

Committees and the International Society on Thrombosis and Haemostasis. Chapel Hill: University of North Carolina at Chapel Hill School of Medicine, 2003.

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## A Novel Coronavirus and SARS

**TO THE EDITOR:** Ksiazek et al. (May 15 issue)<sup>1</sup> report that there is antibody cross-reactivity between serum from a patient with severe acute respiratory distress syndrome (SARS) and antibodies that are reactive with group I coronaviruses. This finding raises the possibility of using existing vaccines against these heterologous coronaviruses for protection against SARS. Unfortunately, the study did not show any virus-neutralization activity. Nevertheless, the close similarity between the SARS open reading frame 1b and other human and animal coronaviruses lends support to the idea of using heterologous coronaviral strains, which are harmless to humans, as vaccines. There are several historical examples of successful heterologous vaccination, such as cowpox virus for smallpox in humans and bacille Calmette–Guérin derived from mycobacterium in cattle for tuberculosis in humans. Furthermore, it has been shown that pathogens cause diseases primarily through their ability to evade immune control and through mimicry of host

proteins.<sup>2</sup> “Fuzzy” antigenic recognition might enable T-cell clones to recognize a spectrum of antigens, even antigens that are not closely similar to one another. Thus, the use of altered heterologous antigens, which are structurally different from self-antigens, may improve immunity against the orthologous pathogens.<sup>3</sup>

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## Pseudo-SARS

**TO THE EDITOR:** We evaluated a possible case of severe acute respiratory syndrome (SARS) that involved issues of hospital admission, an inconsistent travel history, and possible enforced isolation. Some of the problems were similar to those described in a recent account in New York.<sup>1</sup>

On May 12, 2003, a 36-year-old white man (accompanied by his Asian wife) was evaluated in our emergency room for fever and cough. He stated that they had arrived in the United States five days earlier from Taiwan, where he worked as an English teacher for physicians. His symptoms began two days after their arrival in the United States. Emergency room personnel placed masks on the couple and isolated them from other patients. This event coincided with the start of the Top Officials

2 (TOPOFF 2) bioterrorism-response exercise at our hospital. When consulted at 1 a.m., we initially questioned whether this patient might be part of the drill. The drill scenario involved an outbreak of pneumonic plague but was also to include some surprises. The patient had no respiratory distress, and a chest radiograph and the oxygen saturation were normal, but the couple had no local residence. Therefore, the patient was admitted to a negative-pressure isolation room and placed under contact and respiratory-isolation precautions in accordance with the recommendations of the Centers for Disease Control and Prevention.<sup>2</sup>

The following day, the patient's diagnosis was reassessed, because he had no fever and he repeatedly requested narcotics for chest pain. That evening, he

threatened to leave the hospital. Although they were suspicious of his story and motives, members of the hospital administration, hospital attorneys, and the public health department had to consider the potential legal options available for enforcing the isolation of a patient posing a potential threat to the public health.<sup>3</sup> When we were finally able to interview the patient's wife separately, she confirmed that they had come from Taiwan but had arrived one month, not five days, previously. She also confirmed that her husband had lost his job nine months earlier because of a drug problem.

This case was frustrating, not only because of the amount of time and resources it demanded, but also because it occurred in association with the TOPOFF 2 exercise. Given the experience with hospital-based outbreaks of SARS in Asia, as reported by Tsang et al. (May 15 issue),<sup>4</sup> and in Toronto, as reported by Poutanen et al. (May 15 issue),<sup>5</sup> possible cases of SARS must be taken seriously, and appropriate infection-control measures must be implemented immediately. Perhaps some of the lessons learned from the TOPOFF 2 exercise can be translated into a heightened awareness and a readiness to handle a more immediate and real threat to the public health — namely, SARS.

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**DRS. TSANG AND HO REPLY:** In response to the letter by Johnson et al. about their case of “pseudo-SARS,” in Hong Kong, we see numerous patients with respiratory symptoms and fever, many of whom have radiologically confirmed pneumonia. Although most patients with SARS have fever, lymphopenia,

increased levels of alanine aminotransferase and lactate dehydrogenase, and radiographic evidence of ground-glass consolidation, these findings are by no means diagnostic. A small proportion of patients with SARS present with a normal chest radiograph, but in most of these patients, ground-glass opacification or frank consolidation is visible on repeated radiography or on high-resolution computed tomography. More specific tests, such as the demonstration of SARS-associated coronavirus RNA on reverse-transcriptase polymerase-chain-reaction analysis, are still unreliable, and anti-SARS IgG is more than 90 percent sensitive, but only 21 to 30 days after the onset of symptoms.<sup>1</sup> The case described by Johnson et al. strongly reemphasizes the difficulties for front-line clinicians, especially those in Asia, who deal with patients with possible SARS, since there is still no effective, rapid diagnostic test, despite the original optimism about its development.

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**DR. LOW REPLIES:** Although SARS has been brought under control in affected areas worldwide, there is ongoing concern that it could reappear and once again spread widely unless we maintain heightened awareness. Control entails the identification of patients and the quick institution of effective isolation precautions. But the case reported by Johnson and colleagues raises an important question: How many patients will we be willing to put in isolation in order to avoid missing one case of SARS? As with SARS, the most important part of tuberculosis-infection control is the isolation of the patient.<sup>1</sup> In regions where tuberculosis is an uncommon diagnosis, a ratio of isolation of 15 patients without disease to 1 patient with disease appears to be acceptable.<sup>2</sup> However, this ratio is likely to be much higher for SARS, as long as we are using the current case definition, which consists of clinical and epidemiologic criteria. The clinical criteria have low predictive ability.<sup>3</sup> The epidemiologic criteria include travel within 10 days before the onset of symptoms to

an area with current or previously documented or suspected community transmission of SARS. With the number of affected areas in the world rapidly dwindling, the challenge will be to maintain our vigilance as the memory of the outbreaks fades.

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## SARS and the Internet

**TO THE EDITOR:** Your editorial (May 15 issue)<sup>1</sup> describes the speed and power of the Internet in communicating to the world knowledge about severe acute respiratory syndrome (SARS) and the progression of the epidemic. This access is indispensable to those of us in Taiwan, from government officials to basic researchers like me. Because of Taiwan's exclusion from the World Health Organization (WHO),<sup>2</sup> we had to rely solely on the Internet to obtain information about SARS from the WHO's Web site and other Web sites like that of the *Journal*, until a team of epidemiologists from the WHO finally arrived in May to assess the damage here. Inexperienced at containing an outbreak, Taiwan was ill prepared for the task, and the deficiencies in hospital management and the health system were exposed. Since late April, a series of

clusters of infections in hospitals made Taiwan's "the most rapidly growing outbreak,"<sup>3</sup> although the pace slowed after mid-May (Fig. 1). It was said that no single entity can manage SARS on its own.<sup>4</sup> For a while, Taiwan was asked by the world to do just that.

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