Health-Care Personnel Pertussis and Tdap Vaccination

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Advisory Committee on Immunization Practices
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National Center for Immunization & Respiratory Diseases
Division of Bacterial Diseases

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Evaluating Vaccinating Health-care Personnel with Tdap

- Tdap vaccine
  - Second dose of Tdap
  - Effectiveness
- Pertussis in health-care personnel (HCP)
  - Burden of disease
  - Transmission
  - Exposure management
- Impact of vaccinating HCP
- WG conclusions
- Discussion

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Second dose of Tdap is safe and immunogenic.

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Response to Second Tdap at 5- or 10-yr Interval Safety and Immunogenicity

- Safety
  - Generally comparable after first Tdap
  - Majority of local and systemic adverse events: mild to moderate; self-limited
  - Of few serious adverse events reported, none related to second Tdap
  - Rates comparable at the 5- and 10-year interval
- Immunogenicity
  - Tetanus and Diphtheria – essentially 100% protected
  - Pertussis
    - Response at 5 and 10 year intervals similar
    - Comparable to historic and contemporaneous first dose

Halperin 2011; Knuf 2010; Booy 2010, Halperin 2012, Mertsola 2010

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Tdap Revaccination U.S. Clinical Trials

- Sanofi Pasteur – Adacel in adults administered 9-11 years after previous Tdap
  - Study completed and presented to WG and ACIP (2013)

Presented to ACIP, June 2013

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GSK Revaccination Development Program for Boostrix

- GSK is conducting a clinical development program in the US for revaccination with Boostrix 5-10 years after prior vaccination with Boostrix
  - GSK recently completed a revaccination study of young adults, 20-28 years old, who were initially vaccinated 10 years ago when they were adolescents (11-18 years old).
  - Revaccination study in adults, 27-72 years old, who were initially vaccinated approximately 8 years ago, will begin later this year.
  - Another revaccination study will begin next year in individuals 70 years and older who were revaccinated more than 5 years ago
- GSK eventually plans to submit the data to the FDA for consideration of label updates to BOOSTRIX

Slide prepared by GSK

Tdap vaccine is effective but protection starts to wane within three years.

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Tdap Vaccine Effectiveness and Duration of Protection in Population Received Only Acellular Pertussis Vaccines (DTaP)

Overall Vaccine Effectiveness: 1 - < 4 years post-vaccination

	Case (n)	Control (n)	VE, %	95% CI
No Tdap dose	109	154	Ref	---
Tdap dose	342	1092	63.9	49.7 – 74.1

Duration of Protection

Time since Tdap	Case (n)	Control (n)	VE, %	95% CI
No Tdap	109	154	Ref	---
< 1 year	69	332	73.1	60.3-81.8
1 - < 2 years	124	389	54.9	32.4-70.0
2 - < 4 years	148	371	34.2	-0.03-58.0

CDC, unpublished data

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Tdap Vaccination:
Unclear Effect on Preventing Transmission

- Vaccinated person's symptoms not as severe - less likely to transmit
- Australian cocooning experience
  - "Cocoon" vaccination of mother significantly decreases risk of early onset pertussis, but timing of mother's Tdap before infant disease onset crucial
- Baboon model
  - Acellular pertussis vaccines protected from getting sick but infected
  - Nasopharyngeal bacterial colony counts mirror unvaccinated animals
  - Transmitted pertussis to other cohoused baboons

McIntyre P. The cocoon strategy to prevent early pertussis - Australian experience. Presented to ACIP June 2013
Warfel JM et al. Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model. 2014 Jan 14;111(2):787-92.

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Pertussis occurs in health-care personnel but probably not significant contribution to overall burden of disease

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Pertussis in Health-care Personnel

- Occupational exposures to pertussis occur in health-care settings
- Frequency and proximity of patient interaction puts HCP at increased risk for infection with potential to expose many

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Transmission of Pertussis in Health-care Setting

- Documented nosocomial infections in health-care settings
  - Index case: HCP, patient, visitor
- Outbreaks in variety of health-care settings
  - Numerous published reports
  - States recently hard hit with pertussis have not identified or reported health-care outbreaks
    - California, Wisconsin, Washington

Valenti WM, et al. JAMA Pediatr RW, et. al. 1968; Fisher MC, et al. 1988; Addiss DG, et al. 1991; Christie CDC, et. al. 1985; Shefor A, et. al. 1985; CDC. MMWR 2006;55(01); Baxter BR, et. al. 2006; Pascual FB, et. al. 2006; Wonston P, et. al. 2006; Bryant KA, et. al. 2006; Zivna I, et. al. 2007; Baggett HC, et. al. 2007; CDC. MMWR 2008;57(22); Liemna S, et. al. 2009; Yasmin S, et. al. 2011.

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Pertussis in Health-care Personnel

- Measured risk and burden of disease - not well defined
  - National surveillance not collect HCP status for pertussis cases
  - Estimated 1.7-fold increased risk for HCPs compared to adult population
    - Based on 384 reported adult pertussis cases; 32 (8%) were HCP
  - 1.3 to 3.6% - annual incidence in ED residents, nursing and patient-care staff
    - Based on serologic evidence; some asymptomatic
- 1-6% yearly infection rate among adolescent and adults based on serologic studies

Desettes G, et al. Morbidity of pertussis in adolescents and adults. J Infect Dis 2000; 182:174-179.
Wright, SW, Decker MD, Edwards KM. Incidence of pertussis infection in healthcare workers. Infect. Control Hosp. Epidemiol. 1999. 20:120-123.
Cherry JD. The present and future control of pertussis. Clin Infect Dis. 2010 Sep 15;51(6):663-7.

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Impact of Pertussis in Health-care Facilities

- Pertussis exposure management is complicated, time-consuming and costly
- Cost estimates for investigation and control measures can be substantial
  - $84,000-$98,000: cost of managing pertussis exposures over 12-month period
  - $74,000-$263,000 per hospital-based pertussis outbreaks

Zivna I, et al. Impact of Bordetella pertussis exposures on a Massachusetts tertiary care medical system. Infect Control Hosp Epidemiol. 2007 Jun;28(6):708-12.
Caliger A, et al. Nosocomial pertussis: costs of an outbreak and benefits of vaccinating health care workers. Clin Infect Dis. 2006 Apr 1;42(7):981-8.
Baggett HC, et al. Two nosocomial pertussis outbreaks and their associated costs - King County, Washington, 2004. Infect Control Hosp Epidemiol. 2007 May;28(5):537-43.
Yasmin S et al. Healthcare-Associated Pertussis Outbreak in Arizona: Challenges and Economic Impact. 2011. J Ped Infect Dis. 2013 3(1):61-64

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Guidance on Post-Exposure Prophylaxis for Health-care Personnel (ACIP 2011)

- Based on HCP's likely contact with patients at risk for severe disease (e.g., NICU), and not Tdap vaccination status
  - PEP for HCP likely expose patient at risk for severe pertussis (e.g., hospitalized neonates and pregnant women)
  - Other HCP either receive PEP or monitored daily for 21 days after exposure and treated at onset of signs and symptoms
- Data inconclusive on need for post-exposure prophylaxis (PEP) in Tdap-vaccinated HCP
  - Pertussis infection did not develop in
    - 38/44 (86.4%) HCP with no PEP
    - 41/42 (97.6%) HCP with PEP
  - Infection based on serologic evidence; no symptomatic pertussis
  - Predefined non-inferiority criteria not met

CDC. Immunization of Health-Care Personnel Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2011 60(No. 55-7): 1-45.
Goins WP et al. A Comparison of 2 Strategies to Prevent Infection Following Pertussis Exposure in Vaccinated Healthcare Personnel. Clin Infect Dis. 2012 Apr;54(7):939-45.

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Tdap Vaccine for Health-care Personnel

- Since 2006, HCP recommend a single dose of Tdap and routine Td booster every 10 years
- Hospital-based Tdap coverage rates among HCP dependent on institutions Tdap vaccination program
  - 30% - campaign
  - 100% - hospital mandate
- 31.4% - Nationally reported Tdap coverage among HCP

Calderon M, et al. Implementation of a pertussis immunization program in a teaching hospital: an argument for federally mandated pertussis vaccination of health care workers. Am J Infect Control. 2008 Aug;36(6):392-8.
Weber DJ, et al. Assessment of a mandatory tetanus, diphtheria, and pertussis vaccination requirement on vaccine uptake over time. Infect Control Hosp Epidemiol. 2012 Jan;33(1):81-3
CDC. Noninfluenza Vaccination Coverage Among Adults — United States, 2012. MMWR. 63(05);95-102.

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Impact of Tdap Vaccination of Health-care Personnel on Nosocomial Transmission

- Earlier models calculated benefits and costs of vaccination program for HCP in preventing a nosocomial pertussis outbreak
- Vaccinating HCP substantially reduced the risk of hospital-based pertussis outbreak and was cost-effective/cost-saving
  - Inputs included Tdap vaccine efficacy estimates higher than current estimates
  - Assumptions include vaccination would decrease transmission and prevent secondary cases
- No direct evidence; updating model

Greer AL, Fisman DN. Keeping vulnerable children safe from pertussis: preventing nosocomial pertussis transmission in the neonatal intensive care unit. Infect Control Hosp Epidemiol. 2009 Nov;30(11):1084-9.
Greer AL, Fisman DN. Use of models to identify cost-effective interventions: pertussis vaccination for pediatric health care workers. Pediatrics. 2011 Sep;128(3):e591-9.
Caliger A, et al. Nosocomial pertussis: costs of an outbreak and benefits of vaccinating health care workers. Clin Infect Dis. 2006 Apr 1;42(7):981-8.

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WG Uncertainties
Tdap Vaccine

- More learned about acellular pertussis vaccines
  - Acellular-primed adolescents - Tdap effective but protection wanes substantially within a few years
  - Whole-cell primed adults - Tdap protects but unable to measure
  - As population ages, will only be acellular-primed cohort
- Is assumption valid that Tdap vaccination protects contacts?
- Timing of any potential indication on additional doses of Tdap or are we compelled to make an off-label recommendation?

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WG Assessments
Pertussis and Vaccinating Health-care Personnel

- Pertussis transmission occurs in health-care settings
- Frequency and proximity of patient interaction puts HCP at increased risk of exposure to pertussis
  - Unclear how much pertussis exposure results in disease
- Lack of updated disease and vaccine data specific to HCP
- No small thing to implement recommendations for HCP
- No supportive evidence that additional doses would be beneficial in prevention of disease and transmission in a health-care setting
  - Even if additional Tdap doses recommended, no change to risk management of pertussis exposures

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WG Conclusions

At this time, ACIP Pertussis Vaccines WG does not propose changes to the current ACIP Tdap recommendation for HCP.

Focus on current Tdap program

- Improve adult coverage, including HCP
- Vaccinate pregnant women to protect infants

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Pertussis-related Projects
MVPDB & Collaborators

- Pertussis Vaccine
  - Tdap vaccine effectiveness
    - Emergence of pertactin negative strains (Vermont)
    - Cohort Study (HMOs)
    - Case-Control Study (California)
  - Clinical Characteristics of Vaccinated and Unvaccinated Pertussis Cases (EPS)
- Tdap Pregnancy
  - Cocooning/pregnancy Tdap evaluation (CA, CT, MN, NM, NY, OR)
  - Infant blood-spot study - Effectiveness of maternal Tdap against pertussis (WA, NY, CA)
- Health-care personnel
  - Update - cost of an outbreak and benefits of vaccinating HCP (DVD, ISD)
  - Incidence of pertussis in HCP (EPS)

EPS: Enhanced Pertussis Surveillance; ISD: Immunization Services Division; DVD: Division of Viral Diseases

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Additional CDC Activities

- Assessment Branch (ISD/NCIRD)
  - Measuring Tdap coverage among pregnant women
    - PRAMS (with DRH/NCCDPHP)
    - Internet panel survey on pregnant women during influenza season
- Immunization Safety Office (DHQP/NCEZID)
  - Safety monitoring in pregnant women following Tdap administration
    - Vaccine Adverse Event Reporting System (VAERS)
    - Vaccine Safety Datalink (VSD)
    - Clinical Immunization Safety Assessment (CISA) Project
- Health Communications Science Office (NCIRD)
  - Formative Research Plans to Develop a Maternal Tdap Vaccination Campaign

PRAMS: Pregnancy Risk Assessment Monitoring System

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Is additional guidance on repeat doses of Tdap for HCP needed?

Tdap vaccine

- Effective but protection wanes within 3 years
- Unclear effect on preventing transmission
- Second dose safe and immunogenic
- Repeat doses not substitute /change exposure management
- Forthcoming data help fill data gaps
- If change to Tdap vaccine product label, ACIP would revisit Tdap revaccination

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