Vaccines and Pregnancy
Part 1: Influenza

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Grand Rounds Lecture
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Learning Objectives

- Clinical manifestations of influenza
- Maternal and fetal effects of infection
- Mechanism of action of vaccination in pregnancy
- Benefits of flu vaccination
- Safety considerations
Impacts of Influenza Infection
Symptoms of Influenza Infection

- Fever
- Headache
- Myalgias
- Rhinorrhea

- Non-productive cough
- Sore throat
- Mild shortness of breath
- Malaise

Remember: Flu is a CLINICAL diagnosis
Complications of Influenza Infection

- Bacterial pneumonia
- Dehydration/PO intolerance
- Respiratory compromise
- Death

- OB patients with any of the following require urgent intervention
  - Chest pain/pressure
  - Respiratory distress
  - PO intolerance
  - Clinical signs of dehydration
  - Altered mental status
  - Obstetric complications

Jamieson et al, UpToDate Oct 2019
Impact of Flu on Pregnant Women

- Compared to the general population, pregnant women are:
  - Equally likely to contract flu
  - More likely to become severely ill or die from infection
  - Up to 4x more likely to be hospitalized

- These worse outcomes thought to be due to routine physiologic changes of pregnancy
  - Increased heart rate
  - Increased O2 demand/consumption
  - Decreased lung capacity
  - Decreased cell-mediated immunity
Impact of Flu on Fetus/Newborn

- Generally not well-studied
- *In utero* period
  - Transplacental transmission observed, but rare
  - Increased risk of congenital anomalies (esp. hydrocephalus, neural tube defects, cleft lip/palate, heart defects)
  - IUFD
- Post-natal period
  - Low birth weight/SGA
  - Preterm birth
  - Increased risk of hospitalization for flu-related complications

Jamieson et al, UpToDate Oct 2019
ACOG 2018
Influenza Vaccination: Rates, Trends
Flu Vaccination Trends Nationally

- Flu vaccine coverage rates are generally low in the United States, across all groups
  - Rates are highest among those 65+ years and infants
  - Lowest among adolescents and young adults
  - Rates among pregnant women are just above national average for adults, at around 50%

NCIRD report, Sep 2019
Pediatric Flu Vaccination Rates
CA Flu Vaccination Rates—Peds
Adult Flu Vaccination Rates

Figure 3. Flu Vaccination Coverage of Adults 18 years and older, United States, 2010–2019

Error bars represent 95% confidence intervals around the estimates.
CA Flu Vaccination Rates—Adults

Figure 4. Flu Vaccination Coverage by State, Adults, United States, 2018–19 Season
Epidemiology of Flu Vaccines in Pregnancy

Nationally, only about 50% of pregnant women on average receive a flu shot

CDC Survey 2016-2017
Influenza Vaccination: Mechanism of Action
Vaccination of Pregnant Woman

1. Give mom Tdap & flu shots
2. Mom creates antibodies
3. Antibodies pass to baby
4. Mom & baby protected

www.immunizeca.org
Humoral Immunity

- Mechanism of action of flu vaccination
  - Pregnant woman receives injection of inactivated influenza vaccine
  - Develops humoral immune response→ protective, strain-specific IgG antibodies (to viral hemagglutinin proteins)
Maternal Antibody Transfer

- Strain-specific IgG antibodies are transferred across the placenta to fetus (neonatal Fc receptor)
- Transplacental antibody transfer usually starts around 17 wks and peaks at end of pregnancy
  - Premature babies tend to have lower antibody levels
- Usually takes about 2 wks for maternal and fetal antibody levels to be reach high levels
- Strain-specific IgA antibodies are transferred via breastmilk

Nunes et al, 2018
Jamieson et al, UpToDate Oct 2019
Transplacental Antibody Transfer

- May be ideal to administer vaccine during 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester, but in general, administer whenever possible!
- This protection lasts for weeks after birth and is infant’s main source of protection against infection
  - Vaccines not approved for infants under 6 mo—typically cannot mount adequate immune response
  - Highest rates of morbidity/mortality from flu occur in those <12 mo old

Nunes et al, 2018
Jamieson et al, UpToDate Oct 2019
Influenza Vaccination: Benefits, Safety Considerations
Benefits of Flu Vaccination

- For pregnant women
  - Reduction in rates of influenza-like illness and febrile respiratory illness of 24-36%
  - Reduction in rates of illness in their newborns of 41-63%
  - Reduction in risk of stillbirth and possible reduction in SGA, less preterm delivery, and higher BW
  - A 40% decrease in flu-associated hospitalization during pregnancy based on large hospital study from 2010-2016
Benefits of Flu Vaccination

- For newborns
  - Higher birth weights
  - Lower rates of congenital abnormalities
  - Decreased rates of hospitalization (in one study, decreased overall LRTI deaths among babies 3 mo and younger)
  - Decreased mortality from infection

Nunes et al, 2018
Jamieson et al, UpToDate Oct 2019
Side Effects of Flu Vaccination

- Soreness, erythema, induration at injection site
- Mild systemic symptoms (fever, malaise, myalgias), lasting no more than 1-2 d
- More severe effects extremely rare (CDC has database)
- Risk of Guillain-Barré syndrome: no clear association w/ overall with influenza vaccination other than slight increase during swine-origin flu seasons
  - Avoid vaccination if hx of GBS within 6 wks of vaccination in the past
Safety Considerations

- Live, attenuated flu vaccine (i.e. nasal mist) is contraindicated in pregnant women
  - Theoretical risk of vertical transmission
  - However, it IS safe for breastfeeding women
- May be given any trimester
  - May be more beneficial to baby if given in later trimesters, but risk of waiting> benefit

CDC Pinkbook, p. 199-201
ACOG FAQ 189, 2015
Safety Considerations

- There is no increased risk of miscarriage with flu vaccination
  - A small study published in 2017 suggested the possibility of increased risk of spontaneous abortion in women who received H1N1 two years in a row (2010-2012) in the first trimester
  - Several studies since have not found this correlation, including a much larger trial by the CDC using the same Vaccine Safety Datalink project database
  - The CDC’s Advisory Committee on Immunization Practices and ACOG (among other organizations), support the administration of flu vaccine in pregnancy women in any trimester
Myths

- Thimerosal does NOT cause autism in pregnant women, babies born to vaccinated women, or in anyone else
  - Thimerosal is a preservative used in some multidose vaccines including flu
- The inactivated influenza vaccine does NOT cause flu infection
  - Not even theoretically
  - LAIV theoretically can but little evidence for this
Reasons You May Get Sick After a Flu Shot

- Not enough time for vaccine to develop immunity
- Already exposed to flu or flu-like illness
- Not responding fully to vaccine
- Over age 65
- Vaccine doesn’t cover strain of flu

Joshua Seong, Verwell, 2018
The Role of Providers

- Based on a CDC survey of women pregnant during the 2017-2018 flu season
  - 2/3rd reported receiving an offer for flu vaccine
  - 15% reported receiving a recommendation but no offer for vaccine
  - 19% reported receiving no recommendation or offer for vaccine

- Always recommend and offer the flu shot (and any appropriate vaccines) to your patients, pregnant or otherwise!

- If you can’t offer a vaccine, give them a prescription

Kahn et al, MMWR 2018
The End

Thank you for your attention!
Works Cited


Works Cited


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Image Credits

- Pregnancy antibodies graphic: http://www.immunizeca.org/pregnant-women/