Understanding the Purpose and Safety of the Vaccine Schedule: How to Make It Work

TRUDY LARSON, MD

PROFESSOR AND DEAN, SCHOOL OF COMMUNITY HEALTH SCIENCES

UNIVERSITY OF NEVADA, RENO

Disclosures

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Faculty: Trudy Larson, MD and Julie Tomaro, RN, BSN, MPH

CME Committee: David Couch; Kathleen Clanon, MD; Johanna Rosenthal, MPH; Pat Blackburn, MPH; Richard Fischer, MD; Sharon Adler, MD.

CNE Committee: Leigh Casey Wallis, MPH; Paul Throne, DrPH, MPH, MSW; Kristen Wilson-Weiberg, BSN, RN; Liz Jaquette, MPH; Mackenzie Melton, MPH; Ginny Cassidy-Brinn, MSN, ARNP.

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Learning Objectives

By the end of this session, you should be able to:

1. Explain the scientific foundation and justification for the current vaccine schedule
2. Explain the most common vaccine safety events and concerns

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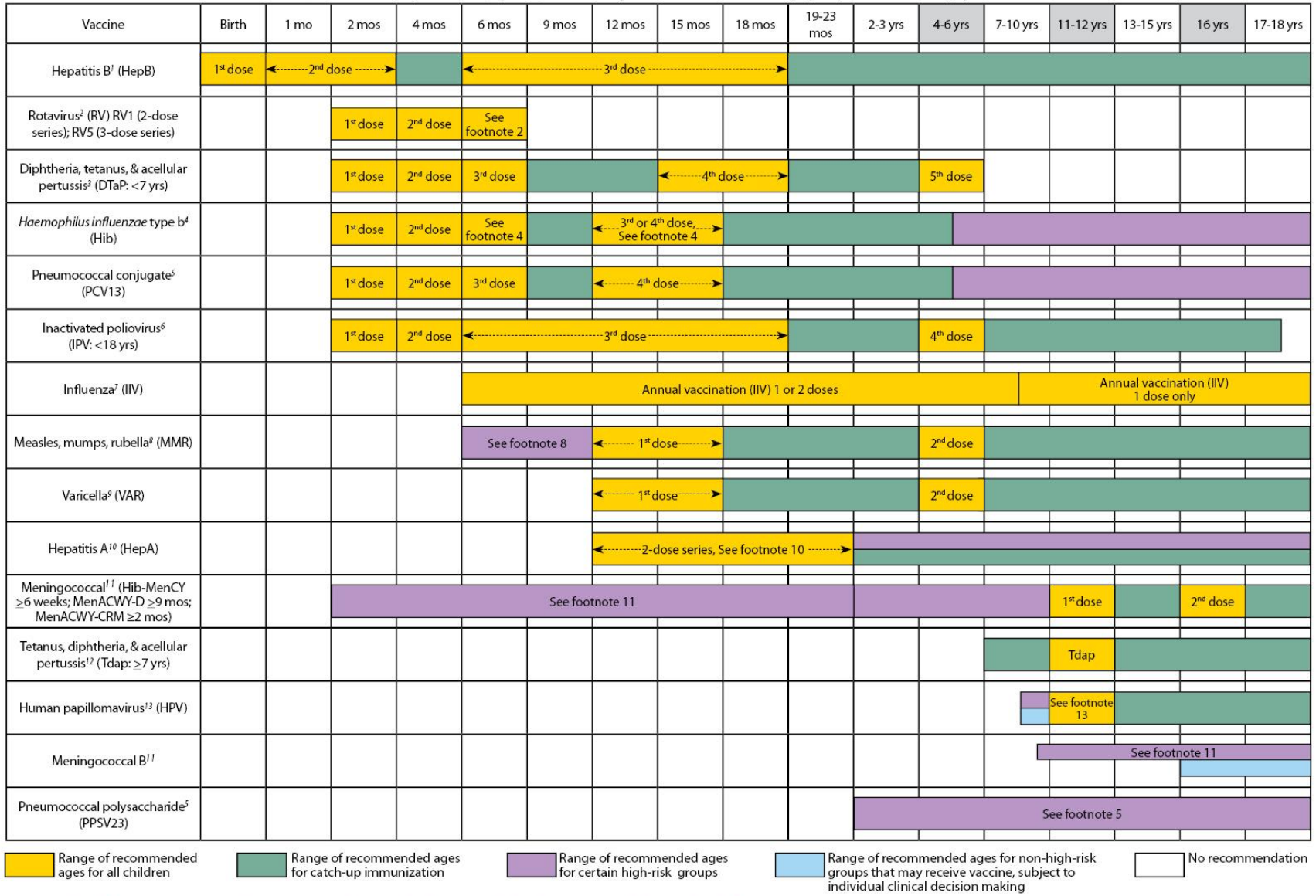
Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2017.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.



NOTE: The above recommendations must be read along with the footnotes of this schedule.

Active Immunity

- Immune system produces antigen-specific humoral and cellular immunity
- Lasts for many years, often lifetime
- Sources
  - infection with disease causing form of organism
  - Vaccination
- Vaccination
  - Active immunity produced by vaccine
  - Immunity and immunologic memory similar to natural infection but without risk of disease

Inactivated Vaccines

- Cannot replicate
- Always require multiple doses
- Immune response mostly humoral
  - Antibody titer diminish with time
  - May require periodic supplemental booster doses
- Whole-cell vaccines
  - viral: polio, hepatitis A, rabies, influenza*
  - bacterial: pertussis*, typhoid*, cholera*, plague*
- Fractional vaccines
  - Subunits: hepatitis B, influenza, acellular pertussis, human papillomavirus, anthrax
- Toxoids: diphtheria, tetanus

Live Attenuated Vaccines

- Attenuated (weakened) form of the "wild" virus or bacterium
  - Must replicate to produce an immune response
  - Immune response virtually identical to natural infection
  - Fragile - must be stored and handled carefully
  - Interference from circulating antibody
- Usually produce immunity with one dose* (except oral)
- Severe reactions possible
- Viral: measles, mumps, rubella, vaccinia, varicella, zoster, yellow fever, rotavirus, intranasal influenza, oral polio**
- Bacterial: BCG**, oral typhoid

Recombinant Vaccines

- Genetic engineering technology
- Viral: hepatitis B, human papillomavirus, influenza (two brands), live attenuated influenza, rotavirus
- Bacterial: *Salmonella* Typhi (Ty21

General Rule:

- The more similar a vaccine is to the disease-causing form of the organism, the better the immune response to the vaccine.

General Recommendations for Immunization

- Timing and spacing of vaccines
- Adverse reactions following vaccination
- Contraindications and precautions to vaccination
- Invalid contraindications to vaccination

Disease Epidemiology and Timing

- Target protection to address peak age for infection and disease
  - Worst pertussis cases in those less than 6 months of age
    - Antibody levels wane over time
  - Hepatitis B infected mothers and chronic Hep B in babies
  - HIB disease peaks in infants and children
    - Meningitis and sepsis
  - Pneumococcal disease seen in infants and children and those over 65
    - Meningitis and sepsis in infants and children
    - Pneumonia in those over 65
  - Meningococcal disease spike seen 15-22 y/o

Timing and Spacing: *Antibody and Measles- and Varicella-Containing Vaccines*

Product Given First	Action
Vaccine	Wait 2 weeks before giving antibody
Antibody (blood, IVIG, HepB)	Wait 3 months or longer before giving vaccine

Timing and Spacing: *Simultaneous and Non-simultaneous Administration*

- **General Rule: All vaccines can be administered at the same visit as all other vaccines.***

* **exception: in children with asplenia, separate pneumococcal and meningococcal vaccines by at least 4 weeks**

- **Combination vaccines are generally preferred over simultaneous administration of single component vaccines**

Spacing of Vaccine Combinations Not Given Simultaneously

Combination	Minimum Interval
Two live parenteral, or live intranasal influenza vaccine	4 weeks
All other	None

Timing and Spacing: *Interval Between Doses of the Same Vaccine*

- **General Rule: Increasing the interval between doses of a multi-dose vaccine does not diminish the effectiveness of the vaccine.**
  - ***Decreasing the interval between doses of a multi-dose vaccine may interfere with antibody response and protection.**
- **Vaccine doses should not be administered at intervals less than the minimum intervals or earlier than the minimum age**

Number of Doses

- For live injected vaccines, the first dose administered at the recommended age usually provides protection.
  - An additional dose is given to provide another opportunity for vaccine response in those who do not respond to the first dose
- For inactivated vaccines, the first dose usually does not provide protection.
  - Needs additional doses for protective immunity to develop.
  - May need boosters.

Immune Response to Doses of Vaccine

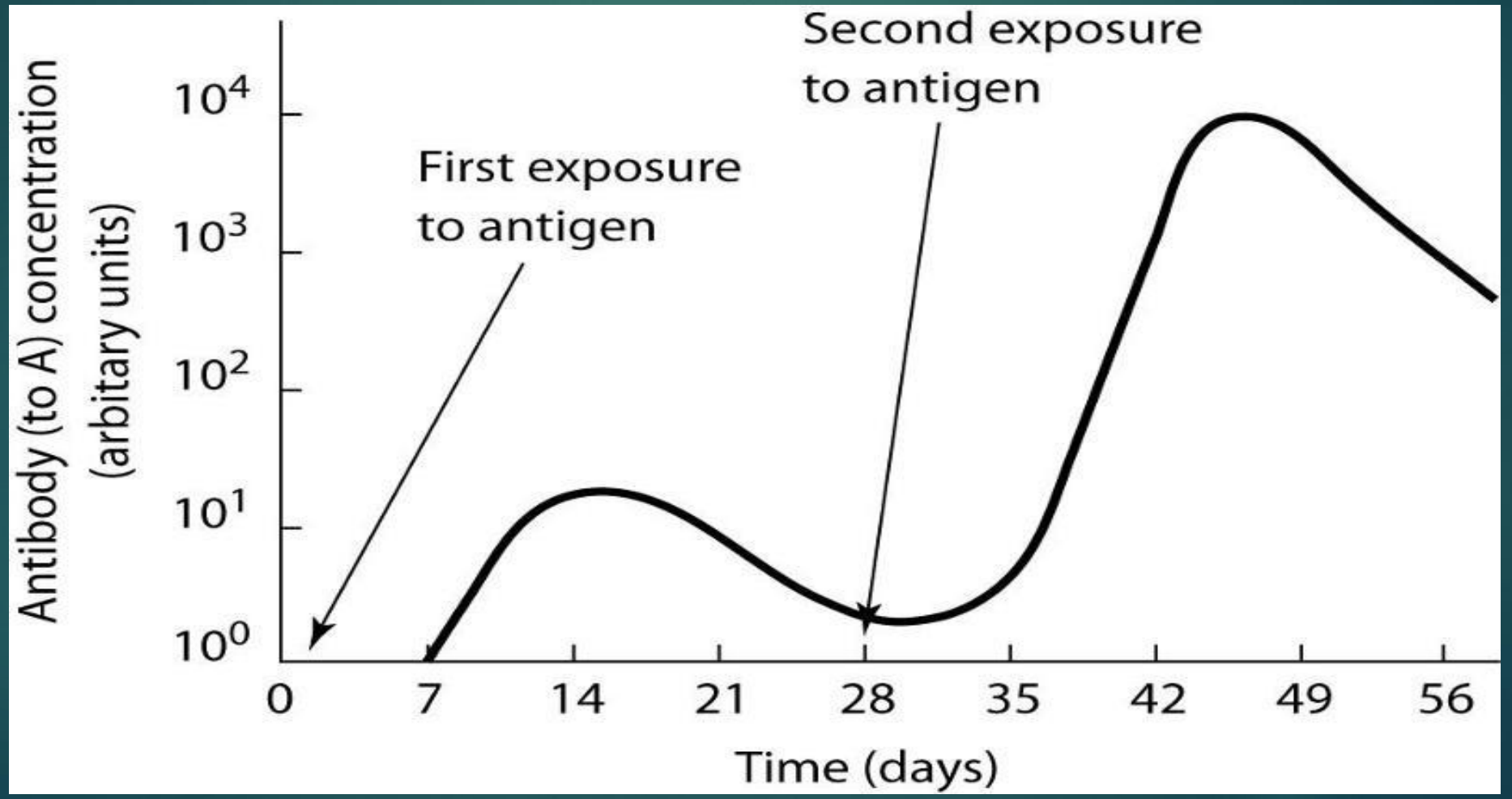
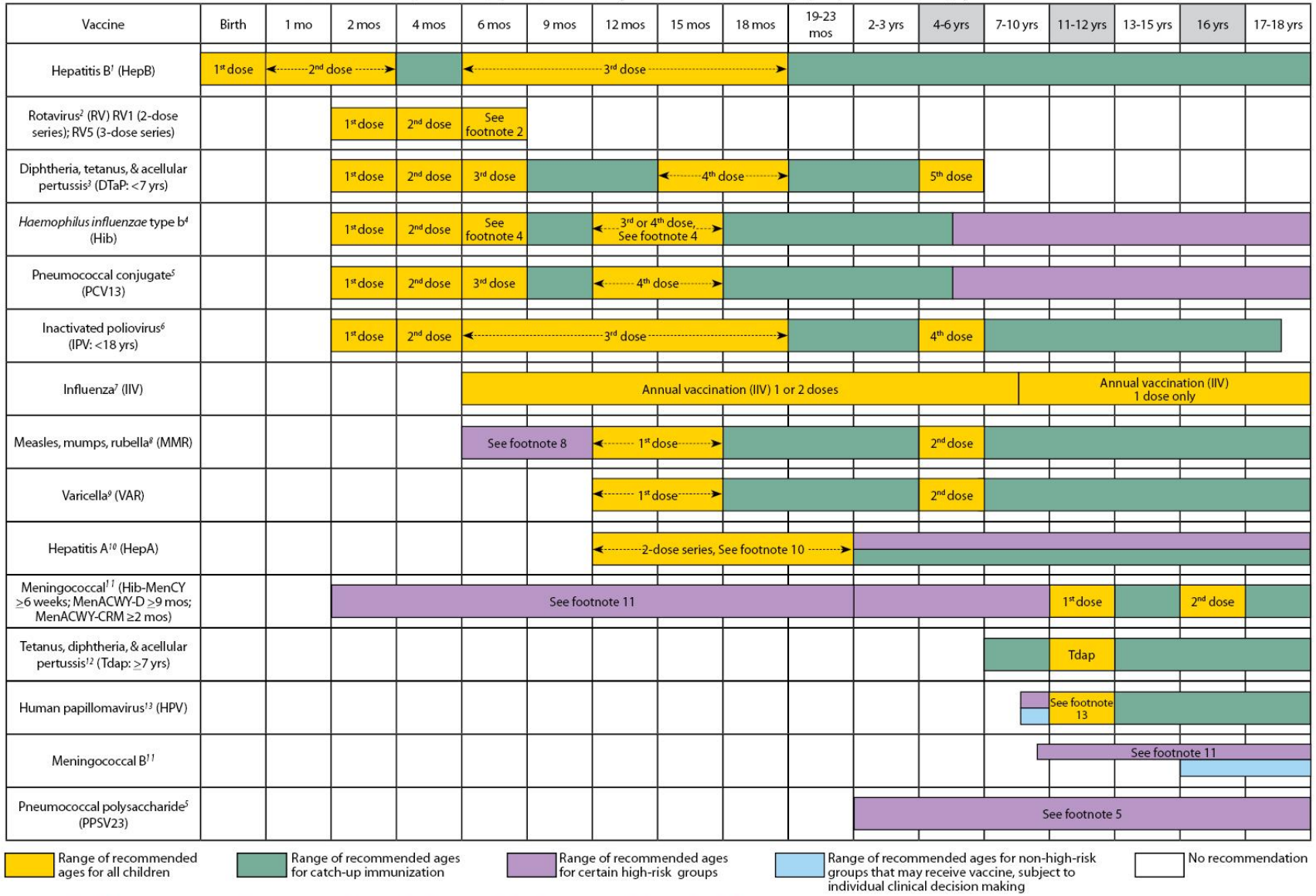


Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2017.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded in gray.



NOTE: The above recommendations must be read along with the footnotes of this schedule.

FIGURE 2. Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind—United States, 2017.

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Figure 1 and the footnotes that follow.

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Children age 4 months through 6 years					
Hepatitis B[1]	Birth	4 weeks	8 weeks *and* at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks.		
Rotavirus[2]	6 weeks	4 weeks	4 weeks[2]		
Diphtheria, tetanus, and acellular pertussis[3]	6 weeks	4 weeks	4 weeks	6 months	6 months[3]
Haemophilus influenzae type b[4]	6 weeks	4 weeks if first dose was administered before the 1st birthday. 8 weeks (as final dose) if first dose was administered at age 12 through 14 months. No further doses needed if first dose was administered at age 15 months or older.	4 weeks[4] if current age is younger than 12 months **and** first dose was administered at younger than age 7 months, **and** at least 1 previous dose was PRP-T (ActHib, Pentacel, Hiberix) or unknown. 8 weeks *and* age 12 through 59 months (as final dose)[4] • if current age is younger than 12 months **and** first dose was administered at age 7 through 11 months; OR • if current age is 12 through 59 months **and** first dose was administered before the 1st birthday, **and** second dose administered at younger than 15 months; OR • if both doses were PRP-OMP (PedvaxHIB; Comvax) **and** were administered before the 1st birthday. No further doses needed if previous dose was administered at age 15 months or older.	8 weeks (as final dose) This dose only necessary for children age 12 through 59 months who received 3 doses before the 1st birthday.	
Pneumococcal[5]	6 weeks	4 weeks if first dose administered before the 1st birthday. 8 weeks (as final dose for healthy children) if first dose was administered at the 1st birthday or after. No further doses needed for healthy children if first dose was administered at age 24 months or older.	4 weeks if current age is younger than 12 months and previous dose given at <7 months old. 8 weeks (as final dose for healthy children) if previous dose given between 7-11 months (wait until at least 12 months old); OR if current age is 12 months or older and at least 1 dose was given before age 12 months. No further doses needed for healthy children if previous dose administered at age 24 months or older.	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus[6]	6 weeks	4 weeks[6]	4 weeks[6]	6 months[6] (minimum age 4 years for final dose).	
Measles, mumps, rubella[8]	12 months	4 weeks			
Varicella[9]	12 months	3 months			
Hepatitis A[10]	12 months	6 months			
Meningococcal[11] (Hib-MenCY ≥6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)	6 weeks	8 weeks[11]	See footnote 11	See footnote 11	
Children and adolescents age 7 through 18 years					
Meningococcal[11] (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)	Not Applicable (N/A)	8 weeks[11]			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis[12]	7 years[12]	4 weeks	4 weeks if first dose of DTaP/DT was administered before the 1st birthday. 6 months (as final dose) if first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday.	6 months if first dose of DTaP/DT was administered before the 1st birthday.	
Human papillomavirus[13]	9 years	Routine dosing intervals are recommended.[13]			
Hepatitis A[10]	N/A	6 months			
Hepatitis B[1]	N/A	4 weeks	8 weeks **and** at least 16 weeks after first dose.		
Inactivated poliovirus[6]	N/A	4 weeks	4 weeks[6]	6 months[6]	
Measles, mumps, rubella[8]	N/A	4 weeks			
Varicella[9]	N/A	3 months if younger than age 13 years. 4 weeks if age 13 years or older.			

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Figures 1 and 2 should be read with the footnotes that contain important general information and considerations for special populations.

Figure 1. Recommended immunization schedule for adults aged 19 years or older by age group, United States, 2017

Vaccine	19–21 years	22–26 years	27–59 years	60–64 years	≥ 65 years
Influenza[1]	1 dose annually				
Td/Tdap[2]	Substitute Tdap for Td once, then Td booster every 10 yrs				
MMR[3]	1 or 2 doses depending on indication				
VAR[4]	2 doses				
HZV[5]				1 dose	
HPV–Female[6]	3 doses				
HPV–Male[6]	3 doses				
PCV13[7]	1 dose				
PPSV23[7]	1 or 2 doses depending on indication				1 dose
HepA[8]	2 or 3 doses depending on vaccine				
HepB[9]	3 doses				
MenACWY or MPSV4[10]	1 or more doses depending on indication				
MenB[10]	2 or 3 doses depending on vaccine				
Hib[11]	1 or 3 doses depending on indication				

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended for adults with additional medical conditions or other indications

No recommendation

Why Combine Vaccines?

- Recommended vaccines have dramatically increased in the first two years of life
  - Currently vaccines against 14 disease, 17 injections, multiple injections in single visit
- Positive effects of combining vaccines in a single syringe
- Concerns include reduced effectiveness, reduced safety and complicated mixing

Benefits of Combinations

1. Fewer injections
2. Reduced trauma to the infant
3. Higher rates of compliance with complex vaccination schedules[3,4]
4. Better vaccine coverage[5]
5. Timely vaccination – vaccination schedule completed on time[5]
6. Reduced administration costs
7. Lower storage space requirements
8. Allows incorporation of new vaccines into immunization schedules[7]

Vaccine	Trade Names	Adjuvant	Schedule
Childhood: DTaP	Tripedia, Infanrix, Daptacel	Alum	5 doses at 2,4,6, 15-20 mos, 4-6 years
DTaP-Hep B-IPV	Pediarix	Aluminum hydroxide Aluminum phosphate	3 doses: 2,4,6 mos.
DTaP-IPV	Kinrix	Aluminum hydroxide	1 dose: 4-6 years
DTaP-IPV-HiB	Pentacel	Aluminum hydroxide	4 doses: 2,4,6, and 15-18 months
Hep-HiB	Comvax		3 doses: 2,4, 12-15 mos
MMRV	ProQuad	Live attenuated	2 doses: 12-15 mos, 4-6 years
Adult: DtaP	Adacel, Boostrix	Aluminum hydroxide	1 dose at 10 years and over
Hep A-Hep B	Twinrix		3 doses: 0, 1, 6 months

Vaccine Safety and Effectiveness

- Vaccines are safe and effective
- However----------

  THEY ARE NEITHER PERFECTLY SAFE

  NOR

  PERFECTLY EFFECTIVE

- Consequently, some persons who receive vaccine will be injured as a result and some persons who receive vaccine will not be protected.

Risk :Benefit Ratio

- To determine some of the issues must look at risk to benefit ratios

- EX: *OPV (oral polio vaccine…..live attenuated) and risk of polio. With lack of wild type polio in US, risks of paralytic polio were 1:2.4 million doses. Changed to IPV (Inactivated polio vaccines) to reduce risk.*

Vaccine Adverse Reactions

- Local adverse reactions
  - pain, swelling, redness at site of injection, occur within a few hours of injection
  - Usually mild and self-limited
- Systemic adverse reactions
  - fever, malaise, headache, nonspecific
  - may be unrelated to vaccine
- Severe allergic (anaphylaxis)
  - due to vaccine or vaccine component, rare
  - risk minimized by screen

Reporting Vaccine Adverse Events

- Providers need to report any clinically significant adverse event
- VAERS (Vaccine Adverse Event Reporting System)
- (800)822-7967
- website: http://vaers.hhs.gov

Contraindications

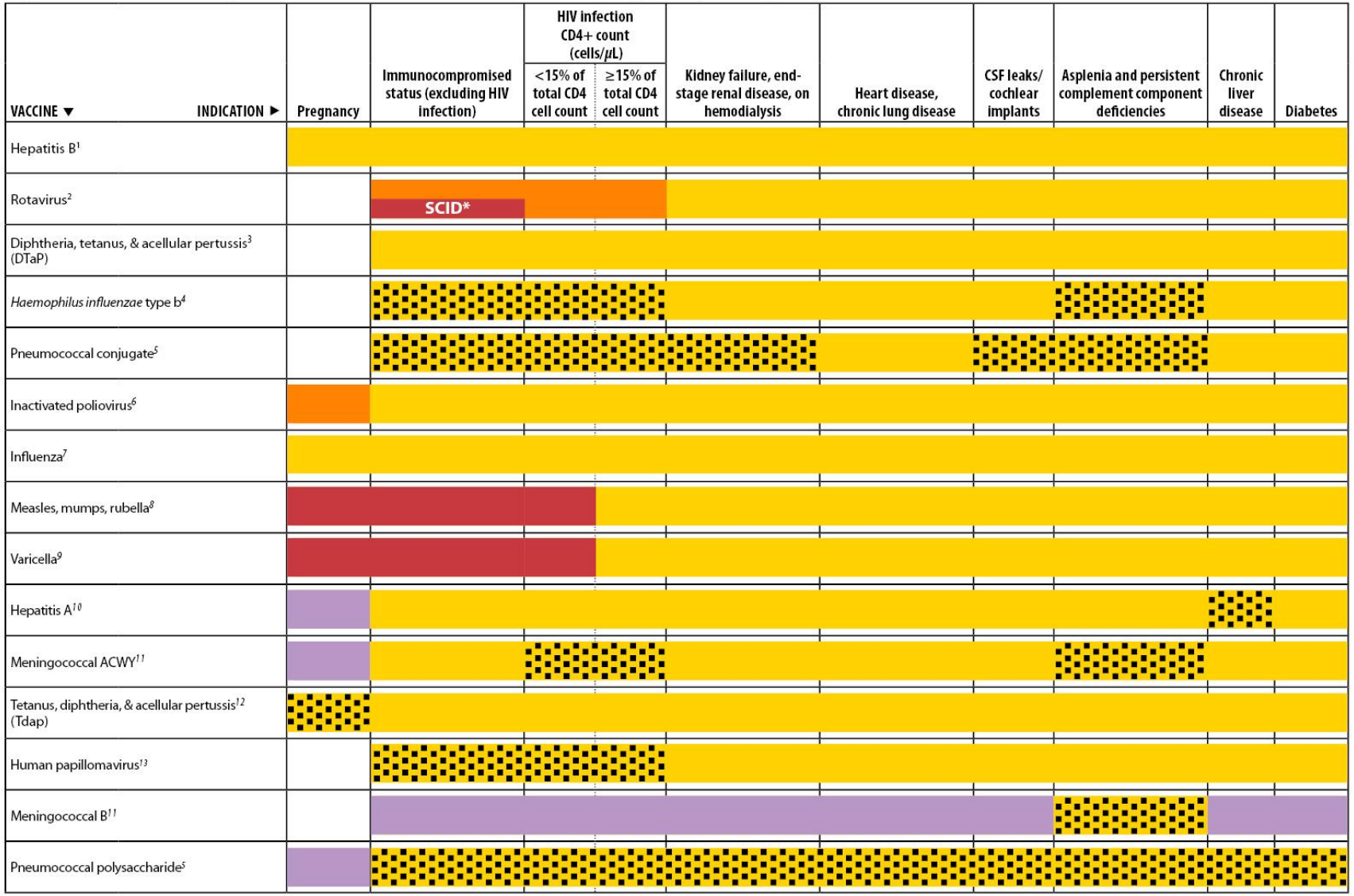
- Permanent contraindications to vaccination:
  - Severe allergic reaction to a vaccine component or following a prior dose
  - Encephalopathy not due to another identifiable cause occurring within 7 days of pertussis vaccination
  - Severe combined immunodeficiency (rotavirus vaccine)
  - History of intussusception (rotavirus vaccine)

Precaution

- Mild to severe illness is a precaution to vaccination
- Vaccine will still be effective and there will not be increased adverse events
  - Main concern is side effects(like fever) might complicate the management of the illness
- Both live and inactivated vaccines should be given after recovery from the illness

Condition	Live	Inactivated
Allergy to component	C	C
Encephalopathy		C
Pregnancy	C	V*
Immunosuppression	C	V
Severe Illness	P	P
Recent blood product	P**	V
C= Contraindication P= Precaution V=OK *except HPV **MMR and Varicella containing (except zoster vaccine) only		

Figure 3. Vaccines that might be indicated for children and adolescents aged 18 years or younger based on medical indications



*Severe Combined Immunodeficiency

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Figure 2. Recommended immunization schedule for adults aged 19 years or older by medical condition and other indications, United States, 2017

Vaccine	Pregnancy[1-6,9]	Immuno-compromised (excluding HIV infection)[3-7,11]	HIV infection CD4+ count (cells/µL)[3-7,9-11]		Asplenia, persistent complement deficiencies[7,10,11]	Kidney failure, end-stage renal disease, on hemodialysis[7,9]	Heart or lung disease, chronic alcoholism[7]	Chronic liver disease[7-9]	Diabetes[7,9]	Healthcare personnel[3,4,9]	Men who have sex with men[6,8,9]
			< 200	≥ 200							
Influenza[1]	1 dose annually										
Td/Tdap[2]	1 dose Tdap each pregnancy	Substitute Tdap for Td once, then Td booster every 10 yrs									
MMR[3]	contraindicated	1 or 2 doses depending on indication									
VAR[4]	contraindicated	2 doses									
HZV[5]	contraindicated				1 dose						
HPV–Female[6]		3 doses through age 26 yrs									
HPV–Male[6]		3 doses through age 26 yrs			3 doses through age 21 yrs						3 doses through age 26 yrs
PCV13[7]		1 dose									
PPSV23[7]		1, 2, or 3 doses depending on indication									
HepA[8]	2 or 3 doses depending on vaccine										
HepB[9]	3 doses										
MenACWY or MPSV4[10]	1 or more doses depending on indication										
MenB[10]	2 or 3 doses depending on vaccine										
Hib[11]	3 doses post-HSCT recipients only	1 dose									

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended for adults with additional medical conditions or other indications

Contraindicated

No recommendation

Invalid Contraindications for Vaccination

- Mild illness
- Antimicrobial therapy
- Disease exposure or convalescence
- Pregnant or immunosuppressed person in the household
- Breastfeeding
- Preterm birth
- Allergy to products not present in the vaccine or allergy that is not anaphylaxis
- Family history of adverse events
- Tuberculin skin testing
- Multiple vaccines

Vaccine Hesitancy concerns are not all the same

Some popular topics are:

- Overloading the immune system
- Neurological side effects including Autism
- Mercury and aluminum exposure

Overloading the Immune System Key Facts about Multiple Vaccines

- An infants immune system has the capacity to respond to thousands of antigens at any given time
  - Exposed every day via toys, shopping carts, playground equipment
  - Immune system constantly replenished so can't be overwhelmed
- While the amount of immunizations have increased, children receive fewer antigens than their parents
- The response to multiple vaccines is similar to the response that occurs when vaccines are given separately

Offit et al. *Pediatrics 2002;109(1)*

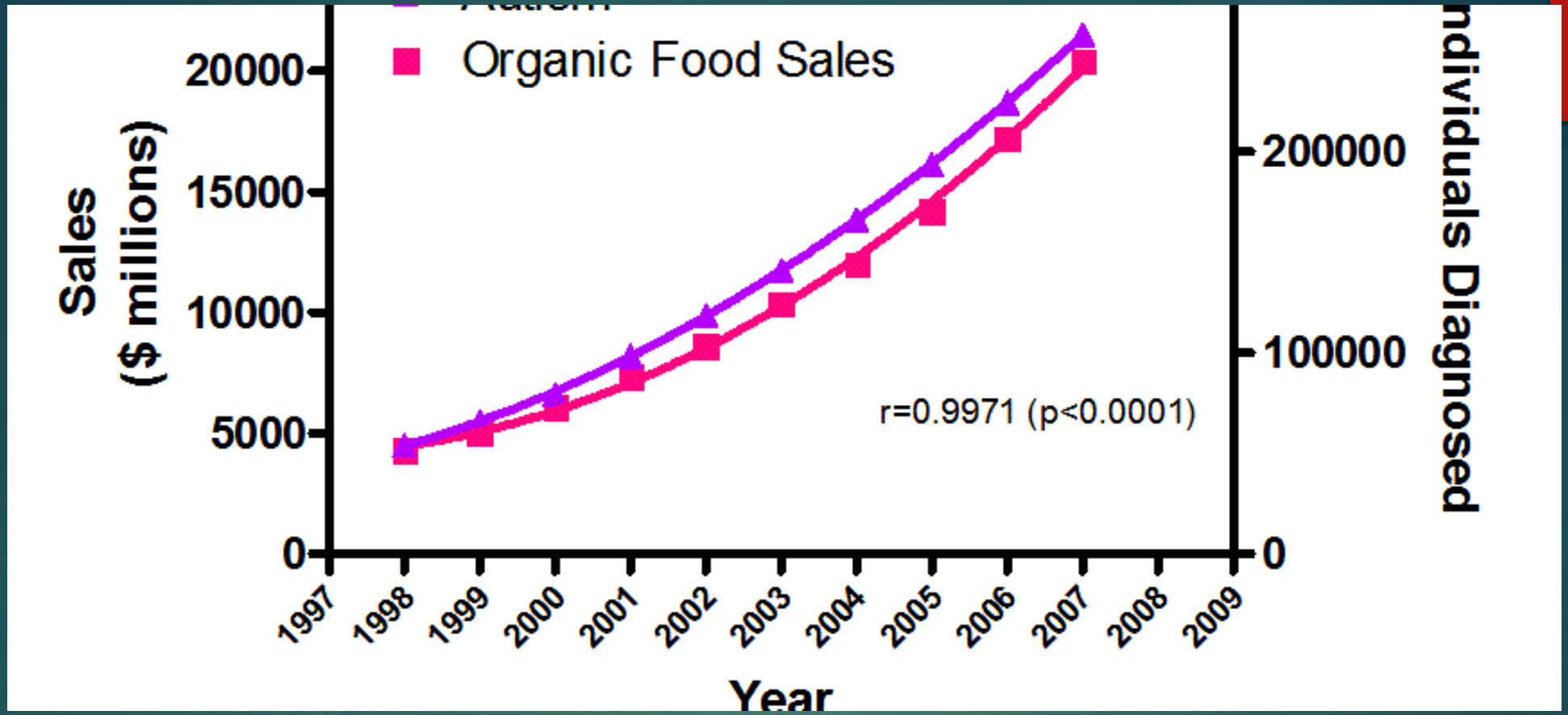
1900		1960		1980		2000	
Vaccine	**Proteins**	**Vaccine**	**Proteins**	**Vaccine**	**Proteins**	**Vaccine**	**Proteins/Polysaccharides**
Smallpox	~200	Smallpox	~200	Diphtheria	1	Diphtheria	1
Total	**~200**	Diphtheria	1	Tetanus	1	Tetanus	1
		Tetanus	1	WC-Pertussis	~3000	AC-Pertussis	2-5
		WC-Pertussis	~3000	Polio	15	Polio	15
		Polio	15	Measles	10	Measles	10
		Total	**~3217**	Mumps	9	Mumps	9
				Rubella	5	Rubella	5
				Total	**~3041**	Hib	2
						Varicella	69
						Pneumococcus	8
						Hepatitis B	1
						Total	**123-126**

Neurodevelopment

- Institute of Medicine has shown that increased number of vaccinations has NOT resulted in higher prevalence of neurodevelopmental problems
- In 2010, the 1998 report alleging the link between MMR and Autism was retracted
  - Several studies since have shown NO link between autism and vaccines
- Vaccine and autism show a TEMPORAL link not a causal link
  - MMR is given around the same time that autism is diagnosed /become apparent despite being present earlier
  - Autism continues to be less understood than many other conditions
  - Parents of autistic children are desperate to find out why and to blame something

Thimerosal, Aluminum and Vaccines

- Large scale studies (as reported by the IOM) found no association between thimerosal and autism or any other developmental delay.
- What vaccines were impacted?
  - DTP, Hemophilus influenza B, Hepatitis B, some influenza vaccines
- MMR never had thimerosal in it
- Aluminum contained in vaccines is similar to that found in a liter (about 1 quart or 32 fluid ounces) of infant formula.
- Given the quantities of aluminum we are exposed to on a daily basis, the quantity of aluminum in vaccines is miniscule.
  - National and Global agencies have determined there is no evidence of health risks with aluminum in vaccines



Correlation does not imply causation

CASE Framework

- C - Corroborate
  - Acknowledge Parent/Patient Concerns
- A - About Me
  - Talk about what you have done to enhance your knowledge
- S - Science
  - Describe what science has to say about the topic in question
- E - Explain and Advise

A parent in your practice does not want his or her child to have the primary series of vaccines at the 2-month visit and is concerned about the number of vaccines the child will receive in the first year of life. The following is an example of an elevator pitch you might develop and reuse in your practice. Additional communication strategies for common parental concern scenarios are available in the CASE video presentation.[26]

- **Corroborate.** "You are correct. Your child will receive more vaccine than you or I did. We both want the same things for your child—to remain healthy and disease free. I know you are concerned, but it is my job to help address your concerns."
- **About me.** "We follow the CDC schedule because it is designed to protect your child when he or she is most susceptible to these diseases. I have spent many years getting education and training in health and medicine, including vaccination. My expertise is why you are here. I have read the recommendations carefully and studied the risks and benefits."

of vaccines using inactivated cells to generate an immune response. This immunological challenge is nothing compared with what your child fights off on a daily basis. An ear infection is a much more significant immune challenge than the vaccines I want to give to your child today."

- **Explain/advise.** "I care about your son/daughter and do not want to practice substandard care. Your child needs to be fully vaccinated to protect against these diseases. I am fully vaccinated and my children are, too."

Abbreviations: CASE, **C**orroborate, **A**bout me, **S**cience, **E**xplain/advise; CDC, Centers for Disease Control and Prevention.

Resources for Vaccine Information for Parents/Caregivers and Providers

Organization	Web site
American Academy of Pediatrics (AAP)	http://www.aap.org/immunization
Centers for Disease Control and Prevention (CDC)	http://www.cdc.gov/vaccines
Immunization Action Coalition (IAC)	http://www.immunize.org
National Network for Immunization Information (NNii)	http://www.immunizationinfo.org
Parents of Kids with Infectious Diseases (PKIDs)	http://www.pkids.org
The Vaccine Education Center at The Children's Hospital of Philadelphia (CHOP)	http://www.chop.edu/service/vaccine-education-center

Giving Vaccines

- Schedules are invaluable in helping time, space, and effectively protect children and adults
- Vaccine information sheets help provide good safety information
- However----actually giving vaccines require other important steps……