Vaccines and Pregnancy Part 2: TDaP

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GRAND ROUNDS LECTURE

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Objectives

- Clinical manifestations of tetanus, diphtheria, and pertussis
- TDaP vaccination rates
- Vaccine mechanism of action in pregnancy
- Benefits of TDaP vaccination
- Safety considerations

The TDaP Vaccine

- Offers protection against three mostly toxin-driven bacterial diseases
  - Tetanus: *Clostridium tetani*
  - Diphtheria: *Corynebacterium diphtheriae*
  - Pertussis: *Bordetella pertussis*
- Acellular pertussis: vaccine used to have whole-cell killed pertussis but caused high incidence SEs including severe swelling and erythema at injection site, and in very small percentage, long crying spells and febrile seizures

CDC Pinkbook, p. 297

Vaccination Rates: Pregnant Women

- Based 2016 National Health Interview Survey, **26.6%** of adults reported receiving Tdap vaccination
- Based on 2018 CDC survey-based study, **54.9%** of pregnant women reported receiving Tdap vaccination
  - Rate was **70.5%** among those who received offer to vaccinate or referral

CDC Survey 2016

Vaccination Rates: Children

- Based on a CDC study for 2017-2018 academic year
  - Nationally: 95.1% of kindergarteners received state-required vaccine doses (ranging from 3-5 doses)
  - California: 96.4% of kindergarteners received 4-5 doses (state requires 5 unless 4th dose was on or after 4 y)

Mellerson et all 2018

Tetanus Infection

Symptoms of Tetanus

- Gram+ anaerobe; releases tetanospasmin exotoxin, forms very hardy spores
- Found in soil and intestinal tract of multiple animals
- Typically enters body through a wound
- Three forms
  - **Localized:** persistent contractions in the same area as location of injury (uncommon and rarely fatal)
  - **Cephalic:** affects facial nerves, can be transmitted via head/facial injuries or otitis media (very rare)
  - **Generalized:** most common form

CDC Pinkbook, p. 341

Generalized Tetanus

- Causes descending pattern of paralysis: trismus (lockjaw)→ neck stiffness→ dysphagia→ abdominal muscle rigidity
- Neonatal tetanus
  - Form of generalized tetanus affecting infants
  - Typically contracted via infected umbilical stump, particularly when unsterilized instruments are used
  - Mostly seen in parts of developing world; rare in US
  - **Occurs in infants w/o passive immunity; ie from non-immune mothers**

CDC Pinkbook, pp. 341-343

Complications of Tetanus Infection

- Laryngospasm
- Fractures
- Nosocomial infections (from prolonged hospitalization)
- Aspiration pneumonia
- Arrythmias
- Pulmonary embolism
- Death

CDC Pinkbook, p. 343

Diphtheria Infection

Symptoms of Diphtheria

- Gram+ aerobe
- Can infect any mucosal tissue in the body including genital and ocular
  - Most common sites are pharynx and tonsils
  - Systemic absorption varies, more likely to cause complications
- Causes localized tissue destruction and pseudomembrane formation
  - Causes fever, pharyngitis, cough, lymphadenopathy, submandibular edema
  - Pseudomembrane formation can cause respiratory compromise

CDC Pinkbook, pp. 107-108

Complications of Diphtheria Infection

- Neuritis
  - Affects motor neurons
  - Can cause paralysis of soft palate, eyes, limbs, diaphragm
- Myocarditis
  - Arrythmias, heat failure
- Secondary pneumonia
- Respiratory failure
- Case fatality rate: 5-10%, 20% in children <5 y

CDC Pinkbook, p. 109

Pertussis Infection

Symptoms of Pertussis

- Gram negative aerobic rod
- Attaches to cilia of pulmonary epithelial cells and releases toxin to paralyze cilia
  - Causes inflammation of respiratory tract and inhibits respiratory secretion clearance
- Disease progresses through three stages
- Catarrhal
  - First 1-2 weeks: rhinorrhea, sneezing, mild cough, mild fever→ like common cold

CDC Pinkbook, pp. 261-263

Symptoms of Pertussis

- Paroxysmal
  - Next 1-6 weeks: spasms of frequent, short coughs followed by long inspiratory effort f/b characteristic "whoop" sound
  - When people are usually diagnosed
  - **Children <6 mo may not make "whoop" noise**
- Convalescence
  - Weeks to months: gradual decrease in sx but may get paroxysms of cough w/ subsequent respiratory infections

CDC Pinkbook, pp. 261-263

Complications of Pertussis Infection

- Secondary bacterial pneumonia
  - Most common complication and cause of death in pertussis infection
- Neurologic: seizures, encephalopathy, insomnia
- Pressure-related: pneumothorax, subdural hematoma, hernia, rectal prolapse, urinary incontinence
- Death

CDC Pinkbook, pp. 261-263

Complications of Pertussis Infection

- Teens and adults typically have milder complications (incontinence, insomnia, etc)
- Children, and especially infants, are highest risk for severe morbidity and mortality
- In one study from the CDC from 2008-2011, >80% of all deaths from pertussis were among those < 3 months old
  - Do not yet have fully developed immune systems
  - Infants typically need 2 doses of DTaP before they are adequately protected from infection

CDC Pinkbook, pp. 261-263, Fouda et al 2018

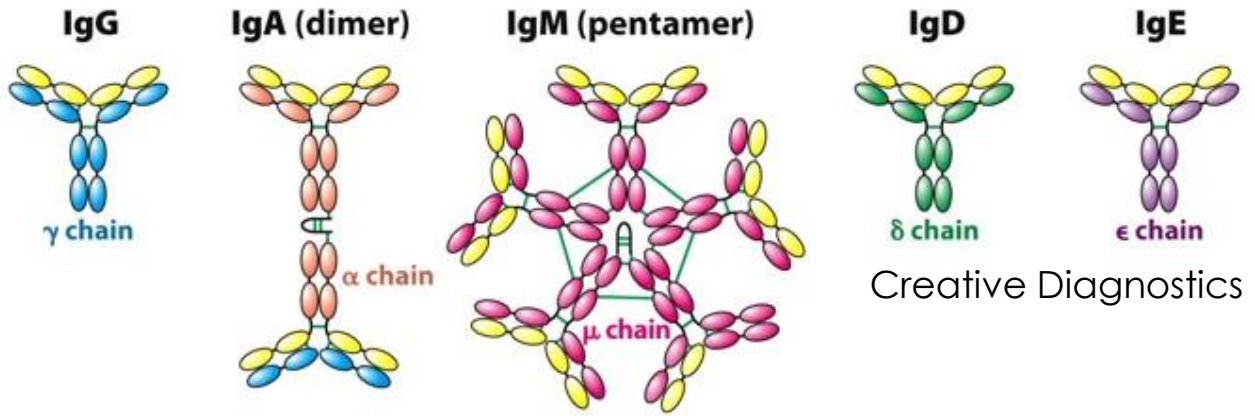
TDaP Vaccination: Mechanism of Action

Vaccination of Pregnant Women

www.immunizeca.org

Humoral Immunity

- Mechanism of action of TDaP vaccination
  - Pregnant woman receives injection of Tdap vaccine
  - Develops humoral immune response→ protective IgG antibodies (against various proteins of each of the three vaccine components)



Creative Diagnostics

Maternal Antibody Transfer

- IgG antibodies are transferred across the placenta to the fetus (via neonatal Fc receptors)
- Takes 2 weeks after Tdap vaccination for antibodies in mother to reach protective levels and transfer to fetus
- IgA antibodies can be transferred to babies via breast milk, but take a couple weeks to become protective
  - Causes potential gap in protection level for infants if mom is vaccinated postpartum rather than while pregnant

Silverman N, 2014; Fouda et al 2018, Schnirring 2011

Maternal Antibody Transfer

- Ideal time to vaccinate pregnant women: 32 wks GA (or between 27-36 wks)
  - Based primarily on pertussis component
  - Vaccinate too early= immunity wanes before infant gets first vaccine but vaccinate too late= not enough time to provide get adequate antibody levels
  - However, any vaccination in mother is better than none
- Passive pertussis immunity is NOT long-lasting
  - Antibody levels take weeks to peak in fetus and wane in months→ can become undetectable in infants as early as 4 months old

Silverman N, 2014; Fouda et al 2018, Schnirring 2011

TDaP Vaccination: Benefits, Safety Considerations

Benefits of TDaP Vaccination

- 3rd trimester Tdap vaccination
  - 77.7% effective in preventing pertussis in infants <2 mo
  - 90.5% effective in preventing pertussis hospitalizations in infants <2 mo
  - When infants do get pertussis, it's less severe than if mother did not get vaccine
- Prevention of tetanus, diphtheria, and pertussis, which cause severe morbidity/mortality on their own
- Relatively little data for fetal effects of any of these infections

Lindley et al, 2019, NCIRD 2017

Public Health Benefits of TDaP Vaccination

- 92% drop in neonatal tetanus mortality globally since tetanus vaccine introduced in 1960s
- Near-eradication of diphtheria worldwide
- Decreased severity of pertussis infection among vaccinated

Fouda et al 2018

Vaccine Frequency

- Tetanus and diphtheria immunity
  - Typically wanes after 10 y in most people, though can be lifelong (need Td boosters q10y)
- Pertussis immunity
  - Wanes significantly within a year (so need w/ each pregnancy)
  - Everyone coming into close contact w/ a newborn should be vaccinated (at least 2 wks before anticipated close contact)

CDC Pinkbook pp. 271 & 348

Side Effects of TDaP Vaccination

- Localized reaction—pain, redness, swelling at injection site (20-40%)
- Fever, to as high as 101 (3-5%)
- Entire arm swelling
- Localized reactions more common after 4th and 5th doses in kids (NOT a contraindication to further vaccination)
- Severe SEs very rare

CDC Pinkbook pp. 275-276

Safety Considerations

- Precaution when administrating TDaP
  - Hx GBS within 6 wks of TDaP/DTaP
  - Hx of severe local reaction following prior dose
  - Moderate to severe acute illness
- Contraindications to future TDaP doses
  - Severe allergic reaction to vaccine components
  - Encephalopathy not due to another identifiable cause occurring within a week of TDaP or DTaP vaccination

CDC Pinkbook pp. 274-275

The Role of Providers

- Based on a CDC survey of pregnant women from March-April 2019
  - 76% reported receiving an offer or referral for Tdap vaccine (70.5%)
  - 5.8% reported receiving a recommendation but no offer for vaccine (19.5%)
  - 18.1% reported receiving no recommendation or offer for vaccine (1.0%)
- Among non-vaccinated, reasons women who reported not getting Tdap vaccination
  - Not knowing it was needed (37.9%)
  - Concerns over safety risks to infant (17.1%)

Lindley et al, 2019, CDC Survey 2016

The Role of Providers

- Always recommend and offer the Tdap shot (and flu shot) to your pregnant patients (and any other vaccines if/as indicated)!!!

- If you can't offer a vaccine, give them a prescription!

Vaccine Schedule

Table 2 Recommended Adult Immunization Schedule by Medical Condition and Other Indications United States, 2019

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 count <200	HIV infection CD4 count ≥200	Asplenia, complement deficiencies	End-stage renal disease, on hemodialysis	Heart or lung disease, alcoholism[1]	Chronic liver disease	Diabetes	Health care personnel[2]	Men who have sex with men
IIV or RIV	1 dose annually										
or										or	
LAIV	CONTRAINDICATED						PRECAUTION			1 dose annually	
Tdap or Td	1 dose Tdap each pregnancy	1 dose Tdap, then Td booster every 10 yrs									
MMR	CONTRAINDICATED	1 or 2 doses depending on indication									
VAR	CONTRAINDICATED	2 doses									
RZV *(preferred)*	DELAY				2 doses at age ≥50 yrs						
or					or						
ZVL	CONTRAINDICATED				1 dose at age ≥60 yrs						
HPV Female	DELAY	3 doses through age 26 yrs			2 or 3 doses through age 26 yrs						
HPV Male		3 doses through age 26 yrs			2 or 3 doses through age 21 yrs						2 or 3 doses through age 26 yrs
PCV13		1 dose									
PPSV23		1, 2, or 3 doses depending on age and indication									
HepA	2 or 3 doses depending on vaccine										
HepB	2 or 3 doses depending on vaccine										
MenACWY	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains										
MenB	PRECAUTION	2 or 3 doses depending on vaccine and indication									
Hib		3 doses HSCT[3] recipients only			1 dose						

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

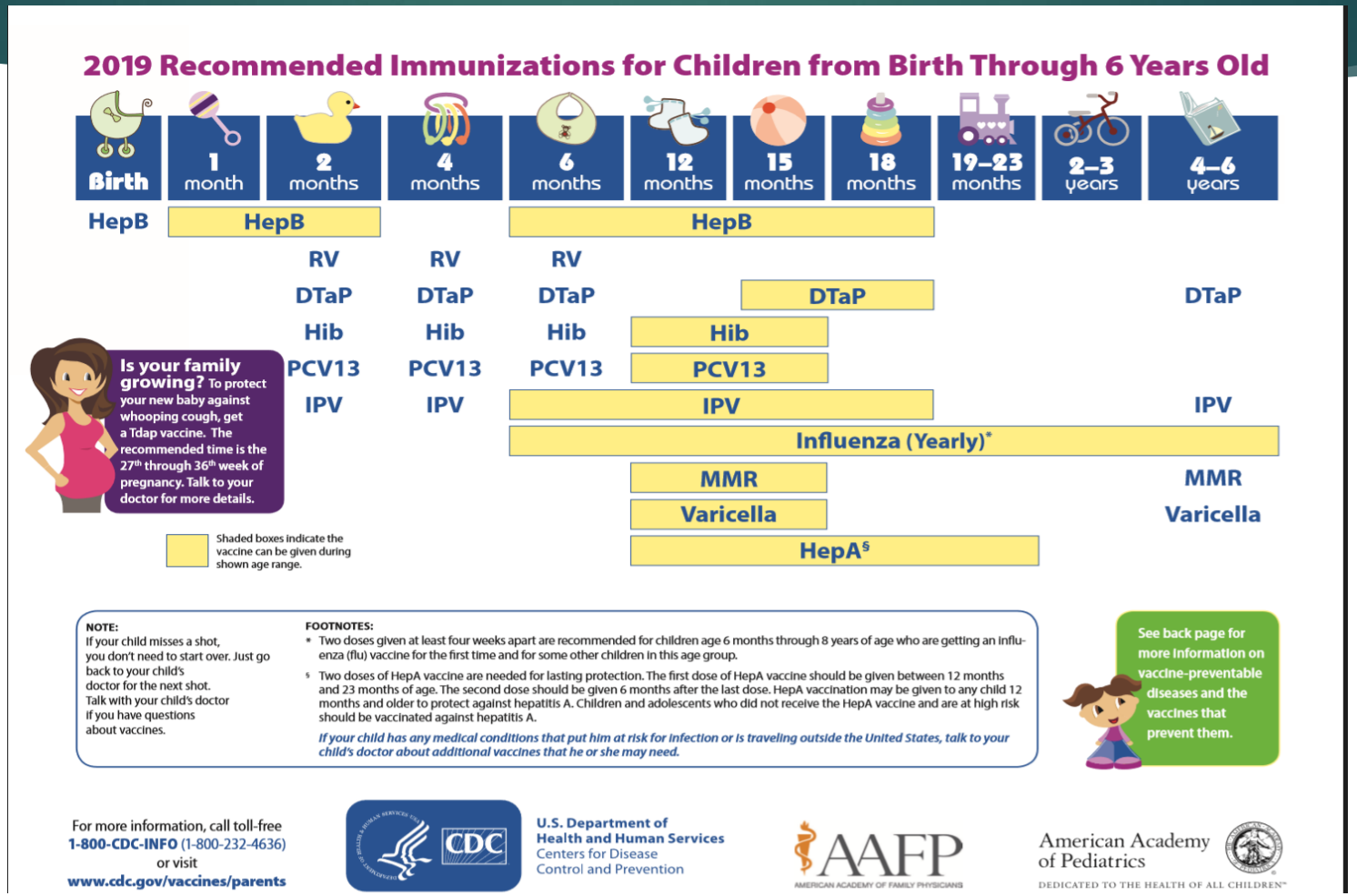
Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction

Delay vaccination until after pregnancy if vaccine is indicated

Contraindicated—vaccine should not be administered because of risk for serious adverse reaction

No recommendation

Vaccine Schedule



2019 Recommended Immunizations for Children from Birth Through 6 Years Old

Vaccine	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
HepB	HepB	HepB			HepB						
RV			RV	RV	RV						
DTaP			DTaP	DTaP	DTaP		DTaP				DTaP
Hib			Hib	Hib	Hib	Hib					
PCV13			PCV13	PCV13	PCV13	PCV13					
IPV			IPV	IPV	IPV						IPV
Influenza (Yearly)*					Influenza (Yearly)*						
MMR						MMR					MMR
Varicella						Varicella					Varicella
HepA§						HepA§					

Is your family growing? To protect your new baby against whooping cough, get a Tdap vaccine. The recommended time is the 27th through 36th week of pregnancy. Talk to your doctor for more details.

Shaded boxes indicate the vaccine can be given during shown age range.

NOTE:
If your child misses a shot, you don't need to start over. Just go back to your child's doctor for the next shot.
Talk with your child's doctor if you have questions about vaccines.

FOOTNOTES:

* Two doses given at least four weeks apart are recommended for children age 6 months through 8 years of age who are getting an influenza (flu) vaccine for the first time and for some other children in this age group.

§ Two doses of HepA vaccine are needed for lasting protection. The first dose of HepA vaccine should be given between 12 months and 23 months of age. The second dose should be given 6 months after the last dose. HepA vaccination may be given to any child 12 months and older to protect against hepatitis A. Children and adolescents who did not receive the HepA vaccine and are at high risk should be vaccinated against hepatitis A.

If your child has any medical conditions that put him at risk for infection or is traveling outside the United States, talk to your child's doctor about additional vaccines that he or she may need.

See back page for more information on vaccine-preventable diseases and the vaccines that prevent them.

For more information, call toll-free
1-800-CDC-INFO (1-800-232-4636)
or visit
www.cdc.gov/vaccines/parents

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

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The End

THANK YOU FOR YOUR TIME!

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Image Credits

- Pregnancy antibodies graphic: http://www.immunizeca.org/pregnant-women/
- Antibodies graphic: https://www.creative-diagnostics.com/blog/index.php/clinical-significance-of-five-immunoglobulin-tests/
- Table 1. Recommended Adult Immunization Schedule for ages 19 years or older, United States, 2019, 5 Feb 2019. https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html
- 2019 Recommended Vaccinations for Infants and Children (birth through 6 years) Parent-Friendly Format. 5 Feb 2019. https://www.cdc.gov/vaccines/schedules/easy-to-read/child-shell-easyread.html
- Valentine comic: Paul White, https://www.acsh.org/news/2019/03/04/top-10-pro-vaccine-or-anti-anti-vaxxer-memes-internet-13853