



This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

<http://www.elsevier.com/copyright>



ELSEVIER

midwifery

www.elsevier.com/midw

Commentary

Pandemic A (H1N1) 2009 influenza—an enhanced hazard during pregnancy

Robert J. Pratt, CBE FRCN (Professor of Nursing, Associate Dean for Research, Director)^{a,b}^aRichard Wells Research Centre, Thames Valley University, London, UK^bParagon Campus, Boston Manor Road, Brentford, TW8 9GA, UKE-mail address: robert.pratt@tvu.ac.uk.

As the second wave of the global pandemic of 2009 H1N1 influenza ('swine flu') continues to escalate during the coming months, countries throughout the world are anticipating a surge of patients with serious, often life-threatening influenza-related complications being admitted to hospitals, many requiring intensive care and advanced technological cardiac and respiratory support. In countries in the northern hemisphere, the simultaneous arrival of the usual epidemics of seasonal influenza ('winter flu') will further exacerbate the impact of influenza on vulnerable populations. There is good quality evidence which shows that pregnant women are among those who may be at a significantly increased risk of severe illness and complications from influenza. If (or when) the numbers of pregnant women requiring hospitalisation rise during the coming weeks and months, midwifery and obstetric services will be tested and stressed as never before.

In Member States of the European Union (EU) and in many other countries throughout the world, national and local influenza preparedness plans are being incrementally deployed. Midwives and all other health-care providers need to ensure that they remain competent in responding appropriately to these strategies and keep up to date with the rapidly changing dynamics of the first global pandemic of the 21st Century.

Influenza viruses

Influenza viruses have endangered human and animal health for centuries, and recurrent patterns of annual seasonal influenza epidemics and less frequent influenza pandemics are familiar. Due to their sudden emergence and their capacity for rapid transnational spread, influenza pandemics are among the most frightening and potentially cataclysmic threats to global public health which exist.

Two types of orthomyxoviruses cause human influenza: influenza A and B viruses. The external surface glycoproteins of these viruses are the antigens that provoke an immune response, which results in infected people producing specific antibodies against the infecting strain of virus. There are two types of external glycoproteins: haemagglutinin and neuraminidase. These are subject to a continuous process of 'antigenic drift' in which their structural characteristics slowly change, thereby escaping immune detection and destruction when they next infect a previously exposed person. This is the reason why the trivalent seasonal influenza vaccine is adjusted each year to ensure the immunogenic components of the vaccine accurately reflect the newly 'drifted' viral strains currently in circulation.

In addition to the gradual changes in the glycoproteins of both viruses as a result of antigenic

drift, type A viruses (but not type B viruses) are able to undergo an abrupt and massive alteration in the structural characteristics of their surface glycoproteins. This 'antigenic shift' can result in the sudden evolution of a new (novel) strain which spreads rapidly and widely as populations will not have acquired immunity to it as a result of previous exposure or vaccination.

Type A viruses are further classified into subtypes according to the variations in these glycoproteins. Sixteen different haemagglutinin subtypes (H1–H16) and nine different neuraminidase subtypes (N1–N9) have been identified (Tortora et al., 2007). Only H1, H2, H3, N1 and N2 influenza A viral subtypes are known to infect humans or cause serious outbreaks (Collier and Oxford, 2006).

Strains of both influenza A and B viruses are involved in causing epidemics of seasonal influenza, but only influenza A virus is capable of causing global pandemics (Nguyen-Van-Tam and Sellwood, 2007).

20th Century pandemics

During the last century, there were three well documented influenza pandemics which occurred in 1918–19 (Spanish flu), 1957–58 (Asian flu) and 1968–69 (Hong Kong flu). The infamous Spanish flu pandemic, caused by a strain of A/H1N1, was the most terrible of them all, scorching its way around the world within months, infecting half the world's population and killing between 50 and 100 million people (Johnson and Mueller, 2002). Later that century, an estimated two million people died during the Asian (A/H2N2) and Hong Kong (A/H3N2) influenza pandemics (Potter, 2001). Mortality rates, principally from pneumonia, were higher in pregnant women with influenza than in non-pregnant populations during the first two of these pandemics (Harris, 1919; Freeman and Barno, 1959).

Pandemic (H1N1) 2009 influenza

In April 2009, the Centers for Disease Control and Prevention (CDC) in the USA reported two cases of human influenza caused by a new strain of influenza A (H1N1) virus in children in different counties in southern California (CDC, 2009a). Within weeks, further cases were then increasingly found throughout the USA and Mexico (CDC, 2009b), and rapid transnational spread occurred massively to all continents (CDC, 2009c) by June 2009 when the World Health Organization declared a global influenza pandemic (WHO, 2009). The viral cause of

pandemic (H1N1) 2009 influenza was identified as a novel swine-origin strain of influenza A virus that had never been seen before. This new virus consisted of a mixture (reassortment) of genetic elements from different but familiar swine, bird and human influenza viruses (Garten et al., 2009), and became known as the 'swine flu virus'. In England, this strain is now referred to as 'pandemic (H1N1) 2009 influenza virus'.

Transmission

Droplet and contact transmission are the principal means by which all influenza viruses spread from person to person. Droplet transmission easily occurs when an infected person generates and sprays uninfected persons with large respiratory droplets when talking, coughing or sneezing. However, susceptible (i.e. non-infected) persons 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 1 m) 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 intubation, cardiopulmonary resuscitation and 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 virus transmission in any other circumstances (Brankston et al., 2007; 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 in pregnant women

Experience to date indicates that like the majority of the population, most pregnant women with

pandemic (H1N1) 2009 influenza will only have mild symptoms similar to seasonal influenza and will recover within a week or so. However, data from past influenza pandemics (Harris, 1919; Freeman and Barno, 1959) and more recent epidemics of seasonal influenza (Neuzil et al., 1998; Dodds et al., 2007) indicate that pregnant women with influenza are at an increased risk of serious influenza-related respiratory illnesses and death. This enhanced vulnerability is thought to be associated with the multiple physiologic changes that occur during pregnancy, including alterations in the cardiovascular, respiratory and immune systems (Jamieson et al., 2006). Pre-existing comorbidities, such as diabetes, pulmonary disease (including asthma), heart disease, renal disease and obesity, will further increase the risk of serious complications in pregnant women with influenza.

Within weeks of the advent of the US (H1N1) 2009 influenza pandemic during April and May, reports were received of pregnant women with pandemic (H1N1) 2009 influenza virus infection with severe complications (CDC, 2009d). A cross-sectional descriptive study of 34 pregnant women with confirmed or probable pandemic (H1N1) 2009 influenza in the USA concluded that they seemed to be at a greater risk of influenza-associated complications (Jamieson et al., 2009) than non-pregnant women with influenza. They had an increased rate of hospitalisation and six died following the development of pneumonia and subsequent acute respiratory distress syndrome requiring mechanical ventilation.

As countries progress through the second wave of the pandemic, more precise risk data will emerge in relation to pregnancy and the associated enhanced likelihood of increased influenza-related morbidity and mortality, especially during the second and third trimesters of pregnancy. In the meantime, preparedness strategies assume that adequate prevention and treatment resources need to be in place to offer the necessary protection to this vulnerable population.

Primary and secondary prevention

An effective strategy to minimise the risk to pregnant women of pandemic (H1N1) 2009 influenza include several elements: ordinary infection prevention and hygiene measures, post-exposure antiviral chemoprophylaxis, immunisation and early treatment. Midwives and other health-care providers need to ensure that all pregnant women they have contact with are counselled about the early

signs and symptoms of influenza, and advised to seek urgent medical assessment if they develop a fever or any other suggestive indications of influenza.

Infection prevention and hygiene measures

Pregnant women and other members of the general public can take basic infection prevention and control measures to minimise the risk of infection during pandemics, both to themselves and to others. These include the following (Cabinet Office and the Department of Health, 2007):

- Staying at home when ill.
- Covering the nose and mouth with a tissue when coughing or sneezing.
- Disposing of dirty tissues promptly and carefully (i.e. bagging and binning them).
- Washing hands frequently with soap and warm water, or using alcoholic hand disinfectants to reduce the spread of the virus from the hands to the face, or to other people particularly after blowing the nose or disposing of tissues.
- Cleaning frequently touched hard surfaces (e.g. kitchen worktops, light switches, door handles) regularly using normal cleaning products.
- Avoiding crowded gatherings where possible, especially in enclosed spaces.
- If suffering with influenza symptoms, wearing a disposable face mask to protect others should it become absolutely essential to go out (e.g. to go to the hospital).
- Making sure that children follow this advice.
- The general wearing of face masks in public places by those who do not have influenza symptoms is not recommended.

Post-exposure antiviral chemoprophylaxis

In certain circumstances, pregnant women, especially those with co-morbid conditions or who are morbidly obese, may be offered antiviral chemoprophylaxis if they have been in contact with someone with symptomatic influenza (Department of Health, 2009; CDC, 2009e). This decision will be taken on a case-by-case basis by their doctor and, if appropriate, a 10-day course of prophylaxis with either oseltamivir (Tamiflu[®]) or zanamivir (Relenza[®]) will be prescribed.

Immunisation

In addition to routine vaccination against seasonal influenza, all pregnant women should be immunised with the pandemic (H1N1) 2009 influenza

Box 1 Online resources

- Royal College of Obstetricians and Gynaecologists (UK)-Questions and Answers: Managing Pregnant Women with Suspected Swine Flu—Advice for Healthcare Professionals. http://www.rcog.org.uk/files/rcog-corp/Influenza%20QA%20-%20final_1.pdf
- Department of Health (England) and the Royal College of Obstetricians and Gynaecologists (UK) - Pandemic H1N1 Influenza: Clinical Management Guidelines for Pregnancy (October 30, 2009). http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_107768.pdf
- Centers for Disease Control and Prevention (USA). H1N1 Flu (Swine Flu): Resources for Obstetric Health Care Providers. http://www.cdc.gov/h1n1flu/clinician_pregnant.htm.

vaccine. This is the most effective measure available to prevent influenza, and every effort needs to be used to persuade pregnant women to be vaccinated. Preventing maternal infection also provides secondary protection to the infant and the transfer of vaccination-related maternal antibodies by breast feeding further reduces the risk of influenza to the infant.

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. It is anticipated that the pandemic (H1N1) 2009 influenza vaccine will have a similar safety profile as seasonal vaccines (CDC, 2009f, 2009g).

A live attenuated influenza nasal spray vaccine (FluMist[®]) is used in some countries (e.g. the USA) but is not approved for use in pregnant women. Pandemrix[®] is the brand name of the principal vaccine used in the UK produced by GlaxoSmithKline, and Celvapan[®] is the brand name of the vaccine produced by Baxter Healthcare Ltd—both of these are inactivated vaccines and safe for use in pregnancy.

Early treatment

Pregnant women who develop a fever should urgently see their general practitioner or family doctor for assessment. Early antiviral treatment with either oseltamivir or zanamivir is important. Current data suggest that neither of these drugs are human teratogens but because of more data about its safety in pregnancy, the use of oseltamivir may be preferred over zanamivir during pregnancy (Tanaka et al., 2009). Fever should be treated with paracetamol (acetaminophen). Urgent hospitalisation is often necessary for managing complications, including influenza-associated viral or bacterial

pneumonia. Many hospitalised pregnant women will require intensive care for respiratory failure, and some of these will need advanced cardio pulmonary support with extracorporeal membrane oxygenation; a scarce technological resource in most countries.

Further resources

A wealth of authoritative guidance is available in each country from government health agencies and the World Health Organization. In the UK, current guidance has been produced by the Department of Health and the Royal College of Obstetricians and Gynaecologists (2009), and the CDC also produce constantly updated information for midwives and other health-care practitioners (Box 1).

Conclusion

Every midwife needs to be a clinical expert in the support and management of pregnant women who are at risk of or affected by pandemic (H1N1) 2009 influenza. Although it is not possible at the beginning of the second pandemic wave to ascertain with any degree of precision how lethal this particular pandemic will be, planning and preparation must proceed on the basis of the 'worst case' assumptions. Pandemics are transformational, they change us and our clients, and the world is different after they have come and gone.

Conflict of interest statement

No financial or personal relationships with other people or organisations that could inappropriately influence this Commentary exist.

References

- Atkinson, M.,P., Wein, L.,M., 2008. Quantifying the routes of transmission for pandemic influenza. *Bulletin of Mathematical Biology* 70, 820–867.
- Brankston, G., Gitterman, G., Hirji, J., Lemieux, C., Gardam, M., 2007. Transmission of influenza A in human beings. *Lancet Infectious Diseases* 7, 257–265.
- Cabinet Office and the Department of Health, 2007. Pandemic Flu—a National Framework for Responding to an Influenza Pandemic. Central Office of Information, London. Available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238055320501 (last accessed May 2008)
- Centers for Disease Control and Prevention, 2009a. Swine influenza A (H1N1) infection in two children—Southern California, March–April 2009. *Morbidity and Mortality Weekly Report* 58, 400–402.
- Centers for Disease Control and Prevention, 2009b. Outbreaks of swine-origin influenza A(H1N1) virus infection—Mexico, March–April 2009. *Morbidity and Mortality Weekly Report* 58, 467–470.
- Centers for Disease Control and Prevention, 2009c. Update: novel influenza A (H1N1) virus infections—worldwide, May 6, 2009. *Morbidity and Mortality Weekly Report* 58, 453–458.
- Centers for Disease Control and Prevention, 2009n. Novel influenza A(H1N1) virus infection in three pregnant women—United States, April–May 2009. *Morbidity and Mortality Weekly Report* 58, 497–500.
- Centers for Disease Control and Prevention, 2009e. Updated Interim Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009–2010 Season. Available at: http://www.cdc.gov/H1N1flu/pregnancy/antiviral_messages.htm (last accessed 20 September 2009).
- Centers for Disease Control and Prevention, 2009f. General Questions and Answers on 2009 H1N1 Influenza Vaccine Safety. Available at: http://www.cdc.gov/h1n1flu/vaccination/vaccine_safety_qa.htm (last accessed 5 September 2009)
- Centers for Disease Control and Prevention, 2009g. General Questions and Answers on Guillain-Barré Syndrome (GBS). Available at: http://www.cdc.gov/h1n1flu/vaccination/gbs_qa.htm (last accessed 5 September 2009)
- Collier, L., Oxford, J., 2006. In: *Human Virology*, third edn. Oxford University Press, Oxford.
- Department of Health, 2009. Antiviral Prophylaxis—Guidance on the Use of Prophylaxis with Antiviral Medicines during the H1N1 (Swine Flu) Pandemic. Department of Health, London. Department of Health and the Royal College of Obstetricians and Gynaecologists, 2009. Pandemic H1N1 2009 Influenza: Clinical Management Guidelines for Pregnancy. London, Department of Health. Available at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_107768.pdf (last accessed 5 November 2009).
- Dodds, L., McNeil, S., Fell, D.B., et al., 2007. Impact of influenza on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. *Canadian Medical Association Journal* 176, 463–468.
- Freeman, D.W., Barno, A., 1959. Deaths from Asian influenza associated with pregnancy. *American Journal of Obstetrics and Gynecology* 78, 1172–1175.
- Garten, R.J., Davis, C.T., Russell, C.A., et al., 2009. Antigenic and genetic characteristics of swine-origin 2009 A (H1N1) influenza viruses circulating in humans. *Science* 325, 197–201.
- Harris, J., 1919. W. Influenza occurring in pregnant women. *Journal of the American Medical Association* 72, 978–980.
- Jamieson, D.J., Theiler, R.N., Rasmussen, S.A., 2006. Emerging infections and pregnancy. *Emerging Infectious Diseases* 12, 1638–1643.
- Jamieson, D.J., Honein, M.A., Rasmussen, S., et al., 2009. H1N1 2009 influenza virus infection during pregnancy in the USA. *The Lancet* 374, 451–458.
- Johnson, N., Mueller, J., 2002. Updating the accounts: global mortality of the 1918–1920 “Spanish” influenza pandemic. *Bulletin of the History of Medicine* 76, 105–115.
- Lemieux, C., Brankston, G., Gitterman, L., Hirji, Z., Gardam, M., 2007. Questioning aerosol transmission of influenza. *Emerging Infectious Disease* [serial on the Internet]. Available at http://www.cdc.gov/EID/13/1/173_174.htm (last accessed 8 June 2009).
- Neuzil, K.M., Reed, G.W., Mitchel, E.F., Simonsen, L., Griffin, M.R., 1998. Impact of influenza on acute cardiopulmonary hospitalization in pregnant women. *American Journal of Epidemiology* 148, 1094–1102.
- Nguyen-Van-Tam, S., Sellwood, C., 2007. Avian influenza and the threat of the next human pandemic. *Journal of Hospital Infection* 65, 10–13.
- Potter, C.,W., 2001. A history of influenza. *Journal of Applied Microbiology* 91, 572–579.
- Tanaka, T., Nakajima, K., Murashima, A., Garcia-Bournissen, F., Koren, G., Ito, S., 2009. Safety of neuraminidase inhibitors against novel influenza A (H1N1) in pregnant and breastfeeding women. *Canadian Medical Association Journal* 181, 55–58.
- Thomas, Y., Vogel, G., Wunderli, W., Suter, P., et al., 2008. Survival of influenza virus on banknotes. *Applied Environmental Microbiology* 74, 3002–3007. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2394922> (last accessed 10 June 2009).
- Tortora, G.J., Funke, B.R., Case, C.L., 2007. In: *Microbiology, An Introduction*, ninth edn. Pearson Education, Inc., San Francisco.
- Weber, T.,P., Stilianakis, N.,I., 2008. Inactivation of influenza A viruses in the environment and modes of transmission: a critical review. *Journal of Infection* 57, 361–373.
- World Health Organization, 2009. New influenza A (H1N1) virus: global epidemiological situation. *Weekly Epidemiological Record* 84, 249–257.

Available online at www.sciencedirect.com