

Would SARS become an endemic disease in Hong Kong?

By Dr Kenneth H Lee

Never before has Hong Kong faced the threat of an epidemic as serious as SARS, the so-called severe acute respiratory syndrome. This epidemic is believed to have originated in November last year in the southern province of Guangdong. Chinese doctors said Guangdong officials responded slowly to the disease and neglected to advise Beijing and neighboring Hong Kong to take precautions against contamination. As a result, about 80 percent of the reported SARS cases have been in mainland China and Hong Kong. Though researchers at Hong Kong University have swiftly identified a new coronavirus as the possible causative agent of SARS, the disease keeps on spreading due to the SAR government's initial indecision to quarantine the infected. Before the epidemic abates, there is fear among experts that SARS, like the avian flu, may become an endemic disease.

From its outbreak in Prince of Wales Hospital in the first week of March, the disease swept through other hospital centers and communities in Hong Kong like wildfire and was carried to more than a dozen countries worldwide by nowadays frequent jet travelers. There are already alarming incidences of rapid global spreading of the disease. Up to May 1, the virus has spread to 26 countries, infecting more than 5,000 people and killing at least 300, according to the WHO. Mainland China has experienced at least 3303 cases of SARS, with 346 previously unreported in Beijing alone and across the nation, at least 88 cases of death. Hong Kong was dealt with the hardest hit, with 1572 cases of infection reported and a death toll of 150.

It is of course not the first time Hong Kong was confronted with outbreaks of large scale epidemics. From recollection of recent epidemic events, during the 1997 outbreak of Avian Flu (Bird's Flu) in Hong Kong, 18 people were

hospitalised, six died and 1.5 million chickens were slaughtered. Further back in history, the 1968 Hong Kong Flu killed 33,800 people in the US alone, although the Colony was then much less affected. Epidemics experts believed that in the past only flu viruses, upon mutation, were most capable of causing super-epidemics or pandemics, on a world-wide scale, but with today's frequent jet travel, even emerging non-flu viruses could cause global pandemics with high death tolls, if they are highly contagious, with little symptoms during a relatively long incubation period, and not virulent enough to kill its hosts instantly, but incurable by known medicine.

SARS may be such an emerging virus. Within one week of its outbreak, Professor John Tam at Chinese University of Hong Kong (CUHK) announced that they had identified samples of the SARS patients paramyxovirus as the possible culprit of the disease. But within days, working with specimens from sick patients received in early March, the Hong Kong University researchers led by Microbiologists Professor Malik Peiris and his colleague Professor Yuen Kwok-yung soon proved that the initial guess may not be right.

Using a host of different types of cell-lines, the HKU researchers found in one of the cell lines a startling result. This cell line, extracted from the kidney of an embryonic green monkey, had previously been used for the culture of the avian virus H5N1 and the HKU team was possibly the only group in the region possessing it. Peering through microscopes, the researchers could see that lurking among the rapidly dying cells was the unmistakable image of a coronavirus, so named because of its spiky-shaped crown.

Subsequently laboratory results from US's CDC (Center of Disease Control & Prevention) run by Larry Anderson and

those from Erasmus University in Rotterdam, the Netherlands hinted that coronavirus could very possibly be the causative agent of SARS. By mid-April, it was confirmed beyond doubt by Dr Albert Osterhaus at the University of Erasmus that the coronavirus is indeed the SARS causing virus upon fulfillment of the last Postulate of Koch*.

The investigators commented that the new virus was not one of the two known human coronaviruses. Nor was it exactly like any of the known animal coronaviruses. Although more genetic analysis needed to be done to be certain, Peiris believed that it may be a new virus which may have originated from animals. He commented: "This report provides evidence that a virus in the coronavirus family is the etiological agent of SARS. However it remains possible that other viruses act as opportunistic secondary invaders to enhance the disease progression, a hypothesis that needs to be investigated further."

The above discovery, combined with the swift development of a PCR-based rapid diagnostic test of coronavirus by HKU, led some local doctors believe optimistically that SARS could be curtailed within months. However, in an editorial in the April Issue of New England Journal of Medicine, US CDC Director Julie L Gerberding made a sobering comment that while the suspect coronavirus was identified with unprecedented speed, it was too soon to predict either the ultimate scope of the disease, or whether drugs and vaccines could be made fast enough to curtail an extensive global outbreak.

"If we are extremely lucky," she said, "the epidemic will be curtailed, develop a seasonal pattern that will improve prospects for regional curtailment, or evolve more slowly than it has in this early stage. If the virus moves faster than our scientific, communications, and

control capacities, we could be in for a long, difficult race.”

If after curtailment, SARS does develop a seasonal pattern, experts believe that this epidemic may become a recurrent disease such as the 1997 Avian Flu which resurged – in form of the H5N1 sub-type - to kill six people and infect 12 others in a small but densely populated area. Nine cases were children under the age of 10. In March 1999, there were two cases of human infection by the H9N2 strain, also in Hong Kong. Ever since local experts believed that the causative influenza A virus of the Avian Flu may have already found its ecological niche in local avian species and that Bird's Flu has become an endemic disease.

Would the same possibility exist with SARS? Now that a new species of coronavirus is proven to be the culprit and it is not found in human, where does it come from? Most experts hint that it may come from animals.

Since the outbreaks of HIV, which was believed to have been transmitted from Africa's Green Monkeys to humans in the early 80's, and the resurgence of Ebola epidemics in Zaire & Uganda in 1989, again a mysterious hemorrhagic fever causing virus proven to be threatening both apes and humans, experts are now convinced that animal viruses are capable of adapting to humans as infecting hosts through mutation if given time and sufficient contacts. Avian flu is already a good example. It is known that viruses from fowl rarely cross over to humans in the past, but H5N1 and its subtype can do so now.

Since it has long been known that the coronavirus family includes viral species involved with the common cold in humans, and with more severe respiratory diseases in cattle, pigs and fowl, could this new species of coronavirus possibly come from farm animals? The investigation team led by WHO epidemics experts visited Guangzhou hospitals with SARS outbreaks in early April, enquiring about the possible viral links with farm animals. They were told that a few of the SARS patients had been kitchen workers, but could not find

any conclusive evidence yet. Scientists believe that the final cue may lie in the analyses of the DNA sequence of causative virus of SARS** . So far, experts believe that there is some possibility that SARS may become an endemic disease of Guangdong and Hong Kong.

Should the SARS become endemic, what can we do? Dr Bing Wong, an expert in plasma fractionation from Boston, said for short term solution, he proposed to the Hospital Authority to adopt the Solvent Detergent technique developed by the New York Blood Centre to ensure that plasma collected from local SARS convalescent patients are free from any residual SARS infectious agents and hepatitis before use, as this technique is capable of inactivating any contaminating viral particles in donated plasma. For long term purpose, he said, the best approach still is to set up a Centre of Community-specific Immunoglobulin (CCI), a charitable body with the mission: 1) To establish HK's first community-specific IG bank for the treatment of coronavirus pneumonia and bird flu, and 2) To help hospitals in HK to treat emerging epidemics of unknown causative agents.

What are community-specific immunoglobulins (IG)? IG is circulating antibodies in blood to neutralise foreign pathogenic (e.g. viral & bacterial) particles. Specificity of IG is highly specialised and directed by the identities of previous infections. As a result, IG have been widely used in the treatment of tetanus, rabies and Hepatitis B. IG derived from locally collected plasma is regarded as HK community-specific IG. For example, if the donor plasma pool consists of convalescent individuals of atypical pneumonia and bird flu, the IG produced could be used for the treatment of the infectious diseases. As the risks of IG therapy are minimal (NIH Consensus Development Program 1990), it could be an alternative choice for certain groups (e.g. renal failure and heart disease) of patients who are not entirely suitable for taking standard drugs. In fact, during the current SARS outbreaks, more than twenty SARS patients in serious

conditions were saved using plasma collected from convalescent SARS patients, because this type of plasma contain high titre of SARS-specific antibodies, capable of neutralising the SARS virus. Should the Hospital Authority have moved more swiftly to set up an official protocol for more front-line doctors to apply this plasma therapy to critically ill SARS patients, more lives could have been saved.

But in the end, in today's shrinking global village in which globetrotters move around constantly, the most effective safeguard of public health against any eventual outbreak of epidemics still lies in the setting up of an epidemics networking system, both nationally and internationally. As Dr Ali, a local public health expert, pointed out earlier, should there be a joint Guangdong and HKSAR communication networking on health issues at all levels (i.e., public health control, identification laboratories, researches and medical treatment, as well as health education), and the recent outbreak of SARS in Hong Kong would have possibly been much better controlled. Under the auspice of WHO, the Mainland along with the province of Guangdong is now in full collaboration with Hong Kong SAR government to set up such an epidemic communication network. It is late, but better than never.

* To be definitively declared the cause of SARS, the novel virus must satisfy three conditions known as Koch's Postulates. These were devised in 1890 by the German scientist Robert Koch, initially for anthrax infections. First, the suspect microbe must be isolated from all, or nearly all, cases; second, it must be cultured in isolation; and third, those cultured germs must be able to re-create the disease in a test animal. Albert Osterhaus of Erasmus University in Rotterdam, the Netherlands, told New Scientist that the coronavirus has now been isolated from patients in several different countries, and grown in several labs. Now results show that the cultured viruses indeed produce symptoms of SARS in the deliberately infected animals as human do.

** Early Saturday morning (April 12, 2003), researchers led by Dr Caroline Astell in at Michael Smith Genome Sciences Centre in British Columbia finished the DNA sequencing work on a sample of a coronavirus from a patient with SARS. The current genome shotgun data file in raw sequence now available in fasta format, contains the first draft genome assembly totalling 29,736 base pairs.

Dr Kenneth Lee obtained his *Docteur de Spécialité* from Lyon University and his PhD in Biochemistry from McGill University. He was the first Science & Technology Editor of Hong Kong Economic Journal and is a well-known columnist in science and technology. He is now CEO of a HK-based biopharmaceutical corporate with R&D in recombinant protein therapeutics.