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Vaccination for Pregnant Women

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No Conflicts of Interest

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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- pregs)

Vandelaer J. Vaccine 2003;21
http://www.who.int/immunization_monitoring/diseases/MNTE_initiative/en/index2.html
ACOG Practice Bulletin #4: Prevention of RhD Alloimunization

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Influenza Immunization

- TIV recommended:
  - *All* pregnant women in *any* trimester
    - USA Decades: during 2nd and 3rd trimester
    - 2004: changed to any trimester
    - 2005 WHO
    - CDC 2010: All persons > 6 mos. age
- ACOG: Essential part of PNC (2004)

Influenza Vaccination Rates During Pregnancy,Canada and United States, 1974-2003

Authors, year (reference)	Population	Study Period	Source of Vaccine Data	Vaccination Rate (%)
Neuzil et al.,1998 (11)	Medicaid population, United States	1974-1993	Medicaid database	<0.1
Mullooly et al.,1986 (10)	Managed care organization, United States	1975-1979	Medical record review	<1*
Black et al., 2004 (18)	Managed care organization, United States	1997-2002	Vaccine Registry	7.5
Munoz et al., 2005 (19)	Clinic population, United States	1998-2003	Clinic Database	3.5
Silverman & Greif, 2001 (35)	Hospital-based survey of postpartum women, United States	2000	Self-report	8
Tuyishime et al., 2003 (44)	Hospital-based survey of postpartum women, Canada	2002	Self-report	2
NHIS,+ 2003 (34)	Population-based telephone survey, United States	2003	Self-report	12.8

*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%**

CDC. MMWR 2010;59. ACOG. Obstet Gynecol 2004;104
CDC. MMWR 2011;60.
Ding H. AJOG 2011;204. CDC. MMWR 2010;59.

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

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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

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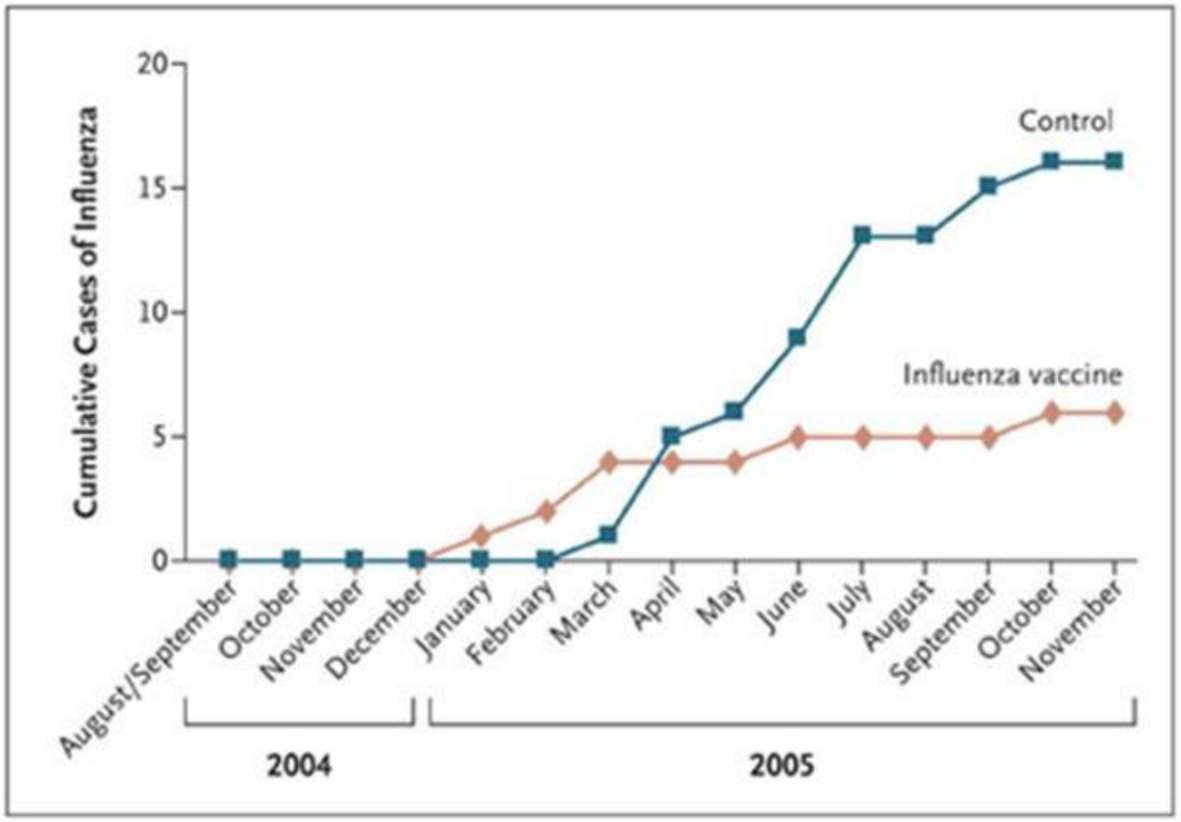
Cumulative Cases of Lab-proven Influenza in Infants Whose Mothers Received TIV vs. Control



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**

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 → 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

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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

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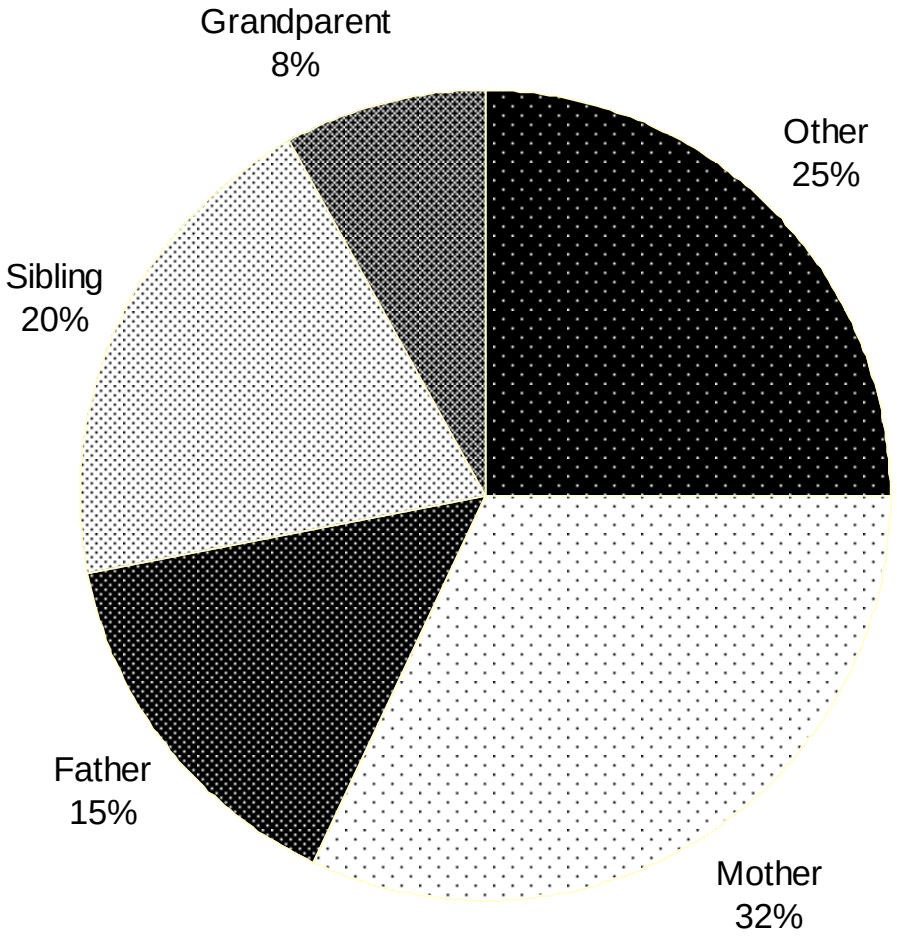
Pertussis Deaths

Pertussis Deaths in Infants Younger than 1 Year of Age in 1938 – 1940 and 1990 – 1999 in the United States				
	1938 - 1940[24]		1990 – 1999[25*]	
Age (mo)	n	%	n	%
0	**396**	**5.6**	**35**	**38.0**
1	**1166**	**16.4**	**33**	**34.8**
2	**1061**	**14.9**	**12**	**13.0**
3	**791**	**11.1**	4	**4.4**
4	646	9.1	3	3.3
5	515	7.2	2	2.2
6	502	7.0	1	1.1
7	458	6.4	3	3.3
8	447	6.3	0	0.0
9	417	5.9	0	0.0
10	361	5.1	0	0.0
11	363	5.1	0	0.0

*Also personal communications with Dr. Tanaka.

Van Rie A. Pediatr Infect Dis J 2005;24

Pertussis Infection Sources in Infants



Bisgard KM, et al. *Pediatr Infect Dis J*. 2004;23:985-989.

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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?

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New Data

Table 1: Newborn antibody levels stratified whether mother Tdap			
Outcome Antibodies	Mother did not receive Tdap, mean (SEM) n=52	Mother received Tdap, mean (SEM) n= 52	P value[a]
Diphtheria	0.571 (0.157)	1.970 (0.291)	<.001
Tetanus	4.237 (1.381)	9.015 (0.981)	.004
PT	11.010 (1.796)	28.220 (2.768)	<.001
FHA	26.830 (4.002)	104.15 (21.664)	.002
PRN	24, 700 (5.765)	333.01 (56.435)	<.001
FIM 2/3	82.83 (14.585)	1198.99 (189.937)	<.002
FHA, filamentous hemagglutnin; FIM, fimbriae; PRN, pertactin; PT, pertussis toxin; TdaP, tetanus, reduced diphtheria, and acellular pertussis antigens vaccine.			
[a] Significant at .05 level.			

Gall S. AJOG 2011;204

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

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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