The SARS Year of Living Dangerously

By Dr Paul Ananth Tambyah

The author taking Corona and SARSi in his stride.

When Han Chong asked me to write about SARS in Singapore, I had a surge of doubt but I had to say yes because he is my good friend and I have a rule about requests. If you agree to the icky ones, then you will get asked to do the juicy ones. Hence, I was hoping someday he would ask me to write about the number of different pulsed-field types of enterococci that could dance on the head of a hydrophobically coated urinary catheter or something that really interests me. After all, what more could be written about SARS in Singapore that has not already been written?

Could I write about the stellar jobs done by certain individuals in turning what could have been a major disaster of biblical proportions into a major disaster of only "Hollywoodian" proportions? Nah, done again and again from National Day onwards. Besides, if I praised our farsighted and generous Chairman of the Medical Board (CMB) too much, I would be accused of angling for a bigger office space or making other CMBs envious. Besides, the word on the wards is that if we did such a stellar job in handling SARS, why did more healthcare workers in Singapore die (5-6) than in Canada (3)? Hong Kong (9) and Taiwan (12) also had relatively few HCW deaths despite larger outbreaks. Most of us healthcare workers who actually treat patients are concerned about the thought that five deaths in active healthcare workers would be considered a success; what happens to us when a less than stellar job is done?

Should I write about the science of SARS from the perspective of a hospital epidemiologist? We who deeply love case-control studies have yet to see a decent one beyond Seto's piece in the Lancet (Lancet. 2003; 361:1519-20). We talk about attack rates but apart from Hsu LiYang's paper in EID (Emerg Infect Dis. 2003; 9:713-7) and the New England Journal by Olsen et al, we are really no wiser about what the true attack rate of SARS is in a ward, ICU, hospital waiting area, or vegetable market. The NEJM paper by Olson et al (NEJM. 2003; 349:2416-22) was really interesting in that one flight with four symptomatic individuals with SARS was associated with an attack rate (for probable SARS) of zero while another flight with a single symptomatic individual was associated with an attack rate of 18%. Our own travel experts have published data (Wilder-Smith, Paton, Goh. Trop Med Int Health. 2003; 8:1035-7) showing that three flights with symptomatic SARS patients resulted in only one transmission. This gives an overall attack rate of much less than 1%, despite one symptomatic individual being a so-called "super spreader" and another being critically ill at the time of the flight. Interestingly, the authors of the New England Journal paper point out that fully 45% of those fellow passengers infected with SARS had no direct contact as defined by the World Health Organization (WHO), with the patient on that ill-fated flight. They do not offer any explanation for the differing attack rates although a careful reader would realise that among the 22 individuals allegedly infected on the flight, ten were travelling together as part of a tour group. Also, the flight with the four symptomatic individuals was much shorter than the flight which was associated with widespread transmission. This is supported by the only cohort study published to date (mid-December) by Scales et al (Emerg Infect Dis. 2003; 9:1205-10) about the experience in a Canadian ICU. Again, time of exposure was considered a major risk factor. Overall, however, what these studies demonstrate is that we need much more detailed analysis to truly understand the epidemiology of this unusual virus. As a "trained" hospital epidemiologist, I have to admit that we have not covered ourselves in glory this time round. Thus, I would not really have much to write about the epidemiology of the SARS coronavirus. Next....

What about the other scientific aspects of the virus? The rapid discovery of the culprit virus, the fulfillment of Koch's postulates in monkeys, the selfless experimenters who worked with live viruses to bring us all the information we now have on it? These individuals work in conditions of extreme discomfort and personal risk with a pathogen which behaves quite differently from any known pathogen. Preliminary data seems to suggest that it can survive on a torn plastic bag far longer than any other similar virus. It has now become customary to vilify researchers who

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are victims of laboratory accidents and label them as irresponsible from the comfort of our armchairs or conference rooms. We often forget that, as the Institute of Medicine put it so succinctly in the title of their document on medical errors, "To err is human". Indeed, the U.S. biological weapons programme during its declared offensive phase (from 1943-1969) was responsible for 456 occupational infections with three deaths (two from anthrax, one from viral encephalitis) in laboratory workers in Fort Detrick (JAMA. 1997;278:412-7). While it is true that we do know a lot about the virus, we know very little about the actual pathogenesis of the illness. In Kuala Lumpur last month, at the Asia Pacific Conference on Medical Virology, Dutch scientists argued that immunopathogenesis was the culprit and the virus is just a trigger. At the same time, Hongkong researchers were pointing out the hazards of over-immunosuppressing individuals who might be at risk for both short term and long term risks of immunosuppression. If we had a set of protocols in place to study the pathogenesis and try the different modalities of therapy based on the different possible mechanisms, then perhaps, that would make a good story, but as far as I can tell, those are far, far over the horizon.

Perhaps, I could write about the clinical features of this illness which would be something that the majority of readers of this publication, being clinicians like myself, would be able to relate to. After all, the vast majority of the publications on SARS have been by clinicians who have described near identical clinical experiences with the virus. Clinicians from Singapore (From ID: Hsu et al. Emerg Infect Dis. 2003; 9:713-7, and Singh et al. Emerg Infect Dis. 2003; 9:1294-8. From critical care: Lew et al. JAMA. 2003; 290:374-80), Hong Kong (in numerous first rate publications in top journals), Canada, Taiwan and China have all reported similar features of a pneumonia which does not begin like a pneumonia. SARS is a non-specific illness with myalgia and malaise in which upper respiratory symptoms do not feature prominently and respiratory symptoms only occur a few days into the illness. Chest X-rays are usually initially normal, as are most lab investigations including full blood counts (except perhaps lymphocyte counts as with most viral infections), liver function tests, and unfortunately, most current molecular diagnostic tests for the SARS coronavirus (negative at least until day 3-4 of the febrile illness). Fever seems to be a hallmark of the illness but, as we in the National University Hospital experienced to our cost, a single individual with NO documented fever who passed through multiple levels of fever screening transmitted the infection to an entire shift of nurses, a physician, other patients and visitors (Fisher et al. Med J Aust. 2003; 178:555-8). Furthermore, our claim to fame as the University Division of Infectious Diseases has been our

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Lancet letter (Lancet. 2003; 361:1740) on atypical cases of SARS which had leukocytosis, no fever or multiple comorbidities, and were near impossible to diagnose without the benefit of careful monitoring and circuitous epidemiologic workups. The X-ray changes are also not specific as our radiologists have reported in major international journals (Pediatr Radiol. 2003. Nov 18) and in the world's first publication on SARS (Kaw et al. Singapore Med J. 2003; 44:201-4), which appeared in print in the Singapore Medical Journal, the sister publication to this, a month ahead of the New England Journal and a week ahead of the Lancet papers.

So, we have a virus which caused devastation to our economy, fear and anxiety among our colleagues, friends and relatives, which we can see very nicely in electron micrographs if we are wearing space suits. We can test for the presence of infection confidently after about a week of illness, by which time many would have been infected or perhaps many more needlessly isolated. We do not know for sure how it is spread, except that some people do not transmit the illness despite being critically ill in airplanes, and others transmit to many people. We do not know how it causes disease except that the immune system is certainly involved, but blocking it might do more harm than good. We do not know how it will present clinically, except that in most cases, it presents no differently from about one third of the patients sitting in any random GP clinic in a HDB estate or downtown. We do not even know for sure about the animal reservoir, although the civet cat has been identified as a natural host, and the seropositive animal market workers were all asymptomatic (Guan et al. Science. 2003; 302:276-8), which is not supposed to happen with SARS. "There are no asymptomatic carriers" is the official mantra.

What we do know is that our hospitals and clinics will never be the same again. Hopefully we have learned some lessons about ourselves, infection control and hospital epidemiology. In the Christmas issue of the BMJ this year, Editor Richard Smith describes the three most important words in medicine as "I don't know." That sums up my reflections on SARS. Now, I do know a bit about urinary catheters, but that is another story..... ■