

Was the fuss overblown?

To the friends and relatives of the 800-plus people slain by severe acute respiratory syndrome (SARS), this might seem like a callous question. But SARS barely registers a blip in the annual body count caused by infectious disease. Influenza is likely to kill up to half-a-million people in 2003, whereas the death tolls from malaria, tuberculosis and AIDS will each run to seven figures. So, when the outbreak is put into perspective, was the panic over SARS really warranted?

Given the economic damage suffered by those countries named by the World Health Organization (WHO) in its warnings against travel to the worst affected regions, some commentators have accused the WHO of overreacting — local officials in the Canadian city of Toronto, in particular, were livid about the agency's advice against travelling there. But the experts contacted by *Nature* are unanimous in rejecting the general idea that health authorities went over the top.



WHO advised against travelling to Toronto during the SARS crisis (Steve Allen / BrandXpictures)

When reports of an unusual respiratory illness began to emerge from southern China late last year, no one knew what caused it. Was this a new super-virulent strain of flu? If so, would it be as deadly as the 1918 pandemic strain, which killed up to 40 million people? Even in mid-March, when outbreaks elsewhere in Asia caused the WHO to release the two global alerts that shot SARS onto the world's news agenda, the culprit remained unknown. Also unclear were the disease's death rate and infectiousness. Health officials could not be sure whether they were dealing with a troubling but ultimately limited threat, or a global mass killer.

Thankfully, it seems that SARS isn't sufficiently infectious to cause a re-run of the 1918 flu pandemic. Even so, the relatively low death count can probably be attributed in large part to the surveillance and patient isolation rapidly introduced in most of the countries that imported the disease. China has been widely criticized for the initially sluggish and secretive response that allowed SARS to take hold within its borders. But after the WHO issued its global alerts, only Taiwan — where officials failed to rapidly establish a central coordinating office for SARS — experienced an outbreak in which there was widespread transmission among people other than health workers caring for SARS victims.

Although experts agree that SARS warranted a vigorous reaction, questions remain about the way in which the threat was communicated to the public. The WHO's executive director for communicable diseases, David Heymann, acknowledges that problems were caused by the agency's second global alert, issued on Saturday 15 March when some ministries of health were closed, after evidence emerged that the disease was being spread internationally. As a result, the media were running with the story before national officials had been briefed

about how to respond. To rectify this, the WHO's general assembly in May urged member states to designate officials who will be available around the clock to be informed about future urgent global alerts.

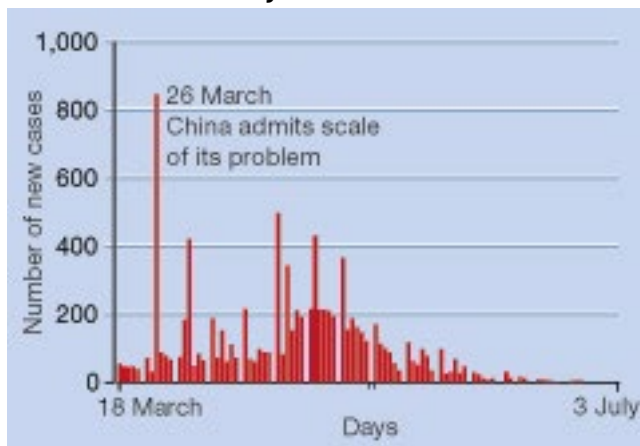
Another problem was that some national agencies, even the respected US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, released information that inadvertently exaggerated the ease with which SARS spreads. For example, in an editorial in *The New England Journal of Medicine*¹ published online on 2 April, CDC director Julie Gerberding wrote: "Airborne transmission may have a role in some settings." No wonder that people in Hong Kong and elsewhere were scared into wearing surgical masks in the street, even though clinical reports suggested that SARS was being spread only by close personal contact.

But these were minor glitches. Experts agree that it is better to be accused of overreacting than of allowing the disease to run out of control. If a similar fuss had erupted in the early days of AIDS, suggests epidemiologist Megan Murray of the Harvard School of Public Health in Boston, maybe HIV would not now be killing three million people each year.

Helen Pearson

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Is the outbreak finally over?



Thanks to global alerts and patient quarantine, the number of new cases of SARS has now tailed off.

With luck, the answer is yes. At the outbreak's peak in early May, some 200 new cases were being reported every day. But as *Nature* went to press, no new cases had been reported since 15 June. "In some senses, we should breathe a sigh of relief," says Roy Anderson, whose team at Imperial College London has been at the forefront of efforts to characterize the spread of the disease.

For Anderson and other epidemiologists who have been crunching the numbers on SARS, the key parameter is known as R_0 . A measure of a disease's infectiousness, R_0 corresponds to how many people, on average, are infected by each patient in the absence of any control measures.

Attempts at modelling the spread of SARS, published online on 23 May by teams led by Anderson and by Marc Lipsitch of the Harvard School of Public Health^{2,3}, gave R_0 a value of between two and four. This was encouraging news, as it confirmed that efforts to isolate patients should bring the disease under control. Contrast this with flu, which boasts an R_0 of about 10. For diseases this infectious, quarantining those who show

symptoms is not enough to bring the average number of new infections caused by each case to below one — the level necessary for an epidemic to go into decline.

But we still know too little about SARS to predict how it will behave should it return. Key unknowns include how quickly a person becomes infectious after they are infected, and how long they remain able to spread the disease. Most importantly, we don't know exactly how the virus is transmitted, to how many people harbour the SARS virus without showing symptoms, and whether these 'silent' cases can infect others.

The relatively sluggish transmission of SARS fits with the idea that it is spread by close contact, requiring its victims to breathe in droplets of virus-laden mucus. That explains why most transmission has been in confined settings, such as hospitals. But unusual foci of infection in Hong Kong show that this isn't the whole story. Most striking was the outbreak at the Amoy Gardens apartment block, where the brother of one resident seems to have infected 321 other people. Scientists tore the block apart, eventually implicating a faulty sewage system that allowed droplets contaminated with faeces to form in the block's bathrooms⁴. Transpose SARS to a developing country with poor sanitation, therefore, and the dynamics of its spread might be different.

If SARS does return at a later date, its epidemiology could be different. For reasons that aren't fully understood, respiratory infections spread more rapidly during the winter. Another crucial question is how long immunity to SARS persists. If this is as short as a few months, and SARS bounces back with the next Northern Hemisphere winter, even those previously exposed to the virus may be just as vulnerable as they were the first time around. "It's quite possible that we haven't seen SARS at its full force," warns Donald Burke, an international health expert at Johns Hopkins University in Baltimore, Maryland.

In the meantime, epidemiologists are trying to work out how many people are silently harbouring the SARS virus. If a sizeable number of symptomless cases can transmit the disease, outbreaks will continue to erupt. Investigating this question will require better diagnostic tests — to detect both antibodies to the SARS virus, and the virus's genetic material. Ideally, these won't require laborious analysis of blood samples. "We need a saliva test," says Anderson.

The greatest danger is if health officials let down their guard now that SARS seems to have waned. A second outbreak in Toronto in late May, weeks after the last new case was reported in the city, provided a timely warning. In this instance, a patient was discharged from hospital with pneumonia — common enough among elderly people who have undergone surgery — that turned out to be SARS.

Tom Clarke

more SARS questions

Are we prepared for the next viral threat?

SARS should be seen as a warning shot. If the virus had been more infectious, we could now be facing millions of deaths. And this nightmare vision doesn't require the emergence of an entirely novel disease: new strains of flu virus arise each year, and every few decades, one appears that wreaks global havoc. So, in the light of our experience with SARS, are we prepared? Scientifically, the answer is a qualified 'yes'. In terms of public health, it's a resounding 'no'.

The most encouraging thing about the response to SARS is the way in which virologists worked together to identify and understand the pathogen responsible. The four collaborating centres in the WHO's Global Influenza Surveillance Network — in Australia, Britain, Japan and the United States — were soon teamed up with seven other leading virology laboratories to probe the mysteries of SARS. Within a few weeks of the WHO issuing

its global health alerts, labs in this network had identified the culprit as a previously unidentified strain of coronavirus⁵⁻⁷, and a prototype diagnostic test was made available⁷.

The network was all about sharing data, resources and time. Results were posted on a password-protected website as soon as they were gathered, and were discussed daily in teleconferences that sometimes stretched over three hours. Most helpful, say insiders, was the prompt reporting, from the word go, of blind alleys. "We had already run through the list of obvious possibilities when the network started, and so could tell the partners not to look for certain viruses," says network member John Tam of the Chinese University of Hong Kong.

Sharing of materials and reagents was also fundamental. The SARS agent was shown to be a coronavirus by amplifying portions of its genetic material using the polymerase chain reaction (PCR), and examining the resulting sequences. But this approach is only feasible if you have the appropriate PCR 'primers', corresponding to short genetic sequences from known virus families. Without the sharing of primers across the collaborating network, says William Bellini, SARS laboratory coordinator at the CDC, the virus would not have been identified so quickly.

WHO officials attribute the rapid scientific progress made by the SARS network in part to the experience of the influenza labs around which it was constructed. "We had a core of people, definitely not ivory-tower people, who were used to working in this way," says Klaus Stöhr, the WHO's influenza project leader, and its resident SARS expert. He is now building further networks to share clinical experience and data from SARS patients, and to link groups trying to identify animal reservoirs of the SARS virus.

Unfortunately, a speedy scientific reaction to an emerging viral threat doesn't guarantee that public-health officials will be able to mount an effective response. Faced with a more rapidly spreading disease, the consensus is that they would have been overwhelmed. And although health authorities might claim that it is unreasonable to expect them instantly to be able to tackle a disease that pops up out of the blue, most nations remain woefully unprepared to deal with a flu pandemic that could emerge at any time.

Through the WHO's efforts, emerging strains of flu virus are constantly monitored in the hope that vaccines can be produced that protect against those in general circulation. But if a pandemic strain does emerge, health officials will also need to deploy anti-flu drugs on a massive scale. "We know that another flu pandemic will occur," says Albert Osterhaus, a virologist at Erasmus University in Rotterdam, the Netherlands, who participated in the SARS network. "But no country has yet started to stockpile antiviral drugs."

Alison Abbott

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