In compliance with continuing education requirements, all presenters must disclose any financial or other associations with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters as well as any use of unlabeled product(s) or product(s) under investigational use.

CDC, our planners, content experts, and their spouses/partners wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

Planning committee discussed conflict of interest with each presenter to ensure there is no bias.

Content will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of the following speakers:
Saad Omer of Emory University will be discussing the safety and efficacy of maternal vaccines. The influenza and Tdap vaccine is not specifically approved by FDA for pregnant women, but is recommended by CDC/ACIP for use by pregnant women.
Tami Skoff of the Centers for Disease Control and Prevention will be discussing the off label use of Tdap vaccination during pregnancy.

CDC did not accept commercial support for this continuing education activity.
Preventing pertussis in newborns: an update on the maternal tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) immunization program

Tami Skoff, MS
Epidemiologist
49th National Immunization Conference

May 16, 2018
Disclosures

- The off-label use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) will be discussed.

- I, Tami H. Skoff, have no commercial relationships to disclose.
Outline

- Epidemiology of pertussis
- Pertussis vaccine recommendations
- Maternal Tdap coverage
- Safety of maternal Tdap vaccination
- Effectiveness of maternal Tdap vaccination
- Key research questions
Pertussis (Whooping Cough)

- Highly contagious respiratory disease
- Severe, debilitating cough illness ("100 day cough") in persons of all ages
- Highest morbidity and mortality among infants
- Estimated 195,000 pertussis deaths in children per year
- Vaccine-preventable
- Poorly controlled, despite high vaccine coverage
Reported NNDSS pertussis cases: 1922-2017*

SOURCE: CDC, National Notifiable Diseases Surveillance System; *2017 data are provisional
Reported pertussis incidence by age group: 1990-2017*

SOURCE: CDC, National Notifiable Diseases Surveillance System; *2017 data are provisional
Reported pertussis incidence among infants aged <1 year: 1990-2016

![Graph showing pertussis incidence among infants aged <1 year from 1990 to 2016. The graph includes data for different age groups: <2 months old, 2-<4 months old, 4-<6 months old, and 6-<12 months old. The incidence is measured per 100,000 population. The data source is the CDC, National Notifiable Diseases Surveillance System.](image-url)
Pertussis deaths by age group: 2000-2017*

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt; 3 months</th>
<th>3-11 months</th>
<th>1+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>15</td>
<td>10</td>
<td>5</td>
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<td>2001</td>
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<td>10</td>
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<td>2016</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>2017*</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

SOURCE: CDC, National Notifiable Diseases Surveillance System; *2017 are provisional
Preventing infant pertussis
Infant pertussis

- Young infants at highest risk of severe disease and complications
  - ~50% of infants with pertussis are hospitalized
- Infants may present with atypical symptoms
  - Cough may be minimal or absent
  - Whoop infrequent
  - Apnea
  - Gagging, choking, vomiting

Pictured: infant survivor of pertussis. As part of her treatment, she received extracorporeal membrane oxygenation and dialysis.

Photo courtesy of her mother, Michelle Razore
Changing pertussis epidemiology – shift in source of transmission to infants

- ~50% of time, source cannot be identified
- Previously, parents commonly identified as source
  - Mothers most often
- More recently, siblings have emerged as the most common source
  - US source of infection analysis (2006-2013):
    - 85% of identified sources were family members; siblings (35.5% most common)

Pertussis vaccines

- DTaP (pediatric vaccine)
  - Diphtheria and tetanus toxoids and acellular pertussis
  - Schedule: 2, 4, 6 mos., 15-18 mos., and 4-6 yrs

- Tdap (adolescent and adult vaccine) (2005)
  - Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis
    - Same as DTaP but reduced quantities
  - Licensed for single use only; preferred administration at 11-12 years
Protecting infants through maternal immunization

- Infants unprotected in the period prior to infant immunization
- ACIP recommended that women receive a dose of Tdap during pregnancy (2011)
  - **Rationale:** to protect infants in the early months of life through the transplacental transfer of maternal antibodies
- Recommendation expanded in 2012 to include a dose of Tdap during every pregnancy
ACIP Tdap recommendation for pregnant women

- Health-care personnel should administer a dose of Tdap during each pregnancy, irrespective of the patient’s prior history of receiving Tdap.

Guidance for use:

Tdap should be administered between 27 and 36 weeks gestation, although it may be given at any time during pregnancy. Available data suggest that vaccinating earlier in the 27-36 week time period will maximize passive antibody transfer to the infant. If a woman did not receive Tdap during her current pregnancy and did not receive a prior dose of Tdap ever, then Tdap should be administered immediately postpartum.

Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP)
Maternal vaccination coverage
Tdap coverage among pregnant women, United States

- PRAMs Survey - 16 States and NYC
  - 9.7% (2011)
- Michigan Medicaid
  - 14.3% (2011-2013)
- Vaccine Safety Datalink sites; 7 health systems
  - 41.7% (2013)
- National Market Scan
  - 44.4% (2014)
- Wisconsin, insured women
  - 35.0% (2013-2014)
- Minnesota
  - 58.2% (2013-2014)
Tdap coverage among U.S. pregnant women, Internet Panel Surveys, 2014-2017*

Receipt of most recent Tdap vaccination among recently pregnant women who had a live birth, Internet panel surveys, United States, April 2014, April 2015, April 2016, and April 2017

*Unpublished preliminary data (2017)
Safety to mother and infant
Safety of maternal pertussis vaccination during pregnancy

- Safety data collected in the United States continue to be reassuring
  - No increased risk of adverse events among women or infants
  - No concerning patterns in maternal, fetal or infant outcomes

- Safety monitoring is ongoing
  - Vaccine Adverse Event Reporting System (VAERS)
  - Vaccine Safety Datalink (VSD)
  - Clinical Immunization Safety Assessment (CISA) Project
Additional discussion of maternal Tdap safety data

- **Session:** Maternal vaccine safety monitoring at the CDC
- **Date:** Thursday, May 17
- **Time:** 10:15-11:15 am
- **Location:** Galleria 2
Impact of maternal vaccination
Maternal immunization in the United Kingdom

- The UK recommended pregnancy vaccination in late 2012 due to a sudden increase in infant pertussis morbidity and mortality
  - high Tdap coverage (>60%) rapidly achieved
- First country to evaluate effectiveness
  - sustained evidence of high VE (>90%)

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study Type</th>
<th>VE (95% CIs)</th>
<th>Infant age</th>
<th>Tdap Vaccination during Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amirthalingam G, et al. 2014</td>
<td>UK</td>
<td>Screening Method</td>
<td>91% (83%-95%)</td>
<td>&lt;3 mths</td>
<td>During pregnancy (rec. 28- to 32 weeks)</td>
</tr>
<tr>
<td>Dabrera G, et al. 2015</td>
<td>UK</td>
<td>Case-Control</td>
<td>93% (81%-97%)</td>
<td>&lt;2 mths</td>
<td>During pregnancy (rec. 28- to 32 weeks)</td>
</tr>
<tr>
<td>Amirthalingam G, et al. 2016</td>
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<td>90% (86%-93%)</td>
<td>&lt;2 mths</td>
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</tr>
</tbody>
</table>
### Maternal Tdap vaccine effectiveness (VE) studies, cont.

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study Type</th>
<th>VE (95% CIs)</th>
<th>Infant age</th>
<th>Tdap Vaccination during Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winter K, et al. 2016</td>
<td>US</td>
<td>Cohort</td>
<td>85% (33%-98%)</td>
<td>&lt;2 mths</td>
<td>27-36 weeks</td>
</tr>
<tr>
<td>Baxter R., et. al. 2017</td>
<td>US</td>
<td>Cohort</td>
<td>91.4% (19.5%- 99.1%)</td>
<td>&lt;2 mths</td>
<td>During pregnancy (most ≥20 weeks)</td>
</tr>
<tr>
<td>Skoff TH, et. al 2017</td>
<td>US</td>
<td>Case-Control</td>
<td>77.7% (48.3%-90.4%)</td>
<td>&lt;2 mths</td>
<td>3rd trimester</td>
</tr>
<tr>
<td>Bellido-Blasco J, et. al 2017</td>
<td>Spain</td>
<td>Case-Control</td>
<td>90.9% (56.6%-98.1%)</td>
<td>&lt;3 mths</td>
<td>28-36 weeks</td>
</tr>
<tr>
<td>Saul N, et. al. 2018</td>
<td>Australia</td>
<td>Case-Control</td>
<td>69%, (13%-89%)</td>
<td>&lt;3 mths</td>
<td>28 - 32 weeks</td>
</tr>
</tbody>
</table>

- VE estimates range from 69%-92%
U.S. case-control evaluation: Methods

- Case-control evaluation; 3:1
  - **Cases**: infants <2 months with cough onset between Jan. 1, 2011- Dec. 31, 2014
  - **Controls**: birth certificates; matched by age group & birth hospital

- Emerging Infection Program Network (EIP) sites: CA, CT, MN, NM, NY, OR

- Interview mother of all case/control infants

- Provider-verified vaccination status:
  - All case/control infants
  - All mothers of case/control infants

- Odds ratios calculated using conditional logistic regression; vaccine effectiveness (VE) was estimated as \((1 - \text{OR}) \times 100\%\)
U.S. case-control evaluation: Results

<table>
<thead>
<tr>
<th></th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Multivariate* VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>104 (43.3)</td>
<td>177 (33.1)</td>
<td>Reference</td>
</tr>
<tr>
<td>Before pregnancy</td>
<td>24 (10.0)</td>
<td>67 (12.5)</td>
<td>50.8 (2.1 – 75.2)</td>
</tr>
<tr>
<td>1st/2nd trimester</td>
<td>5 (2.1)</td>
<td>27 (5.1)</td>
<td>64.3 (-13.8 – 88.8)</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>17 (7.1)</td>
<td>90 (16.8)</td>
<td>77.7 (48.3 – 90.4)</td>
</tr>
<tr>
<td>After pregnancy</td>
<td>90 (37.5)</td>
<td>174 (32.5)</td>
<td>4.9 (-4.9 – 39.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>240</strong></td>
<td><strong>535</strong></td>
<td><strong>--</strong></td>
</tr>
</tbody>
</table>

*The following variables were included in the final model: household size >2 persons, maternal education, household member with pertussis diagnosis, and infant age (weeks)*
U.S. case-control evaluation: Results, cont.

- Vaccine effectiveness against hospitalized cases
  - 157 (65.4%) cases were hospitalized (n=336 matched controls)
  - 3rd trimester: 90.5% (65.2 – 97.4%)
U.S. case-control evaluation: Summary

- Tdap administered during third trimester of pregnancy was 77.7% effective at preventing pertussis among infants <2 months of age
  - VE of Tdap during pregnancy increased to 90.5% against hospitalized cases
- Post-partum vaccination did not offer any protection in our evaluation, emphasizing the importance of vaccination during pregnancy
Key research questions
Key research questions

- Effectiveness of vaccination during pregnancy among aP-primed women
- Optimal timing of vaccination during pregnancy
- Effectiveness and safety of boosting during every pregnancy
- Safety and immunogenicity of concomitant administration of Tdap with influenza vaccine during pregnancy
- Impact of maternal Tdap vaccination on epidemiology of infant pertussis
  - Trends in infant disease
  - Disease severity
  - Blunting of responses to DTaP and other vaccines
Summary

- Infants are at greatest risk for severe pertussis-related morbidity and mortality
  - Protecting infants is a priority
- Maternal Tdap immunization during pregnancy is a highly effective and safe strategy for preventing infant pertussis in the early months of life
- Continue to promote the uptake of Tdap among pregnant women
Print resources

www.cdc.gov/vaccines/pregnancy
Acknowledgements

- Anna Acosta
- Alison Albert
- Carla Black
- Amy Blain
- Karen Broder
- Amanda Faulkner
- Susan Hariri
- Fiona Havers
- Angela Jiles
- Katherine Kahn
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.