mild SARS case is difficult to be differentiated from other atypical pneumonia, it gives the mild SARS-CoV a chance to become an epidemic strain through further trans-genus mutation. Thus, the possibility of SARS outbreak is still there. Although this article was finished 2 years ago, we believe the main points and contents in this article will be still valuable for prevention and control of reemerging of SARS.

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