

## Conference Summary

### Emerging Infections: What Have We Learned from SARS?

Given the current size and mobility of the human population, emerging diseases pose a continuing threat to global health. This threat became reality with the outbreak of severe acute respiratory syndrome (SARS). The emergence of a disease requires two steps: introduction into the human population and perpetuated transmission. Although preventing the introduction of a new disease is ideal, containing a zoonosis is a necessity. The lessons that we have learned from SARS were the topic of a meeting of The Royal Society on January 13, 2004, in London, England.

Zoonoses are responsible for most emerging infectious diseases, including infections caused by Ebola virus, West Nile virus, monkeypox, hantavirus, HIV, and new subtypes of influenza A. In the case of SARS coronavirus (SARS-CoV), serologic evidence indicates that the virus was spread through interspecies transmission from wild game markets in Guangdong, China (Malik Peiris, University of Hong Kong). This finding led to bans in the wild meat trade from Nan Shan Zhong (Guangzhou Respiratory Disease Research Institute) similar to the ban on eating nervous system tissue from cows that was implemented after new variant Creutzfeldt-Jakob disease emerged in Britain.

Ecologic changes, concomitant with increasing contact between humans and animal disease reservoirs, contribute to zoonoses. The emergence of SARS was facilitated by increased contact between people and animal disease reservoirs as the wild

meat industry expanded recently. Global warming will likely contribute to the spread of dengue beyond tropical regions (Tony McMichael, National Centre for Epidemiology and Population Health, Canberra, Australia). Habitat fragmentation by deforestation may increase the contact between people and reservoir species. For example, hemorrhagic fever virus has been linked to deforestation in South America.

Containing an emerging disease depends on rapidly designing and implementing a control strategy appropriate to the epidemiology of the disease. Interdisciplinary and international collaboration occurred with unprecedented rapidity during the SARS outbreak. The network of laboratories in 17 countries organized by the World Health Organization (WHO) coordinated information sharing (David Heymann, WHO) and was instrumental in rapidly identifying the etiologic agent of SARS (1) and in fulfilling Koch's postulates (2) (Albert Osterhaus, Erasmus University, Rotterdam).

As is typical of an emerging disease, no vaccines or drugs to combat SARS existed, making quarantine, patient isolation, travel restrictions, and contact precautions the only means of limiting transmission. Mathematic models provided a framework for evaluating alternative control measures and making predictions about the course of the epidemic (3,4). Previously, similar models had guided public health policy, for example, in halting an outbreak of hoof and mouth disease in the United Kingdom in 2001 (5,6). One of the complications in setting parameters in an emerging disease model is the difficulty in estimating epidemiologic limits from the initially small sample sizes. Thus, openly sharing data and analysis of key model parameters are vital.

The model must be appropriate to the nature of the disease and the accuracy of the parameter estimates (7).

Stochasticity inherent in transmission dynamics will be particularly pronounced when infection prevalence is low. Population heterogeneity and the network structure of human interactions will affect the spread of an emerging disease. In the 2003 SARS outbreak, healthcare workers were at particular risk (8) and acted as bridges carrying the infection from the hospital and causing community wide epidemics. High-risk "core groups" have been a major focus of HIV/AIDS models for years (9), but the movement of SARS patients into the core (i.e., the hospital) adds a further complication (3).

The two waves of SARS clusters in Toronto (Robert Maunier, Mount Sinai Hospital, Toronto) highlight the need for surveillance even after an outbreak appears extinguished. Management of the SARS epidemic also demonstrated that public service infrastructure, which affords the greatest chance of success (3), is essential to the rapid containment of an outbreak. In areas most affected, contact tracing was important (10). In Guangdong, police departments tracked down contacts of infected persons, who were then followed up for 10 days after exposure. Evaluating the surge capacity of public health services and hospitals is one way to assess the preparedness of a medical system.

The case-fatality rate is a key determinant of the public health impact of an emerging disease and was high for SARS at approximately 15% (11). The relationship between infectiousness and onset of symptoms is also important. Patient isolation has greater potential as a control strategy if the illness can be diagnosed before the person becomes infectious (Roy Anderson, Imperial College London). In contrast, persons infected with influenza virus are highly infectious before they become symptomatic.

The rapidity of pathogen turnover means that evolution in pathogen populations can occur on a time scale that

is epidemiologically relevant. Indeed, SARS-CoV evolved during the course of the SARS outbreak in China (12). Similarly, influenza is perpetuated in the human population by the evolution of new antigenic variants every year (Robin Bush, University of California, Irvine) (13). Even if the transmissibility of an emerging disease is initially below the threshold necessary to sustain it in a population, the potential for the organism's evolution to higher levels may exist (14,15). Thus, one should not become complacent about diseases that are repeatedly introduced through zoonosis, but teeter on the edge of sustainability within the human population.

The success with which WHO coordinated the global collaboration in containing SARS galvanized the World Health Assembly to grant WHO greater authority to verify outbreaks, conduct investigations of outbreak severity, and evaluate the adequacy of control measures. The outcome of this new authority will depend on integrating the expertise of public health officials, medical doctors, and epidemiologists worldwide with guidance from disease transmission models. The SARS outbreak demonstrated that an epidemic in one part of the world is not just an individual nation's problem but a global problem.

**Alison P. Galvani\***

\*University of California, Berkeley, California, USA

## References

- Kuiken T, Fouchier RA, Schutten M, Rimmelzwaan GF, van Amerongen G, van Riel, et al. Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. *Lancet*. 2003;362:263–70.
- Fouchier RA, Kuiken T, Schutten M, van Amerongen G, van Doornum GJ, van Hoogen BG, et al. Aetiology: Koch's postulates fulfilled for SARS virus. *Nature*. 2003;423:240.
- Lloyd-Smith JO, Galvani AP, Getz WM. Curtailing transmission of severe acute respiratory syndrome within a community and its hospital. *Proc R Soc Lond B Biol Sci*. 2003;270:1979–89.
- Riley S, Fraser C, Donnelly CA, Ghani AC, Abu-Raddad LJ, Hedley AJ, et al. Transmission dynamics of the etiological agent of severe acute respiratory syndrome (SARS) in Hong Kong: the impact of public health interventions. *Science*. 2003;300:1961–6.
- Ferguson NM, Donnelly CA, Anderson RM. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature*. 2001;413:542–8.
- Keeling MJ, Woolhouse ME, Shaw DJ, Matthews L, Chase-Topping M, Haydon DT, et al. Dynamics of the 2001 UK foot and mouth epidemic: stochastic dispersal in a heterogeneous landscape. *Science*. 2001;294:813–7.
- May RM. Uses and abuses of mathematics in biology. *Science*. 2004;303:790–3.
- Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med*. 2003;348:1986–94.
- Anderson RM, May RM. *Infectious diseases of humans: dynamics and control*. Oxford: Oxford University Press; 1990.
- Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan-Yeung M, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. *N Engl J Med*. 2003;348:1977–85.
- Galvani AP, Lei X, Jewell NP. Severe acute respiratory syndrome: temporal stability and geographic variation in case-fatality rates and doubling times. *Emerg Infect Dis*. 2003;9:991–4.
- Chinese SARS Molecular Epidemiology Consortium. Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. *Science*. 2004;303:1666–9. Epub 2004 Jan 29.
- Treanor J. Influenza vaccine—outmaneuvering antigenic shift and drift. *N Engl J Med*. 2004; 350:218–20.
- Antia R, Regoes RR, Koella JC, Bergstrom CT. The role of evolution in the emergence of infectious diseases. *Nature*. 2003;426:658–61.
- May RM, Gupta S, Mclean AR. Infectious disease dynamics: what characterizes a successful invader? *Philos Trans R Soc Lond B Biol Sci*. 2001;356:901–10.

Address for correspondence: Alison P. Galvani, Department of Integrative Biology, University of California, Berkeley, CA 94720-3140, USA. fax: 410-643-6264; email: agalvani@nature.berkeley.edu

## Conference Summary

### Open Access Publishing

An Open Access Publishing Conference was convened in Atlanta, Georgia, on January 7, 2004, by the libraries of the Centers for Disease Control and Prevention (CDC) and Emory University. Open Access is an emerging publishing model for peer-reviewed scientific research in which authors and their publishers grant free access to their work as long as the authors are acknowledged and the publisher ensures that the work is made freely available in a digital archive (1). The conference brought together key stakeholders including scientists, researchers, publishers, and librarians and included approximately 240 participants with 80 offsite registrants connecting through the simultaneous Web cast.

The keynote address, “The Coming Revolution in the Publication of Scientific Papers,” delivered by Harold Varmus, emphasized that 1) in today's Internet era, the traditional Gutenberg print publishing model is outdated; 2) electronic publishing has the advantages of lower costs, global distribution, content that can be linked to datasets, improved archiving, and full-text searching; and 3) rigorous peer review is possible in electronic and Open Access formats. Open Access publishing challenges include engaging professional societies in this approach, building sustainable business plans, and changing academic culture so that published works are evaluated for content rather than for the journal label. Open Access publishing is typically financed by author fees along with a combination of philanthropic and advertising support. Examples are the Public Library of Science, Journal of Clinical Investigation, and BioMed Central