Immunizations in Pregnancy: a critical element of care

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I have no disclosures
Historical Perspective

Influenza Pandemic 1918-19
1,350 pregnant women reported; 50% developed pneumonia (>50% died); case fatality 27%

Asian Flu 1957
Also noted higher than expected death rate
Second & third trimesters particularly affected

H1N1 Pandemic 2009
56 deaths reported (7.1% 1st trimester, 26.8% 2nd trimester, 64.3% third trimester)

Who is at highest risk?

• Children <5 years of age

• Adults-
  Asthma or COPD
  Immunosuppressed
  Cardiac Disease
  Pregnancy
  Diabetes
  Obesity
Why Pregnancy?

- Lung capacity
- Nasal congestion
- Colloid oncotic pressure
- “Relative compromised immune system”

H1N1 in pregnancy and postpartum women: CA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pregnant (N=94)</th>
<th>Postpartum (N=8)</th>
<th>Nonpregnant (N=137)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range) — yr</td>
<td>26 (16-42)</td>
<td>28 (22-33)</td>
<td>28 (15-44)</td>
<td>0.02‡</td>
</tr>
<tr>
<td>Race or ethnic group — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.24‡</td>
</tr>
<tr>
<td>Hispanic</td>
<td>43/78 (55)</td>
<td>3/8 (38)</td>
<td>47/116 (41)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>15/78 (19)</td>
<td>2/8 (25)</td>
<td>32/116 (28)</td>
<td></td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>9/78 (12)</td>
<td>2/8 (25)</td>
<td>15/116 (13)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>6/78 (8)</td>
<td>1/8 (12)</td>
<td>18/116 (16)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5/78 (6)</td>
<td>0</td>
<td>4/116 (3)</td>
<td></td>
</tr>
<tr>
<td>Chronic underlying illness — no./total no. (%)</td>
<td>32/93 (34)</td>
<td>2/8 (25)</td>
<td>82/137 (60)</td>
<td>&lt;0.001†</td>
</tr>
</tbody>
</table>

Young, healthy women get sick!

H1N1 in pregnancy and postpartum women: CA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pregnant (N = 24)</th>
<th>Postpartum (N = 8)</th>
<th>Nonpregnant (N = 217)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary bacterial or fungal infection — no. (%)</td>
<td>1 (2)</td>
<td>1 (12)</td>
<td>9 (7)</td>
<td>0.05</td>
</tr>
<tr>
<td>Antiviral treatment — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At any time during course of illness</td>
<td>71/88 (81)</td>
<td>2/8 (25)</td>
<td>97/120 (81)</td>
<td>0.98</td>
</tr>
<tr>
<td>48 hr after symptoms onset</td>
<td>30/60 (50)</td>
<td>3/7 (43)</td>
<td>28/82 (34)</td>
<td>0.06</td>
</tr>
<tr>
<td>Antibiotic treatment — no./total no. (%)</td>
<td>42/94 (45)</td>
<td>7/8 (88)</td>
<td>80/137 (58)</td>
<td>0.04</td>
</tr>
<tr>
<td>Median time from symptom onset to hospitalization</td>
<td>2 (0–11)</td>
<td>6 (2–7)</td>
<td>3 (0–20)</td>
<td>0.12</td>
</tr>
<tr>
<td>(range) — days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median hospital stay (range) — days</td>
<td>3 (1–70)</td>
<td>6 (1–36)</td>
<td>4 (1–41)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death — no.</td>
<td>6</td>
<td>2</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Median time from symptom onset to death (range)</td>
<td>20 (14–49)</td>
<td>30 (26–33)</td>
<td>10 (1–22)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Delay in antiviral treatment -> greater death rate!

Louie et al. NEJM, 2010;362:27-35

What did we learn from H1N1?

1. Young, previously healthy women died

2. Death and ICU admission was highest in pregnant and post-partum women who were treated >48 hours after symptoms.

3. Rapid flu screens performed poorly
   (antigen detection tests: 10-70% sensitivity)
   (direct fluorescent tests: 47-80% sensitivity)
Seasonal Flu Vaccine
Who should get it?

Target group- everyone over 6 months of age including pregnant women at any gestational age.

No “adjuvants” used in US formulations
Latex- free formulation exists.

The 2014-15 Flu Vaccines

Trivalent Flu Vaccine
A/CA/7/2009 (H1N1)-like virus
A/Victoria/361/2011 (H3N2 Virus)
B/MA/2/2012 – like virus

Quadrivalent Flu Vaccine
Above + B/Brisbane/60/2008 – like virus
Surveillance of Influenza Vaccination Safety in Pregnancy

**Routine Surveillance**
- Vaccine Adverse Event Reporting System (VAERS)
- Clinical Immunization Safety Assessment (CISA)
- Vaccine Safety Datalink (VSD)

**Enhanced Surveillance By 2009 H1N1**
- Enhanced VAERS
- Real Time Immunization Monitoring System (RTIMS)
- Vaccines and Medications in Pregnancy Surveillance System (VAMPS)
- Defense Medical Surveillance System (DMSS)

**Now**
- Vaccine Adverse Event Reporting System (VAERS)
- Clinical Immunization Safety Assessment (CISA)
- Vaccine Safety Datalink (VSD)
- Vaccines and Medications in Pregnancy Surveillance System (VAMPS)
Prospective Cohort Study (2009 – 2012)

- 1032 exposed pregnant women
- No increase in birth defects, SAb, IUGR
- Vaccinated women delivered 3 days earlier
- H1N1 containing vaccines

Case Control Study (2009 – 2011)

- 4781 subjects (3539 cases and 1242 controls)
- No increase in birth defects
- Increase in PTD in 2009 but not 2010
- Decrease in gestational age – 2 days
Additional Safety Data on Flu Vaccine in Pregnancy


Efficacy of Influenza Vaccination

340 Bangladeshi women randomized to receive pneumococcal vaccine or trivalent influenza vaccine in third trimester
serum samples from 292 babies at 20 and 26 weeks showed significant antibody levels to influenza types passively acquired from the mother


1160 Native American mother-infant pairs who delivered during 3 flu seasons 2002-2005
risk of lab confirmed flu – RR 0.59 (CI 0.37-0.93)
risk of ILI hospitalization – RR 0.61 (CI 0.45-0.84)
HIA titers higher @birth & @2 mo in babies born to vaccinated moms for the 8 flu virus strains tested

Arch Pediatr Adolesc Med 2010; 165 E 1-8
Efficacy of Influenza Vaccination

Double-blind, randomized, placebo controlled trial of IIV3 in 2,116 non-HIV infected and 194 HIV infected pregnant women

<table>
<thead>
<tr>
<th></th>
<th>HIV- IIV3</th>
<th>HIV- Placebo</th>
<th>HIV+ IIV3</th>
<th>HIV+ Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attack Rate (%)</td>
<td>1.8</td>
<td>3.6</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>Efficacy (%)</td>
<td>50.4</td>
<td>57.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Madhi et al. NEJM 2014;371:918-931

Estimates from CDC…

- Coverage among women who were pregnant during the 2013-14 influenza season was 52.2%, similar to the 47% coverage estimate for the 2011-12 influenza season.

- 65% of women reported provider recommendation & offer: 70.5% were vaccinated.

- 15.1% women received recommendation: 32% were vaccinated.

- 19.8% women received no recommendation or offer: 9.7% were vaccinated.

MMWR 9/19/2014
What other vaccines should we be giving routinely during pregnancy?
Tetanus, Diptheria, Pertussis (Tdap)

- Tdap vaccine is recommended for pregnant women during each pregnancy (27-36 weeks gestation).
- Tdap vaccine is recommended for all persons who are close contacts of infants younger than 12 months of age (e.g., parents, grandparents, and child-care providers) and who have not received Tdap previously.
- Other adults who are close contacts of children younger than 12 months of age continue to be recommended to receive a one-time dose of Tdap vaccine.

Effectiveness of maternal pertussis vaccination in England: an observational study

- Maternal immunization program began 10/2012
- Maternal coverage peaked @ 78% ~ 60%
- <3mo. infants (328 cases in 2012 vs 72 in 2013 (-78%, 95% CI -72 to -83)
- <3mo. infants (440 admissions in 2012 vs 140 in 2013 (-68%, 95% CI -61 to -74)
- 91% vaccine efficacy
Safety of pertussis vaccination in pregnancy

- Short-term risks: 17,560 vaccinated ≥ 28 wks
  No signal in stillbirth, preterm ctx or PTD

- Overall, no increased risk stillbirth, maternal or neonatal death, preeclampsia, hemorrhage, fetal distress, low birth weight, neonatal renal failure

*Donegan et al. BMS 2014;349*
**Pneumococcal Disease**

- **Invasive disease from S. pneumoniae**
- Vaccination recommended for persons <65 if immunosuppressed or immunocompetent with:
  - asthma
  - smoking
  - diabetes
- Pneumococcal polysaccharide vaccine (PPSV23) given to immunocompetent.
- PPSV23 + PCV13 (pneumococcal conjugate vaccine) – both given if immunocompromised.

**Other vaccines to consider**

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>WHY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>high risk exposure</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>high risk behavior</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>high risk behavior</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>travel</td>
</tr>
<tr>
<td>Meningococcal conjugate</td>
<td>exposure</td>
</tr>
<tr>
<td>Meningococcal polysaccharide</td>
<td>travel</td>
</tr>
<tr>
<td>Inactivated polio vaccine</td>
<td>travel</td>
</tr>
<tr>
<td>Rabies</td>
<td>travel / exposure</td>
</tr>
<tr>
<td>Smallpox</td>
<td>high risk exposure</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>travel</td>
</tr>
</tbody>
</table>
Pregnancy vaccines in the future...

Cytomegalovirus

RSV

Group B Strep

Select References


Select References (cont.)


Select References (cont.)

