Vaccination for Pregnant Women

Richard H. Beigi, MD, MS
Associate Professor of Reproductive Sciences
Department of OB/GYN/RS
Magee-Women’s Hospital of the University of Pittsburgh Medical Center
No Conflicts of Interest
Outline

- Pregnancy Unique Time
- Maternal Immunization Benefits and Recommendations
- Summary
Pregnancy Unique Time

- Pregnant women motivated to improve own health
  - Pregnancy motivates some to quit smoking
    - Curry. Psych of Add Behav 2001;15(2)

- Frequent HC interactions: PNC

- Motivated to optimize fetus/neonatal outcomes
  - Often preferentially to fetus/newborn
  - Provider input key!
Maternal Immunization Success

- Neonatal Tetanus
  - Substantial progress
    - 14→5% of total neonatal death (‘93-’03)
    - 82 → 57 countries “not eliminated”
  - Maternal Immunization key
    - WHO: Td during pregnancy X2 (up to 5X)

- Rh Alloimmunization [Rho(D)] – 1970’s
  - Previous 9-10% total pregnancies affected
    - Now rare in Rh- women (<1% Rh- pregns)

Vandelaer J. Vaccine 2003;21
ACOG Practice Bulletin #4: Prevention of RhD Alloimmunization
Influenza Immunization

- TIV recommended:
  - All pregnant women in \textit{any} trimester
    - USA Decades: during 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester
    - 2004: changed to any trimester
    - 2005 WHO
    - CDC 2010: All persons > 6 mos. age
Influenza Vaccination Rates During Pregnancy, Canada and United States, 1974-2003

<table>
<thead>
<tr>
<th>Authors, year (reference)</th>
<th>Population</th>
<th>Study Period</th>
<th>Source of Vaccine Data</th>
<th>Vaccination Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuzil et al., 1998 (11)</td>
<td>Medicaid population, United States</td>
<td>1974-1993</td>
<td>Medicaid database</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Mullooly et al., 1986 (10)</td>
<td>Managed care organization, United States</td>
<td>1975-1979</td>
<td>Medical record review</td>
<td>&lt;1*</td>
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<tr>
<td>Black et al., 2004 (18)</td>
<td>Managed care organization, United States</td>
<td>1997-2002</td>
<td>Vaccine Registry</td>
<td>7.5</td>
</tr>
<tr>
<td>Munoz et al., 2005 (19)</td>
<td>Clinic population, United States</td>
<td>1998-2003</td>
<td>Clinic Database</td>
<td>3.5</td>
</tr>
<tr>
<td>Silverman &amp; Greif, 2001 (35)</td>
<td>Hospital-based survey of postpartum women, United States</td>
<td>2000</td>
<td>Self-report</td>
<td>8</td>
</tr>
<tr>
<td>Tuyishime et al., 2003 (44)</td>
<td>Hospital-based survey of postpartum women, Canada</td>
<td>2002</td>
<td>Self-report</td>
<td>2</td>
</tr>
</tbody>
</table>

*Vaccination rate was 6% during the 1976 swine flu vaccination campaign
*NHIS, National Health Interview Survey

Naleway AL. Epidemiol Rev 2006; 28
Influenza Vaccine in Pregnancy

- Prior to 2009
  - Nationally @ 15% pregnant women
  - 2009 H1N1 → @ 50%

- Recent CDC yearly data:
  - @ 49% “pregnant” women
    - Internet panel of 1457 respondents (4-2011)
    - 12% before, 32% during, 5% after pregnancy

- Healthy People 2020 Goal: 80%
Overcoming Barriers

- CDC, 2010-2011
  - Internet panel survey 4-2011
  - N=1457 pregnant in peak flu season (Oct-Jan)
    - 62% women reported offer of flu vaccine by HCP
      - 71% vaccinated
      - 14% if no HCP offer
      } 5X
    - 45% reported previous year’s acceptance
      - 4X increased acceptance (84 vs. 21%)

CDC. MMWR 2011;60
Transplacentally-acquired Influenza Antibody and Disease in Infants

- Correlation between level of cord blood antibody and age at time of influenza A/H3N2 infection, suggesting protective effect (26 infants), Puck, et. Al., J Infect Dis 1980;142:844-9

- Infants of mothers with antibody to influenza A/H1 had delayed onset and decreased severity of influenza disease (39 mother-infant pairs), Reuman et al, PIDJ 1987;6:398-403
Maternal Influenza Vaccination

- **Effectiveness of Maternal Influenza Immunization in Mothers and Infants**
  - Increased risks: pregnant women and infants (< 6 mos)
    - Recc for moms…not licensed for infants < 6 mos age
  - RCT 340 moms 2004-05 - Bangladesh
    - ½ influenza vaccine, ½ pneumococcal vaccine (controls)

- **Results:**
  - 316 mother-infant pairs
  - Babies:
    - 6 vs. 16 cases of lab confirmed influenza (63% effectiveness)
    - Respiratory illness + fever: 110 vs. 153 infants (29% reduction)
  - Mothers: 36% reduced Respiratory illness + fever

Zaman et al. NEJM 2008;359
Conclusion: Maternal vaccination benefits: moms & babies < 6 mos old
*NNT: 5 maternal vaccinations to prevent 1 case ILI in mom or infant
*NNT: 16 maternal vaccinations to prevent 1 proven flu illness in infant

Cumulative Cases of Lab-proven Influenza in Infants Whose Mothers Received TIV vs. Control
Influenza Vaccine Benefits

- Omer et al. PloS Med 2011;8:e1000441
  - PRAMS cohort data in Georgia (2004-06)
    - 4,168 births with maternal flu vaccine data
  - During flu season (October-May)
    - OR = 0.60; (95% CI, 0.38–0.94) for PTB
    - OR = 0.31; (95% CI, 0.13–0.75) for SGA
      - * Not significant for the pre-influenza activity period

- Steinhoff CMAJ 2012;184(6)
  - Less flu (p<0.003) & less SGA (p=0.02) during flu season
    - Babies with maternal immunization
Flu Vaccine CE

- Beigi CID 2009;49(12)
  - Pandemic vaccine (either 1 or 2 doses)
    - Strongly cost-effective $\rightarrow$ Dominant at both seasonal and pandemic disease rates and severity

- **Summary:**
  - Safe, effective (both mom & baby)
  - Fetal benefits
  - Strongly CE (cost-saving)
  - All pregnant women to receive
    - lacking contraindication
Tdap

- Tetanus, Diptheria, Pertussis
- 2 Toxoids and acellular pertussis
  - Pertussis key
- Poorest control for a VPD
- 2 Tdap Vaccines since 2005:
  - ADACEL (Sanofi) – licensed for ages 11-64
  - BOOSTRIX (GSK) – licensed for ages 10-18
# Pertussis Deaths

Pertussis Deaths in Infants Younger than 1 Year of Age in 1938 – 1940 and 1990 – 1999 in the United States

<table>
<thead>
<tr>
<th>Age (mo)</th>
<th>1938 - 1940</th>
<th>1990 – 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>396</td>
<td>5.6</td>
</tr>
<tr>
<td>1</td>
<td>1166</td>
<td>16.4</td>
</tr>
<tr>
<td>2</td>
<td>1061</td>
<td>14.9</td>
</tr>
<tr>
<td>3</td>
<td>791</td>
<td>11.1</td>
</tr>
<tr>
<td>4</td>
<td>646</td>
<td>9.1</td>
</tr>
<tr>
<td>5</td>
<td>515</td>
<td>7.2</td>
</tr>
<tr>
<td>6</td>
<td>502</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>458</td>
<td>6.4</td>
</tr>
<tr>
<td>8</td>
<td>447</td>
<td>6.3</td>
</tr>
<tr>
<td>9</td>
<td>417</td>
<td>5.9</td>
</tr>
<tr>
<td>10</td>
<td>361</td>
<td>5.1</td>
</tr>
<tr>
<td>11</td>
<td>363</td>
<td>5.1</td>
</tr>
</tbody>
</table>

*Also personal communications with Dr. Tanaka.

Van Rie A. Pediatr Infect Dis J 2005;24
Pertussis Infection Sources in Infants

- Mother: 32%
- Father: 15%
- Sibling: 20%
- Grandparent: 8%
- Other: 25%

Controversy: Tdap *During* or *After* Pregnancy?

- Maternal IgG antibody is transferred to the fetus in high levels in the third trimester.
- The most vulnerable time for infant exposure is 0-4 months of age.
- Would “high” maternal to fetal transfer of IgG protect infants in the most vulnerable time (0-4 mo)?
- Only 1/3 of the family member exposures were from the mother: do you get a “two for one” bonus by boosting the Mom during the last trimester?
### Table 1: Newborn antibody levels stratified whether mother Tdap

<table>
<thead>
<tr>
<th>Outcome Antibodies</th>
<th>Mother did not receive Tdap, mean (SEM) n=52</th>
<th>Mother received Tdap, mean (SEM) n= 52</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>0.571 (0.157)</td>
<td>1.970 (0.291)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tetanus</td>
<td>4.237 (1.381)</td>
<td>9.015 (0.981)</td>
<td>.004</td>
</tr>
<tr>
<td>PT</td>
<td>11.010 (1.796)</td>
<td>28.220 (2.768)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PRN</td>
<td>24, 700 (5.765)</td>
<td>333.01 (56.435)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>FIM 2/3</td>
<td>82.83 (14.585)</td>
<td>1198.99 (189.937)</td>
<td>&lt;.002</td>
</tr>
</tbody>
</table>

FHA, filamentous hemagglutnin; FIM, fimbriae; PRN, pertactin; PT, pertussis toxin; TdaP, tetanus, reduced diphtheria, and acellular pertussis antigens vaccine.

<sup>a</sup> Significant at .05 level.
Tdap in Pregnancy

- Apparent safety
  - No signals, no biologic plausibility
- More cost effective during pregnancy
  - Protects mom earlier thereby more protection to neonate
    - 2+ weeks for full Ab response
  - Ab provides direct neonate protection - critical time
    - Remained robust in sensitivity analysis
      - Low efficacy, high blunting

MMWR 2011;60:41
New ACIP Recommendation

- Tdap during pregnancy > 20 wks
  - Unvaccinated moms
  - Preferred method
  - PP, if not given during pregnancy
- Cocooning for < 12 mos age
  - Adolescents/adults (other family members), care providers
    - If not had Tdap previously
  - 2 wks prior to close contact
- > Age 65 -> Tdap
  - Close contact with infant < 12 mos

MMWR 2011;60:41
Summary

- Pregnancy proven successes
- Recommendations:
  - Influenza – all women anytime in pregnancy
  - Tdap – after 20 wks gestation
- Motivation appears present for many mothers
  - Preferentially act for fetus/newborn
  - Much HC contact
  - Challenges do exist
- Depends much on provider recommendations