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Closing in on the cause of SARS

James Hughes, of the Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA), doesn't think SARS (severe acute respiratory syndrome) has the ability to become a pandemic. But he said on April 4 that "we haven't heard the end of this. We have to stay tuned and treat it as the public-health threat that it is".

The number of cases worldwide is still relatively small—2722, with 106 deaths at April 9. But since Feb 15, when the first patient in Hong Kong fell fatally ill with non-typical pneumonia that was later identified as a previously unrecognised infection, SARS has been spread by air travellers to 16 other countries, including Vietnam, Singapore, Thailand, the USA, Canada, and the UK, leading the WHO, for the first time in its history, to recommend that travellers avoid specific geographical areas (Hong Kong and Guangdong Province, China) except for essential business. The USA has introduced compulsory quarantine for SARS patients, ranking the infection alongside smallpox and cholera.

SARS carries a 4% mortality, and it can kill otherwise healthy adults, including a 46-year-old WHO physician who identified Vietnam's first case of SARS. Several cases in the early days of the Hong Kong outbreak were in health-care workers and family contacts. At present there is no specific treatment. The agent seems to be transmitted by droplets or by direct or indirect contact, but airborne and faecal-oral transmission have not been ruled out. According to WHO the incubation period is 3–10 days.

The primary agent of SARS seems to be a new coronavirus, not closely related to coronavirus types 229E and OC43 that cause the common cold. CDC scientists were the first to link the novel virus to SARS (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5212a1.htm>), and other laboratories soon confirmed this finding. Malik Peiris' team at the University of Hong Kong (see page 309), using serological and a reverse-transcriptase PCR assays specific for the novel coronavirus, have found

evidence of infection with the virus in 45 of 50 Hong Kong patients with SARS but no controls (*Lancet* online April 8, http://www.thelancet.com/journal/vol361/iss9364/full/lancet.361.9364.early_online_publication.25242.1).



Thin-section electron micrograph of human pneumonia-associated coronavirus infected cells. Reproduced from Peiris et al. *Lancet*. Published online April 8, 2003

Human metapneumovirus (a paramyxovirus) has been isolated in some outbreaks, including the Canadian one, where it was seen in four of five coronavirus-positive specimens (*N Engl J Med* online March 31, http://content.nejm.org/cgi/reprint/N_EJMoa030634v2.pdf). Chlamydia has also been reported in some SARS patients in China, but its significance is unclear. Peiris et al, who found no evidence of human metapneumovirus infection, conclude: "It is highly likely that this coronavirus is either the cause of SARS or a necessary prerequisite for disease progression". They suggest that other viruses may act as "opportunistic secondary invaders to increase the disease progression".

As we go to press SARS must still be diagnosed clinically, but virologist Maria Zambon at the Public Health Laboratory Service (London, UK), one of WHO's network of 11 laboratories that have been racing since March 17 to identify the cause of SARS, claims to be on the verge of having a reliable "first-generation" diagnostic test for SARS. Zambon, whose PCR and

electron-microscopic studies on infected material "suggest that coronavirus is highly correlated with SARS infection" but who found human metapneumovirus in some specimens, adds that "we have limited information about the nature of coronavirus, so it is hard to speculate about its infectivity". WHO says that three types of diagnostic test available—ELISA, an immunofluorescence assay, and a PCR molecular test—"all have limitations as tools for bringing the SARS outbreak quickly under control". Nevertheless, David Heymann, executive director of communicable diseases at WHO, concedes that a definitive test is "weeks, rather than months" away.

Hong Kong appeared to be the main focus of SARS infection until the end of February, when China admitted to having had 300 cases and five deaths from non-typical pneumonia since November in Guangdong Province—the home of Hong Kong's index patient. China now accounts for about half of all cases (1280 of the 2722 as at April 9). If Guangdong is where SARS started, could the common practice there of keeping fowl and other domestic animals in the house be the key? Virologist John Oxford (Queen Mary College, University of London, UK) says, "There is a good chance that the SARS virus, like H5N1 influenza, crossed species from chickens or animals to man".

If anything good has come out of the arrival of SARS it is the demonstration that WHO and its partners in the Global Outbreak Alert and Response Network are capable of rapid response and international collaboration on an unprecedented scale. "Other new diseases will emerge in the future", says Guenael Rodier, director of WHO's Communicable Disease Surveillance and Response. "We will respond just as we have with SARS—with maximum efforts to contain its spread." Hughes, at CDC, sees the SARS experience as "a fire drill for a number of things", be it the next influenza pandemic or a bioterrorist attack.

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