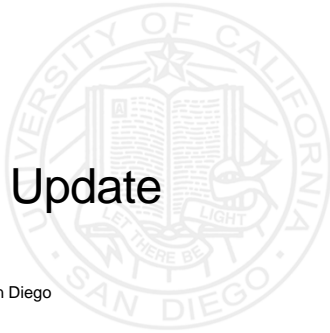


# Red Book Update

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## Disclosures

- I have no financial relationships to disclose or Conflicts of Interest to resolve.
- I will discuss the off label use of Tdap vaccine during pregnancy



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## Objectives

- List some new policies/guidelines coming in the next year from AAP and other partner organizations
- Explain the rationale for preferring the live attenuated nasal influenza vaccine over the injectable vaccine
- Describe the advantages of HPV9 vaccine
- Explain who should receive Tdap vaccine boosters
- List some reasons not to give antibiotics
- Cite some key online sources of infectious disease information



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### The 2015 Red Book



- Available in the Spring of 2015
- Will be available in both hard copy and online versions
- Over 250 Chapters
- The process
  - Primary authors (n=hundreds) write/update every chapter
  - Most chapters reviewed by content experts at CDC and other organizations
  - Every chapter reviewed by two COID members/liaisons
  - Every chapter reviewed by one of the Red Book editors
  - Every chapter discussed in a 3-day "Marathon" meeting (March 2014)
  - Stuff happens and then you get your Red Book



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### Selected new policy statements/clinical reports coming from COID

- Management of Bronchiolitis/Palivizumab-revision Fall 2014
- Vaccine Hesitancy 2015
- Congenital Toxoplasmosis 2015
- Use of Interferon Gamma Release Assays for Tuberculosis Testing Fall 2014
- Infection Control in Organized Sports 2015
- Biologic Response Modifiers fall 2014



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### New Policies from other organizations

- Inappropriate antibiotic use for acute respiratory tract infection (AHRQ)
- Clinical guidelines for diagnosis and antiviral management of seasonal and pandemic influenza in adults and children (IDSA)
- Kawasaki Disease and Endocarditis with Committee on Cardiovascular Disease in the Young (AHA)
- Diagnosis and management of bone and joint infections (IDSA)
- Clinical practice guidelines for the management of candidiasis (IDSA)



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## Palivizumab Preview



- Reduce age for routine administration for premature infants from 32 weeks to 28 weeks gestational age
- Elimination of risk factors to consider in 32-35 week gestational age
- Recommended for infants with chronic lung disease who were <32 weeks gestational age and who have required oxygen for >28 days
- Use in infants with congenital heart disease during the first year of life only and only in selected groups
- Specific recommendations for special populations (cystic fibrosis patients, immunocompromised patients, children with anatomic pulmonary abnormalities)
- Limited use in the second year of life



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## Expected ACIP Influenza Vaccine Recommendations 2014-2015

Same vaccine strains in the vaccine

Continue to support annual immunization for everyone 6 months of age and older

All available vaccine products are acceptable for indicated age groups

Preference for LAIV in children <9 years of age

Ample supply of vaccine



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## LAIV vs IIV

### Background (2)

- ACIP currently expresses no preference for LAIV vs. IIV.
- Recent recommendations expressing some degree of preference for LAIV for children:

Country	Age (years)
Canada	2-17
United Kingdom	2-17
Israel	2-17
Germany	2-6
United States—Oregon	2-5
United States—Washington	2-7



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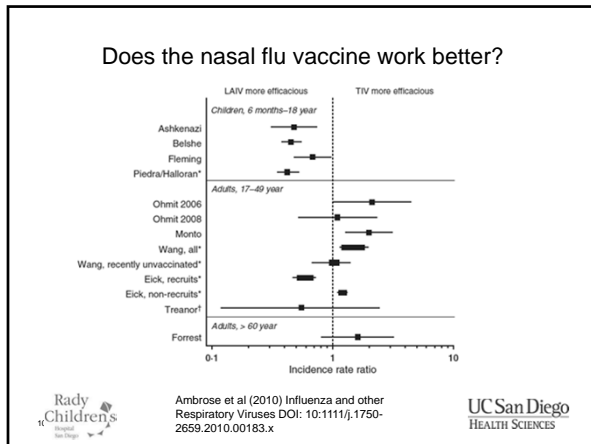
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- ### Probable Upcoming Recommendation-June 2014
- Preferential use of LAIV over IIV for children 8 years and younger
  - No change in recommendation for older children and adults
  - Emphasis on not missing opportunities if a provider doesn't have LAIV
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- ### Is Quadrivalent flu vaccine better?
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- Quadrivalent vaccine composition
    - an A/California/7/2009 (H1N1)pdm09-like virus
    - an A/Texas/50/2012 (H3N2)-like virus
    - a B/Massachusetts/2/2012-like virus (Yamagata)
    - a B/Brisbane/60/2008-like virus (Victoria)
  - Roughly 15% of the flu cases this year caused by influenza B
  - For 2013-2014 (as of 5/23/14) 70% of influenza B strains were Yamagata lineage
  - So, 4.5% of influenza cases potentially protected by the quadrivalent vaccines
  - At least four quadrivalent influenza vaccine products available for 2014-2015
  - In 2013-14 quadrivalent vaccines were 37-95% more expensive than trivalent vaccines
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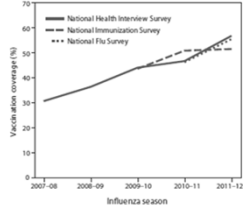
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### Influenza vaccine coverage: Pediatrics

FIGURE 2. Influenza vaccination coverage among children aged 6 months–17 years, by surveillance system — National Health Interview Survey, National Immunization Survey, and National Flu Survey, United States, 2007–08 through 2011–12 influenza seasons\*



MMWR, 2013; 62(ss04): 1-29




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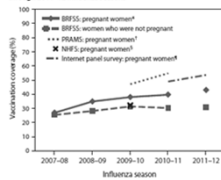
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### Influenza vaccine coverage: Pregnant women

FIGURE 4. Influenza vaccination coverage among pregnant women aged 18–49 years— Behavioral Risk Factor Surveillance System, Pregnancy Risk Assessment Monitoring System, National 2009(H1N1) Flu Survey, and Internet Panel Survey, United States, 2007–08 through 2011–12 influenza seasons



MMWR, 2013; 62(ss04): 1-29




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### How many doses of flu vaccine do I give?

#### Number of Seasonal Influenza Doses for Children 6 months through 8 years of age



FIGURE 2. Number of 2013–2014 seasonal influenza vaccine doses for children 6 months through 8 years of age.

COID, Pediatrics 2013;132:e1089-1104




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## The Good News: HPV9 is coming



- Current HPV vaccines contain two (Cervarix, GSK) or four (Gardasil, Merck) serotypes
- HPV serotypes 16 and 18 are in both vaccines and are the most common causes of cervical cancer
- HPV serotypes 6 and 11 are only in HPV4
- Recommended routinely beginning at 11 years of age
- A new vaccine with 9 HPV serotypes is coming in Spring 2015




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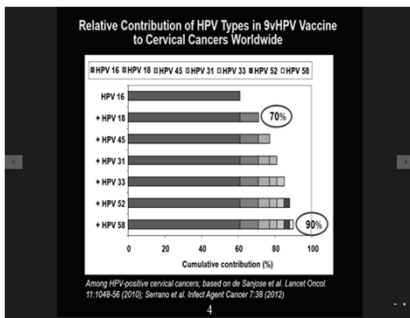
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### Protocol 001: Non-inferiority of Month 7 cLIA Seroconversion Rates in Women Administered 9vHPV Vaccine vs. Women Administered qHPV Vaccine

The non-inferiority criterion was met for all 4 HPV types ( $p < 0.001$ )

Anti-HPV cLIA Response	9vHPV Vaccine		qHPV Vaccine	
	n	%	n	%
Anti-HPV 6	3,393	99.8	3,975	99.8
Anti-HPV 11	3,395	100	3,982	99.9
Anti-HPV 16	4,032	100	4,062	100
Anti-HPV 18	4,539	99.8	4,541	99.7




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HPV 9 issues



- What should we do with people who have already had 3 doses of HPV2 or HPV4?
- What should we do with people who have had only some of their HPV doses?
- Cost?
- Can this be used as a 2-dose vaccine?



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Tdap vaccine during pregnancy



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Rationale for Tdap during pregnancy



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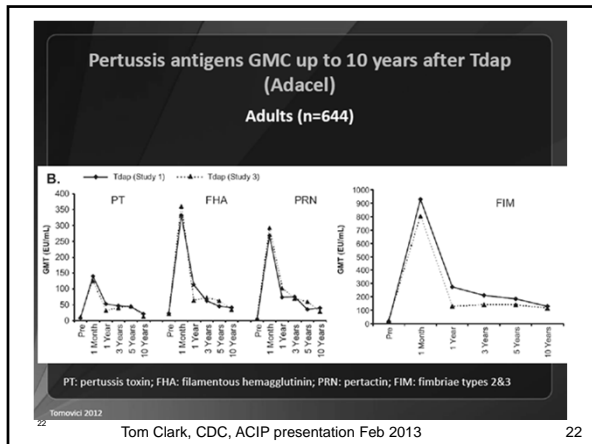
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### Preliminary Results

	Tdap in pregnancy	Unvaccinated	Adjusted Relative Risk (95% CI)
Full cohort N=26,224    N=97,265			
Chorioamnionitis	6.1%	5.5%	RR=1.19 (1.13-1.27)
Preterm <37 weeks	6.3%	7.8%	HR=0.88 (0.83-0.93)
SGA <10 <sup>th</sup> percentile	8.4%	8.3%	RR=1.00 (0.96-1.06)
Vaccinated <20 weeks N=6,083    N=97,265			
Hypertensive disorders	8.2%	8.0%	RR=1.09 (0.99-1.20)
Vaccinated 27-36 weeks N=11,351    N=97,265			
Chorioamnionitis	5.6%	5.5%	RR=1.11 (1.03-1.21)
Preterm <37 weeks	5.3%	7.8%	HR=0.83 (0.77-0.90)
SGA <10 <sup>th</sup> percentile	8.6%	8.3%	RR=1.03 (0.96-1.10)

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## Tdap immunization related to pregnancy

- Do re-immunize pregnant women at every pregnancy to protect their infants
- Do not re-immunize women prenatally or post-partum
- Do not re-immunize the cocoon
- Do immunize the cocoon and everyone else 11 years of age and older one time with Tdap



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## What about Tdap boosters?

Table 2 | Effectiveness of Tdap (reduced acellular pertussis) vaccination in preventing polymerase chain reaction (PCR) confirmed pertussis in selected subgroups defined by childhood pertussis vaccination history

Childhood pertussis vaccination history and comparison group for PCR positive cases	No of cases	No of controls	Vaccine effectiveness (%) (95% CI)	P value
<i>Pre-vaccine era:</i>				
PCR negative controls*	61	1887	24.1 (-58.7 to 63.7)	0.464
KPNC controls	61	2725	26.7 (-65.4 to 67.5)	0.455
<i>All whole cell vaccinees:</i>				
PCR negative controls*	129	4300	68.3 (45.8 to 81.5)	<0.001
KPNC controls	129	4970	63.6 (37.3 to 78.9)	<0.001
<i>All acellular vaccinees:</i>				
PCR negative controls*	181	822	57.6 (34.1 to 72.7)	<0.001
KPNC controls	181	4776	74.4 (60.4 to 83.4)	<0.001

KPNC-Kaiser Permanente Northern California.

\*Each of these models deleted a small number of observations for PCR negative controls because of missing covariate data (one observation in pre-vaccine model, three observations in all whole cell model, and three observations in all acellular model).

Baxter R et al, BMJ 2013




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## What is not coming!

- Tdap booster recommendation for the general population
- ?Tdap booster for those around young infants
- ?Tdap booster for healthcare workers

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## The times they are a-changin

Why it might not be a good idea to prescribe antibiotics

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## Why it might not be a good idea to prescribe antibiotics

- Side effects
- C. difficile
- Antibiotic resistance

# • THE MICROBIOME



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## Adverse Drug Events-Antibiotics

- Every week 56% of children take at least 1 medication
- 19% take a prescription drug
- 158,520 patients <18 years of age treated in ED's for adverse drug events in 2004-2005
- 25% of those due to antibiotics

Table III. Five most common therapeutic categories of drugs causing unintentional overdoses, allergic reactions, and adverse effects in children and adolescents treated in emergency departments—United States, 2004 to 2005

Unintentional overdose (n = 71,214)		Allergic reaction (n = 15,484)		Adverse effect (n = 35,814)	
Therapeutic category	Cases, estimate (n)	Therapeutic category	Cases, estimate (n)	Therapeutic category	Cases, estimate (n)
Antigens	290 (14.1) (25)	Anticancer agents	129 (3.6) (6.8)	Anticancer agents	165 (4.4) (22)
Respiratory medications	454 (11.3) (11.9)	Analgesic medications	137 (3.8) (9.2)	Psychotropic medications	125 (3.6) (13.1)
Psychotropics	281 (7.1) (11)	Plasma agents	118 (3.7) (6.7)	Plasma agents	145 (3.1) (18.4)
Neurologic	301 (7.6) (9.7)	Respiratory medications	104 (3.2) (5.9)	Respiratory medications	78 (2.0) (10.4)
Cardiovascular agents	240 (6.1) (9.2)	Psychotropic medications	42 (1.2) (2.2)	Neurologic medications	91 (2.0) (9.1)



Cohen AL, J Peds 2008;152:416

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## C. Difficile infection (CDI)

- Rates of CDI in children increased from 2001-2006 from 2.6-4.0 cases per 1000 hospital admissions
- Median age=4 years
- Community acquired disease increasing in adults and children
- Children with complex health care needs are at increased risk
- Severe CDI among hospitalized children leads to colectomy in 1.25% of cases
- Management of CDI is challenging

Sammon JS, JAMA Pediatrics 2013;167:567-73



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### Principles of Judicious Antibiotic Prescribing for URI in Pediatrics

- Use stringent clinical criteria for diagnosis
  - Otitis: effusion with inflammation (Pediatrics 2013;131:e964-e999)
  - Sinusitis: high fever/purulent rhinorrhea; persistent rhinorrhea and cough for 10 days; clinical worsening after initial improvement (Pediatrics 2013;132:e262-e280)
  - GAS pharyngitis: only test when 2 findings present (fever, tonsillar exudate/swelling, swollen/tender nodes, absence of cough).
- Understand the benefits and harms of antibiotics



Pediatrics, 2013;132:1146-1154

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### Judicious Use of Antibiotics

- Implement judicious prescribing strategies
  - Narrow-spectrum agents
    - OM, sinusitis, GAS: amoxicillin or Augmentin. No azithromycin
  - Minimize duration of therapy
    - OM: 7 day course for older children
    - Sinusitis: no more than 14 days
  - Consider a period of observation prior to prescribing
    - Otitis-watchful waiting for those older than 2 years
    - Sinusitis-observation for persistent symptom group



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### Where do you look that up...?

- If your nurse inadvertently gives an MMR IM instead of Subcutaneously do you need to repeat it?
  - No, CDC General Recommendations on Immunization
- If your nurse gives an HPV subcutaneously instead of IM do you need to repeat it?
  - Yes, CDC General Recommendations on Immunization
- My patient's family is going butterfly catching in the Mozambique. What is the dose of malarone for a 4 month old?
  - There isn't one, CDC Travel Site
- Is there malaria in the Antigua and Barbuda ?
  - No, CDC travel site
- My patient is on their 3<sup>rd</sup> episode of C. difficile. What do I treat with now?
  - Oral Vancomycin. Consider a taper, IDSA Guidelines
- My patient with Mycoplasma is allergic to azithromycin. Which quinolone is the best drug to treat with?
  - Moxifloxacin, Antimicrobial Agents and Chemotherapy



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### Where do you look that trivia up?

- AAP
  - Recommendations for the Prevention and Control of Influenza in Children
- CDC (CDC.gov)
  - General Recommendations for Immunizations
  - Travel recommendations
- IDSA Guidelines (Google IDSA or [http://www.idsociety.org/idsa\\_practice\\_guidelines/](http://www.idsociety.org/idsa_practice_guidelines/))
  - Community Acquired Pneumonia in Children 2011/CNS Infections
  - C. difficile
  - Candidiasis/Histoplasmosis/Coccidioidomycosis
  - Clinical Practice Guideline for the Immunization of Immunocompromised Hosts
- Don't forget Antimicrobial Agents and Chemotherapy!



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### Summary

- Red Book 2015 is coming
- Look for new guidelines for use of palvizumab this fall
- Consider giving LAIV to young children
- We need to help get pregnant women immunized with Tdap
- We need to give fewer antibiotics
- Remember Antimicrobial Agents and Chemotherapy!



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