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SARS: The emergence of a new epidemic

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At this moment the world health community is struggling to cope with a severe and rapidly spreading new disease in humans, severe acute respiratory syndrome (SARS). So far, the new disease has been diagnosed in more than 28 countries worldwide. It appears to be the first severe and easily transmissible new disease to emerge in the 21st century. What distinguishes the international health community response to this epidemic is the almost instantaneous communication and information exchange that supported every aspect of the response. The World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and national and local health agencies across the globe have disseminated up-to-the-minute information tailored for clinicians, public health officials, health care workers, travelers, household contacts, and many other affected parties. As SARS is moving too fast for traditional medical journals to stay on the top of the story, this brief report documents the chain of events in the emergence of the new epidemic, the state of clinical and virologic knowledge at the outset of this epidemic, diagnostic procedures, treatment and preventive measures based on information collected from the instantaneous and revolutionary information exchange of the world wide web.

The chain of events began on February 11, 2003 when the Chinese Ministry of Health officially informed the WHO of an outbreak and reported 305 cases of acute respiratory syndrome of unknown cause that occurred in 6 municipalities in Guangdong province in southern China. Five deaths were reported, and transmission was particularly prevalent among health care workers and

US specificity is 97.4% with a NPV of 0.97 and accuracy of 96.4%.

The immediate goal of abdominal assessment after multiple system blunt trauma is rapid determination of the necessity for urgent surgery. A diagnostic screening test for abdominal injury should have both a high sensitivity and a high NPV for the need for acute laparotomy. Ultrasound satisfy these criteria and combined with its speed and non-invasive nature makes it a power tool in the initial assessment of trauma victims. Several studies in the literature refer to the potential cost savings when US is used for BAT.¹ Ultrasound technology has evolved to the point that extensive training and specialization are not required to master specific techniques, thereby making it very suitable for use in trauma resuscitation area.^{2,3} From Kuwait, Abu-Zidan et al,⁴ prospectively evaluated US on 53 patients and found a sensitivity of 85%, a specificity of 100% and an accuracy of 95%. They concluded that US is an accurate and safe method for screening patients With BAT. Hoffman et al⁵ favoured US for initial approach to patients with BAT. The results of this study indicate that US is a highly accurate means to objectively evaluate the abdomen in BAT patients. In this study, US detected 94% of injuries (sensitivity). It also identified 97.4% of the 39 patients without intra-abdominal injury (specificity), and overall accuracy of 96.4%. So the sensitivity, specificity and accuracy in this study are consistent with those studies from North America, Europe and Asia.¹⁻⁵ On the basis of the results of this study, US meets the criteria of useful diagnostic test in blunt trauma patients. It provides diagnostic information that is not available from physical examination or plane film x-ray studies. It can be obtained rapidly and integrated easily into the resuscitation. It is easily repeated, portable and fast which makes it suitable for evaluating large numbers of patients, less stable patients and patients undergoing other diagnostic and therapeutic procedures. Ultrasound should not be used at the exclusion of other Diagnostic modalities or clinical judgment but in combination with them.

Ultrasound is a sensitive, specific and accurate test with which to evaluate patients with abdominal injury requiring surgery. Routine abdominal US can be performed at bedside in emergency departments as a timely, non-invasive diagnostic test. This use of screening abdominal US examination can improve clinical decision-making for the use of emergency laparotomy. The results of this study support the continued use of trauma US as the primary technique for the assessment of abdominal trauma.

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Table 1 - Cumulative number of reported probable cases and number of deaths of severe acute respiratory syndrome during the period 1st November 2002 through to 26th May 2003.

Country	Cumulative n of case(s) ¹	n of new cases	Final status		Date last probable case reported	Date for which case is current
			Death	Recovered ²		
Australia	6	0	0	6	12/5/2003	26/5/2003
Brazil	2	0	0	2	10/4/2003	24/4/2003
Bulgaria	1	0	0	0	24/4/2003	28/4/2003
Canada	148	8	26	110	25/5/2003	25/5/2003
China	5316	24	317	2829	26/5/2003	26/5/2003
China Hong Kong ³	1726	2	267	1276	26/5/2003	26/5/2003
China, Macao	2	0	0	0	21/5/2003	26/5/2003
China, Taiwan	585	62	72	112	26/5/2003	26/5/2003
Colombia	1	0	0	1	5/5/2003	5/5/2003
Finland	1	0	0	1	7/5/2003	20/5/2003
France	7	0	0	6	9/5/2003	22/5/2003
Germany	9	0	0	9	9/5/2003	26/5/2003
India	3	0	0	3	13/5/2003	14/5/2003
Indonesia	2	0	0	2	23/4/2003	23/5/2003
Italy	9	0	0	9	29/4/2003	24/5/2003
Kuwait	1	0	0	1	9/4/2003	20/4/2003
Malaysia	5	0	2	3	20/5/2003	26/5/2003
Mongolia	9	0	0	8	6/5/2003	19/5/2003
New Zealand	1	0	0	1	30/4/2003	26/5/2003
Philippines	12	0	2	10	15/5/2003	24/5/2003
Poland	1	0	0	0	1/5/2003	5/5/2003
Ireland	1	0	0	1	21/3/2003	23/5/2003
Korea	3	0	0	2	14/4/2003	26/5/2003
Romania	1	0	0	1	27/3/2003	22/4/2003
Singapore	206	0	31	163	18/5/2003	23/5/2003
South Africa	1	0	1	0	9/4/2003	3/5/2003
Spain	1	0	0	1	2/4/2003	7/5/2003
Sweden	3	0	0	3	18/4/2003	13/5/2003
Switzerland	1	0	0	1	17/3/2003	16/5/2003
Thailand	8	0	2	6	13/4/2003	25/5/2003
United Kingdom	4	0	0	4	29/4/2003	23/5/2003
United States of America	65	2	0	33	17/5/2003	23/5/2003
Vietnam	63	0	5	58	14/4/2003	14/5/2003
Total	8202	96	725	4662	-----	-----

Source: Cumulative number of reported probable cases of severe acute respiratory syndrome (SARS)
Geneva: World Health Organization, 2003 (Accessed 28 May, 2003 at http://www.who.int/csr/sarscountry/2003_05_26/en/)

1. A decrease in the number of cumulative cases and discrepancies in difference between cumulative number of cases of the last and current WHO update are attributed to the discarding of cases
2. Include cases who are "discharged" as reported by the National Health Authorities
3. One death attributed to Hong Kong Special Administrative region of China occurred in a case medically transferred from Vietnam

their household members. The Chinese authority also provided information that cases had been detected as far back as November 16, 2002. However, SARS was first identified in Vietnam on February 28, 2003 by Dr. Carlo Urbani, the 46-year-old WHO physician and infectious disease specialist who died on March 29, 2003 of the disease. On March 12, 2003, as the condition began to spread from China, the WHO issued a rare global health alert instructing health authorities worldwide to be aware of a new atypical pneumonia, termed by the CDC as the Severe Acute Respiratory Syndrome (SARS) and reported in several countries in Southeast Asia.

Following the WHO global health alert, the CDC formed an emergency operation unit to track and investigate the development of the outbreak. Due to the spread of SARS to several countries in a short period of

time, the WHO issued on March 15, 2003 emergency guidance for travelers and airlines. On March 22, 2003 a team of scientists in the Department of Microbiology at the University of Hong Kong announced their success in culturing the viral agent that causes SARS.¹ Using a special cell line, the Hong Kong scientists isolated the virus from the lung tissue of a patient who developed pneumonia following contact with a professor from Guangdong province in southern China. Both the Professor and the contact died. Two days later, scientists at the CDC and in Hong Kong announced that a new coronavirus had been isolated from patients with SARS. On 16 April 2003, WHO officially announced that a new pathogen, a member of coronavirus family, is the cause of SARS. The available sequence data on this new coronavirus suggest that its sufficiently distinct from

those previously reported in animals and humans; that its source may be yet to be discovered. The name Urbani SARS-associated coronavirus has been proposed for the new virus.² The speed at which this virus was identified has been astounding and was the result of the close and unprecedented international collaboration of 13 laboratories from 10 countries. Close collaboration, with findings shared daily in teleconferences and by email, has allowed advances that normally need months to take place in a matter of days.

Despite the early recognition of the cause of SARS, the causality of this new invader is increasing as each day passes by. During the period November 1, 2002 through May 26, 2003 a total of 8,202 cases with 725 deaths officially reported by the WHO from 30 countries in 5 continents. The countries with the largest number of probable SARS cases, as of May 26, 2003, were China (5,316), Hong Kong Special Administrative Region (1,726), Taiwan (585), Singapore (206), Canada (148), the United States (65) and Vietnam (63). Aside from the one case that was reported in Kuwait in April 20, 2003 no cases have been reported in the Gulf region. This is amazing given the large number of expatriates working in the area from Southeast Asia. **Table 1** illustrates SARS' cumulative number of reported probable cases and number of deaths during the period November 2002 through May 26, 2003. As of May 26, 2003 the majority of patients identified as having SARS have been adults aged 24-78-years-old who were previously healthy. Few suspected cases have been reported among children aged 15-years-old and cases among affected children appear to be very mild.

Epidemiologic evidence to date indicates that transmission of SARS is facilitated by close person-to-person contact. There is no evidence of transmission following casual contact. Potential ways in which SARS can be spread include touching the skin of other people or objects that are contaminated with infectious droplets. Airborne transmission may also have a role in some settings and could account for the extensive spread within buildings and other confined areas that has been observed in some places in Asia. Fomites or other modes of transmission could also be relevant, since coronaviruses can survive on contaminated objects in the environment for at least a few hours and have been isolated from the stool of some animals. Shedding of the SARS virus in feces, respiratory secretions, and urine is now well established. On May 5, 2003 scientists in the WHO network of collaborating laboratories reported results of the first scientific studies designed to determine the survival time of the SARS virus in different environmental media and in feces. Results from studies of the effectiveness of different disinfectants commonly used in hospitals were also reported, confirming the validity of currently recommended measures for infection control.³ The new studies confirm that the SARS virus can survive after drying on plastic surfaces for up to 48 hours. Scientists have also determined that the virus can survive in feces

for at least 2 days, and in urine for at least 24 hours. Studies conducted at a second collaborating laboratory in Hong Kong found that virus in feces taken from patients suffering from diarrhea, which has a lower acidity than normal stools, could survive for 4 days.³ However, the dose of virus needed to cause infection remains unknown.

The incubation period for SARS is typically 10 days; however, several reports have suggested an incubation period as short as one day and as long as 11 days with a median of 5 days. The most common presenting symptoms in 10 cases studied in Canada⁴ were fever (in 100% of cases) and malaise (in 70%), followed by nonproductive cough (in 100%) and dyspnea (in 80%). Lymphopenia (in 89% of those for whom data were available), elevated lactate dehydrogenase levels (in 80%), elevated aspartate aminotransferase levels (in 78%), and elevated creatinine kinase levels (in 56%) were also common. Less common symptoms include sputum production, sore throat, coryza, nausea, vomiting, and diarrhea. In another study of 10 patients in Hong Kong (5 men and 5 women 38-72-years-old),⁵ all patients presented with fever (>38.0 C° for over 24 hours) and most presented with rigor, dry cough, dyspnea, malaise, headache and hypoxemia.

Centers for disease control and prevention recommends that initial diagnostic testing for suspected SARS patients should include chest radiograph, pulse oximetry, blood cultures, sputum gram's stain and culture, and testing for viral respiratory pathogens, notably influenza A and B and respiratory syncytial virus. A specimen for legionella and pneumococcal urinary antigen testing should also be considered. To enhance the future understanding of the SARS disease, WHO recommends that clinicians collect and store sequential samples from patients with SARS for testing when diagnostic tests become readily available. This is particularly important for the first cases recognized in countries that have not previously reported SARS. The current imaging protocol indicates that if SARS is clinically suspected, a chest radiograph should be performed. If the chest radiograph is abnormal (for example varying degrees of pneumonia and acute respiratory distress syndrome), then no further imaging investigation is required other than serial radiographs for follow up. However, if the chest radiograph is normal, a high resolution computed tomography is performed. This may show changes one to 2 days before they become radiographically apparent.

The present role of tests in diagnosis has proved more problematic than hoped. At this time, tests for the new human coronavirus are still being refined, and no sensitivity or specificity data are available. Currently, there are 3 tests available and are helping to improve understanding of how the virus causes disease in human. However, all 3 tests have limitations as tools for bringing the SARS outbreak quickly under control. The first test is the enzyme linked immunosorbent assay which, detect antibodies reliably but only from

approximately day 20 after the onset of clinical symptoms. Therefore, it can not be used to detect cases at an early stage before they have a chance to spread the infection to others. The second category consists of serum antibody tests that include both the indirect immunofluorescence antibodies and enzyme immunoassay. Both detect antibodies reliably as of day 10 of the infection, but are comparatively slow tests that require the growth of virus in cell culture. The third and most currently available test, which is useful in the early stages of infection, is the reverse transcription-polymerase chain reaction molecular test for detection of SARS virus genetic material. The test can detect coronavirus ribonucleic acid in clinical specimens including, blood, serum, stool, and nasal secretions or body tissue. However, it produces many false negatives which means that many persons who actually carry the virus may not be detected creating a dangerous sense of false security for a virus that is known to spread easily in close person-to-person contacts. In the absence of a proven diagnostic test(s), SARS will continue to be diagnosed on the basis of symptoms and exposures, as described in the current SARS case definition which is the presence of fever ($>38^{\circ}\text{C}$), and one or more clinical findings of respiratory illness (for example, cough, shortness of breath, difficulty breathing, or hypoxia), and radiographic evidence of pneumonia, or respiratory distress syndrome, or autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause.

At the present time, the most efficacious treatment regimen, if any, is unknown. In several locations all over the world, treatment regimens have included cefotaxime and clarithromycin (or levofloxacin) to target common pathogens causing community acquired pneumonia. Additionally, antiviral agents such as oseltamivir to treat possible influenza infection. If fever persisted for more than 48 hours and the blood count showed leukopenia, thrombocytopenia, or both, oral ribavirin (1.2g 3 times a day) and corticosteroid therapy (prednisolone at a dose of one mg per kilogram of body weight per day) was given as a combined regimen. Patients with persistent fever and worsening lung opacities were given intravenous ribavirin (400 mg every 8 hours) and corticosteroid therapy (an additional 2-3 pulses of 0.5 mg of methylprednisolone daily. Patients in whom hypoxemia developed were given oxygen through a nasal cannula. Patients were admitted to the intensive care unit if respiratory failure developed, as evidenced by an arterial oxygen saturation of less than 90% while the patient was receiving 50% supplemental oxygen, a respiratory rate that exceeded 35 breaths per minute, or both. Corticosteroids have also been administered orally or intravenously to patients in combination with ribavirin and other antimicrobials. However, others warn from using corticosteroids in treating SARS patients.⁶ Serial chest radiographs showing the resolution of lung opacities could demonstrate a successful response to therapy.

The severity of illness might be highly variable, ranging from mild illness to death. Although a few close contacts of patients with SARS have developed a similar illness, the majority have remained well. Some close contacts have reported a mild, febrile illness without respiratory signs or symptoms, suggesting that illness might not always progress to the respiratory phase. The likelihood of dying from SARS in a given area has been shown to depend on the profile of the cases, including the age group most affected and the presence of underlying disease. Based on data received by the WHO to date, the case fatality ratio is estimated to be less than 1% in persons aged 24 years or younger, 6% in persons aged 25-44 years, 15% in persons aged 45-64 years, and greater than 50% in persons aged 65 years or older.

Despite our long experience with other viral respiratory infections, we have no proven, successful population-based strategy for their prevention. In the early stages of a global outbreak, public health authorities rely on many measures to contain the spread of a contagious illness. Isolation and quarantine are 2 common practices in public health and both aim to control exposure to infected or potentially infected individuals. Both measures may be undertaken voluntarily or compelled by public health authorities. Isolation applies to people who are known to have an illness and restricts their movement to stop the spread of that illness. It allows for the focused delivery of specialized health care to people who are ill, and protects healthy people from getting sick. Isolated people may be cared for in their homes, in hospitals, or at designated health care facilities. Quarantine, in contrast, applies to people who have been exposed and may be infected but are not yet ill. It is medically very effective measure in protecting the public from a contagious disease and intended to stop the spread of that disease.

Severe acute respiratory syndrome patients in many affected countries are being isolated until they are no longer infectious. To date, the WHO and CDC have recommended isolation of individuals with SARS, but has not compelled quarantine or isolation for these individuals. However, several countries are introducing maximum measures, including quarantine, to prevent further international spread. The WHO announced on April 28 the removal of Vietnam from the list of affected areas following 20 consecutive days (the duration of 2 incubation periods) since the last new cases of SARS were detected. This announcement makes Vietnam the first country to successfully contain its SARS outbreak. Key actions that helped Vietnamese officials to contain the outbreak include early recognition of the outbreak, the consolidation of SARS patients in a single hospital, strict infection control, diligent contact tracing, and through investigation of all rumored cases. Toronto, Canada was also removed from the list of areas with recent local transmission on May 14, 2003. The most important WHO consideration is whether 20 days, which is twice the maximum incubation of SARS, have passed since the last locally acquired case was isolated or died.

The key word now for medical personnel around the

world is caution not panic. They should be aware of the protean symptoms of SARS and follow the advice available at the WHO Web site (<http://www.who.int/csr/sars/guidelines/en/>) or the CDC website (<http://www.cdc.gov/ncidod/sars/clinicians.htm>). Clinicians evaluating suspected cases should use standard precautions (for example, hand hygiene) together with airborne precautions (for example, an isolation room with negative pressure relative to the surrounding area and use of N-95 filtering disposable respirator for persons entering the room) and contact (for example, gowns and gloves) precautions. Until the mode of transmission has been defined more precisely, eye protection also should be worn for contact with patients or their environment. Clinicians who suspect cases of SARS are requested to report such cases immediately to their public health authorities. Initial steps toward vaccine development have already begun. Vaccines are successful in preventing coronavirus infection in animals. Hence, the development of an effective vaccine against this new coronavirus is a realistic possibility.

In summary, SARS is an emerging disease that has sickened to date over 8,202 persons on 5 continents. A cumulative list of affected countries and numbers of cases and deaths is released each day on the WHO web site. Speed of scientific discovery and speed of communication are hallmarks of the response to SARS and reflect amazing achievements in science, technology and international collaboration. Awareness of the disease is now very high throughout the world. An increase in the number of suspected cases is to be expected in such an atmosphere of heightened awareness as cases being quickly identified and immediately isolated. Surveillance is proving to be sensitive, with suspected cases rapidly detected, reported to national authorities and WHO, and investigated according to the standard case definition which is being updated as more information becomes available. Knowledge regarding its clinical behavior, diagnostic procedures, response to treatment, and modes and risks of transmission are continually evolving.

The world health community is confident that, in the present climate of heightened awareness, rapid and detailed reporting and a cooperative network of scientists and clinicians working around-the-clock on improving the precision of diagnostic tests to put case definition on a laboratory rather than a clinical basis and developing a reliable treatment, it can and will succeed in bringing this epidemic under control. This will be a very welcomed development by some countries such as the Kingdom of Saudi Arabia where preparations are underway for the next pilgrimage season in which over 2,000,000 Muslims from all over the globe are expected to participate.

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End stage renal disease experience in a general hospital in Eastern Saudi Arabia

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Saudi Aramco (the Saudi Arabian American Oil Company) (SA) is a major employer in the Eastern region of the Kingdom of Saudi Arabia (KSA). It is the largest oil producing company in the world. There are currently around 60,000 employees distributed throughout KSA. The main bulk of these employees are located in the Eastern region, where oil production takes place. Saudi Aramco employees are of multi nationalities, the majority of which are Saudi citizens (90%). All major tribes of the Saudi population are represented in SA. Saudi Aramco offers comprehensive medical care to its employees and their dependents: spouses, parents, and children. Approximately 500,000 individuals (employees and dependents) are eligible for medical care at SA. One half of these individuals (250,000) are treated at Dhahran Health Center (DHC), and the rest are contracted for treatment in private hospitals distributed across the KSA. Over the years, the then simple medical facility, DHC has evolved into a state of the art 600-bed referral institution, in addition to several satellite clinics and local hospitals. Dialysis started at DHC in the early 1980's. Within a relatively short period of time the dialysis population rapidly expanded. In this article we retrospectively report our experience with end stage renal disease (ESRD) over a 4 year period starting January 1998 through December 2001.

Patients who developed ESRD and started hemodialysis (HD) or peritoneal dialysis (PD) at DHC were included. Patients who developed ESRD and did