To the Editor: The article by Hsieh et al. analyzed the daily case-report data for severe acute respiratory syndrome (SARS) from May 5 to June 4, 2003, posted on the Web site for the Taiwan Center for Disease Control, to show how this disease had rapidly spread in the 2003 outbreak (1). Hsieh et al. suggested that infection in hospitalized patients who were classified erroneously as suspected SARS case-patients was a major factor in the rapid spread of the disease in hospitals. Slow classification and delayed placement of these patients in negative-pressure isolation rooms contributed to the high percentage (73%) of nosocomial infection in Taiwan (1).

During the outbreak period (stage II), three teams were responsible for classifying SARS cases (2). The team included infectious disease specialists, respiratory specialists, and epidemiologists recruited from major teaching hospitals throughout Taiwan and was organized by the Taiwan Center for Disease Control and the National Health Insurance Bureau. The team met daily and reviewed the clinical data, travel and contact history, and chest radiographic scans of the reported case-patients obtained (by email or fax) from the patients’ attending physicians. The same protocol (Figure) was used by all team members to classify the case-patients as having suspected or probable SARS. All hospitals that treated patients with suspected SARS either had their own committee to classify patients according to World Health Organization guidelines or followed the protocol for classification or reclassification of reported cases by the team members (3).

Although official reclassification might have taken 12.5 days as suggested by Hsieh et al., the conclusion that inadequate isolation of infected patients during this period led to a higher rate of nosocomial transmission cannot be based on the data available to these authors. From the first day that suspected cases were reported to the Taiwan Center for Disease Control, the patients were placed in negative-pressure isolation rooms when available. Suspected case-patients may have been less likely than probable case-patients to be placed in negative-pressure isolation rooms when these were in short supply; however, all other available isolation precautions were used to treat suspected case-patients before they were reclassified. The notion that increased infection transmission occurred despite these isolation precautions is not consistent with the literature suggesting the central role of gloves, gowns, and surgical masks in preventing transmission (4). Thus, the process of reclassification was not associated with the timing of isolation measures shown to have the greatest impact in preventing infection transmission.

The high proportion of patients with nosocomial SARS infection in Taiwan is consistent with the observations of Lingappa et al. (5) and others who have noted that the hospital setting was the primary amplifier of SARS transmission, with significant community transmission occurring in only the largest outbreaks. The high proportion of nosocomial cases in Taiwan is not unique. Moreover, the potential for nosocomial transmission of SARS is high. In outbreaks where nosocomial transmission occurred, stringent infection control measures were not always consistently implemented. Thus, nosocomial transmission of SARS infection can be prevented, but it requires strict adherence to infection control practices and a high index of suspicion among healthcare workers.

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Figure. Flowchart of classification for severe acute respiratory syndrome (SARS) revised on May 1, 2003. ARDS, acute respiratory distress syndrome.
proportion of nosocomial cases suggests that containment measures instituted in Taiwan were ultimately successful in preventing a much larger outbreak. Multiple factors were associated with the nosocomial outbreaks in Taiwan, including inadequate infection control infrastructure and triage screening that led to delayed detection of several highly contagious index cases.

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In Reply: Hsueh and Yang (1) correctly described the case classification procedure in Taiwan during the 2003 severe acute respiratory syndrome (SARS) outbreak as being conducted simultaneously by three teams of local experts in the northern, central, and southern parts of Taiwan; however, they failed to mention that this procedure was implemented only after May 10 (2). More precisely, before May 9, the relevant medical records of all reported SARS cases patients were reviewed by a SARS Advisory Committee at the Taiwan Center for Disease Control, whose members included respiratory specialists, infectious disease physicians, and epidemiologists. After May 10, because the dramatic increase in the number of new cases attributed to the hospital cluster outbreaks in Taipei in late April (3), the SARS Advisory Committee at the Taiwan Center for Disease Control in Taipei could no longer effectively provide care for the rapidly increasing case load. Consequently, three regional offices of the Bureau of National Health Insurance (BNHI) north, central, and south of Taiwan took over the responsibility of case review and used standard operating procedures for case evaluation (2). Local SARS expert committees were established in all three regions, with each committee consisting of the relevant experts. This policy change provides irrefutable evidence that the authorities expedited the case classification process, which was deemed too slow, because the backlog of cases waiting to be reviewed was mounting.

In a subsequent, related study (Hsieh et al., unpub. data), retrospective statistical analysis of the laboratory-confirmed case data conducted with a two-sample t test indicated that the mean time from initial diagnosis of patients with suspected SARS to reclassification as probable SARS, improved significantly after May 10. The estimated mean time from diagnosis to reclassification was 12.56 days from May 5 to June 4 (3). Final classification was substantially delayed in the suspected SARS cases that were reclassified as probable SARS cases in the days after the new procedure was implemented. However, they were well represented in our mean estimation result.

Another issue raised by Hsueh and Yang concerns the evidence of nosocomial infections. From May 5 to June 4, the suspected SARS patients in Taiwan were placed in negative pressure chambers, when available, as soon as they were diagnosed. However, the operative word here is “when available.” In National Taiwan University Hospital, the most established and well-equipped hospital in Taiwan, swift and efficient isolation was accomplished. Only 31 SARS cases, a small fraction of the Taiwan case data, occurred through exposure in the emergency room at the National Taiwan University Hospital Hospital, which culminated in the temporary shutdown of emergency services on May 12 (3,4). Other hospitals in Taiwan had cluster infections on wards as late as the end of May (5,6). Multiple factors were associated with the nosocomial outbreaks in Taiwan. Our modeling result merely suggested that the slow classification process, which was effectively rectified with the policy change on May 10, had been one of the contributing factors, and the change was subsequently instrumental in the quick containment of the outbreak. The intervention efforts helped prevent SARS infection transmission in medical facilities from spreading into the community. Nonetheless, a more proactive and constructive approach is to learn from this experience and to minimize the opportunity for nosocomial infections to occur in the future.

Finally, we stressed that “with more and better data, one could perhaps estimate the parameters over smaller periods of interest during the complete progression of the epidemic, if not the parameter values for each time n” (3). In the last 2 decades, the academic literature contains abundant evidence of how mathematical modeling can provide insights into infectious diseases (7). The purpose of mathematical modeling is to recon-
struct the epidemic events of importance from the data that are available at the time. Our modeling was conducted during the summer before the end of the epidemic and only the data available from various Web sites was used, which did not allow us to compare the difference in classification time before and after May 10. With the laboratory-confirmed SARS case data now available, we are able provide more definitive and detailed results in a manuscript under review (Hsieh et al., unpub. data), as well as in an ongoing modeling of the SARS outbreak in Taiwan that encompasses intervention measures and behavior change of the general public.

With the current void of precise knowledge regarding the chains of infections that led to the in-hospital and inter-hospital infections in Taiwan, mathematical modeling gives the best hope of understanding exactly how the cluster infections occurred, so we can better meet the challenges of future epidemics. Such knowledge is possible only with the interface of detailed epidemiologic and molecular data of the SARS cases with mathematical modeling. During this past winter season, a second wave of the SARS epidemic was averted. Hopefully, retrospective modeling studies such as ours will better prepare us for the emergence of any infectious diseases in the future.

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