# Analysis and comment

*Epidemics*

## What we have learnt from SARS epidemics in China

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China's experience with SARS has important implications worldwide, and may improve preparedness for an epidemic if bird flu spreads to humans

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The mainland of China experienced three outbreaks of SARS between November 2002 and May 2004. The first outbreak resulted in a pandemic and caused huge financial loss and social panic, but rigorous policies and control measures that were established circumvented further pandemics. Such efforts mean that SARS is currently under control. However, these outbreaks revealed some problems in the health system and in public understanding of emerging infectious diseases. The lessons we learn while facing up to these events can improve our medical performance in the future for management of new epidemics, such as human avian influenza.

### What have we learnt?

**Lesson one: honesty is needed**

In an emergent event, an information blackout makes absolutely no sense. The first case of SARS appeared in Guangdong province, China, in November 2002,[1] but information about it was not broadcast on Central TV, the official Chinese television station, until February 2003,[2] though rumours spread via cell phones and the internet. It was not until three months after the breakout of epidemics that a group of healthcare officials were sent to investigate. Before this, the absence of open news was an attempt to maintain social stability. But the silence led to panic buying of vinegar and some Chinese herbal drugs that were believed to help prevent this "mysterious" disease. Soaring prices for these goods extended to others, undermining the intended social stability. Things began to change when information, in the form of daily roundups on SARS epidemics and public education on disease prevention, reached the community.

Honesty is what matters. The public needs to know the truth; concealing what happens may lead to a panic rather than to social stability. Prevention and control of communicable diseases remains critical for the improvement of public health.

**Lesson two: controversy can lead to lost chances**

SARS-associated coronavirus (SARS-CoV) is new to humans. Scientists have sequenced the genome of the virus and noted that SARS-CoV is not closely related to any of the previously characterised coronaviruses.[3] At the beginning of the SARS outbreak, when the disease was being called "atypical pneumonia," the search for the pathogen responsible resulted in widespread arguments over whether the disease was caused by *Chlamydia* or a virus. On 28 February 2003, the health authorities announced that *Chlamydia* was the cause of "atypical pneumonia": it had been isolated from lung tissue in two of three autopies; typical *Chlamydia* particles had been seen under the electronic microscope; and antibody to *Chlamydia* was found in patients who had died of "atypical pneumonia." The authorities proceeded to declare that "sensitive antibiotics were considered very effective against such pneumonia." Some centres carried out trials to support these findings.

Clinicians and epidemiologists did not agree. The disease was too highly contagious (with family and hospital clustering) to be of chlamydial origin; it had progressively deteriorating symptoms within a short period of time—and it did not respond to any standard treatment for *Chlamydia*. Clinicians claimed that no macrolide-resistant (or quinolone-resistant) strains of *Chlamydia* had so far been reported. *Chlamydia* might be one of the pathogens causing death rather than causing the disease. Arguments continued until April, when US and Hong Kong scientists announced that SARS-CoV was the cause of SARS, when the pathogen was looked at again and found to be SARS-CoV.[4]

Scientists at the Military Academy of Medicine had had pictures of the new coronavirus on 26 February, more than a month before the discovery by US researchers, but they kept silent about their findings

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Control of wildlife markets may be vital for preventing outbreaks of SARS because the controversy was raging at that time.[5] China lost the chance to announce the primary discovery of SARS-CoV. This would not have been the case if there had been better collaboration between laboratory workers and epidemiologists and clinicians, and if research data had been shared among scientists and made known to the public.

**Lesson three: conclusions may be premature**

The first and the second outbreaks of SARS clearly showed that SARS-CoV in humans was linked to small wild animals, civet cats in particular.[6–8]

Professor Kathryn Holmes, a former president of the American Society for Virology, told the 2005 annual meeting of American Association for the Advance of Science in February: "the SARS epidemic strain has not been seen in nature since June 2003 . . . the human epidemic strain is not being harbored in animals" and thus "SARS no longer exists in wildlife and has essentially disappeared as a threat."[9 10]

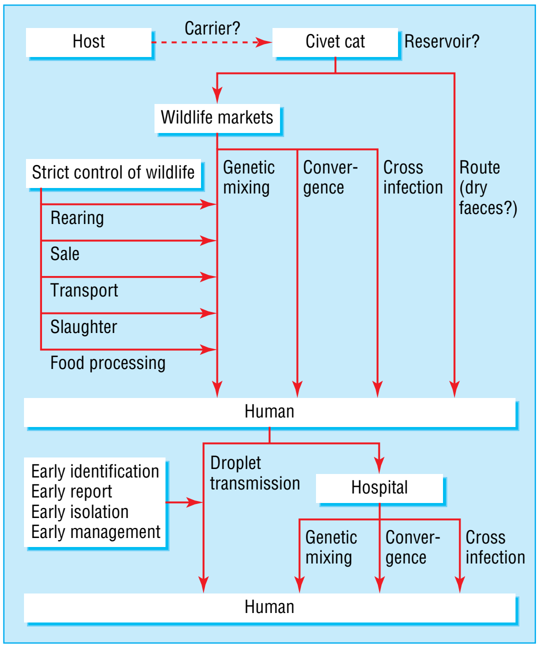
Several factors lead us to believe that it is too early to conclude that SARS-CoV is eradicated outside laboratories:

- The genomic sequences of SARS-CoV from humans and civet cats in the 2003-4 outbreak were nearly identical; there was a cross host evolution of SARS-CoV (spike protein in particular) in civets and humans[11]
- High positive rates of serum SARS-CoV in civets were found at Guangzhou wildlife markets in 2004, but not in other wildlife markets in other cities or provinces[12]
- Civets can be infected experimentally with SARS-CoV[13]
- Other SARS-related coronaviruses have been identified in Chinese horseshoe bats. Bats are a natural reservoir of SARS-like coronavirus.[14]

Wildlife markets represent a dangerous source of possible new infections that could undermine the prevention of SARS (figure). Game foods are believed to "enhance the vitality of the body," and as Cantonese people consume a substantial amount of game as a tonic in cold weather, the wildlife markets in Guangzhou thrive in winter. Many markets are poorly managed and insanitary, so cross infection, interspecies transmission, amplification, genetic convergence, and mixing of coronavirus may be taking place. Animal traders standing in close proximity to these infected animals may be affected, as may the food processors who slaughter infected animals in restaurant kitchens, causing SARS-CoV to spread from wildlife to humans—after which it may spread from human to human, principally by droplet transmission. It is too early to conclude that the SARS threat is over. If no action is taken to control wildlife markets, the SARS-CoV organism may develop into an epidemic strain.

**Lesson four: some centres may be flouting regulations**

During the second SARS outbreak (March 2004), a young postgraduate who was working at an institute of virology in Beijing developed symptoms of pneumonia on 25 March. When she returned home to Hefei, the capital city of Anhui Province, she was diagnosed as having SARS, and she had transmitted the disease to seven people, including her parents and healthcare workers both in Beijing and Hefei. Twenty three days later, another person working at the same institute presented with the same symptoms, also diagnosed as




Transmission of SARS and methods of intervention

SARS. These two cases arose from the same contaminated laboratory but did not infect each other (the incubation period is 2-10 days). The institute was shut down immediately. Nine people with SARS and more than 200 contacts were quarantined, and no further cases occurred.

The two laboratory acquired cases of SARS reflect the ways regulations can be flouted in research institutes: allowing non-professionals to be on SARS research projects; downplaying biosafety regulations; using methods with unconfirmed efficacy to inactivate viruses; improper technical processing in P3 laboratories (those set up according to biosafety level 3 regulations of the World Health Organization); delay in monitoring fever, etc. Strict scientific regulations are urgently needed and policies should be implemented and monitored.

## How can we do better next time?

SARS has not been eradicated, and humans remain vulnerable to emerging infectious diseases like bird flu. As we face up to the threat of future pandemics, we can take encouragement from the fact that many of the uncertainties that arose during the SARS outbreak were resolved over time. Three aspects may influence future strategies.

Firstly, laboratory workers, epidemiologists, preventive medicine professionals, and clinicians must collaborate closely to contain any emergent infections. Clinical trials using inactivated whole SARS-CoV vaccine are underway, and multidisciplinary research on genotherapy using small interfering RNA (SiRNA) shows promise.[15] Lack of coordinated effort could compromise any advances in science. Also, biosafety should be emphasised when conducting studies related to highly pathogenic micro-organisms.

Secondly, constant consultation with healthcare professionals would provide the evidence that an authority needs for developing appropriate, rather than arbitrary, policies. As early as the 2002-3 SARS outbreak, Guangdong's local government and department of public health summoned leading scientists and respiratory specialists to set up an anti-SARS steering committee. Implementation of measures endorsed by this committee achieved the lowest case fatality rate from SARS in the world (3.8%). During early 2004, when four new cases were identified in Guangdong, the government took strong action on strict control of wildlife markets, including a ban on rearing, sales, transport, slaughter, and food processing of small wild mammals, and implemented "four earlies" (early identification, early reporting, early isolation, and early management) to stop transmission from human to human. This control strategy seems to have been effective in preventing the second SARS outbreak from evolving into an epidemic. This policy also holds true in the management of human avian flu, especially in dealing with febrile patients who have a history of contact with live poultry or birds.

Thirdly, an international monitoring system with a far reaching network is crucial for the early alerting of infectious diseases. A nationwide monitoring system for emerging infectious diseases has been set up in China. Surveillance of 185 designated hospitals and a network of 39 laboratories found 16 cases of human avian flu. Most of these patients were identified by doctors working in local hospitals. As a result of targeted education and on-site training for management of avian flu, there was no delay in referrals and quarantines. If doctors providing primary care are alerted and part of a monitory programme, epidemics can be controlled at the outset.

Lessons taught by SARS have given us a new outlook on a devastating human health crisis. Surely, these lessons are not confined to China, and they have important implications worldwide. As Franklin P Jones said, experience is the marvellous thing that enables you to recognise a mistake when you make it again. What has happened with the spread of SARS-CoV must not be allowed to happen again with H5N1. Incessant efforts are needed to improve our preparedness.

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### Summary points

Many of the uncertainties that arose during the SARS outbreak were resolved over time and important lessons learned

To contain emergent infections, laboratory workers and health professionals need to collaborate closely

Consulting healthcare professionals will help in developing appropriate official policies

An international monitoring network for emergent infections is needed


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# Research priorities in traditional Chinese medicine

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Is the current Western model of research—trying out unknown treatments in animals—suitable for studying treatments that have long been used in humans?

## Introduction

Evidence based medicine re-emphasises applied clinical research in human subjects.[1 2] However, research in traditional Chinese medicine has had a mechanism centred approach and has been dominated by studies of basic and intermediate mechanisms. Though tremendous efforts have been made, and despite occasional successes, such as in acupuncture,[3] most questions—for example, the nature of disease in traditional Chinese medicine—have not been satisfactorily answered.[4]

According to Liang, "Since the early 1990s, the search for the nature of disease has descended into a downward spiral. All the breakthroughs once cheerily anticipated seemed to have become an illusion. The entire traditional Chinese medicine research is currently in a state of disarray. Basic research had come to a standstill. What has gone wrong? Where should we go from here?"[4] In this article, I argue that research priorities in traditional Chinese medicine need to be reviewed, and I propose an efficacy driven strategy.

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