Treating emerging viral infections

To the Editor—I read with interest the recently published article on the use of plasma from a convalescent patient to treat severe acute respiratory syndrome.[1] The therapeutic use of serum products in managing infectious disease reminds us of the pioneering work of Robert Koch's students, who developed a sheep antiserum against diphtheria toxin in 1891; a girl dying of diphtheria received the antiserum, recovered within hours and survived.[2] Since then, the strategy of administering plasma from survivors of various epidemics of viral illness has been used with success. Examples include treatment of Bolivian haemorrhagic fever (during an epidemic in the 1960s caused by Machupo virus),[3] Argentinian haemorrhagic fever (caused by Junin virus, a close relative of Machupo virus),[4] and Lassa fever in Nigeria.[5] Reduction in mortality by giving this type of therapy has been attributed to the immunoglobulin fraction of the plasma—the source of neutralising antibody. A perhaps more familiar example is the experimental use of immunoglobin from survivors of West Nile encephalitis,[6] which is being considered for further clinical trials to manage infection with West Nile virus.

Clearly, plasma from convalescent patients who had a viral infection has a unique role in therapeutic medicine, especially in the face of emerging (and often devastating) viral infection outbreaks. Above all, these accounts make a strong case for public health authorities to store batches of hyperimmune plasma in case outbreaks of these diseases strike in the future.

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Authors' reply

To the Editor—We thank Drs Chow, Burnouf and Radosevich for their valuable comments. Dr Chow provided important examples of when convalescent plasma has been used to treat other severe viral illnesses. Drs Burnouf and Radosevich suggested ways of improving convalescent plasma therapy. Our institution has analysed more than 20 patients who received convalescent plasma for severe acute respiratory syndrome. Among patients who had pulsed methylprednisolone for more than 1.5 g, those receiving concomitant plasma had better survival and earlier discharge from hospital (unpublished data).

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Modelling the severe acute respiratory syndrome epidemic

To the Editor—The most direct way to assess the trend in the severe acute respiratory syndrome (SARS) epidemic is to study the number of reported cases. There are two quantities related to reported cases: the cumulative number and the daily number of cases. Based on these observations, epidemiologists try to fit models to describe the epidemic.

Firstly, fitting a statistical model by extrapolation not only ignores the possibility of the effect of interventions,
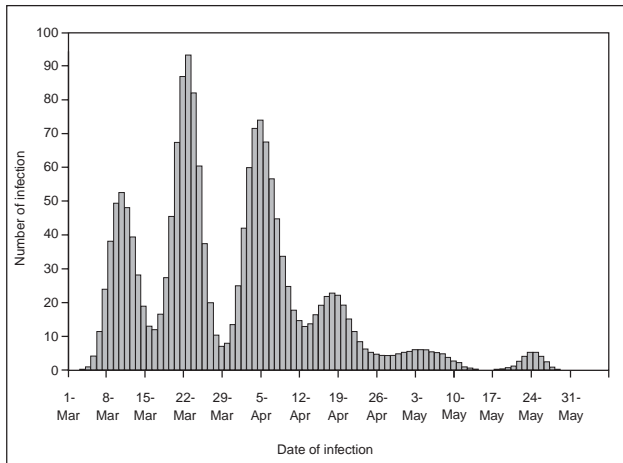
Fig. (a) Estimated daily number of infection of severe acute respiratory syndrome in Hong Kong
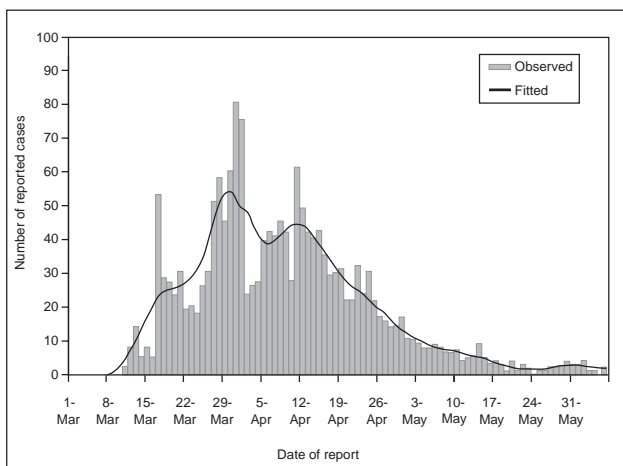

Fig. (b) Observed and fitted daily number of severe acute respiratory syndrome reported cases in Hong Kong

but also ignores unique features of the transmission of the epidemic. That is, useful information concerning the incubation period, the time between infection and onset of disease when there is contact between susceptible and infectious individuals, is not fully utilised.

Secondly, some extraordinary events, such as the major outbreak in the housing estate (Amoy Gardens) in Hong Kong, will greatly distort the shape of the original curve. This will result in a poor fit of the statistical model. Furthermore, initially epidemics tend to experience a period of exponential growth that then levels off when more than half of the population is infected. Modelling the epidemic by extrapolation cannot capture this characteristic. The use of an exponential model or a linear model has also been criticised for these reasons by Razum et al.[1]

Alternatively, there are epidemic models that are specially designed for modelling infectious disease.[2-4] However, the application of such models requires detailed information including, for example, the time of infection and the number of infectious individuals over the course of epidemic. This information is usually incomplete and/or unavailable.

As suggested by Razum et al,[1] studying the daily number of reported SARS cases is easy for the public to understand, and can indirectly show the change in the reproductive number (R_0), defined as the average number of secondary cases generated by one primary case in a susceptible population.[2,3] However, due to the incubation period, there is a time lag between the day of infection and the day of reporting. As a result, the epidemic curve of the daily number of SARS cases may not adequately monitor the change in R_0. Further, as there is variation in the length of the incubation period, people reported on the same day may have been infected on different days.

We propose the back-projection approach to be used to reconstruct the infection curve, based on the daily reported number of cases and an estimated incubation period.[5-7] The SARS infection curve for Hong Kong up to 6 June 2003 was reconstructed using the back-projection method. The estimated curve and the fitted daily reported number of cases are shown in Fig a and b. The estimated infection curve is easy to interpret and the effect of major events on the spread of the epidemic can be readily identified.

Modelling the SARS epidemic using a simple extrapolation model is definitely inaccurate, while a complicated stochastic epidemic model may not be feasible. The back-projection method is thus preferred. Further, the assumptions made for each model need to be explicitly stated when the model is used in order to avoid any misleading conclusions.

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