Bio-Terrorism & SARS

The world has been whipped up into hysteria over terrorist attacks and 'weapons of mass destruction'. Governments want to ban the publication of sensitive scientific research results, and a group of major life sciences editors and authors has concurred. Some even suggest an international body to police research and publication. ***Dr. Mae-Wan Ho*** *looks at the current SARS epidemic and argues why all of those measures to control bio-terrorism are misplaced, and what's really needed.*

The SARS episode

In the weeks that the 'allied forces' were wreaking destruction and death in Iraq to hunt down Saddam Hussein and his elusive 'weapons of mass destruction', a SARS epidemic has been criss-crossing continents carried by air-passengers and spreading like molecular cluster bombs that explode to liberate further millions of infectious particles soon after a target is struck.

SARS – Severe Acute Respiratory Syndrome – is a completely new infectious disease spread by human contact, and kills about four percent of the victims. The epidemic originated in Guangdong Province, South China. The Chinese authority has admitted mishandling the crisis and to have been slow to inform its citizens.

The disease first struck last November. In March, Liu Jianlin, 64 year-old medical professor who was involved in treating patients, went from Guangdong to Hong Kong to attend a wedding. He was taken ill soon after arrival and admitted to hospital. He asked to be put into quarantine, but was ignored; nor did the hospital warn his contacts. As a result, nine guests in the hotel where he stayed caught the disease and carried it to Singapore, Canada, Vietnam and other hospitals in Hong Kong.

On 10 February, news of the disease was posted on ProMed, an international e-mail notification service for infectious diseases outbreaks. The next day, China informed the World Health Organisation (WHO), but refused to let the WHO team into Guangdong until early April. By 8 April, there were 2671 confirmed cases of SARS in 19 countries and 103 deaths.

A palpable sense of panic has gripped the health authorities around the world. "Mother nature is the ultimate terrorist," says an editorial in the journal *Nature*. "Powerless to stop the spread", says *New Scientist* magazine, whose editor decries the lack of international control when it comes to disease epidemics: "The international community has weapons inspectors poised to force entry into a country at the first hint that it may possess chemical weapons. But when it comes to disease, we have no international body empowered to take charge, *even though the disease may be vastly more dangerous*." (italics added)

Eleven laboratories around the world participated in the hunt for the disease agent, a collaborative effort organised via teleconferencing, since March 17, by virologist Klaus Stöhr at the WHO headquarters in Geneva.

The journal *Science* says that Malik Pieris of the University of Hong Kong was the first to identify coronavirus (which causes colds and pneumonia) just four days later. This finding was replicated in other laboratories. The virus and antibodies against the virus were detected in many, though not all infected patients, but were not found in more than 800 healthy controls tested.

The *New Scientist* says it was the death of Carlo Urbani, the WHO doctor who first recognized SARS as a new disease that led to the discovery of coronavirus. It was isolated from his lungs and sent to Joe DiRisi in University of California at San Francisco who made the identification. The virus has since been named after Urbani.

There is some remaining doubt, however, whether the coronavirus is the complete story. John Tam, director of virology at Prince of Wales Hospital in Hong Kong, found another virus, the human metapneumovirus in 25 out of 53 SARS patients, as have laboratories in Canada and Germany. Metapneumoviru belongs to the family Paramyxoviridae, which includes viruses responsible for parainfluenza, mumps and measles, as well as the Nipah and Hendra viruses in recent outbreaks.

Coronavirus showed up in only 30 patients tested while the bacterium *Chlamydia* has been identified in all samples in Hong Kong, though that strain of *Chlamydia* is not known to cause disease.

Could it be that both viruses are bystanders of the disease while an as yet unidentified virus could be responsible for SARS?

The coronavirus was atypical. It rapidly infected cells in culture dishes, something that other human coronaviruses do not do. Viruses from the lung tissue in Toronto patients readily infected monkey kidney cells, and no known human coronavirus infects that cell line.

DiRisi's laboratory has a virus detector chip capable of screening for 1 200 viruses all at once. When samples sent from the Centers of Disease Control and Prevention in the United States (CDC) were screened, several species of coronaviruses lit up, the strongest spots – indicating the closest identity - were the avian bronchities virus and a bovine coronavirus. This appears to fit China's statement that the earliest cases were in bird handlers.

However, more detailed analysis using polymerase chain reaction (PCR) by two groups who just published their results online in the *New England Journal of Medicine* indicate that the new virus is not closely related to *any* known virus at all, human, mouse, bovine, cat, pig, bird, notwithstanding.

Furthermore, the virus was isolated from cell cultures only, and not from the tissues of patients. The PCR fragments of the new coronavirus were not detected in any healthy subject tested so far. But not all patients with SARS tested positive for one of the PCR fragments. Where did this new virus come from?

Genetic engineering super-viruses

While the epidemic has still to run its course, a report appeared in the *Journal of Virology*, describing a method for introducing desired mutations into coronavirus in order to create new viruses. A key feature of the procedure is to make interspecific chimera recombinant viruses. It involves replacing part of the spike protein gene in the feline infectious peritonitis virus (FIPV) - which causes invariably fatal infections in cats - with that of the mouse hepatitis virus. The recombinant mFIPV will no longer infect cat cells, but will infect mouse cells instead, and multiply rapidly in them.

These and other experiments in manipulating viral genomes are now routine. It shows how easy it is to create new viruses that jump host species in the laboratory, in the course of apparently legitimate experiments in genetic engineering. Similar experiments could be happening in nature when no one is looking, as the SARS and many other epidemics amply demonstrate.

It is not even necessary to intentionally create lethal viruses, if one so wishes. It is actually much faster and much more effective to let random recombination and mutation take place in the test tube. Using a technique called "molecular breeding" (see "Death by DNA shuffling", this series), millions of recombinants can be generated in a matter of minutes. These can be screen for improved function in the case of enzymes, or increased virulence, in the case of viruses and bacteria.

In other words, geneticists can now greatly speed up evolution in the laboratory to create viruses and bacteria that have never existed in all the billions of years of evolution on earth.

Controlling bio-terrorism

John Steinbruner, University of Maryland arms control expert, has been calling for mandatory international oversight of inherently dangerous areas of biomedical research, specifically, an international body of scientists and public representatives to authorize such research.

He has taken the proposal to meetings of the American Association for the Advancement of Science and the World Medical Association in recent months, and in April 2003, to a London bio-terrorism meeting, sponsored by the Royal Society of Medicine and the New York Academy of Medicine.

The oversight system would be mandatory and would operate before potentially dangerous experiments are conducted. Access to results could also be limited to those who pass muster.

Requiring scientists, institutions and even experiments to be licensed "would have a devastating chilling impact on biomedical research," said American Society for Microbiology (ASM) president Ronald M. Atlas. His answer is self-regulation, already in line with ethical requirements to prevent the destructive uses of biology.

The ASM orchestrated and supports a statement released February 15 by a group of major life sciences editors and authors, acknowledging the need to block publication of research results that could help terrorists.

Critics say even the self-censorship espoused by the journal editors and authors group is an impediment to the rapid progress of science, which is the best way to defuse the lethal potential of some biological research. But Steinbruner fears that self-regulation does not go far enough to head off terrorists.

Both Steinbruner and Atlas agree, however, that any effort to keep good science out of the hands of ill-intentioned people must be international to be effective. And both point to existing efforts to push a treaty making bio-terrorism an international crime, one long espoused by Harvard University microbiologist Mathew Meselson and chemist Julian Robinson of the University of Sussex.

Steinbruner and his critics, and the critics of his critics are all missing an important point. They have yet to acknowledge that genetic engineering experiments are inherently dangerous, as first pointed out by the pioneers of genetic engineering themselves in the Asilomar Declaration in the mid 1970s, and as we have been reminding the public and policy-makers more recently.

Who needs bio-terrorists when we've got genetic engineers?

But what caught the attention of the mainstream media was the report in January 2001 of how researchers in Australia 'accidentally' created a deadly virus that killed all its victims in the course of manipulating a harmless virus. "Disaster in the making: An engineered mouse virus leaves us one step away from the ultimate bioweapon", was the headline in the *New Scientist* article. The editorial showed even less restraint: "The genie is out, biotech has just sprung a nasty surprise. Next time, it could be catastrophic."

The SARS episode should serve as a reminder of some simple facts about genetic engineering.

In the first place, genetic engineering involves the rampant recombination of genetic material from widely diverse sources that would otherwise have very little opportunity to mix and recombine in nature. And, as said earlier, some newer techniques

will create in the matter of minutes millions of new recombinants in the laboratory that have never existed in billions of years of evolution.

In the second place, disease-causing viruses and bacteria and their genetic material are the predominant materials and tools of genetic engineering, as much as for the intentional creation of bio-weapons.

And finally, the artificial constructs created by genetic engineering are designed to cross species barriers and to jump into genomes, ie, to further enhance and speed up horizontal gene transfer and recombination, now acknowledged to be *the* major route to creating new disease agents, possibly much more important than point mutations which change isolated bases in the DNA.

With genetic engineered constructs and organisms routinely released into the environment, we hardly need the help of terrorists. That may be why we are coming up against new epidemics of viral and bacterial diseases with increasing regularity. Mother nature is not the ultimate terrorist, we are.

What needs to be done instead?

It is pointless to control the publication of sensitive scientific results because there is nothing special about the recombination techniques, they are already well known. "The only way we'll ever understand these natural outbreaks is by first-rate science and getting it published," says Lynn Enquist, editor of the *Journal of Virology*, referring to the creation of a coronavirus that crosses from cat to mouse that's a routine part of a genetic engineering technique.

Open publication is only half of the story. The other half is the importance of biosafety. An international instrument for regulating biosafety already exists, it is the Cartegena Biosafety Protocol agreed in January 2000, now signed by 43 countries including the European Union; though efforts to undermine it has continued unabated, principally by the United States and allies and the biotech industry. All we need to do is to strengthen the Biosafety Protocol both in scope and in substance.

There is also an urgent need for democratic input into the broad areas of scientific research that are to be supported by the public purse. Every sector of civil society has been called upon to be 'accountable', even corporations; so why not scientists?

We have drafted a discussion document, Towards a Convention on Knowledge, which contains some key ideas on how scientists could be socially responsible and accountable.

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