



GUIDELINES FOR OBSTETRIC AND NEONATAL SPECIALIST SERVICES FOR THE MANAGEMENT OF INFLUENZA-LIKE ILLNESSES DURING THE INFLUENZA PANDEMIC ASSOCIATED WITH THE INFLUENZA A (H1N1) 2009 VIRUS

1. INTRODUCTION

This document provides advice for the management of obstetric and neonatal specialist services and common clinical scenarios involving pregnancy during the current influenza pandemic associated with the novel influenza A (H1N1) 2009 (previously known as human swine influenza) virus.

There are over 32,000 births in WA every year. It is estimated that fewer than half of all pregnant women will experience symptoms of influenza during an influenza pandemic and, of those who do, the great majority will have a mild, self-limiting illness. Pregnant women do not seem to be at an increased risk of contracting pandemic (H1N1) 2009 influenza compared to the general population. However, during pregnancy, they do have an increased risk of complications from *any* type of influenza, especially in the third trimester. These complications usually affect the respiratory system (pneumonia) or predispose them to premature labour or premature rupture of membranes. Excess deaths among pregnant women occurred during the pandemics of 1918-19 and 1957-58 and severe infections and deaths have been reported in some pregnant women with pandemic (H1N1) 2009 influenza infection. Whilst some of these cases have had other risk factors for more severe disease, others have not.

WA and other States and Territories are currently in the “PROTECT” phase of Australia’s response to the pandemic (H1N1) 2009 influenza virus. In this phase, the focus of response is on provision of medical care to those with either serious illness due to the virus or to those who are at risk of more serious disease because of underlying medical conditions. During this phase of the pandemic, the vast majority of influenza-like illness (ILI) due to influenza will be caused by the pandemic (H1N1) 2009 virus.

Currently, it is recommended that all pregnant women with an ILI, regardless of gestation, seek medical advice as soon as possible from their usual General Practitioner or Obstetrician.

2. VULNERABLE GROUPS FOR PANDEMIC (H1N1) 2009 INFLUENZA

These currently include:

- Pregnant women, particularly those in the second or third trimesters
- Persons with morbid obesity (BMI > 40)
- Indigenous people of any age (due to increased incidence of underlying medical conditions that confer increased risk)
- Persons with conditions predisposing to severe influenza such as:
 - cardiac disease
 - chronic respiratory conditions including asthma and chronic obstructive pulmonary disease
 - diabetes mellitus
 - chronic metabolic diseases

- chronic renal failure
- haemoglobinopathies
- impaired immunity
- chronic neurological conditions

Please note that these groups are those that have been shown to have an increased risk of severe infection with pandemic (H1N1) 2009 influenza and do not match exactly the high risk groups recommended for annual influenza vaccination by the National Health and Medical Research Council (NHMRC).

Pregnant women in the second and especially the third trimester, who also have other underlying medical conditions, will be at particularly high risk.

Whilst testing is no longer recommended for most patients with ILI, testing of pregnant women may be of benefit in deciding treatment strategies and choice of antiviral medications. Awaiting test results, however, should not delay initiation of antiviral therapy, if indicated. If tests are ordered, a clear and accurate medical history, including gestational age, should be included on the request form, as this will assist the laboratory in prioritising testing.

3. OBSTETRIC SERVICES

3.1. GENERAL ADVICE TO PREGNANT WOMEN TO REDUCE THEIR RISK OF CONTRACTING INFLUENZA

General advice is available at http://www.public.health.wa.gov.au/2/949/2/swine_flu.pm.

It also important to ensure that normal seasonal influenza vaccine is administered to women who will be in the second or third trimester of pregnancy during the influenza season, including those in the first trimester at the time of vaccination, as recommended by the NHMRC.

3.2. OUTPATIENT MANAGEMENT OF PREGNANT WOMEN WITH INFLUENZA-LIKE ILLNESSES DURING THE H1N1 2009 INFLUENZA PANDEMIC

3.2.1. Obtain nose and throat swabs. See guidance for swab collection at

http://www.public.health.wa.gov.au/3/952/3/human_swine_flu_health_providers.pm

or at this specific link:

<http://www.public.health.wa.gov.au/cproot/2244/2/Collection%20and%20referral%20of%20samples.pdf>

3.2.2. Recommend commencement of antiviral therapy (details provided below). Currently, anti-influenza medication is provided free for groups with defined medical conditions, including pregnancy. Specialist advice for clinical scenarios not covered in this guidance is available from the On Call Clinical Microbiologist for PMH/KEMH or the On Call Obstetric Consultant at KEMH, who are contactable via KEMH switchboard on (08) 9340 2222

3.2.3. Advise home isolation for the period of acute illness. Normally, shedding of influenza virus is reduced to very low levels by 5 days, and presence of fever is correlated with viral shedding. Patients are considered no longer infectious 24

hours after resolution of fever, provided they have received 72 hours of anti-influenza medication, or 7 days have elapsed since onset of respiratory symptoms.

3.2.4. Provide information to the patient. The KEMH Pregnancy and Pandemic (H1N1) 2009 Influenza (human swine influenza) fact sheet is available from: http://www.public.health.wa.gov.au/3/952/3/human_swine_flu_health_providers.pm

3.3. MANAGEMENT OF PREGNANT WOMEN WITH INFLUENZA-LIKE ILLNESS OR PROVEN PANDEMIC (H1N1) 2009 INFLUENZA INFECTION WHO REQUIRE ADMISSION TO HOSPITAL.

Definition of influenza-like illness (ILI):

- Fever (measured $\geq 38^{\circ}\text{C}$ or a good history of fever) AND
- Cough and/or sore throat

Pregnant women with an ILI or confirmed pandemic (H1N1) 2009 influenza, who require hospitalisation, are to be admitted to their chosen hospital in the first instance, unless they have severe infection requiring a level of care not available at that hospital.

Specialist advice to assist in their management for influenza and/or secondary bacterial infection and obstetric issues will be available from KEMH (via the On-Call Clinical Microbiologist and/or the On-Call Obstetric Gynaecologist).

Pandemic (H1N1) 2009 influenza-positive pregnant women will deliver at their chosen hospital, unless their condition requires a level of care not available at that hospital.

Please note:

Access to tertiary services at King Edward Memorial Hospital will be assessed on a case by case basis using existing referral processes.

4. CONCEPTION AND PREGNANCY ISSUES AND PANDEMIC (H1N1) 2009 INFLUENZA.

4.1. FETAL CONSIDERATIONS:

There are contradictory studies on the effects of normal seasonal influenza on the fetus with the risks (if any) being small and possibly related to the maternal fever associated with influenza rather than to the virus itself. Risks associated with influenza were reduced for women who received antipyretic medication and for those who had taken folic acid before and during early pregnancy. Importantly, maternal influenza with normal seasonal strains has not been associated with an increased risk of spontaneous abortion or intrauterine death.

However, as we still know little about the potential effects of pandemic (H1N1) 2009 influenza in pregnancy, it may be worthwhile discussing with women who are trying to become pregnant whether they may wish to delay conception during the current period of high influenza activity.

Women who are currently participating in fertility programmes should also discuss the implications of the current pandemic when planning their program.

4.2. USE OF ANTIVIRALS IN PREGNANT WOMEN – GENERAL CONSIDERATIONS

The current pandemic (H1N1) 2009 influenza strain is sensitive to the neuraminidase inhibitors oseltamivir (TamiFlu®) and zanamivir (Relenza®). Whilst there have been isolated overseas reports of oseltamivir resistance, such resistance has not been detected by Australian and Western Australian surveillance. Pandemic (H1N1) 2009 influenza virus is resistant to amantadine and rimantadine.

Oseltamivir and zanamivir are "Pregnancy Category B1" medications, indicating that only a limited number of pregnant women have taken these agents. Studies in animals have not shown an increased occurrence of fetal damage with these agents. No formal clinical studies have been conducted to assess the safety of these medications for pregnant women. However, to date, there has been no increase observed in the frequency of malformations or other direct or indirect harmful effects on the human fetus from over 200 women who received oseltamivir, and nearly 100 women who received zanamivir during pregnancy, or among infants born to women who have received oseltamivir or zanamivir.

These agents would not normally be recommended for use in pregnancy unless the benefit to the mother justifies the potential risk of these antivirals to the fetus. Expert opinion currently recommends that the balance of direct benefits to pregnant women for treatment supports the use of either agent. Such use, by modifying maternal infection and decreasing the fever associated with it, may well benefit the fetus.

The efficacy of both oseltamivir and zanamivir for prophylaxis or treatment of influenza is comparable. Zanamivir reaches lower concentrations in the blood than oseltamivir and may be preferable where concerns of potential in utero fetal exposure to these agents are being considered, especially in the first trimester of pregnancy or when used for prophylaxis. However, respiratory complications (e.g. bronchospasm) and medication delivery system challenges with users unfamiliar with use of inhaled aerosol delivery devices need to be considered, especially in women at risk for respiratory problems.

Oseltamivir is preferred for treatment of probable or proven pandemic (H1N1) 2009 influenza, where systemic levels are required for therapy, including patients with proven or suspected viral pneumonia. Treatment should be initiated promptly upon presentation of pregnant women with clinically suspected infection and especially for those with other risk factors. Do not wait for test results if samples have been collected before starting treatment.

Please note:

Expert advice on the use of antiviral agents in pregnant women is available from KEMH by telephoning the On-Call Clinical Microbiologist or the On-Call Obstetric Consultant. Contact either via the KEMH switchboard (24 hour service) on (08) 9340 2222.

4.3. SPECIFIC SITUATIONS

4.3.1. Pregnant women with influenza-like illness in the second or third trimester

During the "PROTECT" phase, treatment should be initiated for pregnant women in the second or third trimester with ILI (prior to confirmation of diagnosis of pandemic (H1N1) 2009 influenza infection). Oseltamivir is the preferred agent and should be commenced as soon as possible, preferably within 48 hours of illness onset. Swabs should be collected and treatment continued for 5 days (or less, if laboratory results are conclusively negative).

Treatment Dose: Oseltamivir 75mg twice a day for 5 days.

Efficacy of oseltamivir for treatment of pandemic (H1N1) 2009 influenza, when initiated more than 48 hours following symptom onset, is unknown, but in women with significant co-morbidities and disease symptoms, or ongoing disease symptoms alone, initiation of therapy after 48 hours may be considered. Commencement of antiviral treatment for pregnant women more than 4 days after symptom onset is unlikely to be beneficial unless they are hospitalised with severe illness.

Patients should be referred urgently to hospital if they have hypoxia (oxygen saturation measured by pulse oximetry < 95%) and/or tachypnoea (respiratory rate > 24 breaths/min) and/or pulmonary infiltrates. In these patients, an increased dose of oseltamivir (150mg bd in patients with normal renal function) should be considered, especially if the illness has developed despite previous prophylaxis or treatment with oseltamivir. Studies on patients with severe avian influenza (H5N1) have shown that nasogastric administration of this dose achieves good blood levels, even in ICU patients.

Presence of ongoing lower respiratory tract symptoms, lobar changes on a chest X-ray, high neutrophil counts and/or a high C-reactive protein, should prompt consideration of secondary bacterial infection (bronchitis, pneumonia) and need for appropriate antibacterial therapy.

4.3.2. Pregnant women with influenza-like illness in the first trimester

Pregnant women in the first trimester are at lower risk for complications of influenza and women with mild ILI and with no risk factors other than pregnancy do not necessarily require antiviral treatment.

However, if additional medical conditions (other than pregnancy) that confer increased risk are present, then antiviral treatment is indicated. Either oseltamivir or zanamivir may be used, though zanamivir may be preferred, as it is administered by inhalation, achieves high concentrations throughout the respiratory tract with less systemic absorption and has potentially less fetal exposure than oseltamivir. Also, as oseltamivir may cause nausea and vomiting (usually with the first dose and minimised by taking with food), which may compound the nausea of pregnancy; zanamivir may be preferred for that reason. Conversely, the inhalational route of administration of zanamivir can cause bronchospasm and dyspnoea; a potential concern in patients at risk of respiratory problems.

Swabs should be collected and treatment (if initiated) continued for 5 days (or less, if laboratory results are conclusively negative).

4.3.3. Pregnant women who are currently well but are contacts of a proven or probable pandemic (H1N1) 2009 influenza case

Notwithstanding the risks to pregnant women from acquiring influenza from such contact, most will not and the majority will experience mild disease. For this reason, during the PROTECT phase, publicly funded antiviral medicines will not be provided routinely for prophylaxis of pregnant women or persons with other defined high risk medical conditions. Such women should be strongly advised to present early for medical assessment if they develop influenza-like symptoms and close monitoring for ILI is recommended.

However, clinical judgement should be used where women have significant underlying medical conditions and are in the 2nd or especially 3rd trimester. In such circumstances, prophylaxis may be warranted. Prophylaxis should preferably be commenced within 72 hours of the last contact with an infectious influenza case and be continued for 10 days after the last known exposure. In situations where multiple consecutive maternal exposures may occur, such as in families, the overall duration of prophylaxis may be longer than 10 days.

4.3.4. Breastfeeding women with influenza-like illness

The relative immunosuppression of pregnancy and associated physiological changes that result in increased risk for pregnant women with any influenza infection, including pandemic (H1N1) 2009 influenza, are quickly reversed after delivery. Consequently, breast feeding women themselves, without other risk factors, are not considered to be an at-risk group and should be managed in accordance with the latest public health recommendations. These currently state that there is no need for people with mild febrile respiratory illnesses to attend or be referred to and tested for influenza in either hospital Emergency Departments or in General Practice unless the patient's symptoms indicate that they need medical review, including those patients who have underlying medical conditions that place them at increased risk of complications of influenza.

Breastfeeding women with an uncomplicated ILI, who are nursing normal infants, would not normally require antiviral therapy. Appropriate hygiene measures should be followed to minimise the potential for spread to the nursing infant. Also, most experts are not recommending prophylactic use of antiviral agents to protect normal babies from their infected mother or other family members, and use of antiviral medication for treatment of ILI is generally only indicated for those infants requiring hospitalisation.

For mothers breastfeeding an infant with a chronic medical condition (especially cardio-respiratory or immunosuppression), individual case circumstances will need to be discussed with relevant doctors to assess indications for infant antiviral prophylaxis and dosage. In such situations, confirmation of maternal pandemic (H1N1) 2009 influenza infection is recommended to guide decisions about antiviral treatment of the mother to minimise viral shedding and /or use of antiviral prophylaxis for the neonate.

Oseltamivir and its metabolites are both excreted into human breast milk in very small quantities and no infant effects from maternal treatment would be expected. There is no data on zanamivir levels in human milk, but given the low systemic absorption of this inhaled agent, breast milk levels are expected to be extremely small with no infant effects.

Where it is decided that a breastfeeding mother requires treatment, the preferred agent is oseltamivir.

Treatment Dose: oseltamivir 75mg twice a day for 5 days.

4.4. OTHER CONSIDERATIONS

4.4.1. Use of antenatal corticosteroids for fetal maturation in pregnant women with concurrent pandemic (H1N1) 2009 influenza infection

Women at risk of preterm birth are routinely given a dose or course of antenatal corticosteroids. It is likely that, during the current pandemic, some women requiring steroids for this indication will also be infected with pandemic (H1N1) 2009 influenza virus. It is unclear whether prolonged therapy with steroids may worsen concomitant viral respiratory illness due to the relative immunosuppression induced. The effect of currently used antenatal single or two dose steroid regimens on the clinical course of pregnant patients with pandemic (H1N1) 2009 influenza infection is unknown. However, the benefits of such antenatal steroid administration are well established for the neonate. Thus, it is recommended that antenatal steroids be administered according to usual obstetric practise.

4.4.2. Newborns of pandemic (H1N1) 2009 influenza infected mothers

Neonates are known to be at higher risk of severe illness from seasonal influenza virus infection and thus are also likely to be at higher risk for severe illness from pandemic H1N1 2009 influenza infection. Clinical experience in determining the most effective prevention strategies for pandemic (H1N1) 2009 influenza infection in infants is limited.

As the risk of transmission of the virus from mother to fetus is unknown, the neonate should be considered potentially infected if delivery occurs during the 2 days before through to 7 days after illness onset in the mother. Intrauterine infection of the fetus is potentially possible from maternal influenza viraemia and influenza has rarely been detected in vaginal secretions, but it is most likely that the infant will be infected postnatally by the respiratory route. Consequently, the neonate should be considered potentially infected irrespective of delivery route. Appropriate infection control measures should be instituted for the duration of hospitalisation of the mother and/or neonate (see section 4.4.3, below).

The neonate should be closely monitored for evidence of influenza infection and, should symptoms develop, testing should be performed, infection control measures continued and antiviral treatment using oseltamivir considered. Specialist consultation is advised in such scenarios.

Post-delivery chemoprophylaxis of potentially exposed neonates is currently not recommended due to very limited data on safety and efficacy. In critical situations (such as congenital cardio-respiratory conditions or similar), oseltamivir prophylaxis may be considered, but specialist advice should be sought.

As intra-family spread is common with influenza, other visiting family members may be infected or be in the infectious prodrome period of pandemic (H1N1) 2009 influenza during the stay of the infant. Exclusion of symptomatic individuals is strongly recommended.

In some circumstances, preterm infants may require management in secondary or tertiary level intensive care units. Unit infection control policies appropriate for pandemic (H1N1) 2009 influenza should be followed. Potential or proven neonatal infection with pandemic (H1N1) 2009 influenza, in the absence of other factors, is not an indication for automatic transfer to PMH/KEMH.

Access to tertiary services (Princess Margaret Hospital, King Edward Memorial Hospital) will be assessed on a case by case basis using existing referral processes.

4.4.3. Infant feeding

Breastfeeding should be strongly promoted because of the protection from respiratory infection offered by breast milk. Breast milk from an infected mother is not considered infectious, and breast milk from a mother receiving antiviral medications is most unlikely to have any adverse effect on the infant.

It is currently unclear whether the best means of protecting the newborn from post-natal acquisition of maternal pandemic (H1N1) 2009 influenza infection is to recommend temporary separation of the mother from the neonate, with the mother encouraged to manually express and the infant fed by another well person. The duration of this separation would usually be 3 days from the time of initiation of antiviral therapy in the mother. The practical difficulties of such an approach would need careful deliberation, as

it is unclear how effective such a separation strategy would be and it is possible the infant may have already been potentially infected prior to or during delivery.

If the neonate remains with the mother, appropriate infection control procedures by the mother and other family members to minimise transmission should be followed. These include wearing of a surgical face mask by the mother during breastfeeding and other infant care activities, good cough etiquette with use of disposable tissues and regular hand hygiene.

5. NEONATAL SERVICES

Princess Margaret Hospital (PMH) will retain tertiary referral status for both pandemic (H1N1) 2009 influenza and seasonal influenza for neonatal patients requiring tertiary care.

Access to tertiary services (Princess Margaret Hospital) will be assessed on a case by case basis using existing referral processes.

6. ACKNOWLEDGEMENTS

This document was developed by Dr Tony Keil (King Edward Memorial Hospital), in consultation with staff in the Communicable Disease Control Directorate, PathWest, and the Disaster Management, Regulation and Planning Directorate of the WA Department of Health.

7. ADDITIONAL RESOURCES

1. KEMH patient information sheet "Pregnancy and H1N1 Influenza 09 (Human Swine Influenza), is available via the Public Health website at:
http://www.public.health.wa.gov.au/2/949/2/swine_flu.pm
2. A range of additional resources for health professionals are available on the Public Health website at:
http://www.public.health.wa.gov.au/3/952/3/human_swine_flu_health_providers.pm