Addressing Vaccine Concerns

Paul J Carson, MD, FACP

Overview - Goals

- Review the main concerns for vaccine hesitancy and their historical origins
- Review the processes and evidence that assure vaccine safety and necessity
- Discuss what providers can do in the medical encounter to improve vaccine acceptance

Ten Greatest Public Health Achievements in the U.S: 1900–1999*

- Vaccination
- Motor-vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary heart disease and stroke
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard


The Tremendous Impact of Immunization on Our Health

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Mortality</th>
<th>2011 Reported Cases</th>
<th>Percent Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>29,895</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21,053</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>212</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>370</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>15,216</td>
<td>92%</td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>15,216</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,749</td>
<td>4</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>Congenital Rubella Syndrome</td>
<td>152</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>9</td>
<td>98%</td>
</tr>
<tr>
<td>Influenza/Influenza</td>
<td>29,000</td>
<td>8*</td>
<td>&gt; 99%</td>
</tr>
</tbody>
</table>

*Source: JAMA. 2007;298(18):2153–2155

Vaccines have become victims of their own success

Increasingly, parents are skeptical of the safety and necessity of vaccines and are opting out of immunizing their children
### History of the Anti-Vaccine Movement

#### What are the Main Concerns?

- **Birth of the Modern Anti-Vaccine Movement**
  - **Lea Thompson**
  - **Barbara Loe Fisher**
  - *A Shot in the Dark*
  - April 19, 1982

- **A Shot in the Dark**
  - 1985 book claims that DTP vaccine causes neurological damage, including autism
  - Book details 100+ cases of DTP vaccine-induced brain inflammation and immune system dysfunction
    - Including children who developed regressive autism after brain inflammation and encephalopathy following DPT vaccination
  - New DTaP vaccine created

- **Effects of Vaccine Roulette and Shot in the Dark**
  - Media coverage claiming whole-cell pertussis vaccine caused brain damage
  - Flood of lawsuits successfully claiming pertussis vaccine caused SIDS, Reye's Syndrome, coma, mental retardation, epilepsy, and transverse myelitis
  - Price of DTP vaccine rose from $0.19 in 1980 to $12.00 in 1986
  - Number of OPV vaccine makers declined from 3 to 1, measles vaccine makers from 6 to 1, and pertussis vaccine from 8 to 1
  - At President's request, congress stepped in and passed the National Childhood Vaccine Injury Act in 1986

- **Modern Anti-Vaccine Origins**
  - British physician and researcher, gastroenterologist
  - Study published in Lancet 1998
  - Study of 12 children with a history of autism or developmental disorder referred to gastroenterology clinic.
  - Findings:
    - Onset of behavioral symptoms, per parents, started after MMR immunization in 8 of the children
    - Bowel abnormalities in all of the children on endoscopy
  - Conclusions: speculated a connection between bowel pathology after MMR immunization that allowed "toxins" to circulate to brain causing brain damage and autism
Americans Beliefs About Autism and Vaccines

- Online Harris poll of 1756 adults for the National Consumer League in 2013
- Only 39% of parents described themselves as being extremely or very knowledgeable about how vaccines work. Yet........
- 33% of parents of children under 18, and 29% of adults agree with the statement, “vaccinations can cause autism”.

What Do Vaccine-Hesitant Parents Think?

- More likely to believe they can control child’s susceptibility to disease
- Doubt the reliability of vaccine information
- Prefer negative outcomes due to inaction (not vaccinating) versus action (vaccinating)
- More willing to rely on herd immunity to protect their child
- Are frequently unsophisticated at risk-perception (e.g., smallpox vs influenza)
- More likely to believe the diseases are not harmful

What Do Parents Think?

Summary of U.S. Parent/Guardian Survey - 2009

- Vaccinators with no concerns: 43%
- Significant refusers: 4%
- Minor refusers: 10%
- Vaccinators with major concerns: 6%
- Vaccinators with minor concerns: 5%

N = 1,278

ASTHO Survey, 2009

How Hard Is It to Get a Vaccine Exemption by State

Vaccination Rates by State

Percentage of kindergartners vaccinated by state, 2013-2014 school year
### Number of Non-Medical Vaccine Exemptions in the NDIIS (NDDOH 2008 – 2014)

<table>
<thead>
<tr>
<th>Year</th>
<th>Religious</th>
<th>Moral</th>
<th>Philosophic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Vaccination Rates and Parental Exemption Rates For Children Entering Kindergarten or 1st Grade

- **Target for Optimal Herd Immunity**
  - 60%
  - 70%
  - 80%
  - 90%
  - 95%

- **Immunization Rate**
  - 80%
  - 85%
  - 90%
  - 95%
  - 100%

- **Exemption Rate**
  - 2%
  - 1%
  - 0%

### Herd Protection

### Herd Immunity

- [https://www.youtube.com/watch?v=UqKP-ETVvrc](https://www.youtube.com/watch?v=UqKP-ETVvrc)
- The percent of the population that needs to be immune to confer herd immunity varies depending on how infectious is the pathogen:
  - 90-95% for measles
  - 85% for pertussis
- Americans focus on individual, culturally opposed to “public health”

### Measles Immunization and Cases in U.K.

- [Wakefield Paper Published](https://www.youtube.com/watch?v=UqKP-ETVvrc)
- Measles cases in U.S. rise; most unvaccinated, CDC says

### USA TODAY

- Earn Your P.P.I. Online
- Measles cases in U.S. rise; most unvaccinated, CDC says

- Wakefield paper
- Measles cases in U.S. rise; most unvaccinated, CDC says

- USA TODAY
- Earn Your P.P.I. Online
- Measles cases in U.S. rise; most unvaccinated, CDC says

- Wakefield paper
- Measles cases in U.S. rise; most unvaccinated, CDC says
Vaccine Safety

Why the Provider Can be Very Confident

FDA Process for Vaccine Licensure

- Rigorous process to assure safety and efficacy before vaccine is licensed
- Multiple stages
  - File IND – outlines method of manufacture, quality control tests, animal safety and efficacy data, and proposed human clinical trials
  - Pre-licensure trials
    - Phase I – safety and immunogenicity in small number of subjects
    - Phase II – dose ranging studies in hundreds of subjects
    - Phase III – efficacy and safety data collected on thousands of subjects
- Process can take up to 10 yrs before vaccine is licensed

Additional Measures Beyond Usual FDA Process

- Government passed the National Childhood Vaccine Injury Act in 1986
  - Requires health providers to provide a Vaccine Information Statement (VIS)
  - Providers are required to report certain adverse events to the Vaccine Adverse Events Reporting System (VAERS), anyone can report
  - Formed the National Vaccine Injury Compensation Program (NVICP)
  - Tasked the Institute of Medicine to review all science on vaccine safety
- Established the Vaccine Safety Datalink (VSD) collaboration in 1990
- Clinical Immunization Safety Assessment (CISA) Network

No drug, device, process, or procedure in healthcare is as heavily scrutinized and monitored for safety and efficacy as are vaccines!

Specific Parental Concerns

- Risk of autism from the MMR vaccine
- Believe child receives too many shots too soon
- Dangers from the disease are minimal, vaccine not necessary (influenza, chickenpox, neonatal hepatitis B)
- Risks from “toxins” in the vaccines, esp mercury (thimerosol) or aluminum
- Long-term effects of vaccine and possible links to chronic auto-immune disease

Our Brains Are Hardwired to Make Associations

Observation: People who sleep in their shoes frequently wake up with headaches
Conclusion: Going to bed with shoes on causes headaches
Evidence based meta-analysis of vaccines and their association with autism

- 2014 review of 10 well designed studies looking for associations between MMR vaccination and/or thimerosal exposure in children, and the development of autism
- 5 case-control studies, 5 cohort studies

Taylor LE. Vaccine 2014.

Case-Control Studies

- Studies done in USA, Poland, UK, and Japan
- 9,920 total children studied
- No evidence of any association between MMR vaccination, Hg, or thimerosal exposure and any form of ASD

Taylor LE. Vaccine 2014.

Cohort Studies Comparing Risk of Autism/ASD with Exposure to MMR, Mercury, or Thimerosal

- Total number of children studied in these 5 Cohort Studies
  N = 1,256,407
- Avg length of follow up – 8.6 yrs
- Conclusions – No association

Taylor LE. Vaccine 2014.

Cochrane Review of Autism/MMR Link

- Respected independent collaboration that undertakes exhaustive reviews of the medical literature
- Feb 2012 released their review of 27 cohort studies, 17 case-control studies, 5 time-series trials, 1 case cross-over trial, 2 ecological studies, 6 self-controlled case series
- All told – involved 14,700,000 children assessing safety and efficacy of MMR vaccine
- Conclusions: Vaccine was unlikely to be associated with autism, asthma, leukemia, hay fever, diabetes, gait disturbance, Crohns disease, or demyelinating disease
More Childhood Vaccines—But Fewer Antigens

Thanks to advances in technology, vaccines today contain fewer antigens. Even with more vaccines, the total immunologic load is much less.1

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900</td>
<td>200</td>
</tr>
<tr>
<td>1960</td>
<td>1</td>
</tr>
<tr>
<td>1980</td>
<td>1</td>
</tr>
<tr>
<td>2000</td>
<td>~200</td>
</tr>
</tbody>
</table>


“I Prefer to Spread Out the Vaccines”

- 42 in-depth neuropsychological tests performed on 1047 children age 7-10. Outcomes compared between those fully vaccinated on-time, vs those with delayed vaccination.
- In univariate analysis, timely receipt associated with better NP scores on 12/42 tests
- In multivariate analysis (adjusting for social and familiar factors), timely receipt remained independently associated with better performance on:
  - Developmental neuropsychological assessment speeded naming test
  - Scored 2.7 points higher on Wechsler IQ tests

Smith MJ. Pediatrics 2010

Who Do Parents Trust?

- 2009 survey of 2521 parents with children under 17. 62% response rate

<table>
<thead>
<tr>
<th>Treatment</th>
<th># of Children</th>
<th>% of Parents</th>
<th>% of Parental Trust</th>
</tr>
</thead>
<tbody>
<tr>
<td>My child(ren)’s doctor</td>
<td>79</td>
<td>75</td>
<td>2</td>
</tr>
<tr>
<td>Other health care provider</td>
<td>25</td>
<td>70</td>
<td>8</td>
</tr>
<tr>
<td>Government vaccine</td>
<td>25</td>
<td>61</td>
<td>18</td>
</tr>
<tr>
<td>Family and friends</td>
<td>15</td>
<td>67</td>
<td>18</td>
</tr>
<tr>
<td>Celebrities</td>
<td>9</td>
<td>65</td>
<td>27</td>
</tr>
</tbody>
</table>

Freed GL. Pediatrics 2011

Some results in several other studies

Iqbal S. Pharmacoepidemiology and Drug Safety 2013
What can be done at the medical encounter?

What Not To Do

Study Design:
- 2 – wave web-based survey experiment on 1759 parents in U.S.
- 1st wave – surveyed re: attitudes towards vaccination
- 2nd wave - randomly assigned to receive 1 of 4 interventions:
  - CDC information explaining lack of evidence that MMR causes autism
  - Textual information about the dangers of diseases prevented by MMR
  - Images of children with the diseases
  - A dramatic narrative about an infant who almost died

Nyhan. Pediatrics 2014

Results:
- None of the interventions increased parental intent to vaccinate a future child
- Refuting claims of an MMR/Autism link successfully reduced misperceptions that vaccines cause autism; however, it decreased intent to vaccinate among parents who had least favorable vaccine attitudes at preset
- Paradoxical findings:
  - Images of sick children increased expressed belief in a vaccine/autism link
  - Dramatic narrative about infant in danger fr disease increased self-reported belief in serious vaccine side effects
- Conclusion: talking about dangers (either refuting vaccine dangers or highlighting disease dangers) made parents more wary

Nyhan. Pediatrics 2014

How You Frame the Question Study
- Cross-sectional observational study of pediatrician-parent discussions at well-child visits for children age 1-19 mos around topic of vaccination
- Study described to providers and parents only in general terms re: “communication”
- Parents assessed on prior survey for degree of vaccine hesitancy, over-sampled vaccine-hesitant parents
- Video camera recorded the encounter in the pediatrician’s exam room
- Communications experts assessed the manner in which conversation was initiated

Nyhan. Pediatrics 2014
**The C-A-S-E Approach:**

**Robert Jacobson MD, Mayo Clinic**

- **C** – Corroborate the parents concern. Find the area on which you agree. Set tone for respectful, successful dialogue.
  - "What is your main concern"
  - Don’t permit a vague refusal
  - Make parent get specific

- **A** – About me: Describe what you have done to build your knowledge base and expertise.
  - Then
  - That’s a valid question, I glad you take a proactive approach to your child’s health
  - When I heard that, I sought out answers myself
  - We both want your child to be free of illness and injury
  - We both want to avoid unnecessary medications and their side effects

- **S** – Science: relate what the science says

- **E** – Explain and advise your patient based on the science

**About Me**

- Raise doubts about the source of their information and strengthen their natural inclination to trust you, their child’s provider
  - The internet has a lot of information out there that can make things very confusing, but we have to be careful to make sure the sources are reliable
  - Vaccinations represent a major part of my professional effort as your child’s doctor/provider. I consider understanding all the issues around vaccine safety one of the most important aspects of my work
  - I’m committed to your child’s health, and I’ve dedicated my career to that work
  - I’ve been studying medicine and pediatrics now for “x” years
  - One of the areas where I read a great deal is about infections, immunity, and vaccination

**Summary: Framing the Question and Pursuit**

<table>
<thead>
<tr>
<th>Acceptance</th>
<th>Presume</th>
<th>Pursue</th>
<th>Pursue</th>
</tr>
</thead>
<tbody>
<tr>
<td>74%</td>
<td>12%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>88% accept</td>
<td>5% offer mitigated plan</td>
<td>7% reject immunization</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acceptance</th>
<th>Participate</th>
<th>Pursue</th>
<th>Acquiesce</th>
</tr>
</thead>
<tbody>
<tr>
<td>4%</td>
<td>21%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>25% accept</td>
<td>42% offer mitigated plan</td>
<td>33% resist immunization</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acceptance</th>
<th>Participate</th>
<th>Acquiesce</th>
</tr>
</thead>
<tbody>
<tr>
<td>4%</td>
<td>13%</td>
<td>83%</td>
</tr>
<tr>
<td>4% accept</td>
<td>13% offer mitigated plan</td>
<td>83% resist immunization</td>
</tr>
</tbody>
</table>

**Corroborate**

- "What is your main concern"
- Don’t permit a vague refusal
- Make parent get specific

About Me – the Paul Offit Approach

- Recommends being passionate in response to vaccine refusal
- "Look, let me love your child. What you’re really asking me to do is to violate a standard of care. Please don’t put me in that position"

- Regarding vaccine refusal, he comments – "[When you dismiss a patient] you’re saying, ‘It’s so important to me, and you’re making a choice that’s substandard care, and I can’t participate in that position."

![Image](image-url)
Science

- Try to avoid in-depth discussion of side-effects, perceived harms etc. Emphasize safety record and the processes to assure safety
  - “Vaccines are better studied than any other medicine I prescribe or test I order”
  - “Each vaccine is safer than any medicine I prescribe”
  - “Vaccines are not fool-proof, but they are the most effective means to prevent certain injuries and illnesses”
  - “The decision what to give when is based on the vaccine’s effectiveness, safety, and specific need for the child at that particular age”

Explain/Advise

- “That’s why I am recommending this vaccine”
- “If this were my child, I would be vaccinating her today”
- “I made sure my children got these vaccines, and I am very confident this is the best way to keep your child safe and healthy”
- “I got this vaccine”
- “That’s why if I were you, I would be getting these vaccines for your child”

Conclusions of Do’s and Don’t

Do
- Be presumptive.
- Affirm the parent’s desire to do what’s best
- Pursue if meet resistance
- Stick to your guns and strongly advocate
- Highlight your expertise and shared desire to do what’s best for the child
- Refute with science as your last resort

Don’t
- Start the conversation with solicitous language
- Be confrontational, denigrating, or argumentative
- If possible, avoid getting into discussion about dangers (danger priming effect and availability heuristic)
- Fire the patient

Emotion Based Appeals?

- Video images of parents with substantial regrets about choice not to vaccinate
- Nyhan study suggests may not help (but it was pictures or text only)
- Need to validate with further research, but probably worth a try

http://shotbyshot.org/story-gallery/
**Resources**

- AAP: [http://www2.aap.org/immunization/families/safety.html](http://www2.aap.org/immunization/families/safety.html)
- Shot of Prevention: [http://shotofprevention.com/](http://shotofprevention.com/)
- Children’s Hospital of Philadelphia Vaccine Education Center – [http://vec.chop.edu/service/vaccine-education-center/home.html](http://vec.chop.edu/service/vaccine-education-center/home.html)
- Pertussis videos: [http://www.youtube.com/watch?v=Rmlo2to0ogs](http://www.youtube.com/watch?v=Rmlo2to0ogs), [https://www.youtube.com/watch?v=S3oZrMGDMMw](https://www.youtube.com/watch?v=S3oZrMGDMMw)

---

**“Toxins” in Vaccines**

**Dangerous Chemicals?**

- 3-methyl-butyraldehyde
- Ethyl ethanoate
- Tocopherol
- Alpha-terpanine
- Terpinyl-acetate
- Proline
- Octene
- Hexanal
- Benzaldehyde

---

**Common Flaws in Anti-Vaccine Literature**

- Incorrect compound cited for “toxic” effects and limit
- Inaccurate level of exposure reported
- Inaccurate claims of “toxin” presence in all vaccines
- Failure to report “toxin” purpose
- Failure to differentiate acute vs. chronic exposure
- Inaccurate mode of entry referenced
- No understanding of general chemistry and overall fear of “unnatural chemicals”

---

**Components of Vaccines**

<table>
<thead>
<tr>
<th>Type of Ingredient</th>
<th>Purpose</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvants</td>
<td>Improve the body’s immune response to antigens</td>
<td>Aluminum salts</td>
</tr>
<tr>
<td>Preservatives</td>
<td>Prevent contamination</td>
<td>Thimerosal</td>
</tr>
<tr>
<td>Stabilizers</td>
<td>Maintain vaccine potency during transportation and storage</td>
<td>Sorbitol, gelatin</td>
</tr>
<tr>
<td>Residual antibiotics</td>
<td>Prevent contamination by bacteria during manufacturing process</td>
<td>Neomycin</td>
</tr>
<tr>
<td>Residual inactivating ingredients</td>
<td>Kill virus or inactivate toxins during the manufacturing process</td>
<td>Formaldehyde</td>
</tr>
<tr>
<td>Residual cell material</td>
<td>To grow enough of the virus or bacteria to make the vaccine</td>
<td>Egg protein</td>
</tr>
</tbody>
</table>

Source: Centers for Disease Control and Prevention

---

**Paracelsus, “Father of Toxicology”**

1493-1541

“Alle Dinge sind Gift und nichts ist ohne Gift. Allein die Dose macht es, dass ein Ding kein Gift ist.

“The dose makes the poison!”
Thimerosol in Vaccines

- Very effective preservative that prevents bacterial and fungal contamination of vaccines
- Multiple studies have shown it to be safe with no long-term effects
- Removed from all childhood vaccines in 2001. MMR, varicella, and IPV never contained thimerosal
- Still present in multi-dose vials of influenza vaccine (not in individual dose vaccine)

Formaldehyde in Vaccines

- Used to kill the viruses that are used in producing inactivated viral vaccines
- Naturally occurs in many foods and is made by the human body
- Can be toxic when inhaled in large quantities over prolonged periods of time
- The EPA oral reference dose considered safe for long-term exposure is ingesting less than 200 mcg / kg body-weight per day (70 kg man could ingest 14,000 mcg daily for prolonged periods)

Formaldehyde in Vaccines

Concerned about formaldehyde in vaccines? Consider the pear...

- 4 year contains 12,000 mcg of formaldehyde
- Checking contains 130 mcg, that’s 0.008% of the formaldehyde in a pear

Circulating normally in the bloodstream:

- 1100 mcg/mL