

Vaccine Safety Reaction or Coincidence?

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22nd Annual Immunization Conference



Health and Wellness for all Arizonans

azdhs.gov



Cowpox Vaccination Cartoon 1802



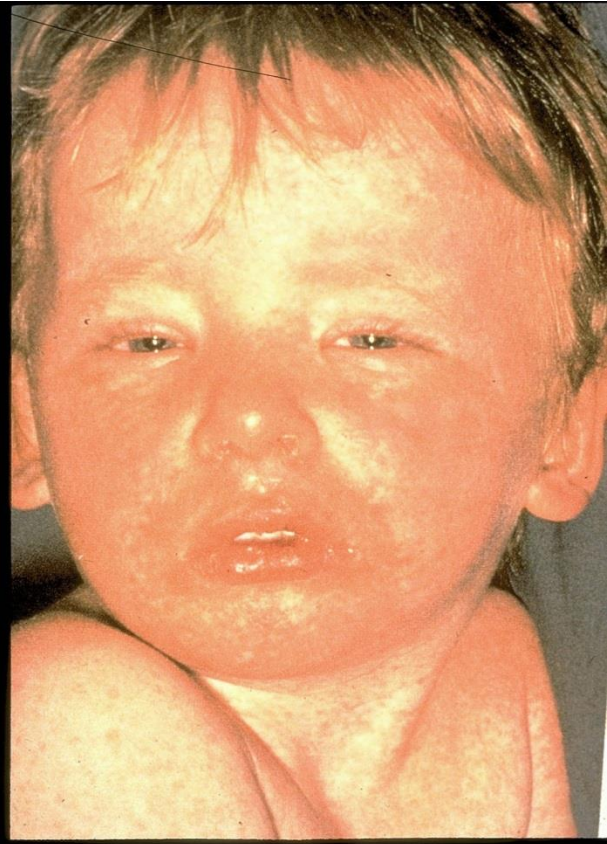
Possible Local Reactions at Vaccine Site

- Common
 - Redness, swelling, warmth, pain
- Local reactions more common when...
 - Pre-existing immunity
 - Strong immune response
 - Adjuvant
 - Subcutaneous versus intramuscular

Examples of Possible Systemic Reactions after Vaccination

- More common
 - Fever
 - Malaise, tiredness, headache
 - Rash
- Rare events
 - Febrile seizure
 - Anaphylaxis
 - Autoimmune
 - Neurologic: Guillain Barré Syndrome, ADEM, seizure

Measles



Source: cdc.gov

US & Measles	1950	2007
Cases	319,124	43
Deaths	468	0

Rubella



US & Rubella	1970	2007
Rubella Cases	57,686	11
Deaths from Rubella	29	1
Congenital Rubella Syndrome	62	0

Source: cdc.gov

Mumps



US & Mumps	1968	2007
Cases	152,209	800
Deaths	25	0

Source: cdc.gov

MMR Vaccine Reactions

- Live attenuated viruses
- Reactions usually within 5-14 days
- MMR recipient is not contagious
- Anaphylaxis (< 1/1,000,000)
- Mild problems
 - Fever (1/6)
 - Mild rash (1/20)
 - Swelling in glands of cheek or neck (1/75)
- Moderate problems
 - Febrile seizure (1/3,000)
 - Temporary joint pain, esp. women (up to 1/4)
 - Temporary low platelet count (1/30,000)

Quiz: Adverse Events after MMR

Likely due to vaccine?

- Fever of 102°F. two days after MMR.
- Swollen lymph nodes along back of the neck one week after MMR
- Low platelets 1 week after MMR
- Small red spots on the trunk 10 days after MMR
- Unilateral swelling of parotid gland 2 months after MMR

CHICKEN POX



CDC PHIL 6121



CDC PHIL 10486

US & Varicella	1972	2007
Cases	154,114	40,146
Deaths	122	6

Shingles (Herpes Zoster)



Source: CDC PHIL 6886

Varicella Vaccine Reactions

- Vaccine site pain, soreness, redness, swelling
 - 1/5 children; 1/3 adolescents and adults
- Fever 5-12 days after vaccine (<10%)
 - Febrile seizure (very rare)
- Generalized maculopapular or vesicular rash within one month after vaccine (4%)
 - Could be contagious until vesicles scab or M/P rash stops appearing for 24 hours
- Pneumonia (very rare)

MMR-V Vaccine

- Combination of MMR vaccine and varicella vaccine
- Nine times as much varicella virus as with separate varicella vaccine
- Fever and febrile seizures more likely after MMR-V than after MMR + Varicella vaccines given at same time but separately

Adverse Events after Varicella Vaccine Likely due to vaccine?

- Generalized vesicular rash 1 day after vaccine
- Fever of 101°F seven days after vaccine
- Maculopapular, generalized rash 2 months after vaccine
- Vesicular, dermatomal, unilateral rash two years after vaccine
- Vesicular, generalized rash 8 days after vaccine

Rotavirus

- Yearly in US before 2006
 - 20-60 deaths
 - 55,000-70,000 hospitalizations
 - 205,000-272,000 emergency department visits
- WHO estimates globally ~527,000 deaths a year



Possible Reactions after Rotavirus Vaccination

- Live, attenuated vaccine
- Most have no problems
- Sometimes
 - Fussy
 - Mild, temporary diarrhea or vomiting
- Rare
 - Intussusception after 1st or 2nd dose
 - 1:20,000-1:100,000 U.S. infants

Pertussis (Whooping Cough)



cdc.gov

Pertussis	1950	2007
Cases	120,718	10,454
Deaths	1,118	9



CDC PHIL 6379

Pertussis (Whooping Cough)



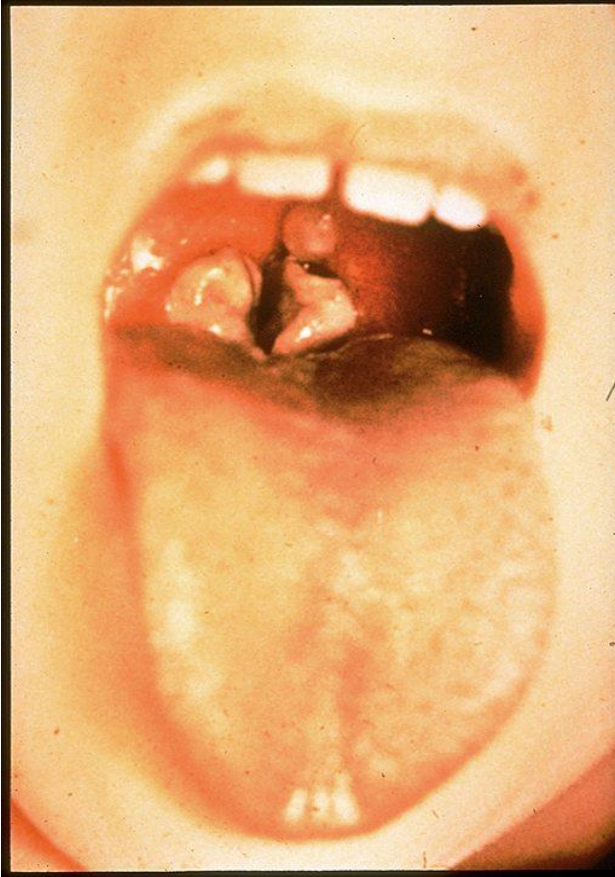
cdc.gov

Pertussis	1950	2007
Cases	120,718	10,454
Deaths	1,118	9



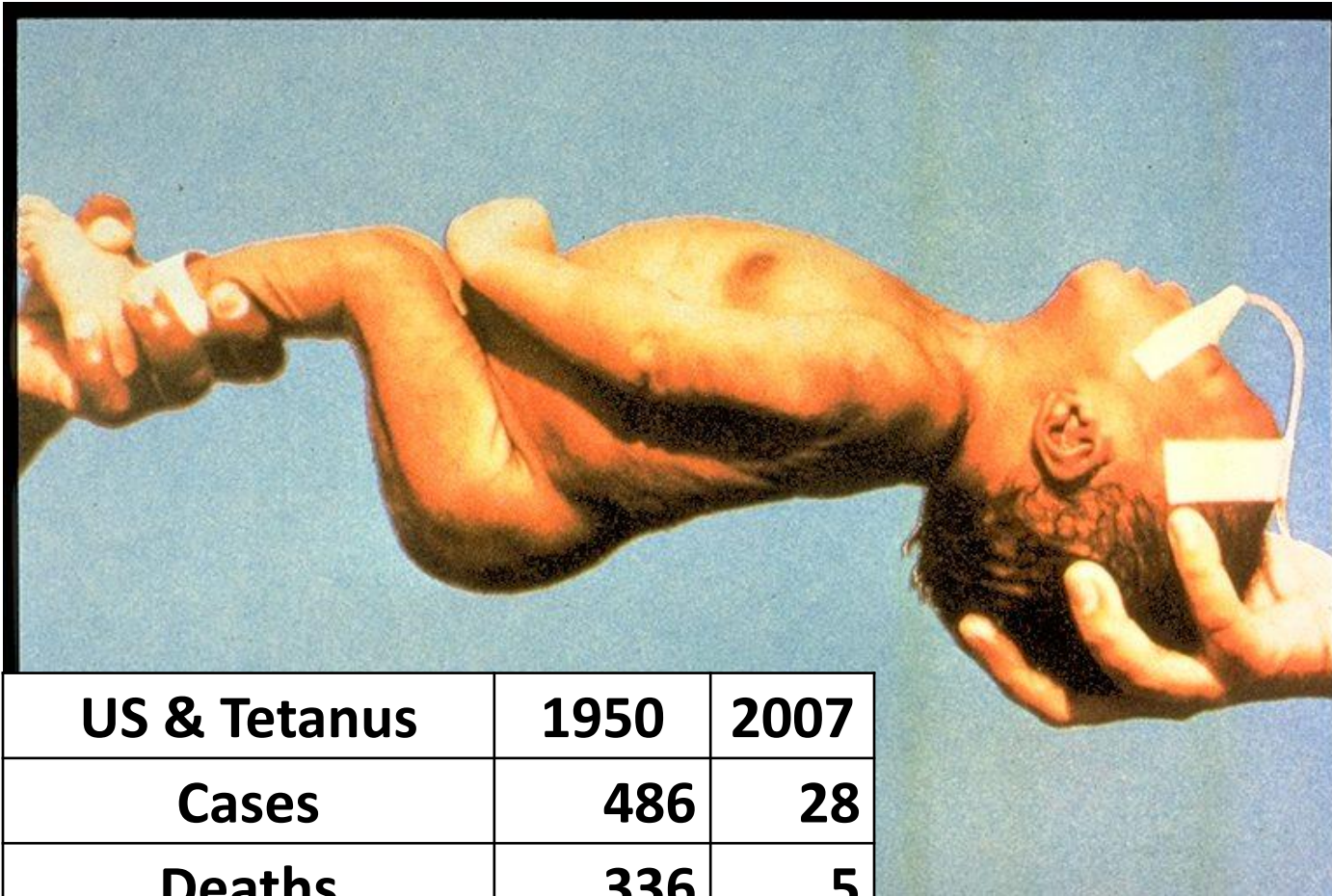
CDC PHIL 6379

Diphtheria



US & Diphtheria	1950	2007
Cases	5,796	0
Deaths	410	0

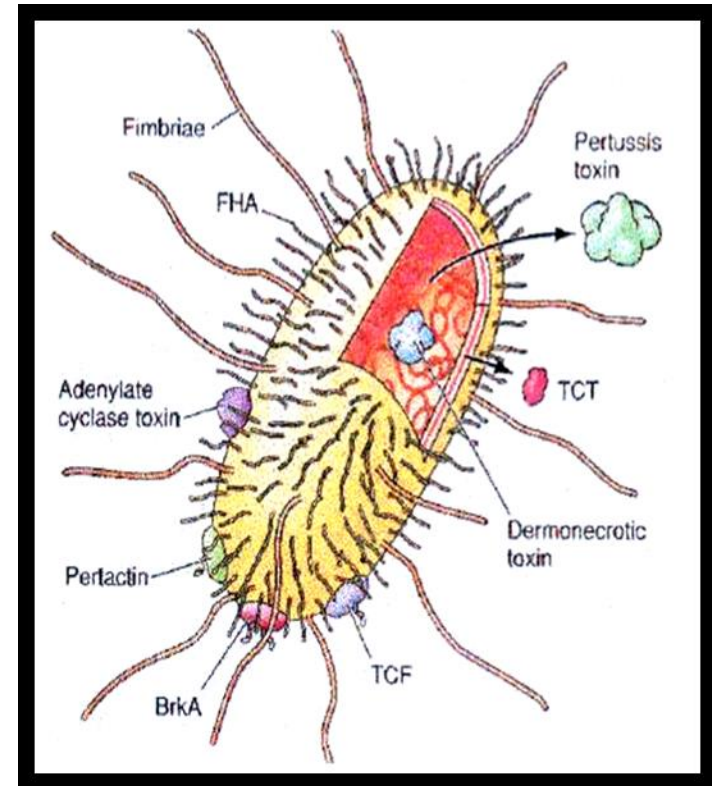
Tetanus



US & Tetanus	1950	2007
Cases	486	28
Deaths	336	5

Antigenic and Biologically Active Components of *B. pertussis*

- pertussis toxin (PT)
- filamentous hemagglutinin (FHA)
- pertactin
- fimbriae
- agglutinogens
- adenylate cyclase
- tracheal cytotoxin
- dermatonecrotic toxin
- adenylate cyclase toxin
- Etc.



Stacey W. Martin, MSc.
CDC Webinar, May 30, 2012

Components of Pertussis Vaccines

Product	Type	PT μg	FHA μg	PERT μg	FIM μg	DIPH Lf	TET Lf
Daptacel	DTaP	10	5	3	5	15	5
Infanrix	DTaP	25	25	8	--	25	10
Pentacel	DTaP+	20	20	3	5	15	5
Pediarix	DTaP+	25	25	8	--	25	10
Adacel	Tdap	2.5	5	3	5	2	5
Boostrix	Tdap	8	8	2.5	--	2.5	5

Adverse Events after DTaP Vaccine

MILD

- Occurring 1-3 days after shot
- Fever (1/4)
- Redness, swelling, pain (1/4)
 - More severe after 4th or 5th
- Fussiness (1/3)
- Tiredness or poor appetite
 - 1/10
- Vomiting (1/50)

MODERATE

- Seizure (1/14,000)
- Non-stop crying for 3 hours or more (1/1000)
- Fever over 105°F. (1/16,000)

SEVERE (very rare)

- Anaphylaxis (< 1/1,000,000)
- Long-term seizures
- Permanent brain damage

Adverse Events after Tdap Vaccine

MILD

- Local Pain
 - 3/4 teens; 2/3 adults
- Local redness/swelling (1/5)
- Fever to 100.4°F.
 - 1/25 teens; 1:100 adults
- Headache (3-4/10)
- Tiredness (1/3-4)
- Nausea, vomiting, diarrhea
 - 1/4 teens; 1/10 adults
- Chills, rash (uncommon)

MODERATE

- Local pain
 - 1/5 teens; 1/100 adults
- Local redness/swelling
 - 1/16 teens; 1/25 adults
- Fever over 102°F.
 - 1/100 teens; 1/250 adults
- Headache
 - 3/20 teens; 1/10 adults
- Nausea, vomiting, diarrhea
 - 1-3/100
- Entire arm swollen (3/100)
- Fainting

Adverse Events after DTaP or Tdap Likely due to vaccine?

- Redness and pain in arm 2 days after shot
- Persistent cough starting the day after the vaccine
- Fever of 105°F. one week after DTaP
- Crying for 4 hours starting 4 hours after DTaP
- Fainting immediately after Tdap
- Sore throat with exudate one week after DTaP

SYMPTOMS OF INFLUENZA

- Rapid onset
- High fever, chills
- Extreme exhaustion
- Muscle aches
- Dry cough
- Runny nose
- Sore throat



Adverse Events after Influenza Vaccines

INACTIVATED

- Soreness, redness, swelling
 - Happen in 15-20%
 - Last 1-2 days
- Fever, chills, malaise, myalgia, fatigue (< 1%)
 - Occur 6-12 hours after shot
 - Last 1-2 days
- Anaphylaxis (< 1 in a million)
- Guillain-Barré Syndrome?

LIVE, ATTENUATED (nasal)

- Runny nose, cough, nasal congestion,
- Wheezing (children)

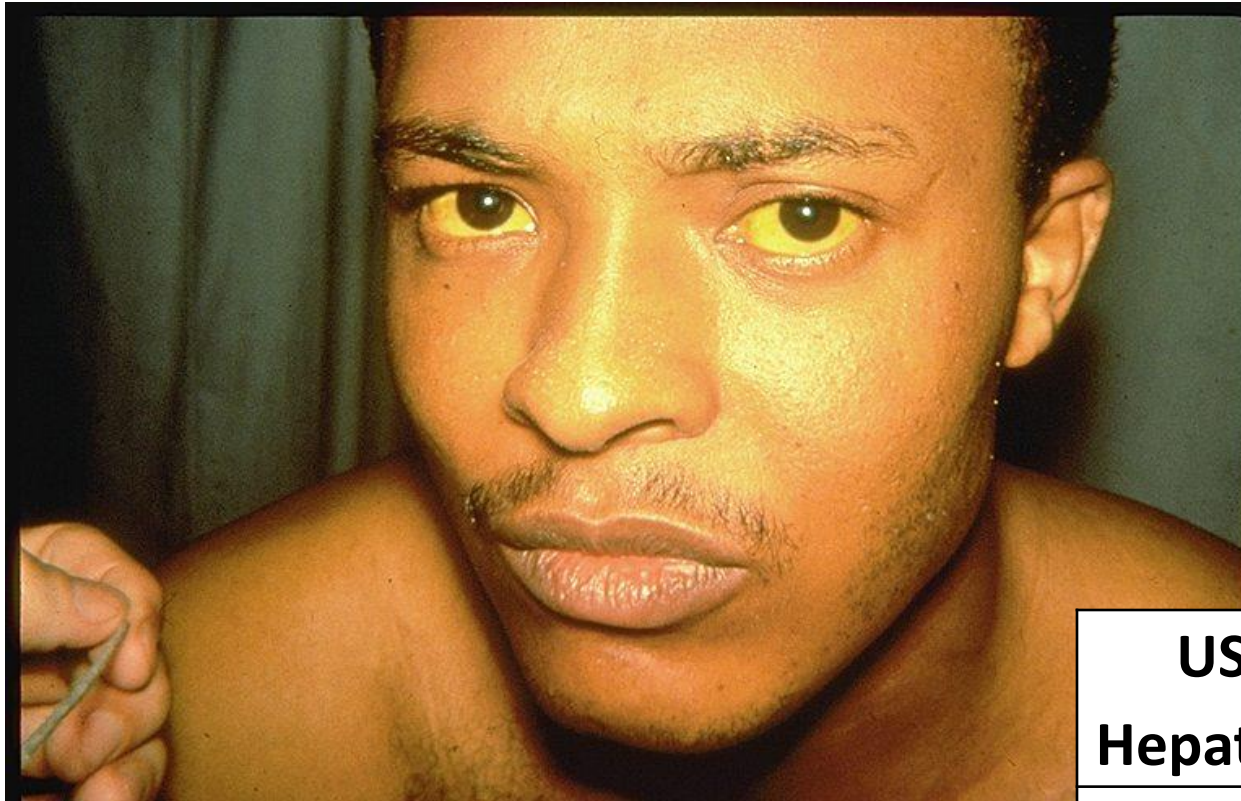
LESS COMMON (after LAIV)

- Headache, muscle aches
- Sore throat
- Tiredness
- Vomiting/diarrhea

Adverse Events after Influenza Vaccine Likely due to vaccine?

- Redness and soreness at vaccine site one day after influenza shot
- Fever of 102°F one week after influenza shot
- Pneumonia diagnosed one week after shot
- Vomiting and diarrhea starting 6 hours after an influenza shot
- Runny nose for two days after LAIV
- Sore throat one month after LAIV

Jaundice from Hepatitis A



US & Hepatitis A	1980	2007
Cases	30,407	2,979
Deaths	129	34

Adverse Events after Hepatitis A Vaccine

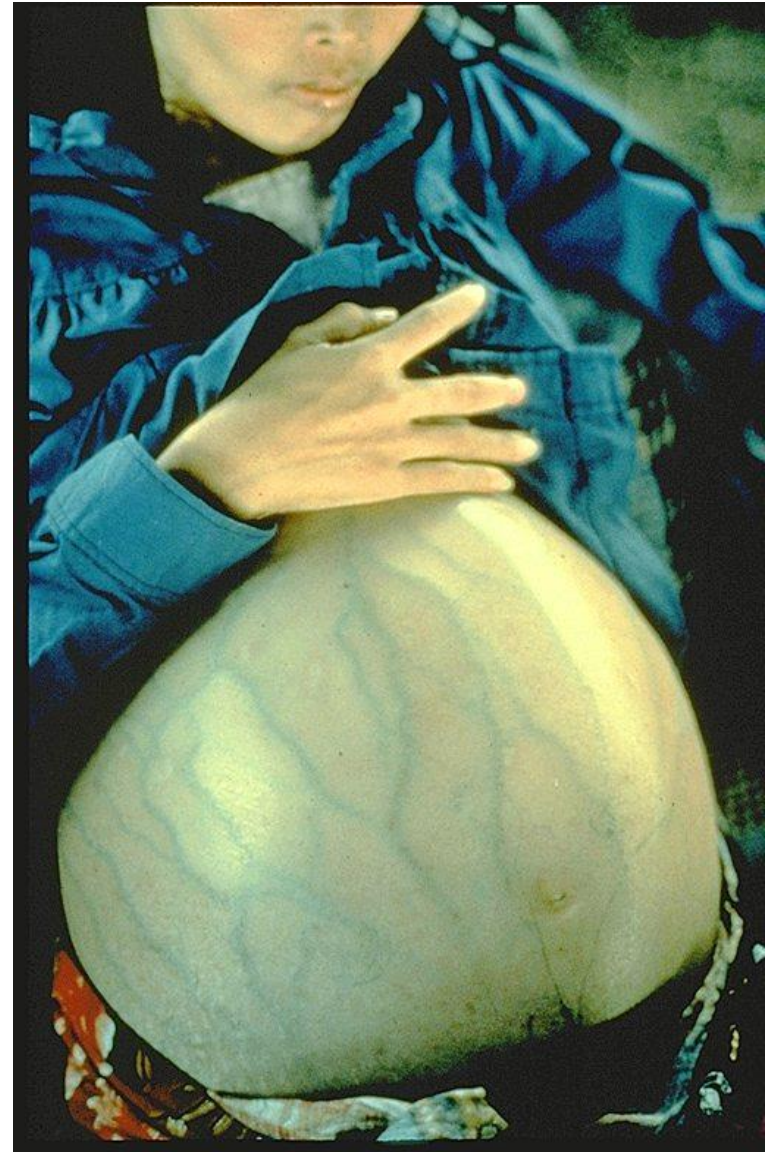
- Mild problems
 - Soreness at vaccine site (Children 1/6, adults 1/2)
 - Headache (Children 1/25, adults 1/6)
 - Loss of appetite (Children 1/12)
 - Tiredness (Adults 1/14)
- Anaphylaxis—very rare
 - Within minutes to hours

Hepatitis B

Causes

Liver Cancer and Cirrhosis

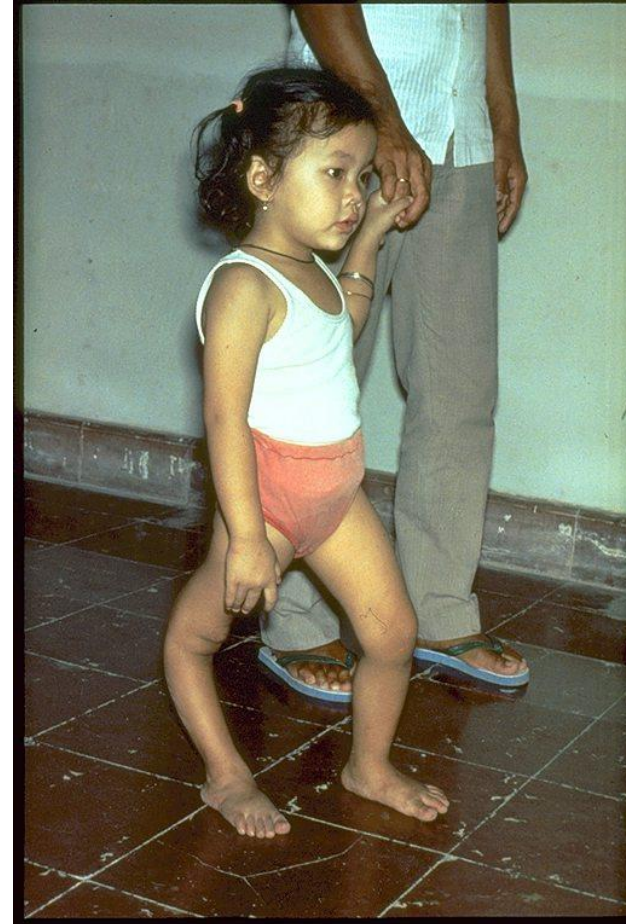
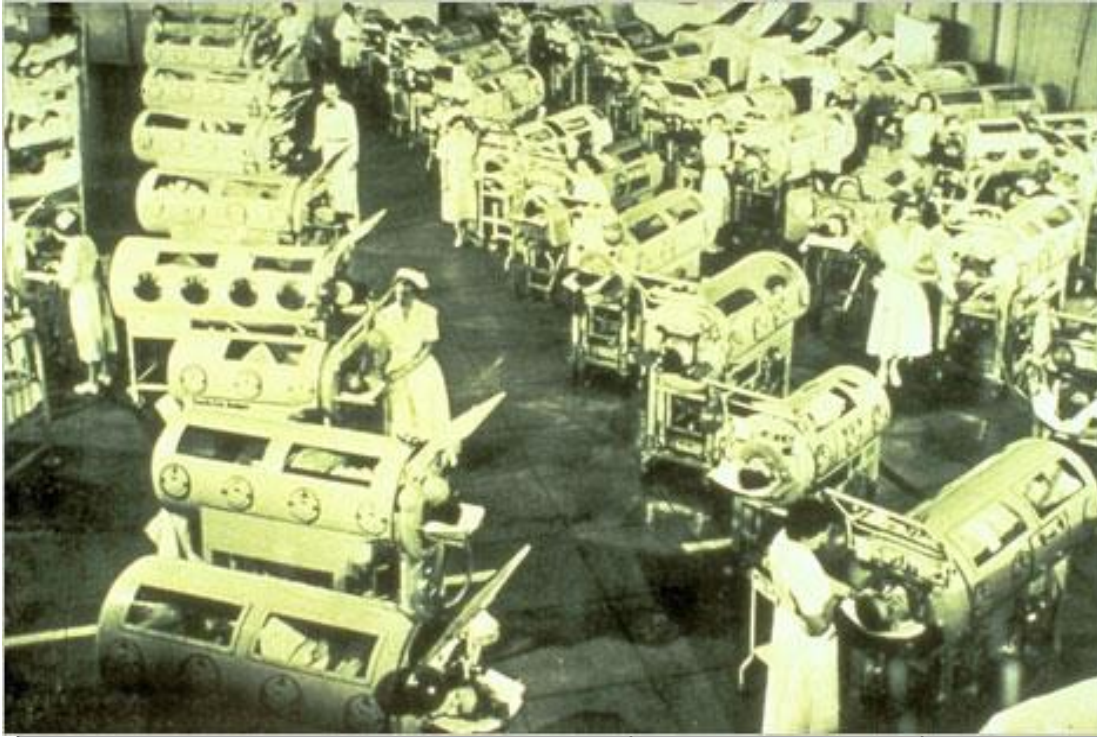
US & Hepatitis B	1979	2007
Cases	15,452	4,519
Deaths	260	719



Adverse Events after Hepatitis B Vaccine

- Mild
 - Soreness at vaccine site (1/4)
 - Temperature to 99.9°F or higher (1/15)
- Test for hepatitis B surface antigen may test positive for up to 28 days
- Severe allergic reactions
 - About once in 1.1 million doses

Poliomyelitis



US & Paralytic Polio	1950	2007
Cases	33,300	0
Deaths	1,904	0

Adverse Events after Polio Vaccines

Inactivated Polio Vaccine (IPV)

- Most people have no problem with IPV
- Soreness at vaccine site
- Anaphylaxis
 - Extremely small risk

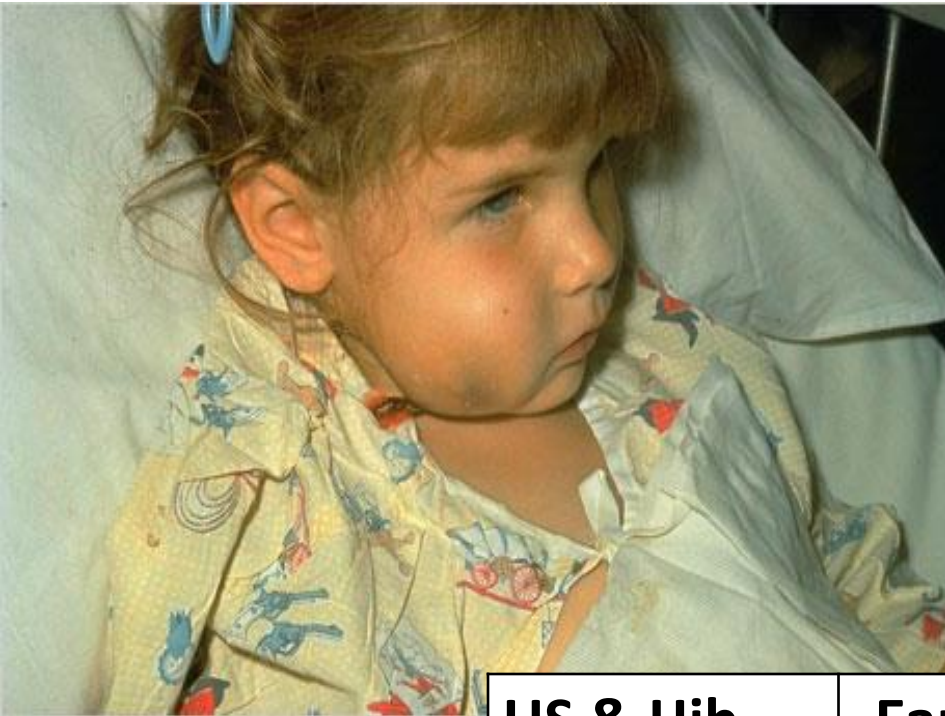
Oral Polio Vaccine (OPV)

- Rarely can cause paralysis from polio infection
 - Risk of 1 case for every 2.4 million doses of OPV
- Close contact of OPV recipient can get infected with OPV and rarely could be paralyzed
- Anaphylaxis
 - Extremely small risk

Adverse Events after Vaccination Likely due to vaccine?

- Jaundice 1 week after hepatitis A vaccine
- Fever 1 day after hepatitis B vaccine
- Vomiting 1 week after IPV
- Runny nose 1 day after hepatitis A vaccine
- Anaphylaxis 6 hours after hepatitis B vaccine
- Paralysis one week after oral polio vaccine
- Diarrhea 1 week after hepatitis A vaccine

Haemophilus influenzae type b (Hib)



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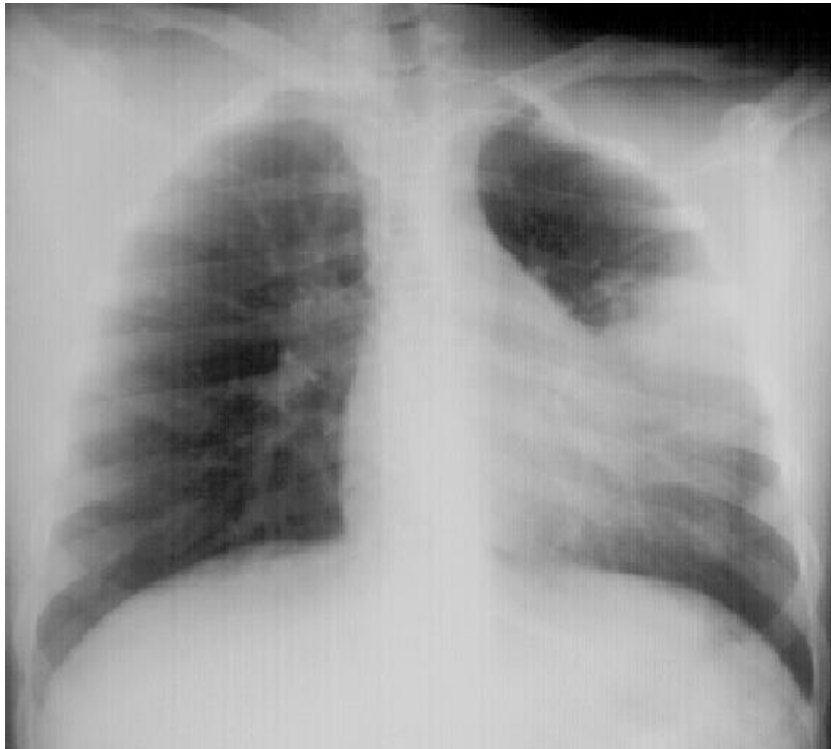
US & Hib	Early 1980s	2007
Cases	~20,000	202
Meningitis	~10,000	N/A

Adverse Events after *Haemophilus influenzae* type b (Hib) Vaccines

- Most people do not have problems
- Mild problems
 - Redness, warmth, or swelling at injection site
 - Problems start soon after shot and last 2-3 days
- Severe shoulder pain at vaccine site—rare
- Fainting—occasional
- Anaphylaxis—very rare

Clinical presentations of *Streptococcus pneumoniae*

- Pneumonia



- Meningitis
- Bacteremia
- Otitis media
- Mastoiditis
- Sinusitis
- Periorbital Cellulitis
- Orbital Cellulitis
- Septic Arthritis

Adverse Events after Pneumococcal Vaccines

PCV13

- Drowsy, loss of appetite, redness or pain at site (1/2)
- Swelling at vaccine site (1/3)
- Mild fever (1/3) or fever over 102.2°F (1/20)
- Fussy or irritable (8/10)
- Anaphylaxis
 - Very rare

PPSV23

- Mild side effects (1/2)
 - Redness or pain at injection site
- Fever (<1%)
- Muscle aches (<1%)
- Severe local reaction (<1%)
- Anaphylaxis
 - Very rare

Neisseria meningitidis



Adverse Events after Meningococcal Vaccines

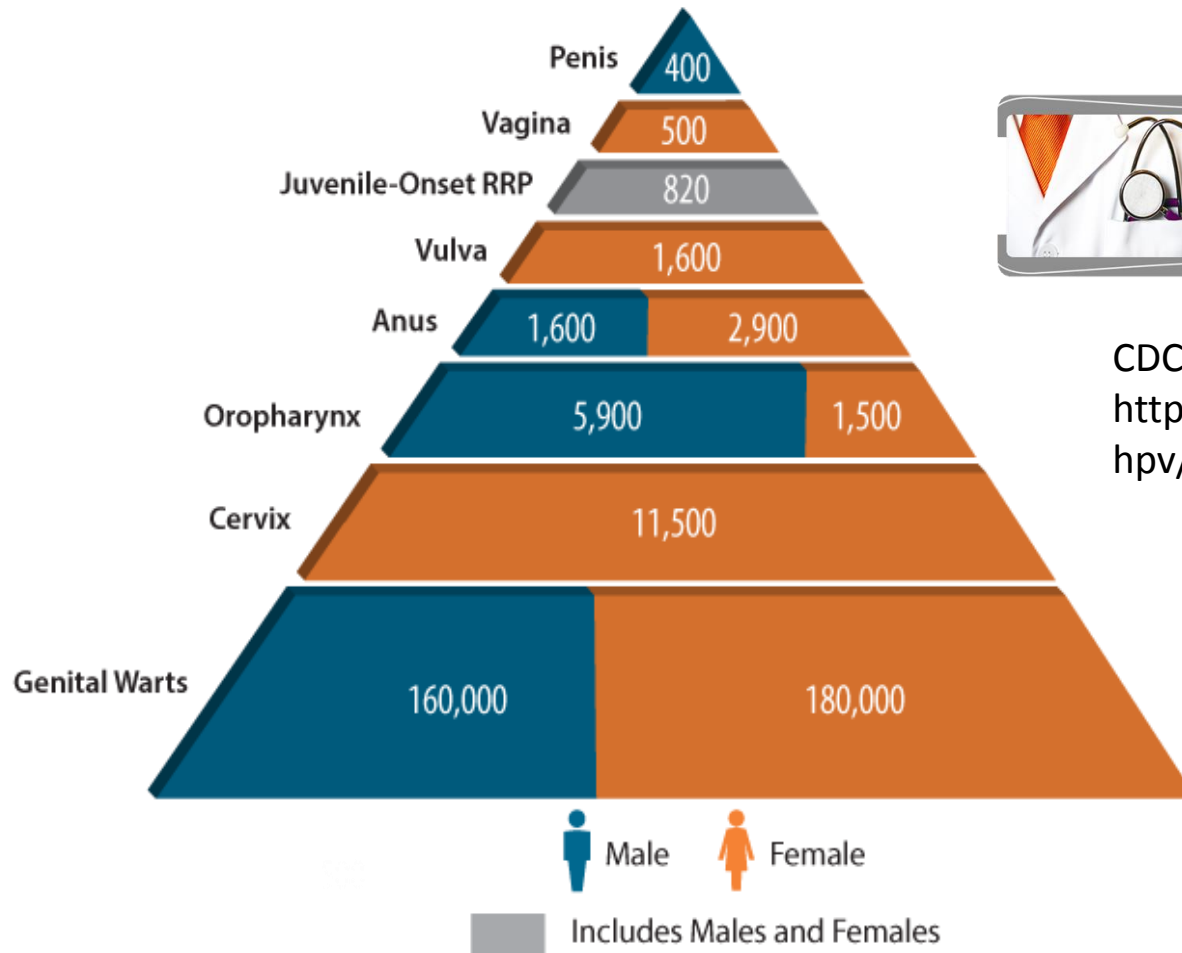
- Redness or pain at injection site (1/2)
 - More common after conjugate vaccine (MCV4) than polysaccharide vaccine (MPSV4)
- Fever
 - Occasional
- Fainting
 - Occasional
- Anaphylaxis—very rare

Adverse Events after Vaccination

Likely due to vaccine?

- Seizure and fever 1 month after meningococcal vaccine
- Runny nose, sore throat, cough starting 1 day after Hib vaccine
- Sore vaccine site for 1-3 days after pneumococcal vaccine
- Diarrhea starting 5 days after meningococcal vaccine

Cancers and Genital Warts Attributed to HPV Infections, U.S.



CDC; 2013. Available at <http://www.cdc.gov/cancer/hpv/statistics/cases.htm>

Adverse Events after Human Papillomavirus (HPV) Vaccines

- Injection site
 - Redness or swelling (4/10)
 - Pain (8/10)
- Fever
 - To 100.4°F. (1/10)
 - To 102°F. (1/65)
- Headache (1/3)
- Fainting
 - Occasional
- Anaphylaxis
 - Very rare

Vaccine Adverse Event Reporting System (VAERS)

- Created as part of National Childhood Injury Act of 1986
 - Established in 1990
 - Co-managed by CDC and FDA
- Report any clinically significant or unexpected event occurring after vaccination

Summary of Vaccine Injury Table

National Childhood Vaccine Injury Act

Containing	Adverse Event Condition	Time interval
Any vaccine	Anaphylaxis / sequela / death	0-4 hrs / NA / NA
Tetanus	Brachial neuritis	2-28 days
Pertussis	Encephalopathy / encephalitis	0-72 hrs
MMR	Encephalopathy / encephalitis	5-15 days
Measles	Thrombocytopenic purpura	7-30 days
	Vaccine infection in immune compromised	0-6 months
Rubella	Chronic arthritis	7-42 days
OPV	Paralytic polio--immune competent	0-30 days
	Paralytic polio—immune compromised	0-6 months
Rotavirus	Intussusception	0-30 days

Vaccine Safety

“I don’t think that word means what you think it means.”

-- Íñigo in *The Princess Bride*

Safety Monitoring after FDA Licensing

- Licensing of manufacturing plant
- Each lot tested at the FDA
 - Safety, potency, purity
- Safety Monitoring
 - Vaccine Adverse Events Reporting System (VAERS)
 - Vaccine Safety Datalink (VSD)
 - Clinical Immunization Safety Assessment Centers (CISA)

Temporal Occurrence Does Not Prove Cause and Effect

