**Ying-Hen Hsieh,* Jen-Yu Lee,* and Hsiao-Ling Chang†**

*National Chung Hsing University, Taichung, Taiwan; and †Center for Disease Control, Taipei, Taiwan

### References

1. Zhou G, Yan G. Severe acute respiratory syndrome epidemic in Asia. Emerg Infect Dis 2003;9:1608–10.
2. Hsieh YH, Chen CWS. Re: Mathematical modeling of SARS: cautious in all our movements. J Epidem Com Health [serial on the Internet]. 2003 [cited 2003 Nov 18]. Available from: http://jech.bmjjournals.com/cgi/eletters/57/6/DC1#66
3. Razum O, Becher H, Kapaun A, Junghanss T. SARS, lay epidemiology, and fear. Lancet. 2003;361:1739–40.
4. World Health Organization. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 [monograph on the Internet]. [cited 2003 Sep 26]. Available from: http://www.who.int/csr/sars/country/table2003_09_23/en/
5. World Health Organization. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS) [monograph on the Internet]. [cited 2003 Oct 17]. Available from: http://www. who.int/csr/sars/en/WHOconsensus.pdf
6. Lee ML, Chen CJ, Su IJ, Chen KT, Yeh CC, King CC, et al. Use of quarantine to prevent transmission of severe acute respiratory syndrome—Taiwan, 2003. MMWR Morb Mortal Wkly Rep. 2003;52:680–3.

Address for correspondence: Ying-Hen Hsieh, Department of Applied Mathematics, National Chung Hsing University, 250 Kuo-Kuang Rd., Taichung, Taiwan 402; fax: 886-4-22853949; email: hsieh@amath.nchu.edu.tw

---

**In Reply**: Our analysis of the dynamics of reported severe acute respiratory syndrome (SARS) clinical cases was conducted in May 2003 during the height of the public panic (1). Our primary goal in that study was to predict "when the epidemic might be brought under control if the current intervention measures were continued." (1). We used the Richards model and successfully predicted the epidemic cessation dates in Beijing, Hong Kong, and Singapore. Our predicted total number of SARS cases was close to the actual number of cases. In addition, we estimated the basic reproductive rate ($R_0$) of SARS infection, and our estimates based on the deterministic model were similar to those based on stochastic models (2,3). Therefore, our analysis provided useful information on the epidemiologic characteristic of SARS infections in three major Asian cities.

Hsieh et al. (4) commented that our article did not address the effect that specific intervention measures might have on the dynamics of SARS infection. Our study was not intended to measure this. As we stated in our article, "the transmission mechanism of the coronavirus that causes SARS and the epidemiological determinants of spread of the virus are poorly understood." Any models built on these unknowns are not suitable for assessing the effects of specific intervention measures. A method suggested by Hsieh et al. (4) to merely "consider a more complicated model with variable maximum case load and growth rate" will not answer the question to any extent.

The retrospective analysis of SARS case dynamics in Taiwan by Hsieh et al. (4) found that "as long as the data include this inflection point and time interval shortly after, the curve fitting and predicting future case number will be reasonably accurate." This notion holds only if the true inflection point is known before an epidemic ends. The main difficulty is how the true inflection point is correctly determined, as noted by Hsieh et al. (4). The time when inflection occurs varies tremendously if truncated data of cumulative SARS case numbers are used. To illustrate this point, we used the cumulative number of reported probable SARS cases in Hong Kong, starting March 17, 2003, but truncated at various dates, and calculated the date when inflection occurred (Table). For example, if the data period from the onset date (March 17, 2003) to the last case reported (June 12, 2003) was used, the date when inflection would occur was estimated as March 19, 2003. If the truncated data ending April 9, April 16, April 30, May 14, and May 28, 2003, were used, the dates when inflection would occur were estimated as April 2, February 7, March 3, March 23, and April 2, 2003, respectively (Table). Clearly, inflection point dates became a moving target as the epidemic progressed. When truncated data ending April 9, April 16, April 30, May 14, and May 28, 2003, were used, the corresponding estimated maximum numbers of cumulative cases (*K*) were 1,107, 1,907, 1,819, 1,749, and 1,733, respectively. Estimation of *K* improved when the data period used for prediction was at least one month past the March 19 inflection point obtained from the entire epidemic period. This analysis highlights the difficulty in identifying an optimal inflection point for prediction purposes during an ongoing epidemic when only a partial cumulative case number is available.

We fully agree with Hsieh et al. (4)

Table. Predicted inflection point and dates when inflection occurs based on truncated data of cumulative number of reported severe acute respiratory syndrome cases in Hong Kong

| Data period (ending date) | $t_m$[a] | Date[b] | *K*[c] | *r*[d] | α[e] |
|---|---|---|---|---|---|
| April 9, 2003 | 16.62 | April 2, 2003 | 1,107 | 0.20 | 0.74 |
| April 16, 2003 | –40.79 | February 7, 2003 | 1,907 | 0.07 | 52.11 |
| April 30, 2003 | –13.52 | March 3, 2003 | 1,819 | 0.07 | 10.21 |
| May 14, 2003 | 6.80 | March 23, 2003 | 1,749 | 0.09 | 2.84 |
| May 28, 2003 | 17.31 | April 2, 2003 | 1,733 | 0.10 | 1.38 |
| June 12, 2003 | 2.63 | March 19, 2003 | 1,751 | 0.09 | 3.77 |

[a] $t_m$ is the inflection point of the model.
[b] Date refers to the date when inflection occurs.
[c] *K* is the predicted maximum number of cumulative cases.
[d] *r* is the intrinsic growth rate.
[e] α measures the extent of deviation of S-shaped dynamics from the classic logistic growth curve.

that the quantitative assessment of the effectiveness of public health intervention measures for SARS is a difficult task for modelers. To make models useful for assessing the effects of specific intervention measures and for predicting the future dynamics during an ongoing epidemic, we need improved knowledge on the transmission mechanisms, pathogenesis, and the epidemiologic determinants of the spread of the virus. Any retrospective analysis of the 2003 SARS epidemic that improves our knowledge of SARS epidemiology is welcome.

**Guofa Zhou* and Guiyan Yan***

*State University of New York, Buffalo, New York, USA

### References

1. Zhou G, Yan G. Severe acute respiratory syndrome epidemic in Asia. Emerg Infect Dis. 2003;9:1608–10.
2. Lipsitch M, Cohen T, Cooper B, Robins JM, Ma S, James L, et al. Transmission dynamics and control of severe acute respiratory syndrome. Science. 2003;300: 1966–70.
3. Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ, et al. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. Science. 2003;300:1961–6.
4. Hsieh YH, Lee JY, Chang HL. SARS epidemiology and cumulative case curve. Emerg Infect Dis. 2004;10:1165–7.

Address for correspondence: Guofa Zhou, Department of Biological Sciences, State University of New York, Buffalo, NY 14260, USA; fax: 716-645-2975; email: gzhou2@buffalo.edu

## Diagnostic Criteria during SARS Outbreak in Hong Kong

**To the Editor:** A novel coronavirus caused more than 8,000 probable cases of severe acute respiratory syndrome (SARS) worldwide (1,2) during the 2003 outbreak. Before the etiologic agent was identified, the diagnosis of SARS was made according to a set of clinical-epidemiologic criteria as suggested by the Centers for Disease Control and Prevention (CDC) (1–3). These criteria remained important in the initial diagnosis and prompt isolation of patients because the overall sensitivity of initial reverse transcriptase-polymerase chain reaction (RT–PCR) testing for SARS-associated coronavirus (SARS CoV) RNA on upper respiratory specimens ranged from approximately 60% to 70% (though sensitivity improved with a second test) (4,5). In a SARS screening clinic at the Prince of Wales emergency department, the positive predictive value (PPV) of these criteria was estimated to be 54% (95% CI 39% to 69%) (6). The relative importance of the clinical versus epidemiologic criteria had not been evaluated. By using paired serologic testing to determine SARS-CoV infection (3), we evaluated the relative importance of the clinical-epidemiologic diagnostic criteria during an outbreak.

Patients with a diagnosis of SARS, and who were admitted to one of five regional hospitals in Hong Kong for isolation and treatment from March 4 to June 6, 2003, were included in this retrospective analysis. Probable SARS case-patients were those who met the CDC clinical criteria for severe respiratory illness of unknown etiology (3), and met the epidemiologic criterion for exposure in either a close or a possible contact. Close contact was defined as caring for, living with, or having direct contact with body fluids of a probable SARS patient (e.g., working in the same medical ward or staying in the same household) within 10 days of initial symptoms. Because Hong Kong was the documented SARS transmission site from February 1 to July 11, 2003, a modified epidemiologic criterion of possible contact was adopted. Possible contact was defined as staying or working in the same hospital compound, or residing in the same building where case clusters of SARS had been reported, within 10 days of symptoms onset.

Laboratory testing of paired immunoglobulin (Ig) G antibody to SARS-CoV was used to determine infection (7). Positive serologic evidence of infection was defined as a four-fold rise in antibody titer or detection of antibody in convalescent-phase serum. Seronegativity was defined as absence of antibody in convalescent-phase serum obtained ≥21 days after symptom onset (3). Seronegativity in this defined time frame (≥21 days – serum collected before July 11, 2003, and beyond 28 days) excluded the diagnosis of SARS (3). Samples from patients showing nonspecific fluorescent signals were considered negative for SARS-CoV infection. RT-PCR was performed on clinical specimens (respiratory, fecal) from all patients (1,3–5).

Demographic and laboratory parameters and history of close contact were compared between the seropositive and seronegative groups. Student *t* test was used to analyze continuous variables. A p value of $<0.05$ was considered statistically significant. Odds ratio (OR) and 95% confidence interval (CI) were calculated for categorical variables.

During the study period, 475 patients were hospitalized with probable SARS. One hundred patients were excluded because their serologic results were either missing (n = 37) or they died before day 21 of illness (no convalescent-phase serum, n = 63). Three hundred seventy-five patients were included in the analyses; 353 (94.1%) patients were serology-positive for SARS-CoV. Two hundred sixty-three of the 353 patients (74.5%) had a 4-fold increase in antibody titers, and 90 of the 353 patients