Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

therapy for patients with acute myocardial infarction is to provide the best care, given the available resources, to such patients in a timely manner at any location. The choice of revascularization method should be decided swiftly, because if angioplasty is delayed excessively its efficacy may well be inferior to that of early thrombolysis, as the reduction in mortality is exceedingly influenced by the rapidity of myocardial reperfusion.

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SARS, Cough, and Fever—or Is It SARS, Fever, and Cough?

In November of 2002, a new atypical pneumonia emerged in mainland China.[1] This infection spread rapidly throughout Southeast Asia and to Canada, and came to be known as the severe acute respiratory syndrome (SARS). A nonspecific case definition was established[2] and a novel coronavirus (SARS-CoV) was identified as the causative agent.[3,4] By the time this pandemic was declared contained in July 2003, almost 800 people had died from > 8,000 infections.[5]

Since July 2003, there has been no documented person-to-person spread of SARS. No one knows for sure if there is a human reservoir, but even if there is not, there is concern that animal and/or laboratory reservoirs could lead to another pandemic. Due to the rapidity of the spread, morbidity, and mortality associated with SARS-CoV, careful monitoring for recurrence of transmission and rapid implementation of control measures is in order.

Although SARS-CoV is less transmissible than previously thought, a few infected persons have been responsible for a disproportionate number of transmissions. These have been referred as *super-spreading events*.[5,6] The incubation period for this infection is 2 to 10 days. Although some asymptomatic and mild infections have been documented, they seem to be uncommon and do not appear to contribute to the spread of disease. Transmission generally has been in close contacts and in health-care and hospital settings. The primary mode of transmission appears to be through direct or indirect contact of mucous membranes with infectious respiratory droplets or fomites.

Several reported series[7–11] have described SARS clinical presentation and course. SARS is manifested by nonspecific complaints such as fever, myalgia, malaise, and chills. Cough is common, but shortness of breath, tachypnea, and pleurisy are prominent later in the course of illness. Laboratory findings include lymphopenia and thrombocytopenia, with increases in d-dimers and activated partial-thromboplastin time. Liver function test (LFT) results may also be elevated. Unfortunately, these symptoms and laboratory findings have not reliably discriminated between SARS and other causes of community-acquired pneumonia. Also, this nonspecificity holds true for the conventional radiograph and high-resolution CT scan findings of SARS.

Reverse transcriptase-polymerase chain reaction (RT-PCR) assays have been developed to assist with the early diagnosis of SARS-CoV infection.[12] Initial tests lacked sensitivity in the first few days of illness. Improved real-time RT-PCR has increased the sensitivity to 80% within the first few days of illness. However, the test still takes hours to complete and will miss 20% of patients with SARS-CoV infection.

Because of the problems with diagnosis described above, case definitions developed for SARS have relied heavily on the contact history. The initial case definition that was published by the World Health Organization (WHO) was shown during an outbreak in Hong Kong to have a sensitivity of only 26% and a specificity of 96%.[13] Clearly, the definition missed too many patients to be helpful in this setting.

In areas where the disease has occurred, there has been an enormous burden on hospitals as well as an emotional strain placed on patients, families, and health-care workers. Obviously, rapid, early diagnosis would alleviate many of these issues.

With these issues in mind, Liu and colleagues report in this issue of *CHEST* (see page 509) the clinical course of SARS during an outbreak of the infection that occurred in Taipei, Taiwan beginning in April 2003. They managed 167 patients who had either suspected or probable SARS according to the WHO case definition. They defined the clinical course and laboratory findings in the subset of 53 patients that SARS-CoV was confirmed either clinically or by polymerase chain reaction (85%) and in whom other diagnoses had been excluded. This is one of the few series to include RT-PCR confirmation of SARS-CoV infection.

The clinical characteristics described by Liu et al are similar to two other reported series, one from Hong Kong (Lee et al[10]) and the other from Toronto, Canada (Booth et al[11]). However, the diagnosis of SARS in the latter two series was based on the case definitions alone. The common symptoms noted in all three series were fever, nonproductive cough, and myalgia. Fever has been found to be almost universally present in patients with SARS. An intriguing finding in the cohort of Liu et al is that the fever in 51 of the 53 patients preceded cough. For the two patients in whom cough occurred first, the patients had a history of chronic cough. By comparison, Booth et al[11] reported that 74% of SARS patients had fever as their first symptom, but 9% of patients had cough or dyspnea alone as the first symptom. However, as the diagnosis of SARS in this series was solely based on case definition, there may have been inclusion of patients without the disease. Both studies suffer from the problems of a retrospective evaluation relying on proper documentation and patient recall. Lee et al[10] (Hong Kong) did not report when symptoms first occurred, simply the frequency in which they were reported. If fever preceding cough were a consistent finding in patients with SARS, it could be used along with other findings as a clue in initially assessing a patient's risk for having SARS.

Other less common symptoms described by Liu et al include headache, dizziness, sore throat, nausea, vomiting and diarrhea, and were consistent with prior reported series.[10,11] Likewise laboratory abnormalities of lymphopenia, thrombocytopenia, and elevated LFT results were frequent and similar to the prior reports. All three series reported chest radiographic infiltrates in a the majority of patients on hospital admission, but no characteristic pattern was noted except in a report[10] from Hong Kong that suggested a predilection of the infiltrates for the periphery. Liu et al described a higher mortality of 21% (11 of 53 patients) than what has been reported previously. Mortality rates of 3.6% and 6.5%, respectively, were reported by Lee et al[10] and Booth et al.[11] The reason for this difference is not clear, but all of the studies confirm the life-threatening nature of the disease.

The experience with SARS to date tells us that effective recognition and rapid institution of infection control practices can limit its spread and bring the disease under control. Thus, the key to controlling SARS is the rapid identification of its presence. Unfortunately, to date no specific clinical, laboratory, or radiologic findings can distinguish with certainty SARS Co-V infection. Even RT-PCR for SARS-CoV presence is fraught with a much higher risk of false-positive results occurring during periods when there is an absence of known person-to-person spread of SARS-CoV infection. Thus, at this time, we are left with using a combination of clinical and epidemiologic factors that suggest this infection. Such factors include the predilection for systemic symptoms (especially fever) to occur prior to respiratory symptoms, for infiltrates on chest radiography

to be peripheral and for lymphopenia and thrombocytopenia as well as elevated LFT results to be present. Obviously, a cluster of patients with such findings and no other explanation should raise suspicion for this disease. Clearly, travel history as well as known exposure to SARS-CoV infected patients is also vitally important. Confirmation of the disease will require laboratory testing that includes rapid RT-PCR and antibody testing using enzyme immunoassay. The antibody testing can only be performed later in the patient course.

If there is a recurrence of SARS, the societal disruption and health-care burden will be tremendous. The earlier the disease is recognized, the sooner infection control procedures can be instituted and the disease brought under control. Further studies of such outbreaks comparing clinical features of SARS (confirmed by laboratory tests) and non-SARS patients may reveal further clues in separating SARS from non-SARS illness from the outset.

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Renal Dose Norepinephrine!

Maintenance of an adequate BP, specifically mean arterial pressure (MAP), is essential for adequate tissue perfusion. When the MAP falls below the autoregulatory range of an organ, blood flow decreases in an almost linear fashion. Decreased blood flow results in tissue ischemia and organ failure. In patients with narrowing of their renal, coronary, or cerebral arteries, and in patients with long-standing hypertension, the fall in organ blood flow will occur at a higher BP. Furthermore, different vascular beds will lose autoregulation at different BP values. The autoregulatory threshold for the mammalian kidney is about 80 mm Hg, while that for the brain is approximately 50 mm Hg. An important goal in the management of critically ill patients is therefore to maintain the MAP above the autoregulatory threshold of the kidney, namely, 80 mm Hg. A higher threshold should be targeted in patients with a history of hypertension and in patients with atherosclerotic vascular disease. In patients who have experienced acute cerebrovascular insults, cerebral autoregulation may be lost, and in such circumstances blood flow is pressure-dependent.[1] In such patients, increasing the MAP beyond the cerebral autoregulatory range may improve tissue perfusion and decrease neuronal loss.[2,3]

Aggressive volume resuscitation is considered to be the best initial therapy for the management of patients with hypotension. Volume resuscitation is initiated with fluid boluses of 500 mL, titrated to BP (*ie*, MAP), heart rate, urine output, and respiratory status. In patients with the systemic inflammatory response syndrome due to sepsis or other causes, hypotension may persist despite vigorous volume expansion. These patients require treatment with a vasopressor agent. Traditionally, dopamine has been regarded as the pressor of choice as it was believed