Editorial

Peter C Doherty

The severe acute respiratory syndrome (SARS) epidemic of 2003 sounded a wakeup call for business and political leaders everywhere. This relatively brief experience with a previously unknown pathogen reminded us that rapidly spreading, lethal respiratory infections are both terrifying and cause substantial economic damage. Although there were only 8000 or so known cases, with about a 10% mortality, the global cost was estimated at between 20 and 40 billion US dollars. We were fortunate that the causative agent was identified quickly and that the epidemic was soon contained. Particularly important was the well established World Health Organization influenza program, which, with its collaborating network of national laboratories, provided the technological and organisational base. SARS illustrated very clearly how the application of contemporary science in the context of open international cooperation serves to protect humanity.

We were also reminded of what happened in 1918–1919, when some 40 to 100 million people, including at least 10 000 Australians, died from the "Spanish flu". Although the accumulation then dispersal of soldiers in the battlefields of Western Europe probably had an effect on transmission, the disease spread everywhere and was by no means confined to countries that had been directly affected by the Great War. At that stage we had no real idea how the pandemic originated, and, in fact, we did not isolate the first human influenza A virus until 1933. Recently, the reconstruction of the 1918 killer has established that this A/H1N1 virus came originally from birds. The same is true for the subsequent 1957 (A/H2N2) and 1968 (A/H3N2) epidemics. For that reason, the influenza research community has been keeping a very close watch on, particularly, aquatic birds — the natural maintaining hosts of these viruses.

Over the years, we have seen other occasional instances where A/H7N7 and A/H9N2 infections have transmitted from birds to humans. Much more concerning was the 1997 occurrence in Hong Kong, where an A/H5N1 avian virus infected 18 people and six died. The outbreak was quickly controlled, but the H5N1 infection continued to circulate in apparently healthy ducks in coastal China and spread east and north to Korea and Japan, and south to Vietnam, Cambodia, Thailand, Laos, Malaysia and Indonesia. Then, in May 2005, a massively lethal outbreak in bar-headed geese at China's Qinghai Lake established the involvement of a much broader range of migratory birds. Monitoring for dead swans and geese showed the virus moving westward to India, Europe and Africa. As at 16 October 2006, there have been 256 human cases with 151 deaths since 2003, including 42 deaths from 93 infections in Vietnam, six from 15 in Egypt and 55 from 72 in Indonesia. Although the virus has been changing rapidly, there is minimal evidence of subclinical "background" infection, and the indications of possible person-to-person spread are very limited.

The combination of low infectivity but great severity in humans could reflect that the distribution of the α2-3 sialic acid receptor used by the avian influenza A viruses is limited to the deeper regions of the lung. One fear is that the virus may mutate to bind the "mammalian" α2-6 sialic acid receptor found in the upper respiratory tract. A further possibility is that simultaneous infection of a pig or a person with, say, "human" H3N2 and "avian" H5N1 viruses could give a "reassorted" H5N1 virus that spreads readily between people. The informed research community is divided on whether either scenario is likely. One school has it that, although the H5N1 virus is a terrible pathogen for birds that sometimes crosses into other species (humans, cats) with disastrous consequences for the individuals concerned, it will remain essentially an avian virus. The alternative view is that it is only a mutation or two away from establishing in people. There's the quandary: the potential threat has horrific proportions, but it is not clear whether anything will actually happen.

As you will read in the following pages, the Australian Government, represented by Health Minister Tony Abbott, and the scientists, epidemiologists and medical professionals who plan for epidemic preparedness have taken this very seriously. I've been watching mainly from the sidelines as, although our research group works with influenza A viruses (including H5N1) in Melbourne and Memphis, we focus on fundamental aspects of T cell-mediated immunity that have little immediate relevance to the current quandary. The pragmatism and willingness to face what are some very difficult choices has been impressive. In a sense, this has been more like developing a national defence initiative than a medical strategy. Significant dollar sums have been spent preparing for something that we all hope will never happen. A national plan is in place, and both private "think tanks" and elements in the business community have also been addressing the issue.

Australians should rest assured that this country is as prepared for a possible H5N1 pandemic as any nation on earth, including the United States, which, with strong leadership from President Bush, has also been very proactive. However, there are no certainties. The virus could mutate to defeat the newly developed "reverse genetics" vaccines or the antiviral drugs (oseltamivir and zanamivir) that are currently being stockpiled. In general, though, the more time goes by, the better off we are likely to be. Also, even if this pandemic does not eventuate, the combination of rapid air travel and greater human population size (threefold increase since 1919) make some such occurrence a certainty for the future. Since 1979, some 30 new viruses (including SARS virus, Ebola virus and HIV) have crossed into humans from animals. Even if we duck the bullet this time, the effort and resources expended here will have ensured that our capacity to deal with an unexpected invader is enhanced.

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