Guidelines on the management of pregnant and postpartum women with suspected Influenza

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6.6	**03/12/2024**	**Update for Winter 2024/2025 influenza season.** • **Align nomenclature to WHO** • **Align to antiviral guidance for the treatment and prophylaxis of influenza**
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Contents

Influenza during pregnancy and the postpartum period

Pregnant women are at increased risk of severe and complicated influenza, including associated hospitalisation and death, compared to non-pregnant women of reproductive age. Normal physiological alterations in heart rate, lung capacity, and immunological function that occur in pregnancy put pregnant women at increased risk of being more severely affected by certain infections, including influenza.

Complications of influenza in pregnancy may include severe pneumonia, early labour (premature birth), reduced foetal growth, low birth weight stillbirth and maternal death. Premature birth can lead to long-term medical and social consequences. The risk of these complications is higher in the second and third trimesters of pregnancy and is greater for pregnant women with at-risk medical conditions.[1]

Postpartum women, who are in transition to normal heart, lung and immune function, are also at increased risk of severe and complicated influenza up to two weeks postpartum (including following pregnancy loss).

These guidelines provide recommendations for managing pregnant, postpartum and breastfeeding women presenting with an influenza-like illness (ILI) or confirmed influenza. The diagnosis of influenza should also be considered in all patients presenting with acute respiratory infections (ARI) regardless of their vaccine status. Of note, the most effective way to minimise the risks of influenza infection and associated complications during pregnancy is through vaccination. Influenza vaccination should be recommended and offered to all women pregnant at any time from October to April. The vaccine can be given at any stage of pregnancy.

Case definitions

Influenza-like illness

Influenza-like illness (ILI) is defined as sudden onset of symptoms

AND at least one of the following four systemic symptoms:

1. fever or feverishness
2. malaise (a general feeling of being unwell)
3. headache
4. myalgia

AND at least one of the following three respiratory symptoms:

1. cough
2. sore throat
3. shortness of breath

Acute Respiratory Infection *

An Acute Respiratory Infection (ARI) is defined as:

Sudden onset of symptoms

AND At least one of the following four respiratory symptoms:

1. Cough
2. Sore throat
3. Shortness of breath
4. Coryza

AND

A clinician's judgement that the illness is due to an infection

Pregnant women should be advised of the signs and symptoms of ILI/ARI and encouraged to present early to their GP or maternity unit if they develop ILI/ARI symptoms or any respiratory symptoms after

* ECDC/EC case definition, available online from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018D0945&from=EN#page=24

close contact with a person who has ILI/ARI or laboratory confirmed influenza. They should be assessed, diagnosed and managed on clinical grounds, noting that there are a number of differential diagnoses for people presenting with ILI or ARI. Influenza typically involves symptoms such as fatigue, headache, muscle aches and pains and patients usually have a fever. In addition, during winter 2024/2025 COVID-19, influenza, Respiratory Syncytial Virus (RSV) and other respiratory viruses continue to circulate and can be difficult to distinguish from symptoms alone without a laboratory test. This needs to be considered when a clinical assessment is being undertaken. The most effective way to avoid the risks of influenza infection is through vaccination.

Testing/Diagnosis

Nose and throat viral swabs should be taken for all women admitted to hospital with ILI or ARI and for women with ILI or ARI being considered for hospital admission (whether for ILI/ARI or obstetric reason). COVID-19 and influenza can be difficult to distinguish from their symptoms alone, and require a laboratory test.

Prevention

Influenza vaccine

The World Health Organization (WHO) has stated that pregnant women are one of the highest priority groups for seasonal influenza vaccination.[2]

In Ireland, the **seasonal influenza vaccine is strongly recommended** by the National Immunisation Committee (NIAC) for all pregnant women. Influenza vaccine **can be administered at any stage of pregnancy** during each influenza season. Pregnant women are recommended to receive the non-live influenza vaccine. As this is not a live vaccine, it is very safe in pregnancy. In the 2024/2025 season, this vaccine is the Quadrivalent Influenza Vaccine (QIV). Influenza vaccines recommended by the WHO are prepared each year, using virus strains similar to those considered most likely to circulate in the forthcoming season. Non-live quadrivalent influenza vaccines contain antigens from two type A and two type B virus strains. Pregnancy increases the risk of complications from influenza because of alterations in heart rate, lung capacity and immunological function. Influenza infection during pregnancy can lead to premature birth, lower birth weight, stillbirth and hospitalisation. The flu vaccine given during pregnancy has been shown to protect both the mother and her baby (up to 6 months old) from influenza infection and associated complications. It takes approximately two weeks after the vaccine has been given to be protected. See further information on influenza vaccine during pregnancy at

flupregleaflet.pdf

Treatment

Scientific evidence attests to adverse outcomes in pregnant women who develop influenza during pregnancy, including increased likelihood of ICU admission and death.[3] Antiviral treatment is recommended for pregnant women or women up to two weeks postpartum (including following pregnancy loss) with suspected or confirmed severe influenza, and can be taken during any trimester of pregnancy.[3]

During the influenza season, treatment for suspected severe influenza should not be delayed while awaiting laboratory test results. Empiric antiviral treatment should be started as soon as possible, ideally within 48 hours of symptom onset, as studies demonstrate that early initiation of treatment is more likely to confer benefit.[3] However, some studies of hospitalised patients with influenza, including an analysis of hospitalised pregnant women, suggest benefit from antiviral treatment even when started more than 48 hours after symptom onset.[3]

Multiple observational studies[4-13] have shown that antiviral treatment with oral oseltamivir or inhaled zanamivir is safe during pregnancy and does not increase the risk of adverse pregnancy outcomes.[3] Oseltamivir remains the first line option for the vast majority of pregnant women with severe influenza and is generally well tolerated, although side effects can occur. There are no data suggesting that tolerability differs between pregnant and non-pregnant women.[14]

Standard dose and duration of treatment with oseltamivir is 75mg orally twice daily for 5 days. Hospitalised patients with severe influenza may require a longer duration of treatment, extension of treatment will be based on clinical assessment. For pregnant women who meet additional criteria for requiring zanamivir first line, further assessment (i.e. rapid diagnostics) and antiviral treatment should be discussed with a local infection specialist

For further guidance for the use of antivirals in pregnancy including definition of severe influenza, follow: *"Guidance on the use of antiviral agents for the treatment and prophylaxis of influenza"* on the HPSC website.

Chemoprophylaxis

Post-exposure antiviral chemoprophylaxis can be considered for certain pregnant women and women who are up to two weeks postpartum (including following pregnancy loss) who have had close contact[†] with someone likely to have been infectious with influenza and who

- cannot receive an influenza vaccination due to a contraindication or because vaccine is not available, or
- have severe immune deficiencies or other medical conditions that make them unlikely to respond to influenza vaccination

Clinical judgement should be exercised in individual cases to determine if the benefit of receiving chemoprophylaxis outweighs the risk. Previous influenza vaccination does not preclude the use of post exposure prophylaxis. Pregnant women and women who are up to two weeks postpartum (including following pregnancy loss) who are given post-exposure chemoprophylaxis should be informed that the chemoprophylaxis lowers but does not eliminate the risk of influenza and that protection stops when the medication course is stopped.[3] Those receiving chemoprophylaxis should seek advice from their doctor if they develop respiratory symptoms that might indicate Influenza infection.

An alternative approach for pregnant and postpartum women (up to two weeks postpartum, including following pregnancy loss) who have had close contact with a patient with laboratory confirmed influenza is to provide information on the early signs and symptoms of ILI/ARI and influenza, and advise them to contact their doctor immediately for evaluation and possible early anti- viral treatment if clinical signs or symptoms develop following a risk assessment.[3]

Oseltamivir is considered the drug of choice for influenza chemoprophylaxis in pregnant women. Standard dose and duration of oseltamivir chemoprophylaxis is 75mg orally once daily for 10 days. For further guidance see *"Guidance on the use of antiviral agents for the treatment and prophylaxis of influenza"* on the HPSC website.

[†] Close contact is defined as having cared for or lived with a person who has confirmed, probable or suspect influenza or having been in a setting where there is a high likelihood of contact with respiratory droplets of such a person, including having talked face-to-face with them.

Pre-Delivery

- Prior to delivery, a hospitalised pregnant woman with ILI/ARI or influenza should be managed in accordance with the Infection Prevention and Control, National Clinical Guideline No. 30 Standard and droplet precautions, with additional precautions for aerosol generating procedures (AGPs) should be employed. This includes patient placement in a single room, cough etiquette including wearing a facemask if being transported outside of their room and additional personal protective equipment (PPE) for staff. Facilities should refer to the Infection Prevention and Control, National Clinical Guideline No. 30 for more detailed information.
- Healthcare staff entering rooms of pregnant women with suspected or confirmed influenza should adhere to standard and droplet precautions, including wearing a facemask, performing hand hygiene, wearing gloves for any contact with potentially infectious material and wearing a gown for any activity where contact with the patients' body fluids may occur.[15]
- International recommendations in relation to the duration of droplet precautions for cases of influenza vary from country to country. As a general rule, the duration of isolation precautions for hospitalised patients with confirmed influenza should be continued for 5 days after illness onset. This may be extended to 7 days for patients who are immunosuppressed following consultation with their doctor. Patients on droplet precautions should be discharged from hospital when clinically indicated, NOT based on the period of potential infectiousness or recommended duration of droplet precautions.
- Patients should be asked to restrict visitors in so far as is possible. Family members and other visitors should be informed of the risks of influenza virus transmission and instructed to adhere to respiratory hygiene and cough etiquette, hand hygiene, and use of PPE according to local policy.[15]

Delivery

- Patients with suspected or confirmed influenza who are in labour and/or in the delivery suite should remain on droplet precautions. Mothers should not be asked to wear a mask during labour and birth. Healthcare staff in the delivery suite should adhere to Standard and Droplet Precautions including practicing hand hygiene before and after handling the newborn.
- If delivery is by planned induction or elective caesarean section, consider deferral, if appropriate. This decision should be taken at senior level weighing up obstetric indication for delivery with risk to mother and baby of delivery while unwell.

Postpartum

- Infection control precautions for mothers with ILI/influenza should continue as above.
- Breast feeding should be strongly encouraged. Appropriate efforts should be made to reduce the likelihood of the baby becoming infected, while minimising the effect on the mother-baby relationship. These include:
    - Treating the mother to reduce the risk of transmission.
    - The mother and baby should sleep at least 2 metres apart (6 feet), in separate beds in the same room (at least while in hospital). When breast feeding, bathing, caring for, cuddling, or otherwise being within 2 metres of the baby, the mother should wear a surgical mask and clean her hands thoroughly with alcohol hand rub or soap and water before interacting with the baby.
    - The mother should try to avoid coughing near the baby and practice cough etiquette.
    - If expressing breast milk using a pump, this should be cleaned as per the manufacturer's instructions.
    - While these measures can be ceased when the mother is no longer infectious, usually five days following symptom onset, continued good hygiene should be encouraged at all times.
    - These measures should also apply to any carer or family member with influenza.
    - Mothers requiring hospital care should not be prematurely discharged because they have influenza.
    - If discharged while still infectious, mothers should be provided with a sufficient supply of surgical masks to take home.

Post exposure prophylaxis for neonates born to mothers with laboratory confirmed Influenza

A particular clinical challenge arises with regard to the neonate if a pregnant woman develops laboratory confirmed seasonal influenza shortly before the onset of labour. The potential mode of transmission to the neonate in such a scenario is via direct contact with the infected respiratory secretions of the mother rather than via breastmilk. The Summary of Product Characteristics (SPC) for Tamiflu® (oseltamivir) oral suspension states that the medicine can be used for post-exposure prevention of influenza in infants aged over 1 year old; therefore, oseltamivir prophylaxis for infants aged less than 1 year old would be an off-label use. Treatment of seasonal influenza in children, including full term neonates, is however, specified in the SPC for capsules and Tamiflu® (oseltamivir) 6mg/ml powder for oral suspension. Relenza® (zanamivir) inhalation powder is not licensed for treatment or prophylaxis in children less than 5 years of age.

There are three potential options which may be considered by mothers and clinicians in relation to neonates born to mothers with laboratory confirmed Influenza.

1. Oseltamivir oral suspension for post-exposure prophylaxis in the neonate, which may be an unlicensed indication if used outside a pandemic influenza outbreak. As prophylaxis reduces but does not eliminate the risk of infection, infants should be closely monitored for signs and symptoms of Influenza.

2. Physical separation of the symptomatic mother and asymptomatic neonate until 5 days after symptom onset.
   Disadvantages would include the effect on the mother baby relationship and for the neonate not being able to benefit from breastfeeding-related transfer of immune factors and nutrients. Throughout the course of temporary separation, and if the mother is severely ill, an option is that all feedings may be provided by a healthy caregiver where possible. These considerations should be included in the discussion with the mother. Women should be encouraged to express breastmilk so that the neonate can receive the benefits of breastmilk, and to maintain the mother's milk supply in order that breastfeeding can continue once mother and baby are reunited. Detailed advice on use of Oseltamivir during breastfeeding should be sought from the Summary of Product Characteristics (SPC) here.

3. No prophylaxis for the neonate and no separation of neonate and mother.
   This will require careful monitoring for symptoms of influenza, a discussion in advance with the mother about prompt antiviral treatment of the neonate, and advance arrangements for rapidly accessing oseltamivir oral suspension if required (as this is more readily available via hospital pharmacies than community pharmacies). There should also be consideration of laboratory testing of a symptomatic neonate, as per existing local arrangements.

   In both scenarios 1 and 3, which doesn't involve physical separation between mother and baby, the mother should be advised of measures to reduce risk of transmission, including respiratory hygiene and cough etiquette, use of facemasks during close contact including during breastfeeding, and handwashing with soap and water, particularly before breast feeding or touching any other item that the neonate may come in contact with. If expressing breast milk using a pump, this should be cleaned as per the manufacturer's instructions.

Decisions regarding the most appropriate course of action should be made on a case-by-case basis and must involve detailed discussion between the mother and physician regarding the relative advantages and disadvantages of each potential option. This advice does not constitute a specific endorsement of the routine use of oseltamivir oral suspension for prophylaxis in neonates, but recognises that this may occur as an off-label use in specific circumstances. Such clinical scenarios highlight the importance of seasonal influenza vaccination of pregnant women; previous research has shown that this was 71% effective in preventing influenza infection in infants aged less than 6 months in England[15-16].

Further advice on the use of antiviral agents for the treatment and prophylaxis of Influenza can be found here.

Neonatal Unit

- Symptomatic mothers, care givers, and family members should not enter the neonatal unit. Digital technology may be used for mother to see her baby.
- Appropriate signage should be displayed at the entrance to the neonatal unit to discourage visitors with ILI/ARI from entering.
- If a newborn infant of a mother with suspected or confirmed influenza is housed in the hospital nursery instead of the mother's room, infants without symptoms of influenza can be cared for by a non-ill person using standard precautions and should be closely observed for signs of infection.
- A newborn that develops symptoms should be placed on droplet and contact precautions and be assessed by a paediatrician.

Visitors

As a general rule during an outbreak, visitors are prohibited from attending the labour unit as they are a possible source of influenza infection for patients. In certain cases, they may be allowed but they should be limited to persons who are necessary for the patient's emotional wellbeing and clinical care. If they are allowed then the following is recommended:

- Visitors should be instructed to limit their movement within the facility.
- Appropriate signage to discourage those visitors with ARI/ILI from entering the hospital should be placed prominently at hospital entrances.
- Facilities should provide instruction, before visitors enter patients' rooms, on hand hygiene, limiting surfaces touched, and use of PPE while in the patient's room.

Discharge

- The NIAC recommend that all pregnant women should receive an influenza vaccine at any stage of pregnancy during the influenza season. One influenza vaccine is recommended in each influenza season. For women who are postpartum, influenza vaccine should only be offered to those who are in recommended groups as per the NIAC guidelines. https://www.hiqa.ie/areas-we-work/national-immunisation-advisory-committee/immunisation-guidelines-ireland.
- The postpartum woman and baby should be discharged from hospital as soon as it is safe to do so.
- The postpartum woman should be given the remaining course of antivirals and advised to complete them.
- Ensure that the GP, home care team and Public Health Nurse (PHN) are informed of the discharge and influenza status of the postpartum woman and newborn baby.
- Ensure the postpartum woman has information on:
    - Influenza and knows that it is important to contact the GP/hospital promptly if the newborn baby develops ARI/ILI symptoms.
    - Avoiding contact, as far as possible, with any individuals in the home who develop ARI/ILI symptoms to minimise exposure to herself and the newborn baby.
    - Hand hygiene and respiratory etiquette when having contact with the newborn baby.
    - Endeavouring, if possible, to have vaccinated, non-ill adults provide care to the newborn at home if the mother develops ARI/ILI symptoms until the mother's illness resolves.

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