

Vaccines: They've Got To Be Used To Work – Lessons from the 2015 Measles Outbreak

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Video Communications and Distance Learning Division

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Disclosures

- I have no current financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity
- Within the past 24 months, I have received research support from Gilead and GSK
 - All monies go directly to UAB and not to me
- I do intend to discuss an unapproved / investigative use of a commercial product / device in my presentation

Rationale For This Presentation

- Vaccines are the most effective medical advance ever created
- Parents too frequently resist having their children vaccinated
- The reality of vaccine confidence and hesitancy impacts pediatricians' work lives every day

Rationale For This Presentation

- More importantly, individual decisions to not vaccinate put vulnerable children and adults at risk

Ten Greatest Public Health Achievements United States, 1900-1999

- Vaccination
- Motor-vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary heart disease and stroke

Ten Greatest Public Health Achievements United States, 1900-1999

- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard

Vaccine Prevention in the 20th Century

- At the beginning of the 20th century
 - Infectious diseases were the most serious threat to human life and well - being
 - 16 out of every 100 children born at the turn of the century died of an infectious disease before the age of 5 years

Vaccine Prevention in the 20th Century

- During the course of the 20th century
 - 300,000,000 people would have died of a vaccine - preventable disease if they had not been vaccinated
 - 160,000,000 people estimated to have been killed in all wars combined during the same century

Reduction in Vaccine - Preventable Diseases, U.S.

Disease	20th Century Annual Morbidity	2013 Reported Cases	Percent Decrease	Annual Deaths Prevented
Smallpox	29,005	0	100%	337
Diphtheria	21,053	0	100%	1,822
Measles	530,217	184	> 99%	440
Mumps	162,344	438	> 99%	39
Pertussis	200,752	24,231	88%	4,007
Polio (paralytic)	16,316	0	100%	1,879
Rubella	47,745	9	> 99%	17
Congenital Rubella	152	0	100%	16
Tetanus	580	19	97%	468
<i>Haemophilus influenzae</i>	20,000	18	> 99%	995

AAP Committee on Infectious Diseases (Red Book Committee)

- 12 Committee Members (voting)
- 1 Section on Infectious Diseases Member (voting)
- 4 Ex Officio Members (Red Book editor and associate editors)

AAP Committee on Infectious Diseases (Red Book Committee)

- 12 Liaisons
 - Canadian Paediatric Society (2)
 - CDC (2)
 - National Vaccine Program (2)
 - NIH
 - FDA (2)

AAP Committee on Infectious Diseases (Red Book Committee)

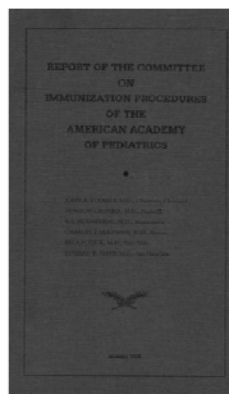
- American Thoracic Society
- COPAM
- Pediatric Infectious Diseases Society

AAP Committee on Infectious Diseases (Red Book Committee)

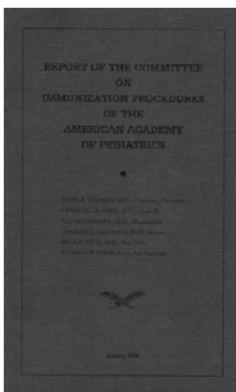
- Committee members appointed for 6 year terms
- Selection influenced by expertise and geography
 - AAP District and Chapter involvement
- Spring and Fall meetings
- Committee members serve as liaisons to ACIP Working Groups

AAP Committee on Infectious Diseases (Red Book Committee)

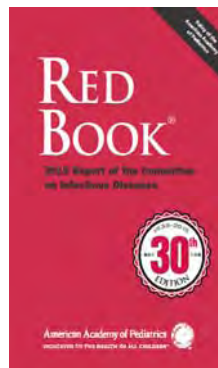
- Red Book® published every 3 years
- Work on next edition begins immediately
- Chapters distributed to primary authors for revision
- CDC and FDA review
- Marathon Meeting in Spring of year prior to publication



- Common Cold
- Diphtheria
- Epidemic Encephalitis
- Erysipelas
- Epidemic Meningitis
- Epidemic Parotitis
- Pertussis
- Pneumonia
- Poliomyelitis
- Rabies



- Measles
- Scarlet Fever
- Staphylococcus
- Infections
- Tetanus
- Tuberculosis
- Typhoid Fever
- Varicella
- Variola



- Author: Committee on Infectious Diseases
 - David W. Kimberlin, MD, FAAP, Editor
 - Michael T. Brady, MD, FAAP, Associate Editor
 - Mary Anne Jackson, MD, FAAP, Associate Editor
 - Sarah S. Long, MD, FAAP, Associate Editor

ACIP History and Charge

- Established by the Surgeon General in 1964
- Provide expert external advice to the CDC Director on use of vaccines in the United States civilian population
- Develop written policy recommendations for FDA - licensed vaccines and related biologics to prevent infectious diseases

Factors Considered by ACIP

- Disease burden (i.e., incidence, morbidity, mortality)
- Vaccine safety and efficacy
- Cost effectiveness

ACIP Members

- Voting members with various expertise (n=15)
- Ex officio members representing federal agencies (n=8)
- Liaison organizations with interests in vaccine development, licensure, and administration (n=26)

Selected Liaison Organizations

- American Academy of Pediatrics (AAP)
- American Academy of Family Physicians (AAFP)
- American College Health Association (ACHA)
- American College of Obstetricians and Gynecologists (ACOG)

Selected Liaison Organizations

- American Medical Association (AMA)
- Council of State and Territorial Epidemiologists (CSTE)
- Infectious Diseases Society of America (IDSA)
- Pediatric Infectious Diseases Society (PIDS)

Selected Liaison Organizations

- National Association of Pediatric Nurse Practitioners (NAPNAP)
- Pharmaceutical Research and Manufacturers of America (PhRMA)

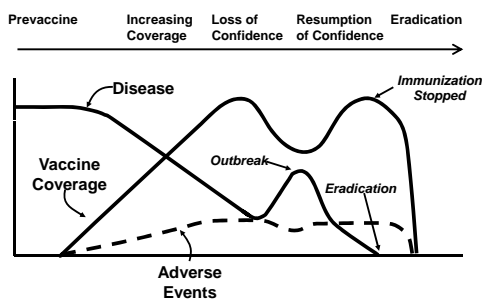
ACIP Recommendations

- “Provisional” recommendations approved by ACIP are posted on the CDC website
- Recommendations are then reviewed by CDC and approved by CDC Director
- Final recommendations are published in MMWR

Progression of an Immunization Program

- Decreased incidence of vaccine - preventable disease
- Decreased awareness of risks associated with disease
- Increased relative prominence of vaccine adverse events
 - Media attention
- Loss of public confidence

Progression of an Immunization Program



Chen, in Vaccines, Plotkin and Orenstein (eds), 1998, 1144-1163

Risk Perception

- Individuals differ in their perception of risk depending on personality, education, and life experience
- Voluntary risks are usually more acceptable than involuntary risks
- Many persons prefer the consequences of inaction rather than action

Vaccine Concerns: Not A New Phenomenon

- “In 1736 I lost one of my Sons a fine Boy of 4 Years old, by the SmallPox taken in the common way. I long regretted bitterly and still regret that I had not given it to him by Inoculation; this I mention for the Sake of Parents, who omit that Operation on the Supposition that they should never forgive themselves if a Child died under; my Example showing that the regret may be same either way, and that therefore the safer should be chosen.”

– Benjamin Franklin

The Epidemiology of Vaccine Refusal

- “The study of what is upon the people”
 - *epi*, Greek meaning “upon, among”
 - *demos*, meaning “people, district”
 - *logos*, meaning “study, word, discourse”
- The study of the patterns, causes, and effects of health and disease conditions in defined populations

The Epidemiology of Vaccine Refusal

- Don't care
 - REJECT – parents today love their children just as much as in prior eras
- Ignorant about risks
 - POSSIBLE – the success of vaccines eliminates seeing the risks associated with the diseases

The Epidemiology of Vaccine Refusal

- Lack of trust
 - DEFINITE – no trust in virtually any institution any longer (government, church, corporations, etc.)
- FEAR
 - ROOT CAUSE – still working on understanding why...

Myths Employed By Anti - Vaccine Movement

- Too many vaccines and vaccine antigens
- Giving vaccines too early in infancy
- Spreading out vaccines is better
- “Bad things” are in vaccines

Recommended Childhood Immunization Schedule, 1983

	0	1 mo	2 mos	4 mos	6 mos	12 mos	15 mos	18 mos	24 mos	4-6 yrs	14-16 yrs
Diphtheria, Tetanus, Pertussis			DTP	DTP	DTP			DTP	DTP		Td
Polio (trivalent)			OPV	OPV				OPV		OPV	
Measles, Mumps, Rubella							MMR				

Immunogenic Proteins and Polysaccharides in Vaccines

1900		1960		1980		2000		2011	
Vaccine	Prot.	Vaccine	Prot.	Vaccine	Prot.	Vaccine	Prot.	Vaccine	Prot.
Smallpox	~200	Smallpox	~200	Diphtheria	1	Diphtheria	1	Diphtheria	1
		Diphtheria	1	Tetanus	1	Tetanus	1	Tetanus	1
		Tetanus	1	WC Pertussis	~3000	AC Pertussis	2-5	AC Pertussis	2-5
		WC Pertussis	~3000	Polio	15	Polio	15	Polio	15
		Polio	15	Measles	10	Measles	10	Measles	10
				Mumps	9	Mumps	9	Mumps	9
				Rubella	5	Rubella	5	Rubella	5
				Hib conj.	2	Hib conj.	2	Hib conj.	2
				Varicella	69	Varicella	69	Varicella	69
				Pncumo conj.	8	Pncumo conj.	8	Pncumo conj.	8
				Hepatitis B	1	Hep A and B	5		
								Rotavirus	15
								Influenza	8
1	~200	5	~3217	7	~3041	11	123-126	14	150-153

Myths Employed By Anti - Vaccine Movement

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Are Infants Too Young to be Vaccinated?

- From birth, infants are challenged by bacteria in the environment (colonizing bacteria on intestines, skin, and throat; bacteria inhaled on dust)
- Vigorous sIgA responses within the first week of life keeps colonizing bacteria from invading

Myths Employed By Anti - Vaccine Movement

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Dr. Bob’s Alternative Vaccine Schedule

2 months	DTaP, Rotavirus
3 months*	Pc, HIB
4 months	DTaP, Rotavirus
5 months*	Pc, HIB
6 months	DTaP, Rotavirus
7 months*	Pc, HIB
9 months	Polio, Flu (2 doses [†])
12 months	Mumps, Polio
15 months	Pc, HIB
18 months	DTaP, Chickenpox

Alternative Vaccine Schedules

- 13% of responders reported using an alternative vaccine schedule
 - 53% refused certain vaccines
 - 55% delayed vaccines until child older
 - 17% refused all vaccines
 - (2.2% of total)

Alternative Vaccine Schedules

- Among those who followed the CDC / AAP schedule
 - 28% thought alternative schedule was safer than recommended schedule
 - 22% disagreed with the statement that the best vaccination schedule was the one recommended by vaccination experts

Harm in Alternative Schedule

- Not science - or evidence - based
- More likely to induce needle phobia
- Increase time during which children are susceptible to vaccine - preventable diseases
- Responsibility to the waiting room
- No benefit

Myths Employed By Anti - Vaccine Movement

- Too many vaccines and vaccine antigens
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Aluminum

- “The alternative schedule suggests only one aluminum containing vaccine at a time in infant years. By spreading out the shots, you spread out the exposure so infants can process the aluminum without it reaching toxic levels.”

– Robert Sears, *The Vaccine Book*, p. 239

Aluminum

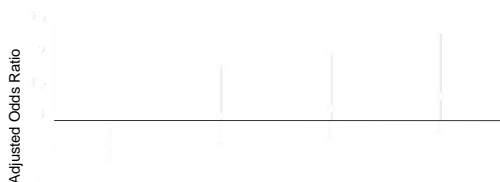
- Aluminum is the third most abundant element on the earth’s surface, and the most abundant metal
- As a consequence, aluminum is in the air we breathe, the food we eat, and the water we drink

Aluminum in Food

- Aluminum is found in breast milk and infant formulas
- By 6 months of age:

– Vaccines	4 mg
– Breast milk	10 mg
– Infant formula	30 mg
– Soy formula	120 mg

Influencing Parental Intent to Vaccinate



Complications of Measles

- Diarrhea (8%)
- Otitis media (7-10%)
- Pneumonia (6%)
- Inclusion body encephalitis (1:1000 cases)
- Acute disseminated encephalomyelitis (ADEM)

Complications of Measles

- Subacute sclerosing panencephalitis (SSPE)
 - ~ 7-10 years after infection
 - 6.5-11 per 100,000 cases
- Keratitis

Complications of Measles

- Hospitalization
 - 19% of cases
- Death (60% from pneumonia)
 - 1-3:1000 cases
- Can cause miscarriages, premature birth or preterm labor in non - immune pregnant women

The Global Perspective on Measles

- In 2012, there were 122,000 measles deaths globally – 330 deaths every day, or 14 deaths every hour

The U.S. Perspective on Measles

- 1962: Challenge to eradicate measles (Langmuir)
 - 1963: 1 - dose recommendation (age 9 mos)
 - 1965: 1 - dose recommendation (age 12 mos)

The U.S. Perspective on Measles

- 1966: 1st measles elimination goal (Sencer et al.)
 - 1967: 1 - dose recommendation (age 15 mos)
- 1978: 2nd measles elimination goal (Hinman et al.)

The U.S. Perspective on Measles

- 1989 - 91: Measles resurgence
 - 1989: 2 - dose recommendation (ages 15 mos and 4-6 years)
- 1993: 3rd measles elimination goal (initiation of VFC)
 - Outbreaks > 1 year ceased

The U.S. Perspective on Measles

- 1994: 2 - dose recommendation (ages 12-15 mos and 4-6 years)
- 2000: Elimination declared

Measles in the U.S., 2014 (Provisional Data)

- 668 cases reported from 28 states, including 23 outbreaks
 - 60 importations (25 from the Philippines)
 - 99% of cases were import - associated
 - 86% of cases were outbreak - associated
 - 77 cases (12%) hospitalized

Measles in the U.S., 2014 (Provisional Data)

- Cases in U.S. residents (n=658)
 - 76% unvaccinated
 - 16% unknown vaccination status (70% of those adults)
 - 9% vaccinated (including 5% with 2 or more doses)

Measles in the U.S., 2014 (Provisional Data)

- Among unvaccinated
 - 80% were personal belief exemptors
 - 2% travelers with missed opportunities age 6 mos to 4 years
 - 8% too young to vaccinate
 - 10% unknown / other

Measles in the U.S., 2015

Provisional Reports to CDC through 4/10/15

- 159 cases reported from 18 states plus D.C., including 4 outbreaks
 - 10 importations
 - 97% of cases were import - associated
 - 27 cases (16%) hospitalized

Measles in the U.S., 2015

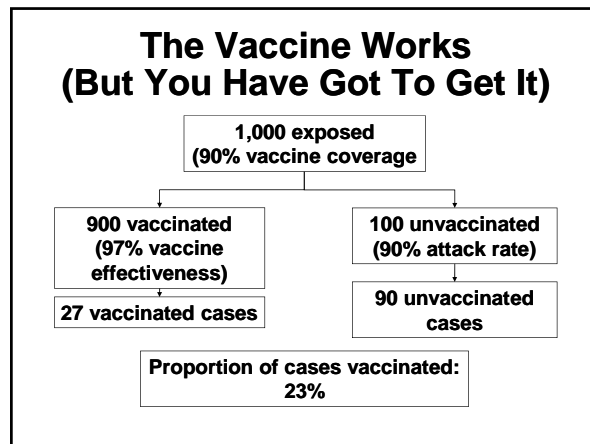
Provisional Reports to CDC through 4/10/15

- Cases in U.S. residents (n=155)
 - 44% unvaccinated
 - 38% unknown vaccination status
 - 18% vaccinated (including 7% with 2 or more doses)

Measles in the U.S., 2015
 Provisional Reports to CDC through 4/10/15

– Among unvaccinated

- 43% were personal belief exemptors
- 35% too young to be vaccinated
- 22% unknown / other



Impact of Vaccine Efficacy and Coverate on Case Distribution*

Example	Vaccine Efficacy (%)	Vaccine Coverage (%)	Attack Rate (%)	Vaccinated Cases	Unvaccinated Cases	Proportion of Cases Vaccinated (%)
Comparator	97	90	90	27	90	23
↓ Efficacy	88	90	90	108	90	55
↓ Coverage	97	85	90	26	135	16

* Theoretical 1,000 Person Cohort

Effects of the 2015 Disneyland Measles Outbreak

- Parents of vaccinated children are mad
- Social media is applying peer pressure that has not been present in prior importations and outbreaks
- State lawmakers are beginning to respond

Status of Bills Related To Exemptions in 2015 Legislative Year

- States with bills and rules that have been enacted:
 - Colorado
 - Montana
 - West Virginia

Status of Bills Related To Exemptions in 2015 Legislative Year

- States with bills that are still viable in current legislative session:
 - California
 - Connecticut
 - Delaware
 - Illinois
 - Maine
 - Massachusetts
 - Michigan
 - Missouri

Status of Bills Related To Exemptions in 2015 Legislative Year

- States with bills that are still viable in current legislative session:
 - New Jersey – Texas
 - New York – Vermont
 - Oregon
 - Pennsylvania

Take - Home Points

- Vaccines save hundreds of thousands of lives every year
- Scientific evidence has proven vaccines are safe
 - Strongly affirmed in recent Institute of Medicine report
- Despite proof, parents are more anxious than ever

Take - Home Points

- We must speak plainly, directly, and passionately, emphasizing:
 - The need to vaccinate each and every child according to scientifically - proven schedule
 - The safety of vaccines
- Additional research into effective messaging needed

References

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- ACIP History and Charge; Smith et al. Ann Intern Med 2009; 150:45
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- Risk Perception; CDC, 1999
- Alternative Vaccine Schedules; A. F. Dempsey, et al, "Alternative Vaccine Schedule Among Parents of Young Children," Pediatrics doi:10.1542/peds.2011-0400

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- Heuristic Psychology; Smith, Appleton, MacDonald. Adv Exp Med Biol 2013;764:81-98