



BIRD FLU: HOW PREPARED ARE WE?

NO ONE KNOWS WHETHER AN H5N1 PANDEMIC WILL STRIKE, BUT THE WORLD CANNOT AFFORD TO SIT BACK AND WAIT. ALISON GOODWIN LOOKS AT THE NATURE OF INFLUENZA AND WHAT IS BEING DONE TO COMBAT THE LATEST THREAT.

PHOTOGRAPHERS: ANDREW PORFYRI + MALCOLM FAIRCLOUGH

Alarmed by the uncontrollable spread of a severe respiratory illness, 15th-century Italians concluded that supernatural influences were at work and gave influenza its name.

The disease struck a chord of fear in those who were helpless to provide effective treatment, let alone prevent it or identify its origins. It is a fear that has parallels with 21st-century concerns about the destructive potential of influenza. But we have one great advantage over medieval observers: an appreciation of the causes of disease.

The electron microscope has unmasked the true culprit, the influenza virus. Fragments of genetic material encased in a protein shell, or capsid, viruses cannot reproduce without a living host cell. Of the three influenza virus types, A, B and C, only A and B cause epidemics in humans. Influenza A, found in pigs, horses and birds, is responsible for the main human epidemics.

Influenza strains are subtyped according to the presence of tiny spikes of the proteins haemagglutinin or neuraminidase on the virus' surface. The

victim responds to these proteins, building up immunity to that strain once infected. But being able to produce seven new generations of themselves in 24 hours, with the possibility of minor or dangerously major mutations in each new generation, makes viruses tough adversaries to deal with.

The minor changes represent the seasonal variations that humans tend to experience on a yearly basis and which our regular flu shots are designed to combat. But when there is an abrupt change in the proteins, a new subtype emerges to which the entire community is



Opposite page & above: Dr David Siebert, a member of the Royal College of Pathologists of Australasia Microbiology Advisory Committee and Virologist for the Queensland Health Pathology Service.

susceptible. It is this major change, or reassortment, that spawns epidemic illness on a regional or national basis, or worse, as has occurred three times in the previous century, a global pandemic. To be designated a pandemic, a disease must be easily transmitted between humans and be genetically unique in that humans have no pre-existing immunity to it.

“It is important to remember that avian flu is not the same as pandemic flu,” stresses Professor Lyn Gilbert, director of the Centre for Infectious Diseases and Microbiology at the Institute of Clinical Pathology and Medical Research, Westmead Hospital, Sydney.

“At the moment avian flu is just that – a bird pathogen that occasionally spreads to humans in close contact with sick birds. For it to become a pandemic strain it will have to change to become easily transmissible between humans, and at this

stage we do not know that will happen,” she says.

There are 15 subtypes of influenza based on different haemagglutinin types, some of which usually infect birds (e.g. H5, H7) and others that usually infect humans (e.g. H1, H3). The current H5N1 avian virus is present in the intestines of infected birds and in their faeces. Handling sick birds or infected carcasses, eating improperly cooked infected poultry or contact with infected faeces can cause disease in humans.

The first documented report of human illness with an avian influenza H5N1 virus strain, in Hong Kong in 1997, coincided with an epidemic of highly pathogenic bird flu in poultry.

Six people died during this outbreak, but it is considered that a human epidemic and possibly a pandemic were averted by the Hong Kong Government’s speedy

decision to destroy the territory’s entire poultry population. There have been dozens of human deaths arising from the current outbreak of avian influenza first recorded in late 2003.

Countries such as China, Indonesia, Vietnam and Turkey have been affected. All cases have been traced to close contact with infected birds and, at the time of publication, there was no indication that the virus had mutated to enable human-to-human transmission.

But Professor Gilbert says the increasing spread around the world of a very virulent flu virus among birds has led many to believe that conditions are right for such an event.

The influenza A we are more familiar with can also kill. Each year across Australia, and most commonly during winter, it is responsible for an estimated 1,500 to 3,000 deaths.

“Though we think of this primarily as a microbiological issue, it will involve all areas of pathology,” Dr Smith says. “We need to ensure that they are informed about the safe handling of samples from cases, and other pathologists and laboratory workers also need to be aware of the potential impact of a pandemic should that occur.”

Dr David Smith, clinical director of the division of microbiology and infectious diseases at PathWest Laboratory Medicine in Perth, Western Australia, says the study of influenza A has “provided us with a sound base on which to plan for avian influenza and for future pandemic influenza”.

His organisation, Westmead’s Centre for Infectious Diseases and Microbiology and the Victorian Infectious Diseases Reference Laboratory in Melbourne form three World Health Organisation national influenza centres working closely with the WHO Collaborating Centre for Influenza in Melbourne.

“We are also members of the Public Health Laboratory Network of Australia, which links all the major public health laboratories in Australia, the Commonwealth Department of Health and Ageing, state and jurisdictional public health units and New Zealand laboratories, and this work is also mirrored on a state level in conjunction with state health departments,” Dr Smith says.

Liaison with animal health experts is also vital and done through various bodies.

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Timely and accurate diagnosis will be a crucial part of the planning and response to any pandemic, but poses many challenges, he says.

“Firstly, we need to develop reliable tests for an infection that is not currently present in Australia; therefore, we need to look at innovative ways to evaluate the new tests.

“We also need to ensure that if we do detect avian influenza, that the virus is adequately contained to protect the public, our staff and our animal populations. If this avian influenza strain, or any other influenza strain, develops into a human pandemic strain, then we will need to potentially provide large numbers of tests to support the public health response as well as individual patient diagnosis.”

Pathology specimens found to contain influenza viruses will be forwarded to state public health laboratories for subtyping using more elaborate tests, says Dr David Siebert, a member of the RCPA’s Microbiology Advisory Committee and Virologist for the Queensland Health Pathology Service. “Once subtyping is complete every state will forward its cache of virus to the WHO Influenza Reference Laboratory at CSL in Melbourne. Many of the specimens will be cultured to obtain live virus, monitor mutations, develop vaccines and provide new material for research and epidemic mapping,” Dr Siebert says.

“The major tool required to contain an influenza pandemic is a widely available and effective vaccine.

“In Australia the common influenza vaccine is a killed ‘split-virus’ vaccine that is first grown in chicken eggs and then chemically disrupted to make it both



Dr David Smith, clinical director of the division of microbiology and infectious diseases at PathWest Laboratory Medicine in Perth, Western Australia

effective at low doses and safe to use. A new formulation is compiled each year containing the latest variants of the common human influenza A types (two) and one influenza B”.

Bird flu vaccine manufacture poses challenges. The virus may re-assort with a human influenza virus, suddenly producing a hybrid that spreads rapidly from person to person and a vaccine based on the current H5N1 strain may be less effective.

“We may have to switch tack and build a whole new vaccine from scratch,” Dr Siebert says.

On the positive side, he says, vaccine research has been moving forward for many years. Australian trials of a split vaccine are under way and new injectors that inject the vaccine into the skin and not deep muscle allow for a lower dose.

Also, new forms of vaccine additives, or adjuvants, increase the immune response to low doses of vaccine, making them more effective and increasing the number of shots that can be made from a single batch. Trials of bioreactors, large cell-culture vats to replace eggs and improve vaccine yields, are under way in the US and Europe. Live recombinant and DNA-based vaccines have been trialed or are under development and an attempt to produce a broad spectrum vaccine using stable components found in all influenza viruses started in 2005.

“We just do not know if the avian agent or a derivative will actually kick start a human pandemic,” Dr Siebert says. “It could happen this year, next year or a decade from now. If we are lucky, it could just fizzle out, but no one is taking bets on that.

“Our capacity to buy time for vaccine production, using antiviral drugs and public health strategy, is limited. We might get one, possibly two, chances to snuff out a local epidemic in the first four to six weeks, if we identify it quickly.”

Dr Smith says Australia also has a responsibility to assist planning and response in the Asia-Pacific region, as it did during the SARS outbreak.

Dr Siebert points out that “we have never been as well prepared to face such a challenge as we are now. Australia has some of the best public health and hospital systems in the world and a

capacity to reach out over long distances in a way few other nations can match”.

It is recognised that the greatest impact of a human pandemic will fall on those least prepared for it and any event matching the size of the 1918 experience would be overwhelming for the people and health systems of poorer countries, he says.

“While the developed nations should fare relatively well, we can only plan effectively up to the limits of our resources and our will to manage large-scale problems. Beyond that, nature is in charge.” 🔥

GPs NOTE: This article is available for patients at <http://pathway.rcpa.edu.au>

Spanish Influenza Pandemic

The first recorded influenza pandemic dates back to 1580, with at least half a dozen more of varying intensity in subsequent centuries. In the past 100 years three pandemics have struck – the first and most serious was the Spanish influenza pandemic of 1918.

Caused by an influenza A (H1N1) strain, it spread widely within six months and continued over a two-year period in which an estimated 200 million people were laid low and an estimated 50 million died. The Spanish prefix was adopted simply because politically neutral Spain was unfettered by censorship and the world got to learn more about the disease’s emergence there.

Reeling from the Great War, the world was well primed for a health catastrophe. Geographical isolation was no protection for Australia and New Zealand; medical historians believe soldiers returning from Europe carried the virus. Australian health authorities had some time on their side but little else as defences against a killer of not only the frail and aged but also apparently healthy young adults.

Australia’s first cases of Spanish flu were in Melbourne early in 1919 and soon strict quarantine measures were in place – citizens were ordered to wear masks on public transport, schools and pubs were closed, sporting and cultural events ceased.

The disease hit in waves and just as health authorities believed it had run its course it flared again. Hospitals overflowed with desperately sick patients and many more had to be cared for at home. New Zealand, with less-stringent quarantine restrictions, had a proportionally higher death rate than Australia.

Newspaper reports told of troops arriving in Sydney at war’s end, only to be marched straight to quarantine at the Sydney Cricket Ground without even the chance to greet the loved ones they had not seen in years.

With the spread of disease came desperate remedies and preventative measures – one US town even banned handshaking. Some pharmacists were prosecuted for inflating the price of their influenza remedies. In western Victoria suspicions fell on commercial travellers as a source of the contagion. Police guards at borders prevented people moving between states.

Australia’s death toll was about 11,500. Sixty per cent were in the 20-to-45 age bracket. Worldwide, while few countries were spared the pandemic, there were varying degrees of infection and death. The two other influenza pandemics of last century were less severe – the 1957-58 Asian flu claimed two million lives and the 1968-69 Hong Kong flu a further one million.