MYTH-BUSTERS: CHILDHOOD VACCINES

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Objectives

- Identify common misconceptions surrounding childhood immunizations
- Evaluate available information in order to address misconceptions surrounding childhood immunizations
- Use various tools when providing education to patients and families regarding childhood immunizations

Background Information

Measles Outbreak

Increasing Risk

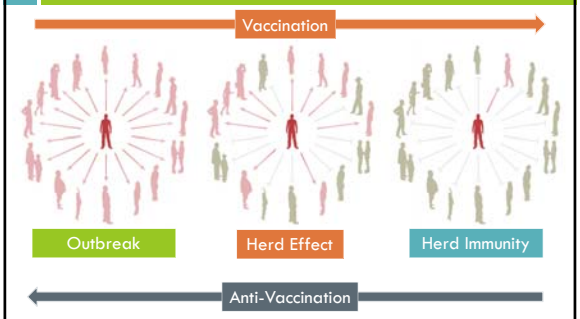
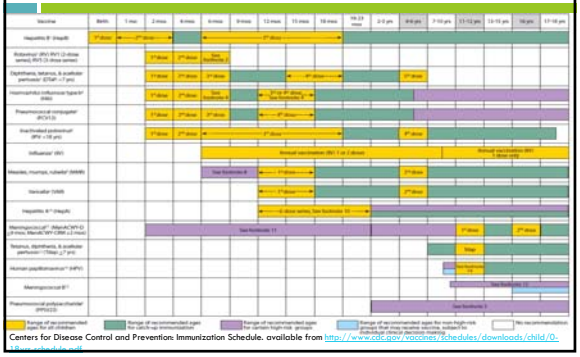


Image: http://www.nytimes.com/interactive/2015/02/02/us/measles-facts.html

CDC Immunization Schedule



Centers for Disease Control and Prevention: Immunization Schedule, available from http://www.cdc.gov/vaccines/schedules/downloads/child/0-

Vaccine Characteristics

- **Vaccine**
  - **Live Attenuated**
    - Weakened form of wild-type
    - Must replicate
    - Response similar to natural infection
    - Usually provide lifelong immunity
  - **Inactivated**
    - Whole or fractional
    - Cannot replicate
    - Generally thought to be safe in immunocompromised individuals
    - Antibody titers wane over time

Centers for Disease Control and Prevention: Principles of Vaccination.

Live Attenuated Vaccines

- Measles, Mumps, and Rubella
- Varicella-Zoster
- Rotavirus
- Nasal Influenza
- Herpes Zoster
- Adenovirus
- Yellow fever
- Typhoid
- Vaccinia
- Tuberculosis (BCG)
- Oral Polio Vaccine

Centers for Disease Control and Prevention: Principles of Vaccination.
Image: http://img2.timeinc.net/health/images/gallery/condition-centers/vaccines-child-needs-400x400.jpg

Inactivated Vaccines

- Hepatitis B
- DTaP/Tdap
- *Haemophilus influnzae* type B
- PCV13
- IPV
- Influenza
- Hepatitis A
- Meningococcal conjugate
- Meningococcal B
- Human papillomavirus
- Pneumococcal polysaccharide

Centers for Disease Control and Prevention: Principles of Vaccination.
Image: https://tinyfeetbigheart.wordpress.com/2013/02/13/dont-worry-mommy-it-will-be-over-in-a-second/

Disease and Vaccine Review

Decrease in Disease

Disease	Pre-vaccine Era	2006	% decrease
Diphtheria	175,885	0	100
Measles	503,282	55	99.9
Mumps	152,209	6,584	95.7
Pertussis	147,271	15,632	89.4
Polio (paralytic)	16,316	0	100
Rubella	47,745	11	99.9
Congenital Rubella Syndrome	823	1	99.9
Tetanus	1,314	41	99.9
H. influenza type b and unknown	20,000	208	99.9
Total	1,064,854	22,532	97.9
Vaccine Adverse Events	N/A	15,484	N/A

Centers for Disease Control and Prevention: Vaccination Safety.

Varicella-Zoster

Background	- Highly infectious, systemic infection typically results in lifetime immunity	
Epidemiology	Pre-vaccine: 15 cases/1000 persons 2-6 hospitalizations/100000 persons 0.6 deaths/1000000 persons	Post-vaccine: Infection declined 82% Hospitalization rates declined 95% Deaths declined 98.5%
Transmission	- Direct contact (respiratory tract, conjunctiva) - Inhalation of aerosols from vesicular fluid of lesions OR infected respiratory tract secretions that are aerosolized	
Incubation	- 10-21days after exposure to rash	
Symptoms	- Itchy, uncomfortable rash - Malaise, headache, fever - Complications: pneumonia, skin infection, encephalitis	
Treatment	- Acyclovir, VZIG	
Other	- Remains dormant in sensory-nerve ganglia and can be re-activated	

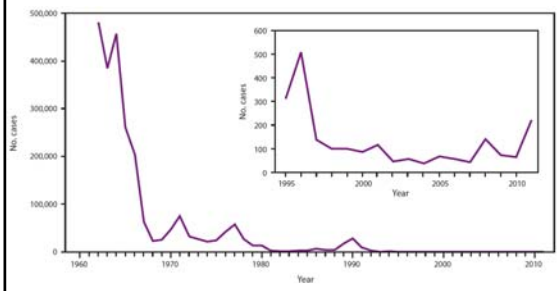
Centers for Disease Control and Prevention. MMWR. 2007; 56(no. RR-4): 1-40.

Measles, Mumps, and Rubella

Epidemiology (Measles)	Pre-vaccine: 500,000 cases 48,000 hospitalizations 500 deaths 1,000 permanent brain damage	Post-vaccine: 2004-2014 37-668 cases
Transmission	- Respiratory droplets	
Incubation (Measles)	- 10-12 days to prodrome - 7-21 days from exposure to rash	
Symptoms	- Rash (Measles, Rubella) - Fever, inflammation of the salivary glands (Mumps) - Complications: pneumonia, encephalitis, arthralgia, thrombocytopenic purpura, hearing loss	
Treatment	- Supportive care, IVIg	

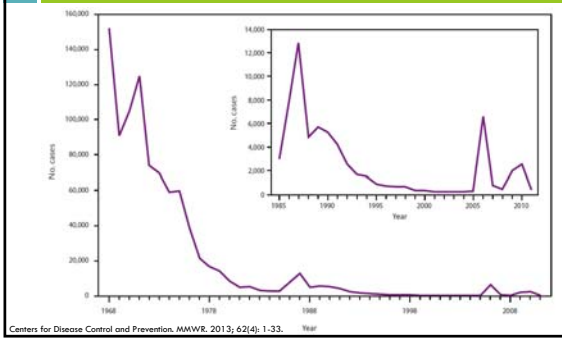
Centers for Disease Control and Prevention. MMWR. 2013; 62(4): 1-33.

Measles Epidemiology



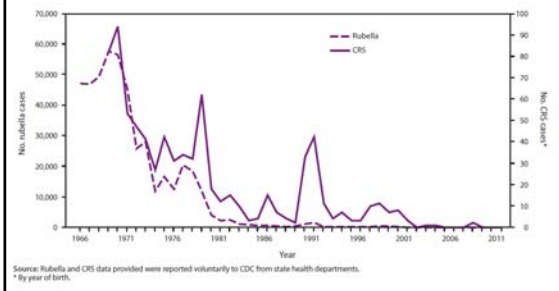
Centers for Disease Control and Prevention. MMWR. 2013; 62(4): 1-33.

Mumps Epidemiology



Centers for Disease Control and Prevention. MMWR. 2013; 62(4): 1-33.

Rubella Epidemiology



Source: Rubella and CRS data provided were reported voluntarily to CDC from state health departments.
* By year of birth.

Centers for Disease Control and Prevention. MMWR. 2013; 62(4): 1-33.

Rotavirus

Background	- Double-stranded RNA virus
Epidemiology	Pre-vaccine: 2.7 million episodes 55,000-70,000 hospitalizations 20-60 deaths
Transmission	- Fecal-oral contamination
Incubation	- < 48 hours
Symptoms	- Fever, vomiting - Mild, watery diarrhea - Severe dehydrating gastroenteritis
Treatment	- Supportive care

Centers for Disease Control and Prevention. MMWR. 2009; 58(No. RR-2): 1-21.

Vaccinate!

- Tremendous impact on the burden of disease in the United States
- Anti-vaccine movement
- Increased risk of wild-type infection in children

Image: http://img.medicalxpress.com/newman/gfx/news/hires/2012/protectingch.jpg

FLU VACCINE

Question #1

JB, a 5 year old boy, presents to your clinic for a sick visit. He has a mild respiratory illness with congestion. Tmax is 38.1C, rapid strep and flu tests are negative. You notice he has not received his annual influenza vaccine. Is it appropriate to vaccinate at this visit?

A. Yes
B. No
C. I am not sure

Centers for Disease Control and Prevention: Vaccination Safety.

Question #1.5

JB, a 5 year old boy, presents to your clinic for a sick visit. He has a mild respiratory illness with congestion. Tmax is 38.1C, rapid strep and flu tests are negative. You notice he has not received his annual influenza vaccine. **You also identify he has an egg-allergy.** Is it appropriate to vaccinate at this visit?

A. Yes
B. No
C. I am not sure

Centers for Disease Control and Prevention: Vaccination Safety.

Flu Vaccine Myths

Acute Illness

- No evidence of reduced efficacy or increased adverse events
- Includes: mild URI, otitis media, diarrhea, etc. , with OR without fever
- OK to vaccinate if on antibiotics

Egg-Allergy

- All children with egg allergy can receive any influenza vaccine
- No additional precautions needed

Centers for Disease Control and Prevention: Vaccination Safety.
AAP Committee on Infectious Diseases. *Pediatrics*. 2017; 140(4):e20172550.

Question #2

JB, a 5 year old boy, is in your clinic for a well child check. You realize he has not received his influenza vaccine. When you discuss with Mom, she mentions she has only ever had the flu when she got the shot and "it doesn't even work this year". How do you respond?

A. Agree with her and recommend against vaccination
B. Continue to recommend vaccination
C. Not sure

Centers for Disease Control and Prevention: Vaccination Safety.

Flu Vaccine Myths

- Interim vaccine efficacy study
- Included 4,562 children and adults from 11/2/17 until 2/3/18 at 5 centers
- Overall adjusted vaccine effectiveness = 36%
  - 25% against H3N2
  - 67% against H1N1
  - 42% against influenza B
  - Children 6 months to 8 years = 59%
- Will still aid in prevention of hospitalization and death

Flannery B, Chung JR, Belongia EA, et al. MMWR. 2018; 67:180-185.

ANTIBODY CONTAINING PRODUCTS AND VACCINES

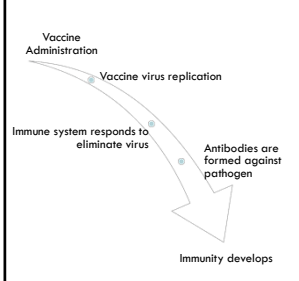
Question #3

JB, a 12 month old boy, is in your clinic for a well child check and his 1 year old vaccines. After reviewing his record, you see that he was treated for Kawasaki disease last month with IVIg and aspirin. Should you proceed with his vaccines (PCV13, Flu, MMR, Varicella); or, should you delay vaccination?

A. Provide all vaccines today
B. Delay all vaccines today
C. Provide PCV13 & Flu today and delay MMR and Varicella

Centers for Disease Control and Prevention: Vaccine Recommendations and Guidelines of the ACIP- Timing and Spacing of Immunobiologics. Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html

Antibody Containing Products



Vaccines affected

- MMR
- Varicella

Vaccines NOT affected

- Yellow Fever
- Typhoid
- Rotavirus
- Zoster
- LAIV

Centers for Disease Control and Prevention: Vaccine Recommendations and Guidelines of the ACIP- Timing and Spacing of Immunobiologics. Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html

Antibody Containing Products

- Blood Transfusion
- Hepatitis A/B Immune Globulin
- CMV Immune Globulin
- Botulinum Immune Globulin
- IVIg*
- Varicella Immune Globulin
- Tetanus Immune Globulin
- Measles Immune Globulin
- Rabies Immune Globulin

Centers for Disease Control and Prevention: Vaccine Recommendations and Guidelines of the ACIP- Timing and Spacing of Immunobiologics. Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html

IVIg Dose and Timing of MMR/Varicella

Indication	Total Dose	Interval
Replacement for Immune Deficiency	300-400 mg/kg IV	8 months
Immune Thrombocytopenic Purpura (ITP)	400 mg/kg IV 800 mg/kg IV	8 months 10 months
Measles contact prophylaxis	400 mg/kg IV	8 months
Post-exposure varicella prophylaxis	400 mg/kg IV	8 months
Kawasaki Disease	2 g/kg IV	11 months

Determine if product administered → Determine dose → Schedule follow up for vaccination

Centers for Disease Control and Prevention: Vaccine Recommendations and Guidelines of the ACIP- Timing and Spacing of Immunobiologics. Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html

SECONDARY TRANSMISSION OF LIVE VACCINES

Question #4

JB, a 12 month old boy, is in your clinic for a well child check and his 1 year old vaccines. His Mom notes his grandma is staying with them and she is undergoing chemotherapy for breast cancer. Should you proceed with his vaccines (PCV13, Flu, MMR, Varicella); or, should you delay vaccination?

A. Provide all vaccines today
B. Delay all vaccines today
C. Provide PCV13 & Flu today and delay MMR and Varicella
D. Not sure

Centers for Disease Control and Prevention: Yellow Book

Lack of transmission of the live attenuated varicella vaccine virus to immunocompromised children after immunization of their siblings

Diaz PS, Au D, Smith S, et al.
Pediatrics. 1991; 87(2): 166-170.

Diaz PS, et al.

Lack of transmission of the live attenuated varicella vaccine virus to immunocompromised children after immunization of their siblings	
Design	- Prospective interventional study in Stanford, California
Patients	- 37 healthy siblings of 30 immunocompromised children with malignancy - 26 receiving maintenance chemotherapy
Intervention/ Assessment	- Measured oropharyngeal cultures - IgG antibodies to VZV measured
Outcomes	- 1 vaccinee had a rash after immunization at injection site - 1 immunocompromised child developed varicella rash - 29/30 immunocompromised siblings had no antibodies at 2 months - 6 vaccinees developed mild varicella after known exposure
Conclusions	- Transmission possible from immunocompromised children with natural infection to healthy siblings - Healthy vaccinees did not transmit to immunocompromised children - Appears risk is related to rash in vaccinnee, not immune status of contact

Diaz PS, Au D, Smith S, et al. Pediatrics. 1991; 87(2): 166-170.

Varicella Summary

Shedding?	• Yes: if development of skin lesions
Transmission?	• Rare • Limited to cases where vaccinee developed skin lesions
Administer?	• Yes • Avoid contact with immunocompromised if skin lesions develop

Horizontal transmission of a human rotavirus vaccine strain- a randomized, placebo-controlled study in twins

Rivera L, Mendez Pena L, Stainier I, et al.
Vaccine. 2011; 29: 9508-9513.

Rivera L, et al.

Horizontal transmission of a human rotavirus vaccine strain- a randomized, placebo-controlled study in twins	
Design	- Phase III, randomized, placebo-controlled, double-blind study in the Dominican Republic
Patients	- Pairs of healthy twins aged 6-14 weeks (GA ≥32 weeks) - Exclusion criteria: - Investigational drug within the last 30 days, immunosuppressed, chronic GI illness, or active illness at time of enrollment

Intervention/ Assessment	- Vaccine strain in stool of placebo group at any time-point considered positive transmission case
	  - Before vaccine/placebo administration
	  - 3x/week up to 6 weeks after dose 1&2, 7 weeks after 2nd dose
	- Stool analyzed with ELISA, confirmation performed with reverse PCR
	- Immunogenicity assessed pre-vaccination, 7 weeks after 2nd dose
	- Safety outcomes:
	  - Gastroenteritis
	  - Intussusception

Rivera L, Mendez Pena L, Stainier I, et al. Vaccine. 2011; 29: 9508-9513.

Rivera L, et al.

Horizontal transmission of a human rotavirus vaccine strain- a randomized, placebo-controlled study in twins	

Outcomes	- Mean age 8.2 weeks
	- 15/80 cases of transmission identified
	- None of the 15 transmission associated with GI effects
	- 50 infants in vaccine group seroconverted
	- 17 infants in placebo group seroconverted
	- 1 possible case of vaccine associated gastroenteritis
	- 11 infants had "serious adverse events"
	  - Bronchiolitis and gastroenteritis most common
	  - No fatalities or intussusception

Conclusion	- Transmission of rotavirus vaccine strain occurred in twins living in the same household - Not associated with any safety concerns

Rivera L, Mendez Pena L, Stainier I, et al. Vaccine. 2011; 29: 9508-9513.

Comparative evaluation of safety and immunogenicity of two dosages of oral live-attenuated human rotavirus vaccine

Dennehy PH, Brady RC, Halperin SA, et al.

Ped Infect Dis J. 2005; 24: 481-488.

Dennehy PH, et al.

Comparative evaluation of safety and immunogenicity of two dosages of an oral live attenuated human rotavirus vaccine	
Design	- Randomized, double-blind study in the United States and Canada

Patients	- Healthy infants 5-15 weeks of age (mean 8.7 weeks)
	- Exclusion criteria:
	  - <36 weeks gestational age
	  - Chronic GI illness
	  - Immunosuppressed OR immunosuppressed household contact
	  - Pregnant household contact

Intervention/ Assessment	- 2 doses of HRV 5.2, HRV 6.4, or placebo separated by 7 weeks - Parent/guardian maintained diary - Laboratory analysis - Prior to vaccination, 2 months after dose 2, at end of study - Stool collected on day of administration and 7 days after vaccine doses - Stool collected on 2 different days within 7 days of onset of symptoms

Dennehy PH, Brady RC, Halperin SA, et al. Pediatr Infect Dis J. 2005; 24: 481-488.

Dennehy PH, et al.

Comparative evaluation of safety and immunogenicity of two dosages of an oral live attenuated human rotavirus vaccine	

Results	- 212 received HRV 5.2, 209 received HRV 6.4,108 received placebo
	- Safety outcomes:
	  - No difference in fever, diarrhea, vomiting during first 15 days
	  - Most common non-serious events were URI and otitis media
	  - 21 serious adverse events (similar between groups)
	  - 6 cases of GI symptoms
	- Immunogenicity
	  - Seroconversion: 67.4%, 78.2%, 6.3%
	  - Vaccine virus shed in stool: 54.1%, 58.2%, 2.6%

Conclusion	- No significant difference in AE between vaccine and placebo

Dennehy PH, Brady RC, Halperin SA, et al. Pediatr Infect Dis J. 2005; 24: 481-488.

Rotavirus Summary

Shedding?	• Yes
Transmission?	• Yes • No reported cases of symptomatic infection
Administer?	• Yes • Severely immunosuppressed should not handle diapers for 4 weeks

MMR Summary

Shedding?	• Measles: no • Mumps: no • Rubella: yes
Transmission?	• No (only through breast milk)
Administer?	• Yes

VACCINES AND AUTISM

Vaccines and Autism

- Theory #1: MMR vaccine damages intestinal lining
- Theory #2: Thimerosal is toxic to the CNS
- Theory #3: Simultaneous administration overwhelms/weakens the immune system

Theory #1: MMR Vaccine

- 12 children
- Chronic enterocolitis and regressive developmental disorder
- Endoscopy with biopsies, MRI, EEG (with evoked potentials), and LP conducted
- Variety of labs collected
- Infectious and vaccine history obtained

Wakefield AJ, Murch SH, Anthony A, et al. Lancet. 1998; 351(1903): 637-641. [RETRACTED FEBRUARY 2010]

Theory #1: MMR Vaccine

- "In 8 children, the onset of behavioral problems had been linked, either by the parents or by the child's physician, with measles, mumps, and rubella vaccination".
- Review of endoscopic findings and histology
- Discussion
  - Potential association between GI disease and behavioral problems
  - Anemia and IgA deficiency may support hypothesis
  - Temporal relationship of vaccine administration and onset of behavioral issues

Wakefield AJ, Murch SH, Anthony A, et al. Lancet. 1998; 351(1903): 637-641. [RETRACTED FEBRUARY 2010]

Theory #1: MMR Vaccine

- Intestinal inflammation allows translocation of peptides that could enter the brain and alter development
- Significant limitations
  - Methods
    - No control group
    - Self-referred patients
    - Un-blinded, data collection not systematic
  - Autism presents around when children receive MMR vaccine
  - Not all children with GI illnesses have autism
  - No evidence to prove hypothesis
  - Financial interests
- Many studies* refute this claim and show no association

Wakefield AJ, Murch SH, Anthony A, et al. Lancet. 1998; 351(1903): 637-641. [RETRACTED FEBRUARY 2010]
Gerber JS, Offit PA. Clinical Infectious Diseases. 2009; 48: 456-461.
Sathyanarayana Rao TS, Andrade C. Indian J Psychiatry. 2011; 53(2): 95-96.

Theory #2: Thimerosal

- Preservative utilized in vaccines
- Implication in autism is far-fetched
  - Mercury poisoning differs significantly from autism
- At least 7 studies show no association
- Thimerosal has been removed from ALL childhood vaccines (except multi-dose flu) since 2001

Gerber JS, Offit PA. Clinical Infectious Diseases. 2009; 48: 456-461.
Image: http://hamiltonsthoughts.com/unsafe-thimerosal-or-mercury-in-vaccines/

Theory #3: Overwhelm/Weaken Immune System

- Autism can develop in a child due to vaccine interaction with the immune system and CNS
- Immune system (even as an infant) can adequately respond to vaccines
- Immunologic load has decreased over time
  - <200 bacterial and viral proteins in 14 vaccines vs. >3000 in the 7 vaccines available in 1980
- Vaccines do not suppress immune system
- No known association of autism with immune system

Gerber JS, Offit PA. Clinical Infectious Diseases. 2009; 48: 456-461

2018 Schedule Updates

2018 Updates

General

- Table with brand names of vaccines
- Footnotes simplified

Medical Conditions

- Specific laboratory parameters for patients with HIV and utilization of live vaccines
- Increased guidance for pneumococcal vaccination

Hepatitis B

- Guidance for vaccination of babies weighing <2,000 grams

Robinson CL, Romero JR, Kempe A, et al. MMWR. 2018; 67: 156-157.

2018 Updates

Flu

- Confirms LAIV should not be utilized this season

MMR

- Guidance for 3rd dose of vaccine during mumps outbreak

Meningococcal

- Separate footnotes for meningococcal conjugate vaccine and meningococcal B vaccine

Robinson CL, Romero JR, Kempe A, et al. MMWR. 2018; 67: 156-157.

2018 Updates

Polio

- Catch up schedule clarified
- Guidance for vaccination of those that received oral polio vaccine as part of series

Rotavirus

- Maximum ages added

Robinson CL, Romero JR, Kempe A, et al. MMWR. 2018; 67: 156-157.

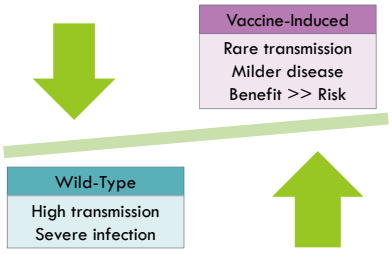
Available Guidelines

Guidelines

- Centers for Disease Control and Prevention
  - Immunizations schedules
  - Pink Book
  - Yellow Book
  - Website
- Advisory Committee on Immunization Practices
- Infectious Diseases Society of America (IDSA)

Take Home Points

Take Home Points



Take Home Points

- You will encounter vaccine misconceptions and parental refusal
- Risk of harm
  - Great enough to report to DSS?
  - Risk of contracting illness and morbidity of illness
- Provide parents with risk/benefit information and attempt to correct misconceptions utilizing available resources
- Child well-being should ALWAYS be primary focus

"Progress is impossible without change, and those who cannot change their minds cannot change anything."

- George Bernard Shaw

QUESTIONS?

Image: http://4s50.files.wordpress.com/2010/08/question-mark-image-7-1-102.jpg

MYTH-BUSTERS: CHILDHOOD VACCINES

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February 21st, 2018