

PANDEMIC INFLUENZA: THE PRIMARY CARE CHALLENGE

As winter approaches, Robert Pratt outlines the essential role played by primary care practitioners in preventing the spread of pandemic influenza

Summary

The UK is on the precipice of the second wave of a global influenza pandemic that will have a massive impact on all primary healthcare services. Primary prevention and vaccinations are critical elements of the UK pandemic preparedness strategy, and it is essential that practitioners are competent and confident in engaging these two aspects of primary health care.

Keywords

Swine flu, pandemic influenza, vaccines, immunisation, primary health care

SEASONAL EPIDEMICS of influenza (winter flu) are familiar to all primary healthcare practitioners, especially practice nurses who each autumn co-ordinate the implementation of flu vaccination programmes, and GPs who prepare for the usual winter onslaught of flu consultations. This is a particularly busy time for practitioners, but with the experience gained in previous years their workload can generally be accurately predicated and well managed. This year, however, everything is different as primary healthcare practitioners now find themselves at the sharp edge of the first global influenza pandemic of the 21st century.

In addition to dealing with the consequences of seasonal influenza, they will have to factor in a significantly increased volume of work resulting from large numbers of patients requiring pandemic influenza-specific immunisation, healthcare advice, treatment and referral or home care. All this will need to be done with an anticipated reduction in human resources as healthcare practitioners themselves become infected and fall ill.

This article describes influenza viruses, discusses how they are transmitted and outlines the clinical

consequences of infection. It also discusses the evolution of the current influenza pandemic and the anticipated burden of infection and illness in the UK and then describes important issues associated with primary prevention, including pandemic influenza vaccination programmes.

Influenza viruses

There are three different types of influenza viruses (A, B and C) but only types A and B cause influenza. The surface glycoproteins – the external ‘spikes’ of these viruses (Figure 1 overleaf) – are the antigens which provoke an immune response that results in infected people producing specific antibodies against the infecting strain of virus.

There are two types of surface glycoproteins: haemagglutinin and neuraminidase. These glycoproteins are subject to a process known as ‘antigenic drift,’ in which the structural characteristics of haemagglutinin and neuraminidase slowly change, thereby escaping immune detection and destruction when they next infect a previously exposed person. That is the reason why the trivalent seasonal influenza vaccine is adjusted each year to ensure the immunogenic components of the vaccine accurately reflect the ‘drifted’ viruses currently in circulation.

Influenza A viruses (but not influenza B viruses) also have the ability to undergo an abrupt and massive alteration in their surface glycoproteins. This ‘antigenic shift’ can result in the sudden evolution of a new (novel) strain of influenza A virus which spreads rapidly and widely as populations will not have acquired immunity to it as a result of previous exposure or vaccination.

A close-up photograph of a human hand, palm facing up, against a black background. The hand is illuminated with a blue and purple glow. Several small, bright, multi-colored spots (red, orange, yellow, green) are scattered across the palm and fingers, representing the spread of viruses. The text 'RCN PUBLISHING COPYRIGHT' is overlaid in the center of the hand.

RCN PUBLISHING
COPYRIGHT

Influenza viruses spread from hand-to-face contact if hands are contaminated by infectious respiratory secretions

Box 1 National Pandemic Flu Service

www.direct.gov.uk/pandemicflu

- Information 0800 1 513 513
- Treatment 0800 1 513 100

Although both type A and B viruses cause seasonal epidemics of influenza, only the emergence of a new strain of Influenza A virus is capable of causing widespread, fast moving simultaneous epidemics in different countries and regions throughout the world, a phenomenon known as a global pandemic.

Major pandemics

There were three major influenza pandemics during the last century, the most terrible occurring in 1918-1919. Known as Spanish flu, this strain swept around the world in the autumn of 1918 infecting 50 per cent of the world's population, half of whom experienced clinical illness. Between 50 and 100 million people died (Brundage and Shank 2008).

Other 20th century influenza pandemics occurred in 1957-1958 (Asian flu) and 1968-1969 (Hong Kong flu), together killing two million people (Potter 2001).

In the early months of this year, outbreaks of influenza caused by a novel influenza – A virus of the subtype H1N1 – were identified in the United States and Mexico and then rapidly spread throughout the world (Centers for Disease Control and Prevention (CDC) 2009a). This strain

of influenza virus, now referred to as 'Pandemic A(H1N1)v' (where the 'v' refers to variant), had never been seen before. It contained a mixture (reassortment) of genetic elements from swine, bird and human influenza viruses and became known as the 'swine flu' virus.

Although it is unclear if the antigenic shift resulting in the emergence of this novel strain occurred in pigs, it is just as likely that it occurred in humans and is now spreading easily from person to person, not from person to pigs or from pigs to humans (Brankston *et al* 2007, CDC 2009a).

By early June 2009, the World Health Organization determined that there was definitive evidence of increased and sustained person to person transmission of this novel A(H1N1)v influenza virus in different countries and declared a global pandemic.

Viral transmission

Influenza viruses spread from person to person via the respiratory route and also from hand-to-face contact if hands are contaminated by infectious respiratory secretions. Droplet and contact transmission are the principal means of viral transmission.

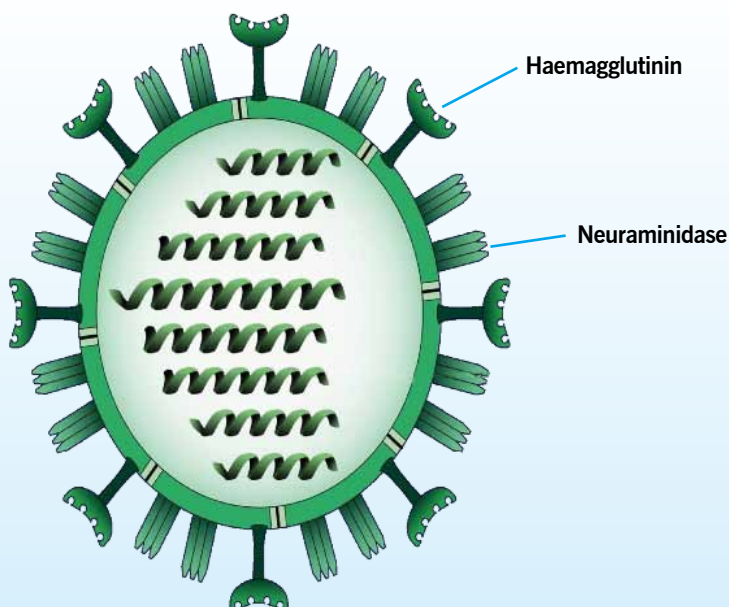
Droplet transmission easily occurs when an infected person generates and sprays uninfected persons with large respiratory droplets when talking, coughing or sneezing. Susceptible (that is, non-infected) people can only become infected by close personal contact as these droplets are too large to become buoyant and can only travel short distances (not more than 1m) through the air.

Transmission can also occur from contact with hands that have been contaminated, for example shaking hands with an infected person who has used their hands to cover their mouth and nose during coughing, or touching surfaces contaminated by infectious respiratory droplets.

Influenza viruses can survive for 24 hours on stainless steel counters, table tops and washing up bowls (Weber and Stilianakis 2008) and, incidentally, on banknotes for several days (Thomas *et al* 2008). Infection can occur when contaminated hands carry the virus to the nose or mouth where the virus can come into contact with and infect respiratory cells.

Although aerosol-generating procedures, such as endotracheal intubation, suctioning, nebuliser treatment or bronchoscopy can increase the risk of viral transmission by producing small particle aerosols, there is no reliable evidence that these are significantly involved in influenza transmission in any other circumstances (Brankston *et al* 2007,

Figure 1 Structural diagram of the influenza A virion



Lemieux *et al* 2007). However, some caution is needed here as other experts advise that small particle aerosols may play a more significant role in the transmission of influenza viruses than previously thought (Atkinson and Wein 2008).

Clinical consequences of infection

People developing respiratory illness are encouraged to telephone or contact online the National Pandemic Flu Service (Box 1) for information and advice on treatment and for contact details for pandemic flu services in Scotland, Wales and in Northern Ireland.

The clinical presentation of influenza in adults is described in Box 2. Most patients will make a quick and full recovery within two weeks and will not require hospitalisation or antiviral medication. In these uncomplicated cases, people in the community with influenza should remain at home until at least 24 hours after they are free of fever (37.8°C [100°F]) without the use of fever-reducing medications, such as paracetamol or ibuprofen (CDC 2009b).

Box 2 Influenza (adults) – clinical presentation

- Incubation period: one to seven days, with an average of 48 hours following exposure.
- Sudden onset of chills, fever – over 38°C/100.4°F – malaise, prostration, cough and generalised aches and pains (especially in back and legs), anorexia.
- Headache, often with photophobia and retrobulbar (back of the eyeball) aching.
- Respiratory symptoms:
 - Initially mild, with scratchy sore throat, substernal burning, non-productive cough and sometimes coryza (upper respiratory infection – the common cold)
 - Later, lower respiratory tract illness becomes dominant, persistent, raspy and productive cough, dyspnoea.
- After two to three days, acute symptoms rapidly subside, but fever may last up to five days. Cough, weakness, sweating and fatigue may persist for several days (occasionally for weeks).
- Complications:
 - both viral and bacterial pneumonia – often the cause of death in severe cases
 - encephalitis, myocarditis, and myoglobinuria
 - all three are infrequent but occur more commonly in pandemic influenza.
- Prominent nausea, vomiting, or abdominal pain and diarrhoea may occur.

Influenza viruses can survive for 24 hours on stainless steel counters, and washing up bowls, and for several days on banknotes

People with influenza who are especially vulnerable to complications include pregnant women, immunocompromised people, infants and very young children, people aged 65 and over and people with underlying chronic disease, such as diabetes mellitus, heart disease and asthma. However, medical assistance should be obtained immediately if patients at home have seizures, develop dyspnoea, cyanosis, are vomiting and unable to keep liquids down, have signs of dehydration (for example, dizziness when standing) and are less responsive than normal or become confused.

Anticipated burden of illness

Influenza pandemics tend to occur in two or occasionally three 'waves'. During late spring and throughout the summer countries in the northern hemisphere experienced the first wave of the pandemic in which we saw that symptomatic disease was fairly benign in the vast majority of the hundreds of thousands of people throughout the world who became infected with the novel A(H1N1)v influenza virus.

Equally fortunate is that this new virus remains sensitive to antiviral treatment with oseltamivir (Tamiflu®) and zanamivir (Relenza®), has not mutated to any significant extent and does not as yet show any tendency to increase in lethality. However, we cannot be sure of anything yet except the inescapable fact that there is a second wave looming and we are not quite sure how it will affect our country and the world.

In September, the Department of Health (DH 2009a) revised its planning assumptions for the UK pandemic during the period September 2009 to mid-May 2010. These include an assumption that:

- 30 per cent of the population may experience influenza-like illness following infection with the A(H1N1) strain (these are the 'clinical cases').
- Up to 15 per cent of the clinical cases may require additional treatment, such as antibiotics but not hospitalisation.
- Up to 1 per cent of the clinical cases may require hospitalisation – of these, 25 per cent could require intensive care at any given time.
- Up to 0.1 per cent of the clinical cases may die during the planning period.
- Absence rates for illness may reach 12 per cent of

Box 3 Seasonal influenza (winter flu) clinical risk group

www.dh.gov.uk/en/Aboutus/MinistersandDepartmentLeaders/ChiefMedicalOfficer/CMOTopics/DH_094790

- Those aged 65 years and over.
- Those aged six months and over with underlying medical conditions such as:
 - Chronic respiratory disease, including asthma*
 - Chronic heart disease
 - Chronic renal disease
 - Chronic liver disease
 - Chronic neurological disease, including stroke and transient ischemic attack (TIA)
 - Diabetes requiring insulin or oral hypoglycaemic drugs
 - People with impaired immunity due to disease or treatment
 - Individuals with multiple sclerosis and related conditions**
 - Those with hereditary and degenerative diseases of the central nervous system**.

* People with asthma who require continuous or repeated use of inhaled or systematic steroids, or with previous exacerbations requiring hospital admission.
 ** GPs should consider on an individual basis the clinical needs of their patients in these groups.

the workforce in the peak weeks of the planning period.

Although these assumptions describe a 'worst-case scenario,' it is not yet possible to predict the magnitude and impact of the pandemic more accurately.

Primary prevention

Immunisation with the newly developed 2009 A(H1N1) pandemic influenza vaccine is the most effective way to prevent illness and is particularly important for those groups of people most at risk of serious complications from influenza or where evidence suggests an increased potential for severity of disease.

The vaccination of household contacts will further protect vulnerable immunocompromised people. Additionally, front line health and social care workers who have regular clinical contact with patients and who are directly involved in patient care, are at an increased risk of exposure to the virus and increased risk of transmitting the virus to vulnerable patients.

People in these groups are prioritised for vaccination in the following order (DH 2009b):

Box 4 Pneumococcal vaccination: childhood clinical risk groups

- Asplenia or dysfunction of the spleen.
- Chronic respiratory disease.
- Chronic heart disease.
- Chronic renal disease.
- Chronic liver disease.
- Diabetes.
- Immunosuppression.
- Individuals with cochlear implants.
- Individuals with cerebrospinal leaks.

- People aged six months and up to 65 years in the current seasonal influenza clinical risk groups (Box 3).
- Health and social care workers directly involved in patient care.
- Pregnant women.
- Household contacts of immunocompromised individuals.
- People aged 65 and over in the current seasonal influenza clinical risk groups (Box 3).

Vaccines

Two 2009 pandemic A(H1N1)v influenza vaccines have been licensed for use in the UK (DH 2009b):

- **GlaxoSmithKline (GSK) Pandemrix®** is the brand name of the GSK vaccine which is a split virion, inactivated adjuvanted vaccine. This vaccine, which is propagated in fertilised hens' eggs, contains an adjuvant (AS03) to help boost the immune response; the vaccine also contains thiomersal as a preservative. Pandemrix® vaccine will be presented in a box of 50 multi-dose vials of 2.5ml suspension and two boxes containing 25 2.5ml vials of adjuvant. Each 5.0ml of reconstituted vaccine should provide ten 0.5ml doses. Each pack should provide 500 doses.
- **Baxter Healthcare Ltd Celvapan®** is the provisional brand name of the Baxter vaccine, which is a whole virion, inactivated vaccine. The whole virion is inactivated both by formaldehyde and ultraviolet irradiation. It does not contain an adjuvant or thiomersal. Celvapan® vaccine will be presented in a pack of 20 multi-dose vials of 5ml suspension per pack. Each 5ml vial should provide 10.5ml doses, with each pack providing 200 doses.

Vaccine storage As for other vaccines, the vaccines need to be stored between 2°C and 8°C.

Dosage A two-dose vaccination schedule with

a three week interval in all age groups (from the age of six months) and including pregnant women is recommended (DH 2009b). For those aged from six months to nine years, half the adult dose (that is 0.25ml rather than 0.5ml) is recommended. The recommendations also allow for one dose to be given to those aged between ten and 60 years. It is likely that the initial recommendations will be updated as needed.

Contraindications There are very few individuals who cannot receive the 2009 A(H1N1) pandemic influenza vaccine. However, those with a confirmed history of anaphylactic reaction to egg (which is a very rare condition) should not be given Pandemrix® but may be offered Celvapan®.

Vaccine safety Influenza vaccines are among the safest vaccines in the world. Billions of doses of seasonal influenza immunisations have been given over many years and serious side effects, including Guillain-Barré syndrome, are rare. The most frequent complaints following immunisation are soreness, redness, tenderness or swelling at the injection site. It is anticipated that the 2009 Pandemic A(H1N1)v vaccine will have a similar safety profile as seasonal vaccines (CDC 2009c, 2009d).

Other relevant vaccines

Clients receiving the 2009 Pandemic A(H1N1)v influenza vaccine will also require the usual trivalent influenza vaccine for this year's seasonal (winter) influenza which can be given at the same time. In addition, pneumococcal immunisation,

recommended as part of the childhood immunisation programme, for children aged two months and over in the clinical risk groups (Box 4) and for adults aged 65 years and over if they have not already received it (DH 2004).

Next month

An update on the epidemiological status of this fast moving pandemic and effective influenza infection prevention and control practice will be outlined in next month's issue.

Implications for practice

- Unless there is a medical contraindication, all front line primary healthcare practitioners have an ethical obligation to be vaccinated against both seasonal and 2009 pandemic A(H1N1) influenza virus infections, to protect themselves and to avoid infecting vulnerable clients.
- Pandemic influenza vaccination programmes need to ensure that patients are also vaccinated with the trivalent seasonal influenza vaccine and receive pneumococcal immunisation if indicated.
- Practitioners need to ensure that they are familiar with and correctly adhere to Department of Health guidance on immunisations contained within the online version of the 'Green Book' (DH 2009c).

Robert Pratt is professor of nursing and director of the Richard Wells Research Centre at Thames Valley University, London

References

- Atkinson MP, Wein LM (2008) Quantifying the routes of transmission for pandemic influenza. *Bulletin of Mathematical Biology*. 70, 3, 820-867.
- Brankston G, Gitterman G, Hirji J *et al* (2007) Transmission of influenza A in human beings. *Lancet Infectious Diseases*. 7, 4, 257-265.
- Brundage JF, Shanks GD (2008) Deaths from bacterial pneumonia during 1918-19 influenza pandemic. *Emerging Infectious Diseases*. 14, 8, 1193-1199.
- Centers for Disease Control and Prevention (CDC) (2009a) Swine Influenza A(H1N1) infection in two children - Southern California, March-April 2009. *Morbidity and Mortality Weekly Report (MMWR)*. 58, 15, 400-402.
- Centers for Disease Control and Prevention (2009b) *CDC Recommendations for the Amount of Time Persons with Influenza-Like Illness should be Away from Others*. Centers for Disease Control and Prevention, Atlanta GA. www.cdc.gov/h1n1flu/guidance/exclusion.htm (Last accessed: October 7 2009.)
- Centers for Disease Control and Prevention (2009c) *General Questions and Answers on 2009 H1N1 Influenza Vaccine Safety*. Centers for Disease Control and Prevention, Atlanta GA. www.cdc.gov/h1n1flu/vaccination/vaccine_safety_qa.htm (Last accessed: October 7 2009.)
- Centers for Disease Control and Prevention (CDC) (2009d) *General Questions and Answers on Guillain-Barré Syndrome (GBS)*. Centers for Disease Control and Prevention, Atlanta GA. www.cdc.gov/h1n1flu/vaccination/gbs_qa.htm (Last accessed: October 7 2009.)
- Department of Health (2004) *Update on Influenza and Pneumococcal Immunisation Programmes. PL/CNO/2004/3*. Department of Health, London. www.dh.gov.uk/en/
- Publicationsandstatistics/Lettersandcirculars/Professionalletters/Chiefmedicalofficerletters/DH_4087289 (Last accessed: October 7 2009.)
- Department of Health (2009a) *Swine flu: UK Planning Assumptions*. Department of Health, London. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_104844 (Last accessed: October 7 2009.)
- Department of Health (2009b) *The H1N1 Swine Flu Vaccination Programme 2009-2010*. Department of Health, London. www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Dearcolleagueletters/DH_107169 (Last accessed: October 20 2009.)
- Department of Health (2009c) *Immunisation Against Infectious Disease - 'The Green Book'*. Department of Health, London. www.dh.gov.uk/en/PublicHealth/HealthProtection/
- Immunisation/Greenbook/DH_4097254 (Last accessed: October 7 2009.)
- Lemieux C, Brankston G, Gitterman I *et al* (2007) Questioning aerosol transmission of influenza [letter]. *Emerging Infectious Disease*. 13, 1. www.cdc.gov/ncidod/eid/13/1/173_174.htm (Last accessed: October 7 2009.)
- Potter CW (2001) A history of influenza. *Journal of Applied Microbiology*. 91, 4, 572-579.
- Weber TP, Stilianakis NI (2008) Inactivation of influenza A viruses in the environment and modes of transmission: a critical review. *Journal of Infection*. 57, 5, 361-373.
- Thomas Y, Vogel G, Wunderli W *et al* (2008) Survival of influenza virus on banknotes. *Applied Environmental Microbiology*. 74, 10, 3002-3007. www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2394922 (Last accessed: October 7 2009.)