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Severe Acute Respiratory Syndrome Epidemic in Asia

Guofa Zhou* and Guiyun Yan*

We analyzed the dynamics of cumulative severe acute respiratory syndrome (SARS) cases in Singapore, Hong Kong, and Beijing using the Richards model. The predicted total SARS incidence was close to the actual number of cases; the predicted cessation date was close to the lower limit of the 95% confidence interval.

As of May 15, 2003, the cumulative number of reported probable cases of severe acute respiratory syndrome (SARS) was $\geq 7,600$ worldwide (1). In the 28 countries reporting SARS cases, the People's Republic of China (PRC), particularly the Hong Kong Special Administrative Region and the Beijing Municipality, reported most of the cases. The Beijing municipal government took various measures to prevent the spread of SARS. As in Hong Kong (2,3), measures in Beijing included wearing masks and handwashing, mandatory home quarantine of persons who had contact with probable SARS patients, suspension of schools and universities for 2 weeks, restrictions on public gatherings, screening body temperatures of air travelers, discouragement of mass migration by air or train, designation of special hospitals for the treatment of SARS patients, and education on SARS transmission and personal protection. The number of new cases reported daily in Beijing were high (e.g., 39 new cases on May 14, 2003), and public and health authorities were concerned about how extensive the SARS epidemic might be and when the SARS epidemic might be brought under control if intervention measures were continued.

The Study

We examined the dynamics of reported SARS clinical cases in three cities in Asia (Beijing, Hong Kong, and Singapore) and used the Richards model (4) to predict SARS infection over several months. For Hong Kong and Singapore, data on SARS cases were extracted from daily reports of the World Health Organization (WHO) from March 17 to May 15, 2003 (1). For Beijing, the number of confirmed SARS cases was published by the Ministry of Health of PRC (5). (The PRC's report was used because WHO did not report SARS case incidence in Beijing; the

WHO report summarized the total number of SARS cases in mainland China.) Although SARS case reporting started in early April 2003 in Beijing, the accuracy of SARS daily case reporting in Beijing before April 21 was questioned (6); thus our analysis for Beijing was based on case numbers from April 21 to May 15, 2003. Data indicated that daily new SARS cases were declining since April 12, April 2, and April 29 in Singapore, Hong Kong, and Beijing, respectively (Figure). The cumulative cases in all three localities resembled S-shaped curves (Figure).

When $S(t)$ is used to represent the cumulative number of SARS cases on day t , the dynamics of S can be modeled as

$$\frac{dS}{dt} = r \frac{S}{F(S)}$$

where r is the intrinsic growth rate, and $F(S)$ measures the effectiveness of intervention measures. The basic reproductive number of an infection, R_0 (defined as the average number of secondary cases generated by one primary case), can be estimated as $R_0 = e^{(rT)}$, where T is the generation time of an infection. This model assumes that 1) the rate of cumulative SARS case increase is proportional to the present number of cases, 2) without control measures the SARS case incidence grows exponentially, and 3) intervention measures will have a negative effect on SARS case increase. This model does not take into account spatial and stochastic processes of SARS transmission. $F(S)$ can be expressed as

$$\frac{1}{F(S)} = 1 - \left(\frac{S}{K} \right)^\alpha,$$

where K is the maximum cumulative case incidence, and α measures the extent of deviation of S-shaped dynamics from the classic logistic growth model ($\alpha = 1$). $\alpha > 1$ or $\alpha < 1$ indicates that the cumulative case numbers grow faster or slower than predicted by the logistic growth model (4). The explicit solution of the model is

$$S = \frac{K}{\left(1 + e^{-r(t-t_m)}\right)^{1/\alpha}}, \quad \text{where } t_m = \frac{1}{r} \text{Ln} \left(\left[\frac{K}{S_0} \right]^\alpha - 1 \right),$$

and S_0 is the number of cases at $t = 0$. Parameter t_m is the inflection point where maximum growth rate occurs; in the case of logistic growth model $S = K/2$ when $t = t_m$. This model predicts that the cumulative SARS case incidence follows an S-shaped curve and gradually reaches a maximum case incidence, K . The end of the epidemic is defined as not a single new SARS case emerging in 3 consecutive months (7). The earliest time to reach this point, t_0 , is calculated through the numerical solution of inequality

$$\int_{t_0}^{t_0+90} (K - S(t)) dt < 1$$

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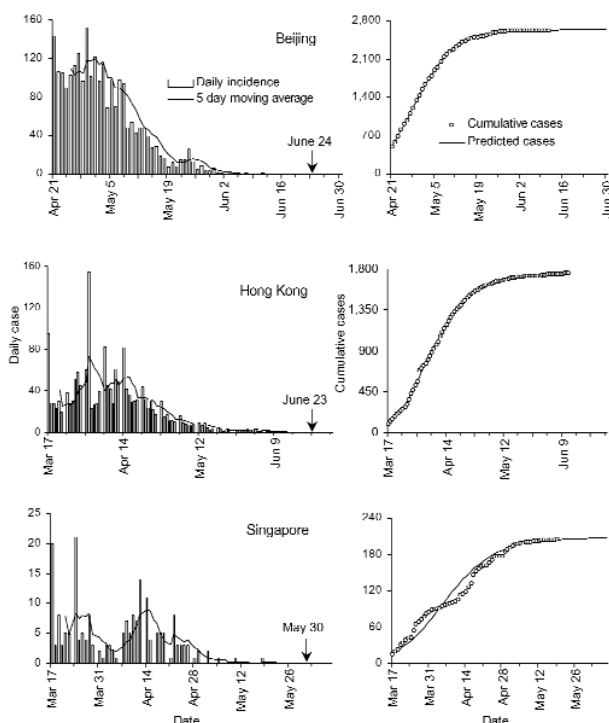


Figure. Epidemiologic depiction of epidemic of severe acute respiratory syndrome (SARS) in Beijing, Hong Kong, and Singapore. The number of daily confirmed SARS cases and 5-day moving average are represented by the left graphs. The observed and predicted cumulative cases since April 21, 2003 (Beijing), and March 17, 2003 (Hong Kong and Singapore), are shown in the right graphs. The modeling used case incidence data up to May 14, 2003. The arrow indicates the date that the World Health Organization removed the locality from the list of areas with local transmission.

Conclusions

The association between cumulative number of cases and time is well described by the Richards model (Figure). For the three localities, highly significant correlations between observed and predicted incidence were found (adjusted $r^2 > 0.98$, $p < 0.01$ for goodness-of-fit of the model) (8). The maximum predicted cumulative incidence, K , was estimated to be 2,595 for Beijing, 1,748 for Hong Kong, and 207 for Singapore (Table). We estimated the 95% confidence interval (CI) of the predicted incidence and time for the epidemic to cease by inverse prediction

based on the relationship $\text{Log}((K/S)^{\alpha}-1)=rt_m-rt$ (8). If we assume that an epidemic is over when no new cases occur in 3 consecutive months, the earliest time for the end of the SARS epidemic, if intervention measures continued and no cases were imported, was estimated to be June 27, 2003, in Beijing; June 29, 2003, in Hong Kong; and May 28, 2003, in Singapore (see Table for 95% CI). Using 8.4 days as the generation time of a SARS infection, as estimated from the mean serial interval between the time from onset of symptoms in index patient to onset of symptoms in secondary case-patient in Singapore (9), we estimated the basic reproductive number of SARS infections, R_0 , to be 2.7, 2.1, and 3.8 in Singapore, Hong Kong, and Beijing, respectively. The higher R_0 value in Beijing likely resulted from delays in exercising effective control measures. The R_0 estimates for Singapore and Hong Kong, when the Richards model and SARS case incidence data through May 14, 2003 were used, were similar to those based on stochastic models (9,10).

The transmission mechanism of the coronavirus that causes SARS and the epidemiologic determinants of spread of the virus are poorly understood (2). Our predictions were based on the trend analysis, assuming effective intervention measures would continue in the three cities. Predicting SARS dynamics on the basis of data from early in the epidemic could have led to untenable conclusions (11); however, we found that the SARS epidemic in Hong Kong and Singapore in May 2003, was not in an early stage. The case data in these two localities clearly indicated S-shaped dynamics. Assuming SARS dynamics in Beijing would follow a similar pattern, we used the Richards model to predict that the SARS epidemic in Beijing would end by late June 2003. This prediction, made on May 21, 2003, was based on the trend analysis and assumed that effective intervention measures would continue.

On May 30, June 23, and June 24, 2003, respectively, WHO removed Singapore, Hong Kong, and Beijing from the list of areas with local transmission (12–14). As of July 10, a total of 8,436 SARS cases had been reported in 29 countries worldwide (15). The actual cumulative SARS cases were 206 for Singapore; 1,755 for Hong Kong; and 2,631 for Beijing (5,15). The observed total SARS incidence was within our predicted 95% CI for all three local-

Table. Predicted epidemic cessation date and maximum number of cases severe acute respiratory syndrome

Locality	Parameter estimation ^a			Maximum no. of cases (95% CI) ^b	Epidemic cessation date (95% CI)
	t_m	r	α		
Beijing	8.94	0.16	1.00	2,595 (2,541 to 2,649)	June 27, 2003 (June 14 – July 10)
Hong Kong	6.11	0.09	2.94	1,748 (1,619 to 1,777)	June 29, 2003 (June 14 – July 14)
Singapore	14.50	0.12	1.51	207 (191 to 223)	May 28, 2003 (May 20 – June 5)

^a t_m , the inflection point of the growth model; r , the intrinsic growth rate; α , the measurement of the extent of deviation of S-shaped dynamics from the classic logistic growth curve.

^bCI, confidence interval.

ities (Table). The error rate (the difference between actual and predicted cumulative incidence divided by actual incidence) is 0.5%, 0.4%, and 1.4% for Singapore, Hong Kong, and Beijing, respectively.

The last probable SARS cases were reported on May 18 for Singapore, June 12 for Hong Kong, and June 11 for Beijing. The predicted SARS cessation date was later than the date the last probable SARS case was reported for all three cities but very close to the lower limit of the 95% CI (Table). Our results suggest that the simple Richards model describes well the SARS case incidence dynamics (under effective control measures) in Singapore, Hong Kong, and Beijing.

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