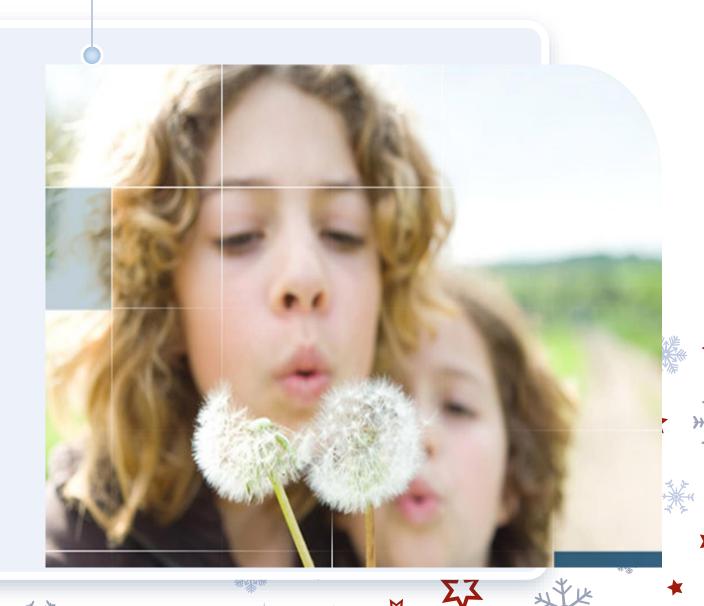
Influenza in pregnancy and Influenza Vaccination

Professor of Obstetrics & Gynecology,
Maternal-Fetal Medicine Fellowship
Iran University of Medical Sciences,
Akbarabadi Teaching Hospital.

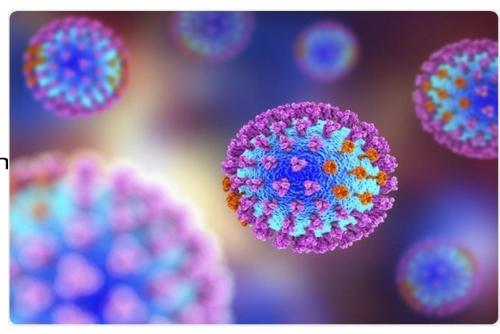


References:



2025





UpToDate®

2025



2024

UK Health Security Agency

2023



Causes, Symptoms, and Treatment



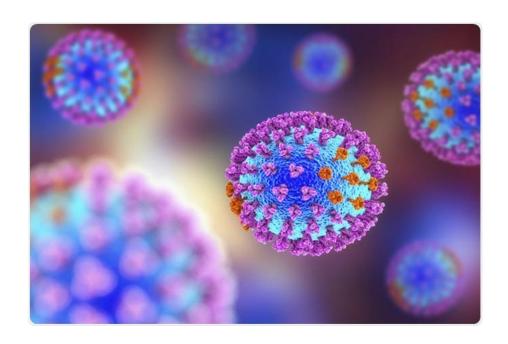
CENTERS FOR DISEASE

CDC 2025

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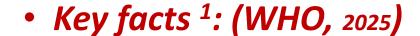
• Infection with influenza virus places a <u>large burden</u> on human health.





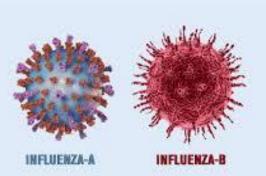






- There are 4 types of influenza viruses, types A, B, C and D.
- Influenza A and B viruses circulate and cause seasonal epidemics of disease.
- There are around **a billion cases** of seasonal influenza **annually,** including **3–5 million cases of severe illness**.
- It causes 290 000 to 650 000 respiratory deaths annually.





- People at greater risk of severe disease or complications when infected are pregnant women, children under 5 years of age, older people, individuals with chronic medical conditions (such as chronic cardiac, pulmonary, renal, metabolic, neurodevelopmental, liver or hematologic diseases) and individuals with immunosuppressive conditions/treatments (such as HIV, receiving chemotherapy or steroids, or malignancy).
 - 1: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)

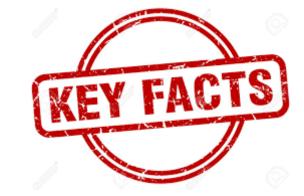






- In the **U.S. alone**, the CDC estimated **35.5 million** people experienced influenza in the 2018–19 season ¹
- Newborns and young infants represent a particularly susceptible population for severe disease following influenza virus infection.
- PEven in countries like the U.S., where health care resources are widely available, those under the age of 6 months are six times more likely to die as a result of influenza virus infection compared to children between the ages of 13 and 17 years ²





- Key facts 1: (WHO, 2025)
- People at high risk or with severe symptoms should be treated with antiviral medications as soon as possible.
- They include people who are 1:
- Pregnant
- Children under 59 months of age
- Aged 65 years and older
- Living with other chronic illnesses
- Receiving chemotherapy
- Living with suppressed immune systems due to HIV or other conditions.





- Key facts 1: (WHO, 2025)
- Vaccination is the best way to prevent influenza.



- Safe and effective vaccines have been used for more than 60 years.
- Immunity from vaccination goes away over time so annual vaccination is recommended to protect against influenza.
- Vaccination is especially important for people at high risk of influenza complications and their carers.
- **Annual vaccination** is recommended for:
- pregnant women
- children aged 6 months to 5 years
- people over age 65
- people with chronic medical conditions
- health workers.



1: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)



WHO (2012) recommends seasonal influenza vaccination for: ¹

A: Highest priority:

Pregnant women and women up to 2 weeks postpartum

B: Priority (in no particular order):

Children aged **6-59 months**

Elderly

Individuals with specific chronic medical conditions

Health-care workers



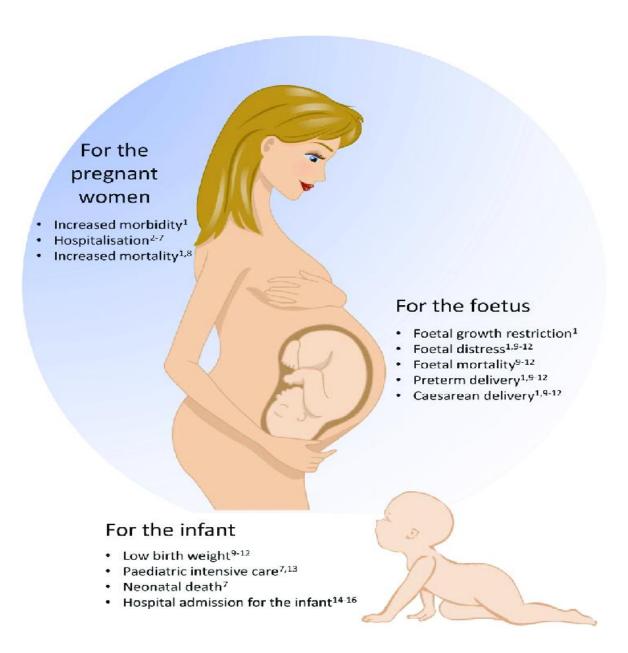


WHO Weekly epidemiological record No 19, <u>2022,</u> 97, 185–208

- Groups at particular risk of severe influenza or complications include:
- Older adults;
- Pregnant women and women up to 2 weeks postpartum;
- Children under 59 months;
- Individuals younger than 19 years of age on long-term aspirin- or salicylate-containing medications;
- People with a body mass index of 40 or higher;
- And individuals with underlying health conditions, including those living with chronic cardiac disease, asthma, chronic pulmonary disease, chronic renal disease, metabolic disorders, endocrine disorders (e.g. diabetes), neurological and neurodevelopmental disorders, liver disease; haematological diseases and immunosuppressive conditions (e.g. HIV/AIDS).

Why is flu so bad in pregnancy?

- Effects of pregnancy on influenza
- Influenza effects on pregnancy

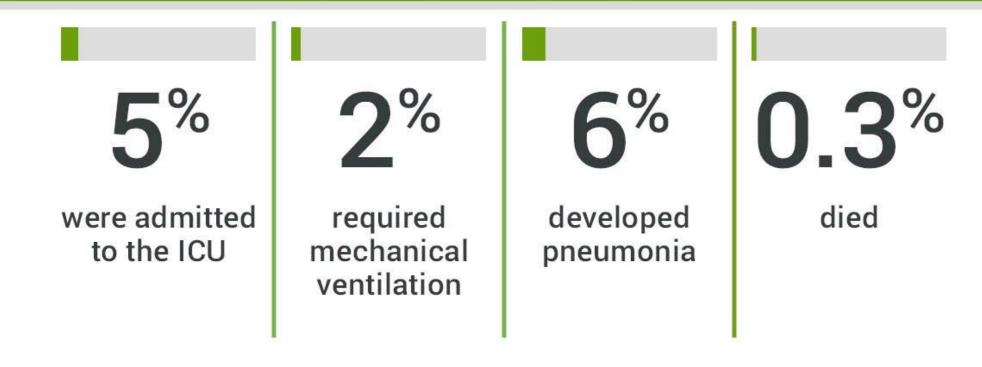




Rachel Holstein, et al.

Characteristics and <u>Outcomes of Pregnant Women Hospitalized</u> with Influenza in the United States, Flusurv-net, 2010–2019. Open Forum Infectious Diseases, Volume 7, Issue Supplement_1, October 2020, Pages \$193-\$194

Among 2,697 pregnant women hospitalized with influenza in the United States



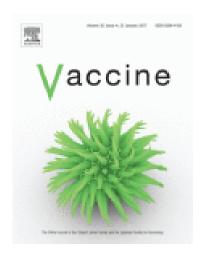


- ACOG (2024)
- Established potential complications of influenza during pregnancy include:
- Preterm delivery,
- Pneumonia,
- Hospital or intensive care unit admission,
- And maternal and fetal death



- Effects of pregnancy on influenza.
 - Maternal effects





Pregnancy as a risk factor for <u>severe outcomes</u> from influenza virus infection: A systematic review and meta-analysis of observational studies. Vaccine <u>Volume 35, Issue 4</u>, 23 January 2017, Pages 521-528

Dominik Mertz¹, Johanna Geraci², Judi Winkup³, Bradford D Gessner⁴, Justin R Ortiz⁵, Mark Loeb⁶

- Pregnant individuals and their infants may be at increased risk of adverse pregnancy outcomes when infected with influenza.
- A systematic review in **2017** and a meta-analysis in **2019** showed that influenza during pregnancy resulted in a:
- **7 times higher risk of hospital admission** (OR 6.8, 95% CI 6–7.7)

 The risk of severe infection in pregnancy is exacerbated by the presence of comorbidities, such as asthma, HIV infection, diabetes mellitus and obesity.

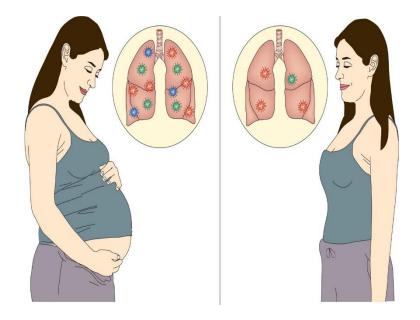


<u>Pregnancy as a risk factor for severe influenza</u> infection: an individual participant data meta-analysis

•<u>Dominik Mertz, Calvin Ka-Fung Lo, Lyubov Lytvyn, Justin R. Ortiz</u> & <u>Mark Loeb</u>, <u>BMC</u> <u>Infectious Diseases</u> volume 19, 683 (**2019**)

- A total of **33 datasets** with data on **36,498 eligible women** of reproductive age and **known pregnancy** status.
- In the multivariable model, pregnancy was associated with a 7 times higher risk of hospital admission.

- The increased severity is thought to be related to normal physiologic changes during pregnancy:
- Heart rate and oxygen consumption increase,
- Lung capacity decreases, and
- Lower cell-mediated immunity.
- **Pregnant** and recently **postpartum** women with influenza are **more likely**:
- To develop severe illness and
- To die
- Than the general population,





 Influenza effects on pregnancy

• Fetal effects of Maternal influenza during pregnancy:



Fetal effects of Maternal influenza during pregnancy:1

- Flu also may be harmful for a pregnant woman's developing baby.
- Trans-placental transmission is rare.
- Might have adverse effects on the fetus even in the absence of trans-placental transmission.
- A common flu symptom is fever,
- Which may be associated with neural tube defects and other adverse outcomes for a developing baby.



Fetal effects of Maternal influenza during pregnancy: 1

- **Hyperthermia** is a **risk factor** for certain birth defects and other adverse infant outcomes.
- This risk appears to be **attenuated** by use of **antipyretics**.
- In the first trimester was associated with an increased risk of:
 Congenital abnormalities (AOR 2.00), Including:
- Cleft lip (OR 3.2),
- Neural tube defects (OR 3.3),
- Hydrocephaly (OR 5.7), and
- Congenital heart defects (OR 1.6).



Fetal effects of Maternal influenza during pregnancy



Severely ill pregnant women is associated with an **increased** risk for :

- Spontaneous abortion,
- Preterm delivery,
- Low birth weight,
- Small for gestational age,
- > And fetal death.





Meta-Analysis
Int J Infect Dis. . 2021 Apr:105:567-578.

The effect of influenza virus infection on pregnancy outcomes: A systematic review and meta-analysis of cohort studies

Ruitong Wang 1, Wenxin Yan 1, Min Du 1, Liyuan Tao 2, Jue Liu 3

 A systematic review of cohort studies involving more than 2 million participants showed that influenza infection during pregnancy:

• Increased the risk of stillbirth (RR) 3.62, 95% Cl 1.60-8.20),

- But had <u>no significant effect</u> on:
- Preterm birth (RR 1.17, 95% CI 0.95–1.45),
- Fetal death (RR 0.93, 95%CI 0.73–1.18),
- Small for gestational age (RR 1.10, 95% CI 0.98-1.24)
- Low birth weight (RR 1.88, 95% CI 0.46–7.66)

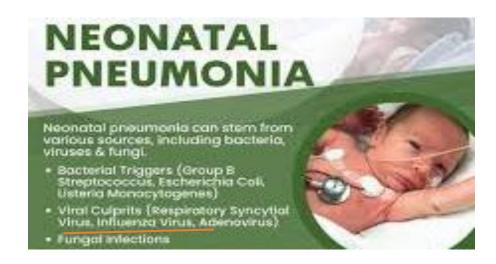
- Influenza effects on pregnancy
- Neonatal effects of Maternal influenza during pregnancy:



Neonatal effects of influenza

- Influenza in newborns can lead to serious illness, hospitalization, and death.
- "The **neonatal immune system**:
- Is not able to effectively clear pathogens, bacteria, viruses,
- And lacks a robust immune memory
- Because neonates don't have the same antigen exposure as older children and adults,











- ✓ Because of the increased severity of influenza in pregnancy and postpartum;
- ✓ Inactivated influenza vaccine is recommended for these women, regardless of trimester of pregnancy.
- ✓ Flu vaccines have been shown to reduce the risk of flu illness, hospitalization and death.¹
- ✓ In addition, pregnant and postpartum women with suspected or confirmed influenza should receive prompt empiric treatment.







Since 2004, the US CDC Advisory Committee on Immunization Practices has recommended that 1:



All women who are pregnant or will be pregnant during influenza season receive any licensed, age-appropriate, recommended influenza vaccine, regardless of trimester.

Annual influenza vaccination is recommended for all persons aged ≥6 months who do not have contraindications, including pregnant and postpartum women.

- Both a quadrivalent vaccine (2 influenza A viruses and 2 influenza B viruses) and a trivalent (containing 2 influenza A viruses and one influenza B virus) inactivated vaccine are available.
- The CDC's Advisory Committee on Immunization Practices does not preferentially recommend a specific formulation of influenza vaccine, trivalent or quadrivalent,
- As **comparative effectiveness data** in large populations are **not available** to support a specific recommendation.





- Pregnant women should not receive a live-attenuated influenza vaccine due to concerns about the safety¹.
- Pregnant and postpartum women do not need to avoid contact with individuals who have recently received the live-attenuated influenza vaccine,
- Live-attenuated influenza vaccine is safe for use postpartum.
- Pregnant women with a history of egg allergy of any severity may receive any licensed, recommended, and age-appropriate influenza vaccine (not live-attenuated vaccine).
- However, if the allergy is severe, then administration should be supervised by a health care provider who is able to recognize and manage anaphylaxis.
- ☐ **Egg-free trivalent and quadrivalent** influenza vaccines are also **available**.
- 1: CDC; Addressing Concerns Pregnant Women Might Have about Influenza Vaccine Safety.

HIGH-DOSE Vaccine

Age 65 or older

NASAL SPRAY

- Healthy, non-pregnant
 - Ages 2 to 49
 - Physician advice recommended

CDC

Annual flu vaccine for everyone 6 months & older

STANDARD Vaccine

- Infants > 6 months
 - Healthy Adults
- Pregnant Women

"NEEDLE-FREE" Vaccine

• Ages 18-64

EGG-FREE Vaccine

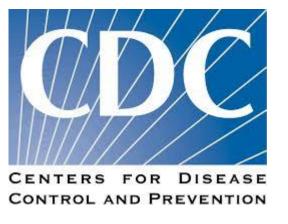
- Severe egg allergic adults
 - Ages 18 and older



Recommendations and Reports / August 29, 2024 / 73(5);1–25

Lisa A. Grohskopf; Jill M. Ferdinands; Lenee H. Blanton; Karen R. Broder; Jamie Loehr.

- Pregnant and postpartum persons are at higher risk for severe illness and complications from influenza, particularly during the second and third trimesters.
- ACIP and the American College of Obstetricians and Gynecologists recommend that persons who are pregnant or who might be pregnant or postpartum during the influenza season receive influenza vaccine.
- IIV3 (Inactivated influenza vaccine, Trivalent) or RIV3 (Recombinant influenza vaccine, Trivalent) can be used.



Recommendations and Reports / August 29, 2024 / 73(5);1–25

Lisa A. Grohskopf; Jill M. Ferdinands; Lenee H. Blanton; Karen R. Broder; Jamie Loehr.

- LAIV3 (Live, attenuated influenza vaccine, trivalent) should not be used during pregnancy but can be used postpartum.
- Influenza vaccine can be administered at any time during pregnancy (i.e., during any trimester), before and during the influenza season.
- Early vaccination (i.e., during July and August):
- Vaccination during July and August should be **avoided** unless there is **concern** that vaccination later in the season might **not be possible**.

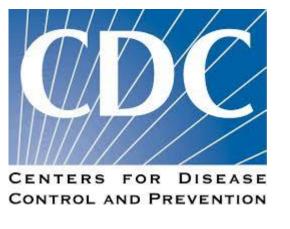


Recommendations and Reports / August 29, 2024 / 73(5);1–25

Lisa A. Grohskopf; Jill M. Ferdinands, ; Lenee H. Blanton; Karen R. Broder; Jamie Loehr.



- Early vaccination (i.e., during July and August):
- Can be considered for persons who are in the third trimester during these months if vaccine is available because this can provide protection for the infant during the first months of life when they are too young to be vaccinated.
- For pregnant persons in the first or second trimester during
 July and August, waiting to vaccinate until September or
 October is preferable, unless there is concern that later
 vaccination might not be possible.

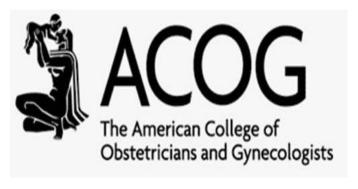


Recommendations and Reports / August 29, 2024 / 73(5);1–25

Lisa A. Grohskopf; Jill M. Ferdinands, ; Lenee H. Blanton; Karen R. Broder; Jamie Loehr.



- **Revaccination** (i.e., providing a **booster** dose) to persons who have been **fully vaccinated** for the season is **not recommended**, regardless of when the **current season vaccine was received**.
- For most persons who need only 1 dose of influenza vaccine for the season, vaccination should ideally be offered during September or October.
- However, vaccination should continue after October and throughout the influenza season as long as influenza viruses are circulating and unexpired vaccine is available.



- ✓ **Despite** these **recommendations**, (ACOG), coverage rates have remained **low for many years**.
- ✓ Coverage rates for pregnant women in the **US is** approximately 49%-54 %.



%

✓ Rates of influenza vaccination during pregnancy are:

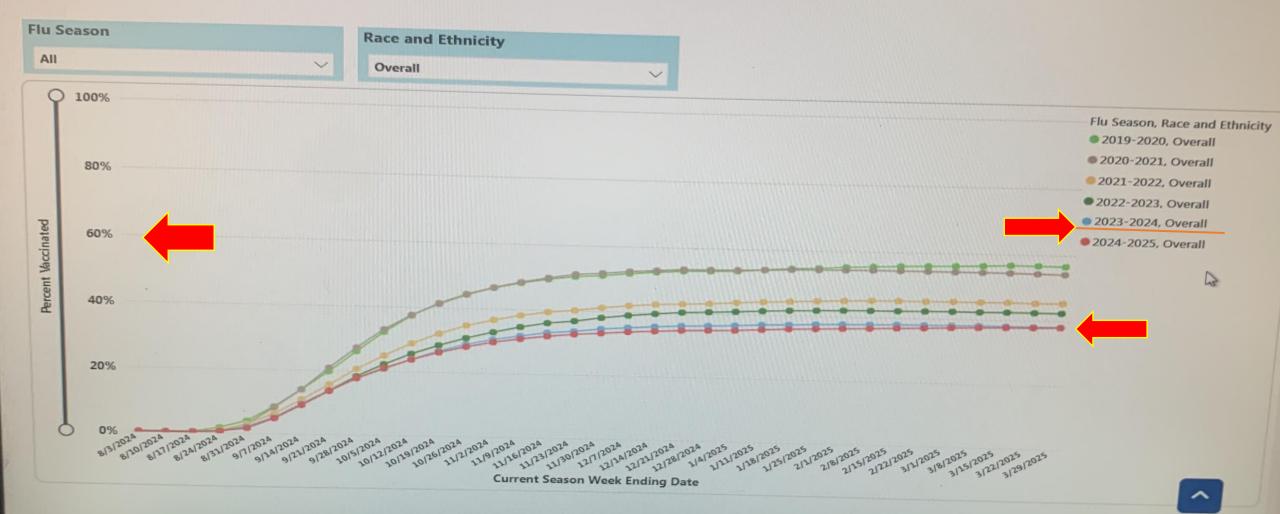
✓ Higher in women whose providers specifically recommend it and

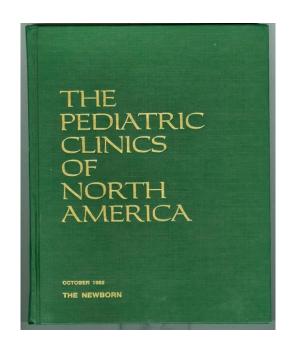
- Coverage
- ✓ Highest when the provider both recommends and offers the vaccine.
- ✓ These findings **highlight** the **importance** of **provider involvement** to **increase influenza vaccination** of pregnant women.

Fig. 3A: Pregnancy Line Graph

Fig. 3B: Pregnancy Bar Graph

Figure 3A. Percent of Pregnant Women Ages 18–49 Years Who Have Received an Influenza Vaccine Overall, by Race and Ethnicity, and Season Data Source: Vaccine Safety Datalink





Cynthia M Rand et al. Maternal Vaccination and <u>Vaccine Hesitancy.</u>
Pediatr Clin North Am. 2023 Feb 24;70(2):259–269.

Contextual Conditions

Vaccine Hesitancy

Vaccine Acceptance

Accurate Information Shared Decision-Making

Key points:





- Obstetric care providers and their office staff should continue
 to offer vaccines even if a pregnant person refused the vaccine
 previously.
- Vaccine safety is the most common concern for patients; future studies in vaccine communication and counseling for obstetric care providers are needed.



Benefits 1,2

- Reduction in maternal influenza illness (up to 50%)
- Reduction in maternal influenza hospitalization (up to 40%)
- Improvement in pregnancy outcome :
- Reduction in risk of stillbirth (RR 0.73)
- Reduced risk for SGA infants and preterm delivery
- An increase in birth weight
- No significant effect on risk of miscarriage (RR 0.91),
- Infant protection (protects the infant for several months after birth) (41 % 63 %)
 reduction in laboratory-confirmed influenza.
- 1: Phadke et al. Maternal vaccination for the prevention of influenza: current status and hopes for the future. Expert Rev Vaccines. 2016 Oct; 15(10): 1255–1280.
 - 2: ttps://www.who.int/biologicals/expert_committee/Clinical_changes_IK_final.pdf



Infant protection of influenza vaccination during pregnancy 1,2

- ✓ Protects the infant for several months after birth.
- ✓ **Induces** substantial levels of **anti-influenza-specific serum (IgG)**, which are actively **transferred** across the **placenta** to the **fetus**,
- ✓ And anti-influenza-specific IgA in breast milk, which is transferred to the infant during lactation .
- ✓ Thus, it is an effective strategy for reducing influenza-related morbidity and mortality among infants, who are not eligible for vaccination until six months of age because they fail to mount an adequate immune response.

1: Nunes et al. Prevention of influenza-related illness in young infants by maternal vaccination during pregnancy. F1000Research 2018, 7(F1000 Faculty Rev):122 Last updated: 29 JAN 2018. 2: ACOG, Committee Opinion Number 732, 2019

Infant protection

- Reduce hospitalizations before three months of age.
- The vaccine's efficacy IS approximately:
- 86 % in infants ≤8 weeks of age and
- **25 30 % in infants 8 24 weeks** of age ¹ (2049 infants).
- Maternal immunization in the third trimester would improve passive protection for the newborn;
- However, delaying maternal immunization places the mother at risk for influenza and its sequelae (maternal and fetal) and is not recommended.



Safety for pregnant women

- No increased risk of complications for inactivated influenza vaccines compared with the general population.
- Although rare, all vaccines, including influenza vaccine, have some background risk of adverse effects, such as Guillain-Barré syndrome.
- However, no specific concerns for pregnant women, their fetuses, infants, or school-age children have been identified from multiple research studies on the safety of all types of influenza vaccination.

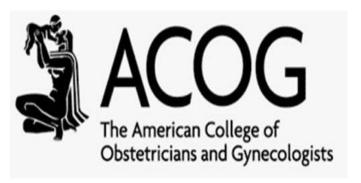


- The **only contraindications** to influenza vaccines are:
 - Anaphylaxis following a previous dose of any influenza vaccine



- Common side effects from a flu shot include:
- Soreness, redness, and/or swelling where the shot was given,
- Headache (low grade), fever, nausea, muscle aches, and fatigue.
- The flu shot, like other injections, can occasionally cause fainting.





• If the timing of the influenza vaccine aligns with other inactivated or non-virus-containing vaccines recommended in pregnancy, such as:



- The tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine;
- Respiratory syncytial virus (RSV) vaccine;
- Or coronavirus disease 2019 (COVID-19) vaccine,
- It is safe and effective to administer these vaccines during the same visit.
- It is also **safe** for **lactating individuals** to receive the **influenza vaccine** if they did **not receive it during pregnancy**.





Treatment (Key Principles)

- Sero-protection rates similar to non-pregnant women
- Influenza vaccine is not 100 % effective,
- Pregnant women and postpartum women (within 2 weeks of delivery or pregnancy loss) with suspected or confirmed influenza should receive empiric treatment as early as possible regardless of vaccination status,
- Treatment should **not be withheld** while **awaiting results of diagnostic testing.**
- Initiating treatment of pregnant women early (generally <2 days)
 after onset of influenza symptoms IS associated with less severe
 disease and fewer deaths compared with treatment begun later.

TREATMENT (Key principles)

Although the benefits are greatest when initiated within the first 48 hours following symptom onset,

► Treatment should still be administered to women who present >48 hours after illness onset and have not begun to improve.

► Health care providers can facilitate early treatment by informing pregnant and postpartum women about signs and symptoms of influenza.



Infection control measures (CON)

- Symptomatic women:
- Pregnant women with confirmed or suspected influenza infection who come to the hospital for delivery

- Should be placed in a private room.
- Should be treated with appropriate antiviral therapy immediately;
- ► Treatment should not be delayed while awaiting the results of diagnostic testing.



- ► In <u>outpatient</u> settings:
- They should wait in a separate waiting area or be asked to sit as far away from others as possible.

- Infant caregivers and household contacts:
- All individuals who live with infants younger than 6 months of age should be vaccinated against influenza.
- Breastfeeding:
- Women with suspected or confirmed influenza who are breastfeeding should be encouraged to continue breastfeeding if possible.
- During temporary separation, mothers should be encouraged to express their breast milk, which a healthy caregiver can use to bottle feed the newborn.





- Temporary separation from her newborn until three criteria were met:
- The mother receive antiviral medications for 48 hours,
- Is afebrile without antipyretics for >24 hours, and
- Is **able to control her cough** and respiratory secretions.
- Mothers who intend to breastfeed should be encouraged to express their milk.
- If temporary separation is not feasible or acceptable, then environmental controls should be considered, such as physical barriers and keeping the newborn >6 feet away from the ill mother.
- Influenza vaccines are recommended for children
 ≥6 months of age.



Antiviral medications

► Treatment decisions, especially those involving **empiric treatments**, should be **informed by knowledge** of **influenza activity** in the community.

The vast majority of currently circulating influenza viruses have been susceptible to the neuraminidase inhibitors, oseltamivir, zanamivir, and peramivir.

► Although information on the safety of oseltamivir, zanamivir, and peramivir during pregnancy is limited, the benefits of treatment outweigh the potential risks.

► Although some reports of increased fetal risk following prenatal exposure to influenza antiviral medications have been published, the number of first-trimester exposures has been small.





- Oseltamivir is generally preferred over inhaled zanamivir and intravenous peramivir for treatment of pregnant women, assuming that prevalence of oseltamivir resistance is low among circulating influenza viruses.
- Oseltamivir is the drug of choice because of its systemic absorption and the greater clinical experience using this drug in pregnancy,

- But pregnancy is not a contraindication to use of zanamivir or peramivir.
- ► Zanamivir is relatively contraindicated in patients with asthma or chronic obstructive pulmonary disease.



Based on limited data, the dose of antiviral therapy for treatment of influenza during pregnancy is the same as in non-pregnant adults:



- Oseltamivir 75 mg twice daily (preferred), OR
- •Zanamivir 10 mg (two 5 mg inhalations) twice daily



- The usual duration of treatment is five days,
- But longer treatment courses can be considered for patients who remain severely ill after five days of treatment.

- Some clinicians have recommended that **severely ill patients** be treated with **double-dose oseltamivir** (ie, 150 mg twice daily);
- However, no data are available to suggest that higher doses are more effective.

 The oral formulation of oseltamivir appears to be adequately absorbed following nasogastric administration.

 Until more safety data on baloxavir marboxil use in pregnancy are available, oseltamivir remains the preferred drug for use in pregnancy. Fever should be treated with acetaminophen.

▶ Antipyretics:

► Use of acetaminophen for treatment of fever may be important, since hyperthermia during the first trimester has been associated with neural tube defects and possibly other birth defects.

In addition, fever during labor is a risk factor for neonatal seizures, encephalopathy, cerebral palsy, and neonatal death.

Other antipyretics (eg, aspirin, ibuprofen) have been associated with adverse pregnancy and infant outcomes; therefore, acetaminophen appears to be the best option.



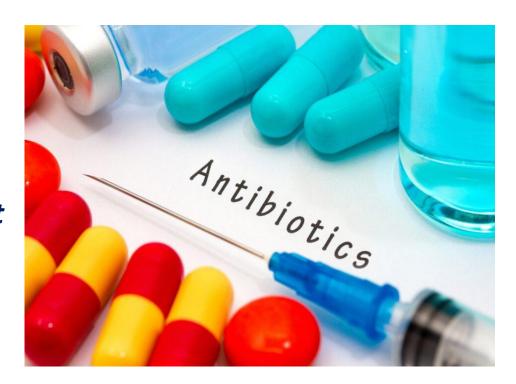
- Symptomatic therapy :
- Many pregnant women will seek advice about symptomatic therapy for cough, rhinorrhea, sore throat, headache, and myalgia.
- Symptomatic therapy is **similar** to that for the **common cold**.

What is a symptomatic treatment?



• Role of antibiotics:

- Antibiotics are indicated only for bacterial complications of acute influenza, such as bacterial pneumonia, otitis media, or sinusitis.
- **Treatment is similar** to that in **non-pregnant** adults,
- Except for avoidance of antibiotics with potentially harmful effects in pregnant women or the fetus.



- Obstetric Management:
- There are **no published guidelines** for **monitoring the fetus** during or after maternal influenza infection.
- The **type** and **frequency of fetal surveillance** should be guided by the health care provider's **judgment** on a case-by-case basis.



Infection control measures



- Standard precautions :
- For **reducing the transmission** of influenza include:

- Hand hygiene (eg, washing with soap and water, use of alcohol-based disinfectant),
- ► Respiratory hygiene/cough etiquette (covering the nose and mouth when coughing, disposing of used tissues promptly, and practicing hand hygiene after contact with respiratory secretions).
- ► Health care workers should use gloves, gowns, masks, and eye protection, as appropriate, when in contact with infected patients.

Protection of pregnant health care workers

► Is the same infection control procedures as all health care personnel;

► Avoiding involvement with aerosol-generating procedures on patients with suspected or confirmed influenza to avoid potentially high-risk exposures.







- Pregnant women with seasonal influenza are at increased risk for serious complications requiring hospitalization and intensive care unit admission, and death.
- Severe maternal illness increases the risk of adverse pregnancy outcome.
- ► The diagnosis of seasonal influenza should be made clinically, without waiting for results from diagnostic testing.

- •Infection control measures are indicated in outpatient and inpatient settings to reduce the risk for transmission of virus among mothers, newborns, staff, and non-staff (eg, infant caregivers, household contacts) in contact with mothers and newborns.
- ► •All women who are pregnant or will be pregnant or postpartum during influenza season should receive either the trivalent or quadrivalent inactivated influenza vaccine, regardless of pregnancy trimester.





Thank You