Pandemic influenza (H1N1) 2009 (swine flu)

The current outbreak of pandemic influenza (H1N1) 2009 demonstrates yet again how enigmatic, unpredictable and challenging the influenza virus is. First isolated in 1933 by Laidlaw, Andrews and Smith and one of the first human viruses to be isolated, it has been intensively studied in the minutest of details over many decades. Yet in 2009 this remarkable virus still baffles virologists and perplexes epidemiologists with its unpredictability and its penchant for upsetting prevailing dogmas.

For almost a decade, the global community had been anticipating that the avian influenza A (H5N1) virus would be responsible for the next pandemic, which should be imminent if the 15-50-year cycle of pandemics were to hold. This would also fit in with influenza A (H5N1) being a new subtype of virus to humans, as was the case with previous pandemics—H1N1 in 1918, H2N2 in 1957 and H3N2 in 1968. Today, 40 years after the last pandemic, it is the novel swine influenza virus that has launched the current pandemic even though it is not a new subtype—H1N1 subtype has circulated in humans since 1977. It is, however, certainly a virus novel to humans, antigenically and biologically quite distinct from human H1N1. Where has this virus come from, and what does it hold for the world and for South Africa in particular?

Classic swine influenza virus of the H1N1 subtype was identified as far back as 1913 as a cause of respiratory disease in pigs. The virus is endemic in pig herds in North and South America, parts of Europe, East Asia and Africa (Kenya). Human infections with this virus have been an occupational risk resulting in sporadic cases of an influenza-like illness but with little or no human-to-human transmission. In 1976, however, an outbreak of swine flu in a military camp (Fort Dix, New Jersey) was responsible for 230 cases and severe illness in some 13 soldiers with 1 death. Here there was clear human-to-human transmission, but the infection mysteriously died out. More recently a derivative of the classic swine influenza virus was detected. Pigs are susceptible and are frequently infected by influenza viruses from birds and humans. It is therefore not too surprising that a novel swine influenza virus arose as a result of the exchange of genetic material, referred to as reassortment, from influenza viruses from swine, avian and human sources. This triple reassortant swine influenza A (H1N1) virus was first detected in human patients in December 2005 in the USA and, until the present novel influenza A (H1N1) outbreak in April 2009, 11 cases of infection had been reported, in 10 of which there had been contact with pigs. While the clinical presentation resembles human influenza illness in many respects, some important differences have been described. The disease was mainly found in children and young adults (median age 10 years), the incubation period was somewhat longer than human influenza (median 3.5 days), and unusual clinical signs were described in about a quarter of the patients, who presented with gastro-intestinal symptoms of vomiting and diarrhoea.

The current pandemic influenza (H1N1) 2009 virus arose from a subsequent reassortment event from the triple reassortant swine influenza A (H1N1) virus. The latter virus contains 5 genes from the classic swine virus (haemagglutinin HA, nucleoprotein NP, neuraminidase NA, matrix M, and non-structural NS), 2 genes from avian influenza virus (polymerase PB2 and PA) and a single gene from human influenza virus (polymerase PB1). In the case of pandemic influenza (H1N1) virus, the NA and M swine genes, which were of North American origin, were replaced by genes of Eurasian origin.

The effect has been to create a novel reassortant virus able to transmit efficiently from human to human and spreading within a matter of 6 weeks throughout the world. Early in June, the WHO declared a global pandemic. The virus is now well established in the human population—the 100 000 mark having been passed in mid-July, although the true tally is greatly in excess of this. Fortunately the disease has been relatively mild in the majority of cases—no more serious than the regular annual seasonal influenza. What is different is the greater involvement of younger individuals (median of 10-20 years of age and relative sparing of older persons), a pattern quite unlike seasonal influenza and more akin to past pandemics. Risk factors for severe disease include those conventionally described for seasonal influenza (with the exception of the elderly) but now also including obesity and pregnancy.

Well over 100 laboratory-confirmed cases have been detected in South Africa as at mid-July and therefore, as has been internationally recommended, routine testing of all suspect cases as well as daily number counting has been stopped as this would add very little value in managing the outbreak, which has undoubtedly spread well beyond the numbers confirmed through laboratory testing. The winter season could well promote significant spread of the virus, as it does for seasonal influenza, further aggravated by the crowded and inadequately ventilated living conditions of a large proportion of our population. Underlying immunosuppressive diseases such as HIV and TB are clearly also aggravating factors—again focusing on the young adult population. The effect of immunosuppression on viral excretion and the epidemiological consequences will also need to be investigated. Influenza is an infection of very high transmissibility and very little can be done to prevent the virus spreading through a non-immune population. It is hoped that an effective vaccine will become available for widespread use by the end of the year. For the individual, personal hygiene practices such as cough and sneeze etiquette, frequent hand washing and social distancing will reduce the chances of transmission.
Given the notorious unpredictability of influenza virus, the long-term future of the pandemic cannot be forecast. Unlike previous pandemics, pandemic influenza (H1N1) 2009, although not a new subtype of influenza virus, does represent a virus that is new to the human population both antigenically and biologically. The extent of cross-protection from prior exposure to human H1N1 influenza, either from past natural infection or from vaccination, still needs to be defined although the relative sparing of older individuals probably does represent some degree of cross-protection.

At present, oseltamivir remains the drug of choice for both treatment and post-exposure prophylaxis in high-risk persons, although the clinical efficacy for pandemic influenza (H1N1) has not yet been adequately established. The virus remains sensitive to both oseltamivir and zanamivir; however, the explosion of resistance to oseltamivir by H1N1 human influenza virus over the past 2 years has taken virologists back – in South Africa all 2008 H1N1 isolates tested highly resistant to the drug.

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