The current threat of avian influenza A is real and not a mirage

The greatest outbreak of influenzas in history, the so-called Spanish pandemic of 1918, provides us with a number of lessons which could be learnt. Studies from pathologists working in the British army tell us that the influenza outbreak started in northern France a year earlier, in the vast sprawling British army camp at Etaples (Oxford et al, 2002). Suddenly a new disease emerged with a case fatality of 50%, attacking young soldiers but only in low numbers and inducing a unique clinical feature, heliotrope cyanosis. The reproductive number, being the number of contact infections from an index case (Ro), was low (probably <1) and the outbreaks appeared to be confined to Etaples and Aldershot barracks.

We hypothesize that this progenitor virus with high virulence but low spreadability mutated to give the 1918 pandemic virus with a higher Ro of 3 and lower case fatality of 2%. During these pre-1918 outbreaks the total mortality was only 150 persons but within 18 months the virus became global causing 50 million deaths. The observation alone explains the seriousness with which the World Health Organization and the UN is taking the current situation with the avian influenza H5N1. The 1918 virus, as with the 1957 and 1968 pandemic viruses, was an avian influenza virus.

It is less appreciated that the avian influenza A (H1N1) virus of 1918 mutated and re-invented itself as an epidemic virus and caused problems worldwide for the next 38 years until displaced by another avian emerging pandemic (H2N2) in 1957. The totality of deaths between 1918 and 1957 exceeded the huge mortality in 1918. So we need to be on guard against these two faces of influenza, the sudden emergent pandemic and thereafter, the epidemic virus.

A different concern

But strangely there is a second lesson to be learnt from the Spanish influenza, after all these years have passed, and a thoroughly unpleasant lesson at that. Beware the virus that attacks young children and babies in arms. The demographer Langford (2002) has burrowed more deeply than most into the influenza death roll of 1918 both in Ceylon and in the UK. Most analyses of 1918 deaths at the time and since have highlighted changes in the proportional distribution of deaths by age compared to earlier 'normal' periods. This type of snapshot has highlighted the deaths in young adults. In contrast Langford views the mortality figures for age-specific death rates which is the ratio of the numbers of deaths to individuals in a particular age group in a year to the number of individuals in that age group. His surprising conclusion was that while the largest proportional increases in age-specific mortality rates were indeed for young adults, nevertheless children under the age of 5 years suffered the greatest absolute increases in mortality rates.

This disturbing and yet timely re-focus on the under-fives is reflected in Poehling et al's study (2006) which described an hitherto unquantified burden of epidemic influenza in young children. In hospitals in three counties in the USA outpatient visits by under-fives associated with influenza were 10–250 times as common as hospitalizations and few of these influenza infections were recognized clinically.

Therefore the international concern about pandemics is also leading to new knowledge about the yearly influenza outbreaks and, importantly, about the disease itself and the spread of virus in the community. The global investment, $3 billion being contributed by the US government alone, is leading to the development of new influenza vaccines and adjuvants and stockpiling and more extended use of antivirals. Research into the molecular mechanisms of deaths and illness is expanding. Could over-reaction of the immune system play a part? These are the important topics explored in the articles in this issue.

New knowledge is at the heart of these observations and they are now more often based on molecular biology or mathematics combined with computer power. The new sensitive and accurate diagnostic tests for influenza involving reverse transcriptase polymerase chain reaction (Yuen et al, 1998) mean that influenza illness in a child can be diagnosed with precision while mathematical modelling tells us that a new pandemic could actually be stopped in its tracks should we be so sensible as to concentrate our energies into this erstwhile theatre of infection (Ferguson et al, 2005). Who would have thought in 1918, 1957 and 1968 that the pandemics could have been prevented by breaking a chain of infection from a virus migrating from geese to domestic chicken and ducks to their keepers? Simple hygiene backed by new antivirals and vaccines are the three tools, but new knowledge underpins everything. BJHM

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KEY POINTS

- The three influenza pandemics of the 20th century were all caused by avian influenza virus.
- A weak link between chickens and humans has been indetified as an Achilles heel of the virus transmission.
- Stockpiles of antivirals and H5N1 vaccines and more attention to hygiene are key munitions.