Swine Flu (S-OIV) Pandemic

Influenza is a disease of global dimension occurring in annual epidemics, and infrequently as pandemic with high attack rates. The annual epidemics result in the host population updating its pool of humoral immunity by exposure to the most recent viruses carrying altered antigenic specificity caused by ‘antigen shift’ in the haemagglutinin (H) ligand. Pandemics are caused by ‘antigen drift’. They occur at intervals and give rise to high morbidity and mortality. Influenza viruses are RNA viruses with a segmental genome comprising eight parts. ‘Antigen drift’ and ‘shift’ arise from these characteristics (Fig. 1).

The RNA genome is transcribed by the polymerase that the virus carries. The transcription is associated with many point mutations persistently causing changes in virus proteins including surface proteins HA and NA (neuraminidase), and thereby causing the ‘antigen drift’ [1]. Antigen drift enables the virus to escape onslaught by the host’s immune defences. Segmentation of the genome facilitates reassortment when two or more viral variants happen to infect the same cell. The progeny virus gets a mixed genome with a different viral structure. The emergence of H3N2 virus, as indeed of several other variants, has been traced to such a genomic reassortment [2].

Two envelope proteins stick out as spikes which the virus uses for entry into host cells (H, agglutinin) and exit by the progeny of the virus (N, neuraminidase). Influenza A viruses are subtyped into 16 H (H1 to H16) and 9 N (N1 to N9) giving a theoretical possibility of 144 serological subtypes. Up to now 105 influenza A subtypes have been discovered, of which all are endemic in water birds (ducks, geese and gulls). Some subtypes have adapted to other species. Species that are considered important from the point of view of humans are pigs, chickens and mammals (pigs, horses and humans) [3].

Influenza pandemics occur when an influenza virus strain is transmitted to humans from another animal species. Species that are considered important from this respect are pigs, chicken and ducks. For example, in 1997 during an outbreak in chickens in Hong Kong the avian influenza virus H5N1 crossed the species barrier and infected 18 persons of whom six died. Since then antigenic variants of the virus have continued to appear in domestic and wild birds. During the 20th century, four pandemics of influenza have been recorded (Table 1). The current swine flu pandemic is the first one of the 21st century.

Viruses of the H5N1 subtype are highly pathogenic for humans [4]. Currently both H1N1 and H3N2 influenza viruses are continuing to circulate in the human population. They are comparatively low pathogenic variants except for the elderly during the winter months. H3N2 infections have caused almost 14 times more influenza-related deaths than H1N1 infections since 1970 [5]. Worldwide the annual seasonal influenza A epidemics result in about 3–5 million cases of severe illness and about 250 000–500 000 deaths (http://www.who.int/mediacentre/factsheets/fs211/en/index.html).

The receptor sites on the host cell are sialic acid residues in the glycolipid components of the cell membrane. The cell membranes of birds have a different configuration of sialic acid compared with mammals. In the pig trachea, however, epithelial cells contain both avian and mammalian configuration which explains why pigs are susceptible to both avian and mammalian viruses. Thus, while aquatic birds are the reservoirs of influenza virus, pigs provide a ‘mixing cauldron’ for reassortments from which may arise a pandemic strain [6].

Pandemics are believed to be rare events in which viruses that circulate among humans acquire a new HA ligand of avian origin. The H1 variants have circulated among humans from 1918 to 1957, and again from 1977 to the present. Following the pandemic of highly virulent H5N1 ‘bird flu’ in chicken and evidence of its transmissibility to humans, there have been warnings of an impending pandemic of H5N1 bird flu in the human population [7]. Hence the scientific community was taken by surprise when a pathogenic new strain of influenza A was identified in Mexico in March 2009, and within days hundreds of more suspected cases were being diagnosed. In 2 months’ time, 33 countries had officially reported 5 728 cases resulting in 61 deaths, and by June 2009 WHO reported 30 000 confirmed cases in 74 countries. Currently WHO has raised the pandemic alert level to 6, the highest level. The new variant has been identified as originating from the H1N1 form of swine influenza—a descendant of the strain that caused the 1918 pandemic (http://www.cdc.gov/h1n1flu). The virus is now labelled as ‘swine origin influenza A virus’ (S-OIV in short). The current strain has a high human-to-human transmission rate, the secondary attack rate being 25–30% to family members compared with 5–20%
Influenza A H1N1 viruses of swine origin containing genes from avian, human and swine influenza viruses first began to circulate in the pig population in North America at the end of 1990s. S-OIV is a recent reassortant. It contains classic swine RNA segments of North American origin, a segment from human seasonal H3N2 virus, a segment of avian origin and segments from the Eurasian swine lineage [8]. The two groups of viruses behave differently. Triple assortant swine influenza A viruses are found in pigs and may occasionally be transmitted to humans, but have not spread from humans to humans. S-OIV is not epidemic in pigs although transmission may occur by exposure to humans, but has spread rapidly in human population.

Epidemiologic features of S-OIV suggest some protection from previous exposure to H1 variants circulating among human populations. In a report from Mexico, out of a group of 60 confirmed cases compared with 180 healthy controls, the latter were more likely to have received seasonal flu vaccine. Among the unvaccinated people in the study \((n = 179)\), 29% became infected with S-OIV compared with 8 out of 61 (13%) vaccinated. All of the eight vaccinated people survived, whereas among the unvaccinated 18 of the 52 who were infected with S-OIV died. [9].

The outcome of influenza virus infection is determined by the host’s immune response and the virulence of the influenza strain. S-OIV has a unique combination of gene segments from several sources. Comparison of the amino acids forming the haemagglutinin of the seasonal H1N1 and S-OIV reveals marked differences, which means antibodies against one protein are unlikely to work against the other [10]. Analysis of epitopes (regions of an antigen with the ability or potential to elicit and combine with specific antibody) revealed that only 31% of B-cell epitopes present in seasonal H1N1 influenza A virus are conserved in S-OIV; 41% of the CD4\(^+\) and 69% of CD8\(^+\) T-cell epitopes are conserved. Furthermore, only one epitope was found between the haemagglutinin (H) and neuraminidase (N) surface proteins which are the primary targets of neutralizing

<table>
<thead>
<tr>
<th>Year</th>
<th>Virus subtype</th>
<th>Deaths (estimated)</th>
<th>Ressortment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918–19</td>
<td>H1N1</td>
<td>50 million</td>
<td>All segments of avian origin</td>
</tr>
<tr>
<td>1957–69</td>
<td>H2N2</td>
<td>2–4 million</td>
<td>Five segments of H1N1 + (PBI;HA;NA) of avian origin</td>
</tr>
<tr>
<td>1968–70</td>
<td>H3N2</td>
<td>1–2 million</td>
<td>Six segments of H2N2 + (PBI and HA) of avian origin.</td>
</tr>
<tr>
<td>1977–79</td>
<td>H1N1</td>
<td>0.7 million</td>
<td>Identical with 1918–19 virus</td>
</tr>
</tbody>
</table>

PBI = polymerase basic protein 1.

with seasonal influenza (http://www.cdc.gov/mmwr/preview/mmwrhtml).

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antibodies [11], being the envelope proteins. The T-cell responses do not prevent infection. Instead they contribute to the clearance of infected host cells. Any such pre-existing immunity may lead to a less severe course of disease [12].

Several lessons have been learnt from the S-OIV pandemic. In particular, the way scientific community has collaborated to unravel the lineage of the new virus. Within days after the first case identification of S-OIV, the complete genetic sequence of envelope proteins was worked out and disseminated worldwide. Within 6 months of first case identification vaccines were undergoing clinical trials for safety and efficacy, followed soon after by immunization of priority groups. Many will consider this not soon enough. It is fortuitous that S-OIV turned out to be not highly pathogenic [13]. For future pandemics of pathogenic variants more timely delivery of vaccines may be needed. Better still a universal broad-spectrum vaccine based on highly conserved proteins of the influenza A virus ought to be the ultimate goal [14]. Expedient vaccine delivery systems in developing countries particularly to the crowded urban squatter slums need to be developed if the tragic experience of 1917–18 pandemic is not to be repeated.

G. J. Ebrahim

References