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

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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 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.

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Mortality</th>
<th>2013 Reported Cases</th>
<th>Percent Decrease</th>
<th>Annual Deaths Prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>29,005</td>
<td>0</td>
<td>100%</td>
<td>337</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21,053</td>
<td>0</td>
<td>100%</td>
<td>1,822</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>184</td>
<td>&gt; 99%</td>
<td>440</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>438</td>
<td>&gt; 99%</td>
<td>39</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>24,231</td>
<td>88%</td>
<td>4,667</td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>16,316</td>
<td>0</td>
<td>100%</td>
<td>1,879</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>9</td>
<td>&gt; 99%</td>
<td>17</td>
</tr>
<tr>
<td>Congenital Rubella</td>
<td>152</td>
<td>0</td>
<td>100%</td>
<td>16</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>19</td>
<td>97%</td>
<td>468</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>20,000</td>
<td>18</td>
<td>&gt; 99%</td>
<td>595</td>
</tr>
</tbody>
</table>

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)

- American Thoracic Society
- COPAM
- Pediatric Infectious Diseases Society

#### Committee Information

- 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

#### Red Book

- 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

#### Topics Covered

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

#### Authorship

- 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

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

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

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>12 mos</th>
<th>18 mos</th>
<th>24 mos</th>
<th>4-6 yrs</th>
<th>14-16 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria, Tetanus, Pertussis</td>
<td>DTP</td>
<td>DTP</td>
<td>DTP</td>
<td>DTP</td>
<td>DTP</td>
<td>Td</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polio (inactivated)</td>
<td>OPV</td>
<td>OPV</td>
<td>OPV</td>
<td>OPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mumps, MMR, Rubella</td>
<td>MMR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Immunogenic Proteins and Polysaccharides in Vaccines

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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

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

Dr. Bob’s Alternative Vaccine Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>DTaP, Rotavirus</td>
</tr>
<tr>
<td>3 months*</td>
<td>Pc, HIB</td>
</tr>
<tr>
<td>4 months</td>
<td>DTaP, Rotavirus</td>
</tr>
<tr>
<td>5 months*</td>
<td>Pc, HIB</td>
</tr>
<tr>
<td>6 months</td>
<td>DTaP, Rotavirus</td>
</tr>
<tr>
<td>7 months*</td>
<td>Pc, HIB</td>
</tr>
<tr>
<td>9 months</td>
<td>Polio, Flu (2 doses!)</td>
</tr>
<tr>
<td>12 months</td>
<td>Mumps, Polio</td>
</tr>
<tr>
<td>15 months</td>
<td>Pc, HIB</td>
</tr>
<tr>
<td>18 months</td>
<td>DTaP, Chickenpox</td>
</tr>
</tbody>
</table>

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
- Giving vaccines too early in infancy
- Spreading out vaccines is better
- "Bad things" are in vaccines

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)
- 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)
  - 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

The Vaccine Works
(But You Have Got To Get It)

Impact of Vaccine Efficacy and Coverage on Case Distribution*

<table>
<thead>
<tr>
<th>Example</th>
<th>Vaccine Efficacy (%)</th>
<th>Vaccine Coverage (%)</th>
<th>Attack Rate (%)</th>
<th>Vaccinated Cases</th>
<th>Unvaccinated Cases</th>
<th>Proportion of Cases Vaccinated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparator</td>
<td>97</td>
<td>90</td>
<td>90</td>
<td>27</td>
<td>90</td>
<td>23</td>
</tr>
<tr>
<td>Efficacy</td>
<td>88</td>
<td>90</td>
<td>90</td>
<td>108</td>
<td>90</td>
<td>55</td>
</tr>
<tr>
<td>Coverage</td>
<td>97</td>
<td>85</td>
<td>90</td>
<td>26</td>
<td>135</td>
<td>16</td>
</tr>
</tbody>
</table>

* 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

Example

1,000 exposed
(90% vaccine coverage)

900 vaccinated
(97% vaccine effectiveness)
100 unvaccinated
(90% attack rate)

27 vaccinated cases
90 unvaccinated cases

Proportion of cases vaccinated: 23%
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

- ACIP History and Charge; Smith et al. Ann Intern Med 2009; 150:45
- Progression of an Immunization Program; Chen, in Vaccines, Plotkin and Orenstein (eds), 1998, 1144-1163
- Risk Perception; CDC, 1999

References

- Influencing Parental Intent to Vaccinate; Nyhan et al. Pediatrics 2014; 133:e835-e842