ISSN 1021-366X

Center for Disease Control
Department of Health
Taiwan, R.O.C.

Vol. 21/ No.6/ JUNE. 25, 2005

Epidemiology Bulletin

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A Retrospective Review on the 2003 Multinational Outbreaks of SARS and the Preventive Measures of Its Nosocomial Infections

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Introduction

Severe Acute Respiratory Syndrome (SARS) was the first emerging infectious disease that caught global attention in the 21st century. The outbreak started in November 2002 when an unknown disease exploded and began to spread in the vicinity of Heyuan City, Guangdong Province of Mainland China. The patients reportedly suffered from fever, chills, dizziness, cough, and other symptoms of respiratory illness, such as pneumonia, and even death. Shortly afterwards, Chinese news programs reported a rush in purchases of "indigowoad root" (a Chinese medicine, English name: Radix Isatidis, the root of *Isatisoin digotica*) happening among certain people living in that region. Since no official communication channels had ever been established between the public health authorities on both shores of the Taiwan Strait for decades, we had no way to get detailed information of this outbreak until February 10, 2003 when Guangdong Health Department publicly announced that the province had an outbreak of some sort of pneumonia with an "unidentified cause," which for the moment they called "atypical pneumonia". By February 9, 2003, it was also revealed that there had been already as many as 226 cases in Guangzhou alone, the capital city of the Guandong province. However, that announcement still failed to catch the attention of global public health professionals. It was not until the end of February that the World Health Organization (WHO) finally became alarmed at the problem for the first time by discovering the same dreadful disease in Hanoi, Vietnam, and it subsequently issued a worldwide alert on March 12, 2003. After that, the new disease spread out of Mainland China again and caused outbreaks in Hong Kong, Singapore, Canada, and Taiwan[1]. Just within a few months, Taiwan's economy, social order, and medical system suffered colossal damages during this unfortunate ordeal, and its health care system was hit the hardest. All these incidents showed once again the importance of nosocomial infection control[2].

Public health scholars and government officials in the affected countries soon realized that they were facing a critical trial, in which important public health policies would have to be formulated and put into practice in a timely manner in order to respond to unexpected epidemics in the future. Since the winter of 2003-2004, the human cases of a novel avian influenza A (H5N1) have been reported in the Southeast Asian countries such as Vietnam and Thailand, WHO epidemiologists have been worrying about novel infectious diseases that have a serious health threat and possibly emerging like a pandemic of new type of influenza virus in the near future. Likewise, the most immediate task facing us in case SARS returns or some other new emerging infectious disease breaks out is to apply those experiences and lessons we amassed during the past SARS crisis at the expense of many deaths so that we might be able to minimize the social costs.

Here, we would like to review the epidemiology and the preventive measures taken in each of eight SARS epidemic countries (including Vietnam, and Mainland China, Hong Kong, Singapore, Canada, and Taiwan) in 2003, with particularly emphasis on the nosocomial infections among healthcare workers. For instance, why did we not have subsequent incidents of nosocomial infection right after the first two confirmed SARS cases that had been discovered in Taiwan? How did a series of hospital SARS outbreaks spread one after the other in different parts of Taiwan in late April of 2003 and how was one hospital in Vietnam successful in preventing the nosocomial infections? What were the successes or failures from the 2003 SARS cross-country epidemic that can be applied to future years? Under what conditions would SARS-coronavirus (SARS-CoV) be easily spread? The answers to these questions will help remind high risk populations the extreme importance they play in the transmission of infectious diseases, such as the mass movement of population during the holiday season, especially after the Chinese Lunar New Year in Chinese countries. These answers will also better protect the health of healthcare workers (HCWs) face the challenge of future epidemics with a scientific mind and attitude, and to curb any possible “negative” impacts on the society due to social panics. We are hoping the future public health endeavors, changing policies and actions should be established on scientific evidences from epidemiological data.

A retrospective Review on the 2003 SARS epidemics

A. Epidemiology of SARS

1. An Etiological Agent

On April 16, 2003, the WHO officially announced that the etiological agent of SARS is a new coronavirus named SARS coronavirus (SARS-CoV). Before this discovery, conventional coronaviruses had been divided into three groups: the first two groups are capable of infecting mammals while the third group can infect birds only. The past known human coronavirus had been documented to cause some mild upper respiratory tract illness in about 30% of the infected people but it never causes so severe a disease in humans as SARS. The differences between SARS-CoV and the conventional human coronaviruses are summarized as follows: (1) this new virus can be cultivated and isolated in Vero E6 (green monkey kidney) cell line; (2) the characteristic clinical outcome of this new virus infection is diffuse pneumonia and respiratory failure, which may be more severe than "atypical pneumonia" reportedly caused by other viruses or bacteria, and that is why the disease was later named severe acute respiratory syndrome (SARS); (3) its antigen-antibody reaction has a specificity of its own, which differs from that of the conventional human coronavirus; and (4) a phylogenetic analysis found that this new coronavirus belongs to a separate cluster, which has quite different viral genetic sequences from those of the conventional ones[3].

2. Case Definitions:

To detect a newly emerging infectious disease (EID), we have first to establish a clear-cut case definition. The Centers for Disease Control and Prevention in the United States (US CDC) used a rather broad definition of so-called "suspect cases." before the etiological agent was identified. The rationale behind this broadness is to involve all the mild and severe SARS-like cases, similar to setting up a big net cast by a fisherman to catch all fishes. At such an early stage when "the disease etiology was unclear, we would not worry later that some "escaped mild case" turned into the source of more outbreaks. Meanwhile, we can compare the epidemiological characteristics of "suspect cases" with those from "probable cases" for the improvement of case definition later on. In this way, each "probable case" is reviewed by the Taiwan CDC SARS Advisory Committee with integrating clinical manifestations and epidemiological characteristics till the end of April 2003. After the standardized laboratory diagnosis methods of SARS-CoV were set up since May 1, 2003 and on, the definition of a "confirmed SARS-CoV case" has required positive laboratory results. It is worthwhile paying attention to that SARS cases also might have "atypical presentations", and its epidemiology is also dynamic, which means SARS is no longer just limited to those having traveled recently to epidemic areas. Rather, the key lies in whether the patient himself, or his contacted relatives and friends, have direct contacts with a SARS patient prior to the onset of illness. As to the scientific diagnosis performed in a laboratory, its accuracy depends much on the enthusiastic help provided by the healthcare personnel involved in the specimen collecting work. It is advisable to substantiate a confirmed case by at least two positive laboratory test results from the clinical specimens collected on separate dates, or two different specimens (eg. feces, throat swabs) by HCWs. This was also one of the successful factors for scientific breakthroughs made at Hong Kong University during the hard time of SARS epidemic there. On May 1, 2003, WHO published a revised version of case definitions for "Severe Acute Respiratory Syndrome," as follows[1,4]:

a) Suspect Case:

This case definition places much emphasis on epidemic time, location, and broader clinical symptoms.

(i) The appearance of the **following three criteria or conditions** with onset since November 1, 2002:

* High fever (>38℃), **and**

* Cough or breathing difficulty, **and**

* **One or more of the following exposures during the 10 days prior to onset of symptoms:**

  • Having close contact with a person who is a suspect or probable SARS case (in case the patient has visited or taken part in certain group activities in association with a hospital or community that has large-scale outbreaks of SARS lately, it is regarded as "having close contacts").

  • Having travel history to an area with recent local transmission of SARS.

  • Residing in an area with recent local transmission of SARS.

(ii) A person with **an unexplained acute respiratory illness resulting in death** after 1 November 2002, but no autopsy has been performed

AND one or more of the following exposures during the 10 days prior to onset of symptoms:

• Having close contact with a person who is a suspect or probable SARS case (in case the patient has visited or taken part in certain group activities in association with a hospital or community that has large-scale outbreaks of SARS lately, it is regarded as "having close contacts").

- Having travel history to an area with recent local transmission of SARS.
- Residing in an area with recent local transmission of SARS.

b) Probable Case:

(i) A suspect case with **radiographic evidence of infiltrates** consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR).

(ii) A suspect case of SARS that is **positive for SARS coronavirus** by one or more assays. See the section of "Laboratory Confirmed SARS-CoV Case".

(iii) A suspect case with **autopsy findings** consistent with the **pathology of RDS** without an identifiable cause.

c) Laboratory Confirmed SARS-CoV Case[1]:

A person with symptoms and signs that are clinically suggestive of SARS and with positive laboratory findings for SARS-CoV based on one or more of the following diagnostic criteria:

(i) PCR positive for SARS-CoV, which uses a validated method from:

* At least **two different clinical specimens** (e.g. nasopharyngeal and stool), or
* The same type of clinical specimens but collected on **two or more occasions** during the course of the illness (e.g. sequential nasopharyngeal aspirates), or
* **Two different assays** (e.g. one might be the qualitative method of RT-PCR while the other one might be the quantitative real-time PCR that both methods have been applied to detect SARS-CoV from the reported SARS cases in Taiwan-CDC to increase efficiency) or repeat

PCR using a new RNA extract from the original clinical sample on each occasion of testing.

Different positive and negative controls at several important steps are required for better quality control in the method of molecular diagnosis.

(ii) Serological Tests [enzyme-linked immunosorbent assay (ELISA) or immunofluorescence assay (IFA)]

* **Seroconversion:** Negative antibody test on acute serum followed by positive antibody test on convalescent phase serum tested in parallel, or
* **Serotiter Changes:** Four-fold or greater rise in antibody titer between acute and convalescent phase sera tested in parallel.

The convalescent serum samples must be collected at 21-28 days after the disease onset date to avoid possible false negative results for better final conclusions.

(iii) Virus Isolation

* Isolation in cell culture of SARS-CoV from any specimen and further confirmed by the above-mentioned molecular assay RT-PCR.

3. Modes of Transmission[3]:

Up to now, the commonly held knowledge is that the transmission of SARS-CoV appears to be either through close distance aerosol (i.e. droplet) or person-to-person contact.

(a) Aerosol Transmission: The principal mode that SARS-CoV spreads from person to person is through droplets in "short distance" (usually within a one meter); namely, when SARS patients with symptoms of coughing or sneezing, their small droplets are propelled through the air and someone else breaths them in or touches a surface or object contaminated by those infectious droplets.

(b)Contact transmission: Having direct or indirect contact with secretions or body fluids of a patient with SARS, such as tears, sniffle or nasal discharge, saliva droplets, sputum, urine, and mucus.

4. **Clinical Manifestations:** Major clinical symptoms and signs expressed by SARS patients are listed in Table 1[5].

   The infectivity of a SARS patient mostly appears after the patient starts to have fever. Researchers in Hong Kong used a molecular quantitative assay of RT-PCR to demonstrate that in some nasopharyngeal secretion specimens, the SARS-CoV RNA peaked on the 10^{th} day after the onset of disease (with a 95% positive rate), and dropped to a 47% positive rate on the 21^{st} day. However, the viral load in the stool specimens was delayed with the peak (100% positive rate) appearing between the 12^{th} and 14^{th} days after the onset, and remained about a 67% positive rate on the 21^{st} day. On the contrary, that SARS-CoV in the urine samples was only 21% positive on the 21^{st} day instead[6]. This also explains why a combination of fever-monitoring and quarantine measure proved to be effective in preventing SARS[2,4]. Incidentally, it must be noted that the onset of SARS is quite different from that of other communicable diseases, such as chickenpox, measles, and influenza, which normally possess infectivity before the symptoms become evident[2]. Furthermore, since stool and urine specimens collected two weeks after the disease onset still contain significant amount of the SARS-CoV RNA, it is important to strengthen this issue through heath education to the patient and his/her family members.

B. The 2003 Global SARS Epidemics

According to the WHO (http://www.who.int) statistics up to December 31, 2003, there were 8096 reported probable SARS cases from November 2002 to

July 31 2003 worldwide and 774 of them were fatal cases with a case fatality rate of about 9.6%. Among the reported cases, 1706 (21.1%) were healthcare workers representing the extremely important "high risk population" during the 2003 SARS epidemic.

There were a total of 29 countries/regions worldwide with reported probable SARS cases and eight of them had indigenous cases, including mainland China, Hong Kong, Taiwan, Canada, Singapore, Vietnam, Mongolia, and the Philippines (Table 2) [1,2,7-10,27]. Among them, the case fatality rates varied among different regions and China and Hong Kong were the two regions with the most fatal SARS cases. With the exception of Mongolia, each of these SARS affected region also had a rather high proportion (19-57%) of healthcare workers diagnosed with probable SARS. Undoubtedly, this epidemic had strong association with ethnic Chinese social networks. Besides the unclear situation in Russia, the remaining 20 regions had only "imported cases". In this article, our objective was to understand the major risk factors for nosocomial infection, the relationship between the level of prevention efforts, and the epidemic trend to avoid future epidemics.

Nosocomial infections

Before the pathogenic microorganism causing the global SARS outbreaks was identified, patients infected with the SARS-CoV in the early stages of the epidemic were often diagnosed as having just a normal respiratory infection and medical care was sought at hospital emergency rooms once the disease progressed. In order to prevent an environment favorable for the transmission of SARS-CoV, it is important that attending medical personnel have alertness to take immediate infection control measures. Furthermore, SARS-CoV viral load peaked on the 10th day after onset of disease, which coincided with the time when patient needs intensive care and tracheal intubation[6],in particular, thus hospital healthcare workers are at a higher risk of being infected than family or community members. Consequently, many hospital healthcare workers, patients, and visitors were infected after exposures to SARS-CoV, and the transmission went on to infect others within the medical institution. Chinese frequently like to visit and take care of their sick and hospitalized family members and friends that unfortunately keep the transmission chains from breaking apart. Literature review showed that “nosocomial infections” is a very important factor for SARS-CoV to start accelerating its spread among the “susceptibles” under such unnatural circumstances. Here we briefly review the epidemic situations in those countries/regions with significant nosocomial infections taking place.

1. Mainland China:

SARS cases originated from severe atypical pneumonia first identified in Guangdong Province of southern Mainland China on November 16, 2002. At that early stage, the disease already had higher attack rates among hospital healthcare workers. In order to cut down on “nosocomial spread,” some hospitals even set up a rule to temporarily suspend those medical staff members who have just treated and taken care of an “atypical pneumonia” patient from their work for one week and resume their duties only if they themselves did not develop any symptoms during the week. Until April 30, 2003, 24% of the total China SARS cases were healthcare workers in hospitals [7,8].

An epidemiological study through international collaborations was conducted to trace the origin of one important atypical pneumonia case which ended up being SARS. A 64-year old, male nephrologist and professor, who traveled from Mainland China to Hong Kong to attend a friend’s wedding, was the "infection source" with important epidemiological linkages that subsequently led to the outbreaks in Hong Kong, Vietnam, Singapore, and Canada. He died on March 4, 2003, and also even resulted in at least 16 travelers or visitors staying at the same hotel in Hong Kong and thus acquired the infection. Since SARS has a long incubation period (10-14 days) and transportation among countries is rapid nowadays, an international traveler may inadvertently get infected abroad, return home before the onset of the disease, and spread the disease to local people when symptoms occur and thus lead to SARS quickly cross the Chinese border to initiate many outbreaks in different countries [1].

Seroepidemiological studies discovered that civets or civet cats (*Paguma larvata*) bought at certain animal market as well as the animal attendants and vendors at the market in Mainland China appeared to be SARS-CoV antibody positive. It suggested that preparing wild animals for food may provide an opportunity for this virus to spread across host-barriers to infect humans [3].

During the 2003 SARS epidemic, Beijing health authority quickly built up a few dozen outpatient fever clinics to exclusively care and treat feverish patients. Researchers found that many feverish patients with unknown infection source were strongly associated with having prior contacts with patients with fever in those hospitals and clinics having fever screening, the matched odds ratio (OR) was 13.4 (95% confidence interval [CI] 3.8-46.7, $p<0.001$). This figure suggested that Beijing's forceful closure of traditional fever outpatient departments in those hospitals with poor nosocomial infection control practice was an effective preventive measure [11]. In conclusion, once the central government of Mainland China initiated the top-down health policies by mobilizing all lower-level provincial and municipal health authorities to take part in the preventive actions, the control activities became much more effective.

2. Hong Kong:

In the 2003 SARS outbreaks, Hong Kong played a significant role in both case number and scientific discovery. Not only were its case number and number of deaths just second to those of Mainland China, it was also the key place that connected all SARS cases around the globe to the ones on Mainland China. The first wave of outbreaks in Hong Kong started on March 10, 2003 at the Prince of Wales Hospital. Among the 138 cases, 69% were hospital healthcare workers. It was later noted that the first index case was in fact received nebulizer treatment, which might have led to the fast spread of the SARS-CoV through tiny droplet nuclei of mist, and the main reason for the epidemic expanding so swiftly[10,12,13]. Taiwan learned from this important lesson and soon stopped this therapy. Therefore, SARS-CoV was initially transmitted only to one family member of the index case, which subsequently transmitted to another family member and one healthcare worker who took care of the index case before a total halt to this first cluster in March. On March 14, the department head of infection control at the same hospital in Taiwan noticed an unusual family-clustering (involving two cases) of pneumonia. He immediately launched infection control measures at the highest possible level and strengthened the classification process in "triage." Such prompt response enabled Taiwan to successfully prevent SARS from spreading within medical institutions in the first wave of SARS outbreaks, unlike the situation in Hong Kong. Apparently, any newly emerging infectious disease in the very early stages without "clear knowledge" would have the greatest impact on the health of hospital healthcare workers. Therefore, the earlier the hospital healthcare workers are aware of the outbreak of the disease and alert others for quick responses with effective preventive measures all together, the better chance we would have to keep the epidemic under control easily.

Another study shows, among the 1755 Hong Kong SARS probable cases, there were 405 hospital healthcare workers (23.1%), including 210 nurses (52% of HCWs), 114 hospital assistants (28% of HCWs), and 64 physicians (only 16% of HCWs). In other words, relevant authorities in charge of prevention and control of nosocomial infection in the future must pay more attention to the occupational health of those professional groups having “shorter distance” or more frequent contacts with the patient. The percentages for each of the eight different classified sources of probable SARS case-clusters for Hong Kong in 2003[7] were summarized in Table 3. A factual reality during the SARS epidemic was that the public hospitals shouldered the most responsibility in taking care of the majority of the SARS patients. The distribution of the occupation in public hospitals, private hospitals, and private clinics were summarized in Table 4[7,14].

Although nurses accounted for the highest percentage among the affected Hong Kong hospital HCWs[10], other non-medical personnel (such as secretaries, assistants, janitors, etc.) were nonetheless under high risk to the nosocomial SARS spread as well. Even though the hospital administration provided those employees with some training in infection control, there were still some discrepancies between the quality and quantity of the trainings they received and what they actually understood and practiced. The shortcoming suggested that in the future, the hospital administration should provide various trainings and policies in infection control with more thoughtful and practical approaches in order to meet the different educational backgrounds and occupational needs. On the other hand, a 33-year-old male suffering from chronic kidney failure was hospitalized in early March 2003 at the Prince of Wales Hospital for treatment. He was found showing symptoms of some severe acute respiratory system illness on March 14. Meanwhile, he visited his younger brother at the latter's home in E Apartment Building of Amoy Garden on March 14 and 19. During the visits, the man used the bathroom because he had diarrhea. After that, his younger brother, his sister-in-law, and two nurses taking care of him at Prince of Wales Hospital were all confirmed to have SARS infection. Certainly, if nosocomial infection control practices had not been timely implemented, another wave of community outbreak could have taken place through epidemiological linkages.

3. Vietnam:

An ethnic Chinese American businessman brought SARS to Hanoi, Vietnam after he was infected at a Hong Kong hotel. An Italian epidemiologist named Carlo Urbani, who worked for the WHO in Vietnam at the time, recognized for the very first time that the man suffered from a brand new lethal infectious disease and reported his finding to the WHO headquarters on February 28, 2003, which led to the later international prevention measures. Unfortunately, Dr. Unbani died of SARS[1]. In Vietnam, there were a total of 63 cases and 36 (57%) of them were hospital healthcare workers, however, it happened to be the first country taken off from the SARS region list by WHO on April 28, 2003. This removal invisibly increased the confidence of other affected countries/regions to accelerate their epidemic-containing endeavors.

The Vietnam outbreak involved two hospitals, and neither of which had a negative-pressure isolation ward. One of the hospitals had an outbreak of nosocomial infections soon after the start and eventually spread into the Vietnam epidemic. The wardrooms designated to treat the SARS patients were quite small but each was equipped with an independent air-conditioning unit. The other hospital belonged to a local medical institute of tropical diseases and they were very familiar with infectious diseases that none of the hospital healthcare workers ever got infected when treating and taking care of SARS patients. Its wardrooms had rather high ceilings and the doors and windows were kept wide open. There was also a rotating fan in front of hospital bed to disperse the virus particles inside the room. Surprisingly, it became the most successful example in professional prevention against SARS. However, the lower severity of the patients treated at this hospital probably was also affected by the situation that they did not have any patients intubated or died[15].

4. Taiwan:

The first reported SARS case in Taiwan was a businessman who went to Guangdong and stopped by Hong Kong on his way home. He had fever on February 26, 2003 and only transmitted the disease to one physician who took care of him and his two family members shortly after. The epidemic preventive measures were conducted in an extremely cautious manner. Additionally, a male resident of Amoy Garden in Hong Kong came to Taiwan to visit his younger brother for tomb sweeping. Soon after the man returned to Hong Kong, he died from SARS, and so did his brother in Taiwan. The etiology of both deaths was confirmed. Fortunately, the first two waves of SARS outbreaks in Taiwan started with two imported cases affected a handful people and was not wide spread indicating that the epidemic control approaches at the very beginning of the Taiwan SARS outbreak worked well. Until late April, a great deal of nosocomial infections suddenly broke out[1,16]. Worse yet, because some patients, patients' visitors, or even hospital healthcare workers visited people at other hospitals, plus dishonest contact history of having visited the hospital with nosocomial SARS cases, it subsequently led to seven hospitals having nosocomial outbreaks one after the other. Among the total 346 probable SARS cases reported in Taiwan, about 80% were hospital-associated SARS cases[2].

The SARS epidemic in Taiwan, made us realize the important role that "hospital emergency rooms" play during an outbreak of newly emerging infectious disease (EID) for the first time. They were not only the first line of defense to fight the SARS epidemic, but also relatively the most accessible location to be in contact with new EID cases. Noticeably, the medical center in Taiwan that cared and treated the first SARS patient only resulted in the infection of one physician. However, two factors led to the sudden increase of SARS patients in emergency rooms and the subsequent infections of the healthcare workers in these hospitals. The first factor was that two other hospitals had nosocomial infections in later late April. The second factor was that some patients were transferred from one nosocomially-SARS-infected hospital to another hospital without informing the other hospital on the possible diagnosis of SARS. The circumstances forced the closure of the emergency room of a major teaching hospital in May. The lesson we learned here is that we have greater responsibility to strengthening the preparedness of healthcare workers at hospital emergency rooms to face the future challenges of EID since their daily 24-hours work period put them in contact with patients with various types of severe infectious diseases[17-19].

The key issue is why nosocomial infections took place so quickly in many hospitals in Taiwan, which is definitely worthwhile exploring for the sake of future occupational safety. Literature shows that in the beginning stage of the 2003 SARS outbreak, an improper distribution of protection materials was the major barrier to provide the highest quality of care by the hospital healthcare workers during the period of crisis. This reminds us that we must stockpile and keep an appropriate amount of such materials all the time to prepare for the unexpected epidemic[20].

5. Canada:

Toronto had two outbreaks of SARS and both were mostly due to nosocomial infections. The first outbreak was started by a hospitalized male patient whose mother traveled to Hong Kong to visit her other children and returned to Toronto but infected with SARS and died. This wave of infection resulted in 128 probable SARS cases, and among them 47 (37%) were the hospital healthcare workers and 36 (28%) were inpatients and their visitors. The second outbreak happened on May 14, 2003 when Toronto was already removed from the infected region list by the WHO. While the surveillance efforts of hospital inpatients and visitors with fever and respiratory symptoms were no longer as tight as before, nosocomial outbreak occurred again[1,16]. This reemphasizes that the preventive measures against nosocomial infections should be kept in high gear all the time, since even a little lapse or negligence may lead to another round of outbreak.

6. Singapore:

In Singapore, hospitals were also the major sites for the transmission of SARS-CoV and more than 80% of the SARS cases occurred among SARS patients' visitors, attending healthcare personnel, and their roommates before their SARS status was identified[21]. On May 22, 2003, in order to allow normal operation of healthcare system in other parts of the nation, Singapore government made an unprecedented quick decision to convert their second largest hospital, the Tan Tock Seng Hospital, into a SARS-designated hospital to take care exclusively SARS patients. In addition, they rushed into transferring the remaining non-SARS inpatients from this hospital to other hospitals to receive more appropriate treatments and care. However, this move in fact led to an unexpected crisis. While four other hospitals consecutively had nosocomial transmission of

SARS, some of those “non-SARS patients” were already infected with the SARS-CoV through contacts (such as sharing a wardroom or taking X-ray together) before the move. This unpleasant experience taught us another valuable lesson, i.e. all patients having any possible physical contacts with SARS patients should be given first priority to be kept in isolation and under observation (quarantine) for a certain length of time to make sure that no SARS symptoms appeared before he or she is allowed to be transfer to other hospitals[22].

C. Prevention Measures during the 2003 SARS Epidemic

Different countries adopted many different measures to prevent epidemic from taking place in 2003, including fever screening and quarantine for travelers on arrival before entering the country, home quarantine, strengthen laboratory diagnosis, and nosocomial infection control measures, all had their effectiveness in prevention[11]. Here we concentrated on those measures targeting mainly at minimizing nosocomial infections in medical institutions and transmissions to healthcare personnel, and divided the issues into the following three major aspects:

1. Early Detection and Screening

Medical institutions played a vital role at the very beginning stage of SARS-CoV transmission since healthcare personnel, patients, and visitors in hospitals had opportunities to come in contact with or be exposed to a SARS patient and acquire the risk of the disease from there. Both outbreak experiences in Taiwan and Toronto demonstrated how difficult it was to successfully detect a SARS index patient in the early stage, especially when the patient’s symptoms were “atypical” and not easily recognized or differentiated. Once the hospital had a SARS patient incidentally escaped the screening system and become an unknown “source”, then a series of subsequent infections would be inevitable.

Therefore, timely screening and detecting of SARS patients in the "early stage" is very important to launch a series of preventive efforts.

Noticeably, the major site for SARS transmission to take place was the hospital emergency rooms (ER) both in Taiwan and Canada. Many important preventive measures such as triage screening had to be done at the ER, i.e. anyone admitted to the hospital has to fill out a special questionnaire, having body temperature measured and documented, having hands washed, and wearing a surgical mask. With no rapid diagnosis available, the attending physician has to rely on patient's travel and contact history to make a judgement[16]. Healthcare personnel stationed at the emergency department of NTU Hospital initiated a score system to screen and reasonably guess whether a new patient was a SARS case or not, based on the deduction from clinical observations and their previous experiences when they did not have available laboratory diagnosis tests during the early period of the epidemic [23]. Chi Mei Hospital in Tainan County and Municipal WanFang Hospital in Taipei City initiated a computerized approach to track SARS patients and prevent nosocomial SARS. In fact, Hong Kong actually used clinic criteria to screen possible SARS patients and did it much earlier than anywhere else.

In order to arrest the spread of the new SARS-CoV, Taiwan as well as Canada faced the same dilemma at the peak of the epidemic: Since a feverish patient with respiratory symptoms was potentially a SARS patient and might transmit the virus to other patients, the government tried its best to isolate them by establishing SARS-designated hospitals, or converting some other buildings into fever clinics, exclusively examining feverish patients. These so called "fever-screening stations" in Taiwan was developed with the objective of creating places with little risk where feverish people could be screened and examined and thus minimizing the spread and incidental contact other low-risk people with this dreadful new SARS-CoV. Indeed, no evidence of any secondary transmissions ever took place at those fever clinics in Toronto or fever-screening stations in Taiwan[16]. Therefore, to confront a future EID: we must first grasp the clinical signs and symptoms of a few cases at the earliest stage of an outbreak and also investigate the involved epidemiological characteristics and risk factors to find out the disease's period of communicability; and then proceed to figure out the most effective way to interrupt the chains of transmission.

2. Strict Adherence to Infection Control Practices

The SARS patients frequently transmitted the virus onto the hospital healthcare workers at close range, however, no definitive laboratory diagnostic methods was available and the mode of transmission was unclear at the beginning of the global outbreak. Health authorities of countries with SARS used the strictest personal protective gear to fend off possible transmission through air and contact. That is, each hospital healthcare worker who cared for SARS patients was required to put on a complete set of personal protective equipment (PPE), including isolation gown, gloves, eye protection, and N95 face mask or even better respiratory filtration. Such high level of protective equipment was widely used in the past to protect healthcare personnel against diseases like tuberculosis and small pox.

According to a retrospective cohort study[9] on 43 nurses who worked at the two Toronto critical care units that admitted and treated SARS patients during the 2003 outbreak, three patient care activities were associated with the SARS infection: intubation [relative risk (RR): 4.20, 95% confidence interval (CI): 1.58-11.14], suctioning before intubation (RR: 4.20, 95% CI: 1.58-11.14), and manipulating an oxygen mask (RR: 9.0, 95% CI: 1.25-64.89). Health workers engaged in these three activities ran great risk of being infected. It also showed that continuously wearing a N95 or surgical mask would reduce the risk of acquiring SARS by near 80%. This observation was quite similar to the results of a study conducted in Hong Kong[9]**.** On protective factors, studies in Hong Kong and Singapore showed that strong protection of healthcare workers was conferred by hand washing [odds ratio (OR): 0.06, 95% CI: 0.007-0.5] and wearing of N95 masks (OR: 0.1, 95% CI: 0.03-0.4). Also, receiving more than two hours of educational training on infection control was very helpful in facilitating their understanding of the measures for infection control (OR 7.29, $p < 0.001$). They were all very important for nosocomial infection control with statistical significance[14,24,25]. However, based on Toronto's experience of the second outbreak found that one ought to pay particular attention to the correct procedures in taking off the gloves and hand washing while leaving a SARS infected risk areas to avoid contaminating the environment or cause infection among other patients (the wearing gloves unadjusted odds ratio: 2.42-20.54, $p < 0.05$). In addition, physicians, nurses, and other ancillary staff at healthcare facilities required rapid intensive training to understand the concepts and frequent practiced standard operational procedures (SOP) of infection control before the arrival of possible prevailing season. In Taiwan, health officials developed many informative teaching materials (including posters, videos, short television features, etc.) to educate and remind healthcare workers. Studies also reveal that such educational activities reduced nurses' fear to newly EID, and improve their willingness to take care of patients. In the future, this sort of rapid trainings should involve family members and hired long-term caretakers of the hospitalized patients[16].

The strategies on reinforcing nosocomial infection control measures, quickly completing epidemiological investigation, and contact-tracing of SARS did help to rapidly reduce the SARS transmission in Toronto. Another study on the Toronto SARS outbreak discovered two more important risk factors[26]. One involved intensive care units (ICU), but the problem was solved after they strengthened infection control measures of the ICU and no more ICU transmission of SARS occurred since then. The other factor was the level of alertness for the epidemic. As we mentioned earlier, the second outbreak in Canada in 2003 was due to a lapse in infection control practices after the official ending of the first outbreak and a patient with an underlying disease was admitted to an orthopedics ward, which was indeed infected with SARS virus but still in the incubation stage. When infection control measures were re-tightened plus the implementation of an active surveillance for hospitalizing patients, the Toronto outbreak eventually truly ended[16].

These experiences taught us that healthcare workers must always keep "high level alertness" to patients with either acute respiratory disease symptoms or chronic respiratory ailments, especially when feverish clusters appear among patients, healthcare workers, and/or hospital visitors[16,26]. The worst scenario seems to be that the infection spreads quietly inside the hospital without notice and is overlooked until it is much too late when one of the infected individual becomes seriously ill or fatal. These also warned us that health authorities should always take seriously on infectious disease surveillance and nosocomial infection control within medical facilities. They should routinely check and evaluate the appropriateness and effectiveness of various infection control practices, or to identify the areas that need improvement, and timely investigate any possible transmissions. In fact, once these infection control measures were seriously put to practice, the number of SARS cases dropped strikingly right afterward. Other prevention approaches such as monitoring infections or fever with unknown origin among travelers and densely populated institutions for early detection of cases are particularly important for minimizing public health threat of a newly EID in its brewing stage.

Hand washing is the simplest infection preventive measure and is equally important in hospitals and other public premises. In hospital public sites, wherever may be touched by public "hands," such as elevator push-buttons and handrails of escalators, can all be made safer to touch by minimizing the transmission of SARS-CoV among people. For instance, disinfectant dispensers activated by elbow (instead of hand) at the hand washing sites could be provided. Besides, should hospital healthcare workers come across any patient with respiratory illness, they must wear oral masks by all means[14,16]. A quite regrettable situation was that many people at large indiscriminately wore N95 masks in all circumstances in Taiwan even after the nosocomial SARS outbreak was over. This unnecessary use led to a serious supply shortage of such masks at places where they were most needed. Therefore, our health authorities immediately launched a public education campaign on "Standards and Protocols of How to Use Masks Properly." through mass media in May 2003.

D. Isolation Precautions of SARS Patients[16]

Negative-pressure isolation wardrooms were emphasized to prevent "possible" air-borne transmission of SARS when the mode of SARS transmission was unclear at the beginning of the 2003 outbreak. This approach apparently worked well as the few early Taiwan SARS cases were soon brought under control and no nosocomial infections happened. However, along with the quick increase in case number, hospitals soon ran out of negative-pressure isolation rooms. Therefore, we can readily realize that keeping good habits against nosocomial infections is far more important than merely relying on negative-pressure isolation rooms. Of course, there are two ways to solve the problem of negative-pressure isolation room shortage. One is quite straightforward: the government can financially support in building more such wardrooms. The alternative is that the hospital may rearrange the air-exchange system of its buildings, so they can put SARS patients into wardrooms having isolated air-conditioning system of their own and separated from the rest of the hospital.

From the successful SARS-control experiences in Taiwan and Toronto, Two important preventive strategies stood out from the successful SARS-control experiences in Taiwan and Toronto. One was rigorous entrance control and surveillance of newly coming patients and visitors entering the hospital plus daily body temperature monitoring for hospital healthcare workers. The other was converting several hospitals into SARS-designated hospitals to ensure adequate medical care for SARS patients right at the peak time of the epidemic. However, when these two strategies were first put into effect, relevant government officials faced many challenges and different opinions from the public. The Canadian health authorities simultaneously selected four hospitals which admitted and treated SARS patients during the second outbreak based on the rationale that this approaches would only enhance the alertness of healthcare workers in each of all four hospitals.

Conclusions and Recommendations

Summing up the above outbreaks in various countries, we can obviously find that the start of rapid SARS spread in 2002-2003 was mostly related with nosocomial infections. This is not surprising because modern medical-settings often simultaneously operated on acute patients, chronic patients, inpatients, and outpatients, which makes the hospital particularly vulnerable for easily spreading communicable diseases among people in all walks of life including the hospital workers. When the hospital healthcare workers on duty got infected themselves, the treatment and caring work routines for other patients during the SARS epidemic would definitely be severely jeopardized or at least face great difficulties. In fact, global experiences indicated that no SARS epidemic of a region or country could be rapidly terminated before the regional nosocomial infections were first put under control.

However, many infection control measures that were once strictly adhered and practiced during the 2003 SARS outbreaks apparently lost the subjective reasons to be emphasized and kept on in the post-SARS era. Furthermore, some of those measures are only appropriate when the level of epidemic suits them right. Therefore, they need not to be restarted unless outbreak explodes somewhere else in the world. Such an upgrade entirely relied on the warning that this outbreak country actively notified other countries or honestly reported to the WHO as early as possible by transparently providing all the epidemiological information. From now on, whether SARS or another newly EID (avian flu for instance) would be spread swiftly across country borders as SARS did in 2003, or whether its epidemiology would be similar to that of SARS, the severity of disease and the needs for patients' medical care will be very likely to put healthcare workers in great risk again[16]. Therefore, it is the responsibility of the health authorities to strengthen infection control and protection at all local hospitals and clinics continuously, enhance the alertness of healthcare personnel, and fortify the public health tasks involving monitoring fever patients in medical facilities as well as dense-population institutions. Taken together, all these efforts are exceptionally important during the prevailing season and ahead of it[2].

In future perspectives, we must prepare ourselves through the root of medical education, routine practices in nosocomial infection control, and the universal health insurance system in Taiwan. However, modern medical institutions put the economic concerns as the top priority leading to solid efforts in nosocomial infection control which would be a very costly investment with no sure timely profit shown. Particularly, for the cost benefit concerns nowadays, all public and private medical facilities trim their regular staff significantly in size and rely more and more on temporary hired hands in order to cut down on day-to-day running costs. These contingent workers may not be professionally competent to take care of SARS patients and immediately contain the epidemic. This managerial change not only causes difficulties in personnel training and management, but also creates another potential worry in shortage of "courageous and well-trained" healthcare workers who would be working willingly on the front line, treating and taking care of patients, and winning the battle confidently and swiftly whenever large-scale epidemics would break out in the future.

Based on the epidemiological characteristics of the 2003 SARS outbreak in Taiwan, we would like to sincerely make the following four recommendations for status quo improvement:

1. We should continuously implement the routine fever screening of hospital visitors and newly admitted patients, along with the subsequent triage categorization, traffic control for the infected ones, and what-to-do mandates. Do not ever take it lightly only because there is no outbreak in the news at this moment. For every feverish patient, we should inquire the travel history, and contact history of animal and humans.
2. Always try to boost the alertness of the healthcare workers on the front line.

Besides, since nursing jobs have a rather high turn over rate, not only more frequent regular educational training should be held, emphasis also needs to be placed on pre-job training for new staff members and then further evaluation on the effectiveness of trainings afterwards.

3. Contracted outside employees working in the medical facilities, such as laundry attendants, hired caretakers, who easily become the weak links in nosocomial infections, should also be included in the regular training program and pre-job courses.
4. During the SARS outbreak, there were protests among healthcare workers, which were mainly caused by the lack of protective equipments. Therefore, we highly recommend each of all medical facilities should have a management information system (MIS) set up and regularly monitor their stockpile of prevention materials to make sure they will have enough materials whenever the need arises.

In conclusion, the most worry of WHO at this moment is the potential of pandemic influenza which similar to SARS, also requires the detection of the probable cases as early as possible. Also, both diseases can easily bring about large numbers of patients and infected healthcare workers in short period. In particular, influenza may result in larger-scale epidemic than that of SARS. In fact, during that 2002-2003 SARS global outbreaks, the so-called three regions on both shores of the Taiwan Strait, i.e. Mainland China, Hong Kong, and Taiwan, accounted for 91.7% of the total SARS cases in the world. In the current atmosphere with the cross-Strait "small three direct transportation links" having been highly promoted at government as well as private sector levels, some drastic changes like direct flights seem to be imminent. Since Taiwan is a region with unique geographic importance, how to detect future outbreaks instantly and efficiently and send out "early" alert immediately will be the greatest challenge for epidemic prevention in public health, the biggest breakthrough needed, and the most contributory opportunity to the global health as well.

Acknowledgements

The authors would like to heartedly thank all public health government personnel and health authorities, worked at central and local departments of health during the 2003 Taiwan SARS outbreak. Sincere thanks also go out to healthcare workers of infection control and emergency departments, and administrators and leaders of the SARS most affected hospitals for their full devotions, and contributions. Because of their sincere concerns and accumulated efforts in public health, Taiwan was able to contain the epidemic and return to normal life within one month after May of 2003 while the majority of folks were in panic. We also feel indebted to the US CDC and WHO infectious disease experts, who voluntarily came to Taiwan to lend us a helping hand. Their honorable and passionate deeds broadened the heart of our younger generation on international view, and their relentless pursuit of true answers when facing such a severe public health threaten outbreaks also served the best role model. We greatly appreciate Dr. Sam Shih and Ms Po-Ju Chen for their efforts in English translation and polishing, respectively. Last but not the least, we want to express our gratitude to Dr. Mei-Shiang Ho, Dr. Clement C.S. Hsu, Dr. Yee-Chun Chen, Dr. Shan-Chwen Chang, Dr. Ih-Jen Su, Dr. Po-Ren Hsueh, and Dr. Day-Yu Chao for their invaluable discussions and suggestions.

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Table 1. Clinical Symptoms and Signs Usually Associated with SARS Patients[5]

Clinical presentation	Symptoms and signs usually appear after the infection of SARS-CoV
Early symptoms	1. First 2-7 days may have the following symptoms, but no respiratory symptoms: (a) High fever* (d) Fatigue (b) Chills (e) Muscle ache (c) Headache (f) Diarrhea 2. 2-7 days after the onset of the above symptoms, respiratory symptom will follow, and it has the following features: (a) Dry cough with no sputum (b) Breathing difficulties 3. Without the appearance of upper respiratory track symptoms. *Be aware that elder people may have fever of lower temperature [12].
Laboratory findings	1. Normal or lower white blood cell count. 2. Lower lymphocyte count. 3. Blood platelet count lightly lower. 4. Higher LDH* reading. 5. Higher CPK* reading. 6. Higher GOT* reading. 7. Delayed activation time of local thrombin. (*CPK: Creatine Phosphokinase *LDH: Lactate Dehydrogenase *GOT: Glutamyl Oxaloacetic Transaminase)
X-ray finding	Most patients start to show chest X-ray abnormalities in the second week after the disease onset.

Table 2. Statistics of the 2003 Global SARS Epidemic in Eight Regions with Indigenous Cases and No of Infected Healthcare Workers

Region	Probable case no.	Median age (Range)	No. of deaths	Case Fatality rate (%)	No. of imported cases (%)	No. of infected healthcare workers (%)	Onset date of the first probable SARS case (Y-M-D)	Onset date of the last probable SARS case (Y-M-D)
Mainland China	5327	Not available	349	7	Unknown	1002 (19%)	2002-11-16	2003-06-03
Hong Kong	1755	40 (0-100)	302	17	79 (4.5%)	405 (23.1%)	2003-02-15	2003-05-31
Taiwan	346	42 (0-93)	37	11	21 (6%)	68 (20%)	2003-02-25	2003-06-15
Canada	251	49 (1-98)	43	17	5 (2%)	109 (43%)	2003-02-23	2003-06-12
Singapore	238	35 (1-90)	33	14	8 (3%)	97 (41%)	2003-02-25	2003-05-05
Vietnam	63	43 (20-76)	5	8	1 (2%)	36 (57%)	2003-02-23	2003-04-14
Philippines	14	41 (29-73)	2	14	7 (50%)	4 (29%)	2003-02-25	2003-05-05
Mongolia	9	32 (17-63)	0	0	8 (89%)	0 (0%)	2003-03-31	2003-05-06

(Data borrowed from http://www.who.int)

Table 3. A Cluster Analysis on the Type of Source of Infection for the 2003 SARS Cases in Hong Kong[7]

Categories of SARS Clusters based on the Source of the Infection	SARS Patient Number	SARS Patient Percentage
Hospital, elder or nursing homes	866	49.3%
Residents of Amoy Gardens	330	18.8%
Neither hospital nor community infections	152	8.7%
Unknown infection source	134	7.6%
People living in the vicinity of Amoy Gardens 【Note1】	128	7.3%
Imported cases	79	4.5%
Residents of other buildings (not Amoy Gardens)	47	2.7%
On flight infections	19	1.1%
Total	1755	100%

【Note1】: People living in the vicinity of Amoy Gardens means they were living in housing projects next to Amoy Gardens and somehow related to the outbreak of Amoy Gardens, but they were not Amoy Gardens residents.

Table 4. Statistics on Case Numbers and Occupation Categories of Healthcare Workers with SARS in Hong Kong [7]

Occupational Categories	Public Hospitals		Private Hospitals		Private Clinics	
	Case no. (%)	Mortality (95% Confidence Interval)	Case no. (%)	Mortality (95% Confidence Interval)	Case no. (%)	Mortality (95% Confidence Interval)
Physicians	56 (13.8%)	3.6% (0.4-12.3)	0 (0%)	—	8 (2.0%)	25.0 (3.2-65.1)
Nurses	188 (46.4%)	0.5% (0.0-2.9)	16 (4.0%)	0 (0.0-20.6)	6 (1.5%)	0 (0.0-45.9)
Medical Assistants & Others	108 (26.7%)	2.8% (0.6-7.9)	6 (1.5%)	0 (0.0-45.9)	1 (0.3%)	0 (0.0-97.5)
Medical School Students	16 (4.0%)	0 (0.0-20.6)	—	—	—	—