Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

Vaccine Safety

Chapter 4

September 2018

Comparison of 20th Century Annual Morbidity and Current Morbidity: Vaccine-Preventable Diseases

Disease	20th Century Annual Morbidity†	2014 Reported Cases ††	Percent Decrease
Diphtheria	21,053	1	> 99%
Measles	530,217	628	> 99%
Mumps	162,344	1,151	99%
Pertussis	200,752	32,971	86%
Polio (paralytic)	16,316	0	100%
Rubella	47,745	8	> 99%
Congenital Rubella Syndrome	152	0	100%
Tetanus	580	21	96%
Haemophilus influenzae	20,000	27*	> 99%
Total	999,159	34,807	97%
Vaccine Adverse Events	Not available	~30,000	Not available

† JAMA. 2007;298(18):2155-2163
†† CDC. MMWR January 9, 2015 / 63(53);ND-733-ND-746. (MMWR 2014 provisional week 53 data)
* *Haemophilus influenzae* type b (Hib) < 5 years of age. An additional 12 cases of Hib are estimated to have occurred among the 226 reports of Hi (< 5 years of age) with unknown serotype.

Importance of Vaccine Safety

- Vaccinations universally recommended or mandated
- Ongoing safety monitoring needed for the development of sound policies and recommendations

Importance of Vaccine Safety

- Decreases in disease risks and increased attention on vaccine risks
- Public confidence in vaccine safety is critical
  - Higher standard of safety is expected of vaccines
  - Vaccinees generally healthy (vs. ill for medications)
  - Lower risk tolerance = need to search for rare reactions
  - Vaccination universally recommended and mandated

What is "Safe"?

- SAFE = No harm from the vaccine?
  No vaccine is 100% safe
- SAFE = No harm from the disease?
  No vaccine is 100% effective
- Remind parents that to do nothing is to take a risk

Pre-licensure Vaccine Safety Studies

- Laboratory
- Animals
- Humans

Pre-Licensure Human Studies

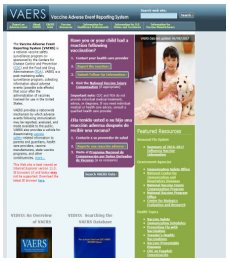
- Phase I, II, III trials
- Phase III trials usually include a control group which receive a placebo
- Common reactions are identified
- Most Phase III trials include 2,000 to 5,000 participants
- Largest recent Phase III trial was REST (rotavirus) – around 70,000 infants

Post-Licensure Surveillance

- Identify rare reactions
- Monitor increases in known reactions - Identify risk factors for reactions
- Identify vaccine lots with increased rates of reactions
- Identify "signals"–reports of adverse events more numerous than would be expected

Vaccine Adverse Event Reporting System (VAERS)

- Jointly administered by CDC and FDA
- National reporting system
- Receives ~30,000 reports per year
- Passive–depends on healthcare providers and others to report



https://vaers.hhs.gov/index

Vaccine Adverse Event Reporting System (VAERS)

- **Detects:**
  - New or rare events
  - Increases in rates of known events
  - Patient risk factors
- **VAERS cannot establish causality**
  - Additional studies required to confirm VAERS signals and causality
- **Not all reports of adverse events are causally related to vaccine**
- **Reportable Events Table (Pink Book Appendix D-2)**

Post hoc ergo propter hoc

"After this therefore because of this"

- **Temporal association does not prove causation**
- **Just because one event follows another does not mean that the first caused the second**

Elements Needed To Assess Correlation of Vaccine Adverse Events

	Disease	No disease
Vaccine	a	b
No vaccine	c	d

$$\frac{\text{Rate in "vaccine" group}}{\text{Rate in "no vaccine" group}} = \frac{a\ /a + b}{c/\ c + d}$$

If the rate in "vaccine" group is higher than the rate in the "no vaccine" group, then vaccines may be the cause

Risk of Autism Spectrum Disorder (ASD) Among Children in Denmark, 1991-1998

	ASD	No ASD
Vaccine	345	440,310
No vaccine	77	96,571

$$\frac{\text{Risk in "vaccine" group}}{\text{Risk in "no vaccine" group}} = \frac{7.83/10{,}000}{7.96/10{,}000}$$

Relative Risk = 0.98

Madsen et al. *N Eng J Med* 2002;347:1477-82

Post-Licensure Vaccine Safety Activities

- **Phase IV Trials**
  - ~10,000 participants
  - Better but still limited
- **Vaccine Safety Data Link**
- **Clinical Immunization Safety Assessment Project (CISA)**

Vaccine Safety Datalink

- **Vaccine Safety Datalink:**
  - Large linked databases
  - Connects vaccination and health records
  - Partnership with large health plans: population under "active surveillance"
    - 9 HMOs
    - 3% (~10 million) of U.S. population
- **Plans, executes immunization safety studies**
- **Investigates hypotheses from medical literature, VAERS reports, changes in schedules, introduction of new vaccines**

- Improve understanding of vaccine safety issues at individual level
- Evaluate individual cases with adverse health events
- Develop strategies to assess individuals
- Conduct studies to identify risk factors

Vaccine Injury Compensation Program

- Established by National Childhood Vaccine Injury Act (1986)
- "No fault" program
- Covers all routinely recommended childhood vaccines
- Vaccine Injury Table (Appendix D-5,D-6)

- Picture of website

Vaccine Injury Compensation Program website: www.hrsa.gov/vaccinecompensation/index.html

The Provider's Role

- Immunization providers can help ensure the safety and efficacy of vaccines through proper:
  - Vaccine storage and handling
  - Timing and spacing of vaccine doses
  - Screening of contraindications and precautions
  - Patient/parent education–benefit and risk communication
  - Vaccine administration
  - Management of adverse reactions
  - Documentation
  - Reporting to VAERS as needed

Common Concerns

Childhood Immunization Schedule and Safety

- **National Academy of Medicine–Mission**
  - Review scientific findings and stakeholder concerns related to the safety of the recommended childhood immunization schedule
  - Identify potential research approaches, methodologies, and study designs that could inform this question
  - Issue a summary report
- **Findings**
  - Committee finds no evidence that the schedule is unsafe
  - Following the complete childhood immunization schedule is strongly associated with reducing vaccine-preventable diseases
  - Committee calls for continued study of the immunization schedule using existing data systems

www.iom.edu/childimmunizationschedule

National Academy of Medicine, August 2011

- **Committee findings:**
  - CAUSAL RELATIONSHIP between some vaccines and adverse events
    - MMR, VZV, Influenza, etc., and anaphylaxis
  - REJECTION OF 5 RELATIONSHIPS
    - Including MMR and autism, TIV and asthma
- **Overall, the committee concluded that few health problems are caused by, or clearly associated with, vaccines**

http://nationalacademies.org/HMD/Reports/2011/Adverse-Effects-of-Vaccines-Evidence-and-Causality.aspx

Multiple Vaccines

- **Early vaccination is important to prevent diseases**
- **Vaccines are given at a young age because infants and children are at highest risk of getting sick or dying if they get these diseases**
- **Newborn babies have antibodies to some diseases from their mothers**
  - However, this immunity lasts a few months–passive immunity
  - Most babies do not get protective antibodies against diphtheria, whooping cough, polio, tetanus, hepatitis B, or Hib from their mothers. This is why it's important to vaccinate a child before she or he is exposed to a disease.

Multiple Vaccines

- **Babies are exposed to thousands of germs and other antigens in the environment from the time they are born**
  - When a baby is born, his or her immune system is ready to respond to the many antigens in the environment and the selected antigens in vaccines
  - Vaccines contain weakened or killed versions of the germs that cause a disease
- **Getting multiple vaccines at the same time has been shown to be safe**
  - The recommended vaccines have been shown to be as effective in combination as they are individually
- **ACIP childhood vaccine schedule ensures children get the best protection**

Vaccine Adjuvants

- **An adjuvant is a substance that is added to a vaccine to increase the body's immune response to the vaccine**
  - Vaccines containing adjuvants are tested for safety in clinical trials before they are licensed for use in the United States, and they are continuously monitored by CDC and FDA
- **Adjuvants have been used safely in vaccines for many decades**

Vaccine Adjuvants

- Only some vaccines contain adjuvants including hepatitis A, hepatitis B, diphtheria-tetanus-pertussis (DTaP, Tdap), Haemophilus influenzae type b (Hib), human papillomavirus (HPV), one influenza vaccine and pneumococcal and recombinant zoster vacine

Autism and Vaccines

- Multiple population-based studies have examined the rate of autism among vaccinated and unvaccinated children
- Available evidence does not indicate that autism is more common among children who receive MMR or thimerosal-containing vaccines than among children who do not receive vaccines

http://www.cdc.gov/vaccinesafety/Concerns/Autism/Index.html

Studies of Autism and Vaccines*

- Kaye JA, et al. Measles, mumps, and rubella vaccine and incidence of autism recorded by general practitioners: a time-trend analysis. Brit Med J 322:460-463, 2001.
- Madsen KM, et al. A population-based study of measles, mumps, and rubella vaccination and autism. N Engl J Med. 2002;347:1477-1482.
- Frambonne E, et al. Pervasive developmental disorders in Montreal, Quebec, Canada: prevalence and links with immunizations. Pediatrics 118:e139-50, 2006.
- Thompson WW, et al. Early thimerosal exposure and neuro-psychological outcomes at 7 to 10 years. N Engl J Med 2007; 357(13):1281-92.
- Schechter R, Grether JK. Continuing increases in autism reported to California's developmental services system: mercury in retrograde. Arch Gen Psychiatry 2008;65(1):19-24.
- Taylor LE, Swerdfeger AL, Eslick GD. Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies. Vaccine. 2014 June;32(29):3623–3629

*Partial listing of representative studies


Vaccines and Autism: What you should know

References

http://media.chop.edu/data/files/pdfs/vaccine-education-center-autism.pdf

What Do You Think?

The Vaccine Adverse Event Reporting System (VAERS) detects new or rare events, increases in rates of known events, and patient risk factors associated with vaccination. VAERS cannot establish causality.

a. **True**

b. **False**

Questions?