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The outbreak pattern of the SARS cases in Asia

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Abstract **The severe acute respiratory syndrome (SARS) caused tremendous damage to many Asia countries, especially China. The transmission process and outbreak pattern of SARS is still not well understood. This study aims to find a simple model to describe the outbreak pattern of SARS cases by using SARS case data commonly released by governments. The outbreak pattern of cumulative SARS cases is expected to be a logistic type because the infection will be slowed down due to the increasing control effort by people and/or due to depletion of susceptible individuals. The increase rate of SARS cases is expected to decrease with the cumulative SARS cases, as described by the traditional logistical model, which is widely used in population dynamic studies. The instantaneous rate of increases were significantly and negatively correlated with the cumulative SARS cases in mainland of China (including Beijing, Hebei, Tianjin, Shanxi, the Autonomous Region of Inner Mongolia) and Singapore. The basic reproduction number R_0 in Asia ranged from 2.0 to 5.6 (except for Taiwan, China). The R_0 of Hebei and Tianjin were much higher than that of Singapore, Hongkong, Beijing, Shanxi, Inner Mongolia, indicating SARS virus might have originated differently or new mutations occurred during transmission. We demonstrated that the outbreaks of SARS in many regions of Asia were well described by the logistic model, and the control measures implemented by governments are effective. The maximum instantaneous rate of increase, basic reproductive number, and maximum cumulative SARS cases were also calculated by using the logistic model.**

Keywords: severe acute respiratory syndrome (SARS), outbreak, epidemiology, logistic model.

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Severe acute respiratory syndrome (SARS) inflicted huge chaos and damages in Asia and some other regions in 2003. Recently, Lipsitch et al.[1] and Riley et al.[2] reported the transmission epidemic of SARS in Singapore and Hong Kong. Both teams made use of mathematical models based on a system of four subpopulations: susceptible, exposed, infectious, and recovered (immune) individual, also called a SEIR model[3]. They estimated that the basic reproduction number R_0 at the early stage without control is of order 2 to 4. The basic reproductive number is a good indicator of the severity of epidemic diseases and effectiveness of control[4—6]. If $R_0<1$, it means that the disease will eventually disappear, while $R_0>1$ implies that the disease will persist[6]. Estimation of R_0 from disease outbreak data is not an easy job because the actual process of infection is not observable, data are often incomplete and the rate of infection is often nonlinear[7—13]. In most situations, detailed epidemical data are lacking. It is time consuming and labor consuming to trace the secondary infection cases from a single SARS case. It is necessary to find an alternative model to describe the outbreak pattern of SARS cases by using simple data of number of SARS cases commonly released by governments.

1 Methods

In population ecology, the continuous exponential model of population growth is described by

$$\frac{dN}{dt} = rN,$$

where N is the population size, and r is the instantaneous rate of increase. The discrete model is written as

$$N_{t+1} = \lambda N_t,$$

where N_t is the population size at time t, λ is the finite rate of increase, and $\lambda=e^r$. Because resources are limited, the instantaneous rate of increase usually decreases with the increase in population size, which is called the effect of density dependency. The logistic model has been widely used to describe the population growth under limited resources. The continuous logistic model is written as:

$$\frac{dN}{dt} = r_{\mathrm{m}}(1-N/K)N, \tag{1}$$

where r_m is the maximum r, K is the carrying capacity of a population in specific environment. With eq. (1), we can prove that when $N=K/2$, $\frac{dN}{dt}$ will reach the maximum. Let

$$\left[\frac{dN}{dt}\right]'' = \left[r_{\mathrm{m}}\left(1-\frac{N}{K}\right)N\right]' = 0, \quad N = K/2.$$

Therefore, depending on the value of $\frac{dN}{dt}$, K can be roughly estimated as

$$K_{\mathrm{H}} = 2N_{\mathrm{H}}. \tag{2}$$

N_H is population size when $\frac{dN}{dt}$ reaches the maximum. According to eq. (2), the maximum of cumulative SARS cases (K_{H}) can be roughly estimated if the outbreak pattern follows the logistic model. Fig. 1 shows how the population size (N) and increase rate $\left(\frac{dN}{dt}\right)$ vary with time t, and how r varies with N, as described by eq. (1). When

$\frac{dN}{dt}$ reach to the peak at time t_p, K can be estimated from the N at time t_p, i.e. K=2N (Fig. 1(a)). There is a negative linear relationship between r and N (Fig. 1(b)).

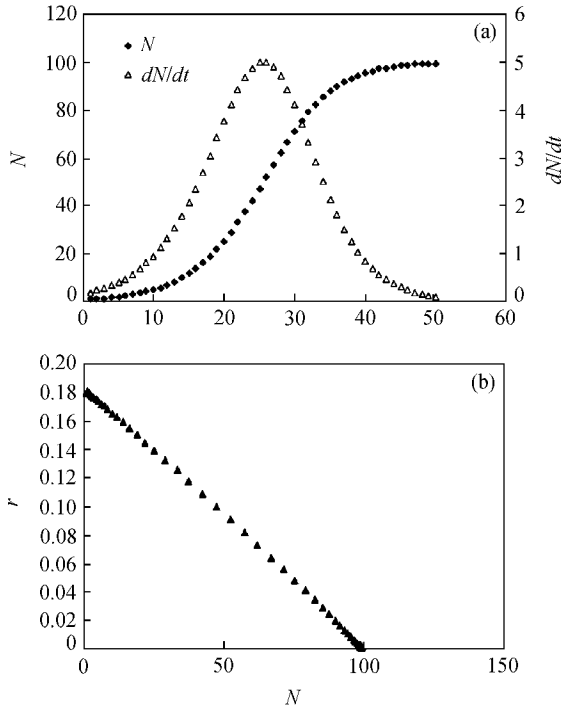

Fig. 1. (a) Simulation results of population size (N) and increase rate (dN/dt) in a continuous logistic model. Model parameters: r_m = 0.2, K=100; (b) illustration of negative relationship between the instantaneous rate of increase (r) and population size (N).

The discrete logistic model of eq. (1) is written as:

$$N_{t+1} = e^{r_m(1-N_t/K)} N_t,$$

$$\ln(N_{t+1}/N_t) = r_m - \frac{r_m}{K} N_t. \quad (3)$$

From eq. (3), r_m and K can be estimated. The equation is also widely used to testify if the population growth is density-dependent or not, depending on whether $\ln(N_{t+1}/N_t)$ is negatively correlated to N_t[14]. In fact, except for population growth, many other biological processes, e.g. the growth of body size of organisms, can be well described by using the logistic model.

The outbreak pattern of cumulative SARS cases is likely of a logistic type because at the initial stage, it grows exponentially, later due to the increasing control effort by people and/or due to depletion of susceptible individuals, the infection will be slowed down. The increase rate of SARS cases is expected to decrease with the cumulative SARS cases, which corresponds to the density-dependent effect in the logistic model. The total cumulative SARS cases in a region correspond to the carrying capacity (K) in the logistic model. The "density dependency effect" in this study refers to the fact that the numbers of new SARS cases become smaller over time as the result of the efforts of both control and natural immunization in the whole population. In this paper, the outbreak patterns of cumulative cases of SARS in the regions of Hong Kong, Taiwan and the Mainland of China, and Singapore were investigated by using the logistic model. The original data of the cumulative cases of SARS are collected from the related governmental websites (e.g. http://www.who.int/csr/don/archive/disease/severe_acute_respiratory_syndrome/en/; http://www.moh.gov.cn/).

2 Results

Figure 2(a) gives the curves of cumulative cases and new cases of SARS in Singapore. The instantaneous rate of increase is significantly negatively correlated with the cumulative SARS cases (Table 1, Fig. 2(b)), indicating that strong negative linear "density dependency" exists in the growth of SARS cases.

Except for Taiwan, China, the results of Beijing, Hebei, Tianjin, Shanxi, the Autonomous Region of Inner Mongolia, Hong Kong, and the mainland of China are similar (Fig. 3(a) and (b); Fig. 4(a) and (b); Table 1). The

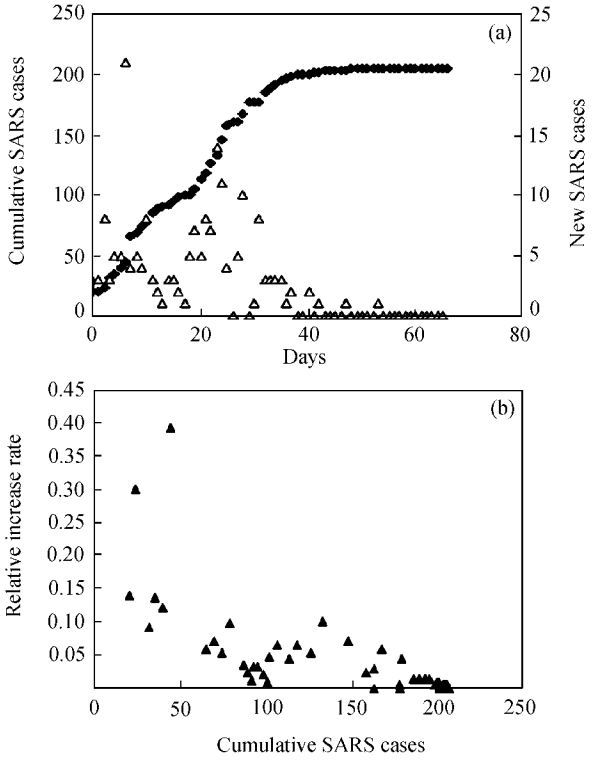

Fig. 2. (a) The observed values of cumulative SARS cases (◆) and new SARS cases (△) in Singapore on March 17, 2003; (b) negative relationship between the instantaneous rate of increase (▲) and cumulative SARS cases in Singapore.

significant and negative linear "density dependency" of the instantaneous rate of increase on the cumulative cases of SARS indicates that the outbreak pattern of SARS can be well described by the logistic model(Fig. 1(a) and (b)).

In Table 1, according to eq. (3), b_0 is the estimation of r_m and $K_L=r_m/b_1$, K_L is the estimation of the maximum SARS cases K (Table 2). According to eq. (2), K_H is also an estimation of K (Table 2). The accuracies of estimation of K by using both methods are very high, further sup porting the conclusion that the growth pattern of SARS cases is generally a logistic curve. The variation of r is larger at the early stage with smaller cumulative SARS cases, probably due to smaller number of cumulative cases.

Table 1 Linear regression models between the instantaneous rate of increase (r) and the cumulative SARS cases (N_s). $r=b_0-b_1N_s$

Country	Region	R^2	d.f.	F	Sigf	b_0	b_1	R_0
China	Mainland	0.940	36	564.29	0.000	0.1204	0.00002	2.0468
	Beijing	0.949	36	674.96	0.000	0.1783	0.00007	3.0311
	Hebei	0.379	25	15.24	0.001	0.3493	0.0018	5.9381
	Tianjin	0.306	23	10.15	0.004	0.3312	0.002	5.6304
	Shanxi	0.616	23	36.96	0.000	0.1463	0.0003	2.4871
	Inner Mongolia	0.331	17	8.43	0.010	0.2388	0.0008	4.0596
	Hong Kong	0.777	51	177.97	0.000	0.1761	0.0001	2.9937
	Taiwan	0.086	25	2.37	0.137	0.0906	0.00007	1.5402
Singapore		0.476	52	47.16	0.000	0.1575	0.0008	2.6775

Table 2 Estimations of maximum cumulative SARS cases in Asia by using two methods. N_H is the cumulative SARS cases when numbers of new SARS cases reach the highest. $K_H=2\ N_H$. K_L is the maximum cumulative SARS cases estimated using eq. (3). K is the observed maximum cumulative SARS cases.

Region	N_H	K_H	K_L	K
Beijing	1199	2398	2547	2520
Hebei	79	158	194	216
Inner Mongolia	190	380	299	288
Shanxi	266	532	478	445
Tianjin	73	146	167	176
Mainland	3106	6212	6020	5328
Hong Kong	530	1060	1761	1713
Singapore	133*	266	197	206

* The second highest N_H

3 Discussions

Mathematical models have been widely used to calculate and describe the dynamic evolution of epidemic threshold values and severity[15,16], among which the most widely used is the Kermarck-McKendrik model, i.e. the SIR model[17]. Various epidemic models have been developed from the classic SIR model for different purposes, or with different assumptions, e.g. the SIRS model[18], SEIR model[19], two-level or two-stage SIR model[20], SIR models for immunity[21], intermediate class[22], and nonlinearity of infection[23—25]. The two SARS models recently proposed by Lipsitch et al.[1] and Riley et al.[2] are also variants of SIR model[3]. These models are relatively complex, and we often need to consider the susceptible people, exposed people, removed people, etc. when establishing such kind of models. Data collection for estimating model parameters is not only time consuming but also labor consuming. In most situations, it is hard to estimate the basic reproduction number (R_0), and it is often impossible to predict the maximum cumulative cases in the early stage of disease outbreak, which limited its application. We do not consider the different populations when establishing a logistic model; only the number of infectious patients is sufficent. The logistic model is also tolerable to the variation of survey interval.

Though simple, the logistic model enables us to easily estimate the maximum relative increase rate (r_m) and maximum cumulative SARS cases (K). From r_m, R_0 can be estimated if only the infection period from a single case to the secondary case is given. According to the epidemic studies on SARS in Hong Kong, China and Singapore[1, 2], the mean serial interval, defined as the sum of incubation period and the duration of infectiveness of SARS person, is estimated as 8—12 d with an average of 8.4±3.8 d in Singapore, and R_0 is estimated to be from 2.2 to 3.6. Since the incubation period is about 5 or 6.4 d[1], the duration of infectiveness (D_1) is about 3 d. Hospitalized SARS persons would also infect front-line doctor staff in hospital, and the average duration of SARS person in hospital (D_2) is about 14 d[26]. As shown in Table 1, r_m is estimated to be0.1761 in Hong Kong, and 0.1575 in Singapore. There R_0 can be estimated by using the equation: $R_0=r_m*(D_1+D_2)$. R_0 of Hong Kong and Singapore are estimated to be 2.99 and 2.68, which is very close to the estimation by Lipsitch et al.[1] and Riley et al.[2]. Wang et al.[27] estimated the R_0 of Beijing to be 1.0698—3.2524 by using a modified SIR model containing six compartments. As shown in Table 1, our estimation on R_0 of Beijing is 3.0311, being the upper limit of that estimated by Wang et al. The R_0 of regions in China ranged from 2.0 to 5.6 (except for Taiwan, China). The R_0 of Hebei and Tianjin were very high, indicating

that there might be new strains more infectious than that of Beijing and Shanxi, and SARS virus might have different origins or new mutations might have occurred during transmission.

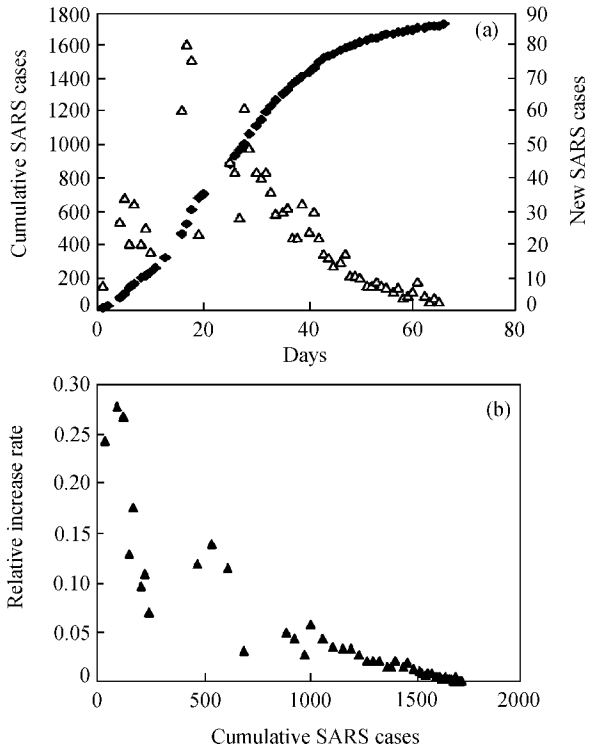

Fig. 3. (a) The observed value of cumulative SARS cases (◆) and new SARS cases (△) in Hong Kong, China on March 14, 2003; (b) negative relationship between the instantaneous rate of increase (▲) and cumulative SARS cases in Hong Kong, China.

The maximum cumulative SARS cases in many provinces or cities in the mainland of China were fitted very well byusing eq. (2) based on the peak values of new SARS cases or by using eq. (3) (Table 2). The maximum cumulative SARS cases in Beijing were estimated to be 2398 and 2547 respectively by using the two methods, very close to the observed value 2520; the maximum cumulative SARS cases in whole mainland of China were estimated to be 6212 and 6020 respectively, very close to the observed cases 5328 (Table 2). The prediction accuracy was very high. Therefore, the model could play an important role in prediction of outbreak of SARS accumulative cases. However, prediction using both ways would become difficult if the variation of increase rate is large for a small number of cumulative SARS cases.

Our study clearly indicates that the outbreak pattern of the SARS virus in China is of a logistic type, and there is strong negative "density dependency" of the instantaneous rate of increase against the cumulative SARS cases in China and in Singapore. This is also a good indication that the control measures, mostly strict isolation of SARS persons and persons with experience of close contact to

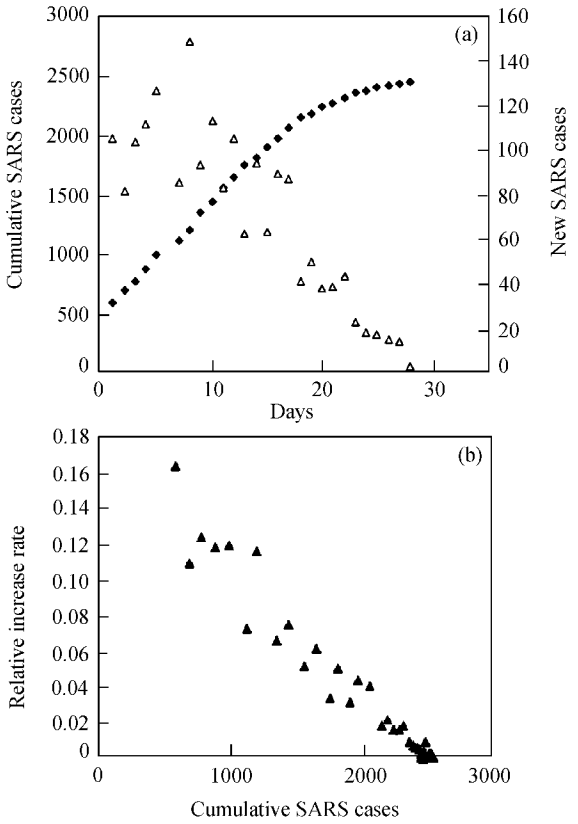

Fig. 4. (a) The observed value of cumulative SARS cases (◆) and new SARS cases (△) in Beijing, China on April 21, 2003; (b) negative relationship between the instantaneous rate of increase (▲) and cumulative SARS cases in Beijing, China.

SARS persons, implemented by government, are effective, and these measures were also causative factors in the negative correlation between rate of increase and total cumulative SARS cases.

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