Vaccine Safety: Considerations for Primary Care Providers

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EDUCATIONAL DAY TALK
FEBRUARY 19, 2020

Objectives

- Explain Adverse Events Following Immunizations (AEFIs)
- Understand true contraindications/precautions to vaccination
- Learn about select vaccine- and population-specific safety guidelines
- Learn about national vaccine safety regulations
- Recognize the multiple available resources to help with decision-making around vaccination

Patient & Parent Concerns

Health Concerns

Pain of injection

Side effects (prior history vs anecdotes)

Currently healthy and do not want to develop new disease

Introducing too many and/or toxic substances into body→ “overwhelming the immune system”

“Unnatural” method of developing immunity

Societal Concerns

Losing personal liberties

-e.g. parental authority over child's healthcare decisions

Financial motives of providers and manufacturers

Conspiracy theories

-e.g. vaccine preservatives, inadequate research, experimenting on the public

US Vaccination Schedule

United States Vaccination Schedule

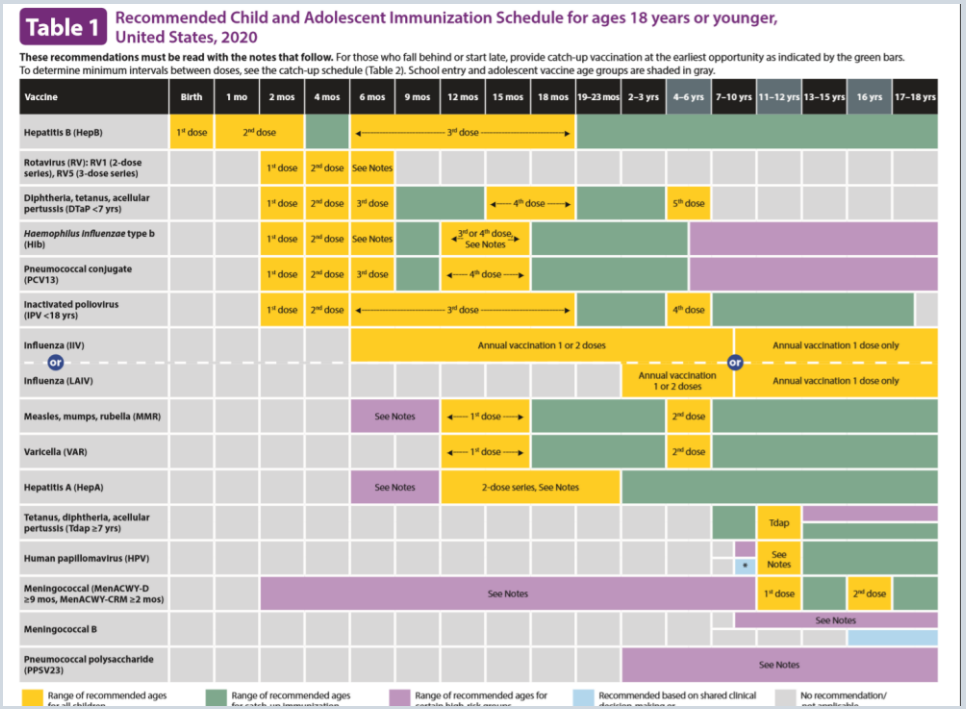


Table 1 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2020

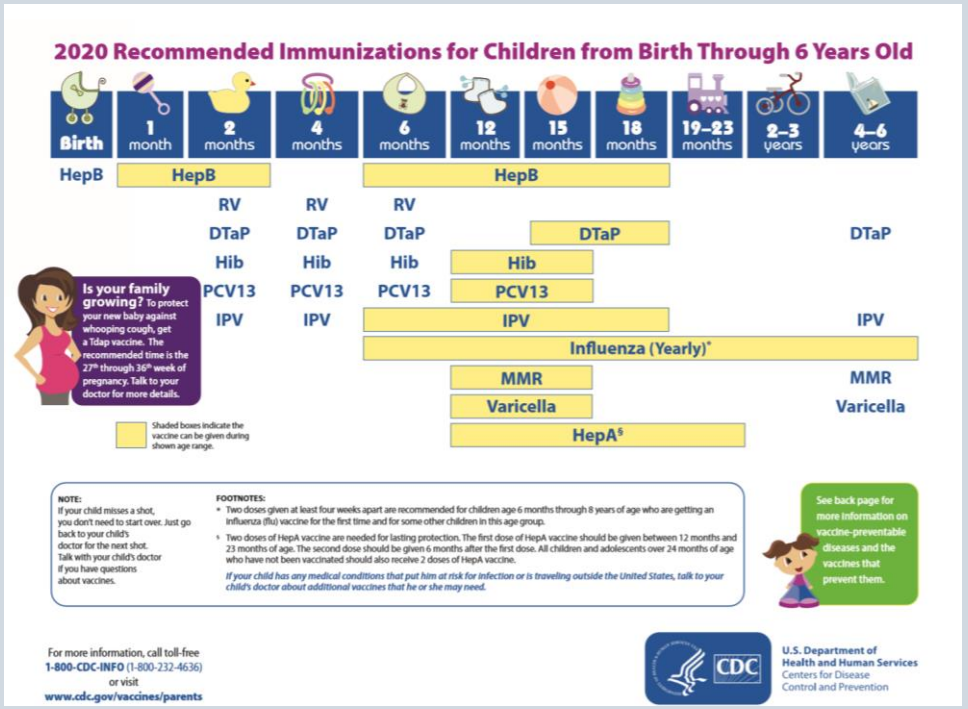
These recommendations must be read with the notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars. To determine minimum intervals between doses, see the catch-up schedule (Table 2). School entry and adolescent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

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
Hepatitis B (HepB)	1st dose	2nd dose			3rd dose												
Rotavirus (RV): RV1 (2-dose series), RV5 (3-dose series)			1st dose	2nd dose	See Notes												
Diphtheria, tetanus, acellular pertussis (DTaP <7 yrs)			1st dose	2nd dose	3rd dose			4th dose				5th dose					
Haemophilus influenzae type b (Hib)			1st dose	2nd dose	See Notes		3rd or 4th dose, See Notes										
Pneumococcal conjugate (PCV13)			1st dose	2nd dose	3rd dose		4th dose										
Inactivated poliovirus (IPV <18 yrs)			1st dose	2nd dose	3rd dose							4th dose					
Influenza (IIV)					Annual vaccination 1 or 2 doses									Annual vaccination 1 dose only			
or																	
Influenza (LAIV)												Annual vaccination 1 or 2 doses		Annual vaccination 1 dose only			
Measles, mumps, rubella (MMR)					See Notes		1st dose					2nd dose					
Varicella (VAR)							1st dose					2nd dose					
Hepatitis A (HepA)					See Notes		2-dose series, See Notes										
Tetanus, diphtheria, acellular pertussis (Tdap ≥7 yrs)														Tdap			
Human papillomavirus (HPV)														See Notes			
Meningococcal (MenACWY-D ≥9 mos, MenACWY-CRM ≥2 mos)			See Notes											1st dose		2nd dose	
Meningococcal B														See Notes			
Pneumococcal polysaccharide (PPSV23)												See Notes					

Range of recommended ages | Range of recommended ages | Range of recommended ages for | Recommended based on shared clinical | No recommendation/

https://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html

Provider Version



https://www.cdc.gov/vaccines/schedules/easy-to-read/child-easyread.html

Parent-Friendly Version

Advisory Committee on Immunization Practices (ACIP)

- US Vaccine schedule set by CDC's ACIP recommendations
  - 15 voting members from research and medical specialties
  - 8 members representing national agencies involved in immunization policy
  - 30 liaison organizations with immunization expertise
- Meets together three times per year and in smaller working groups year-round

https://www.cdc.gov/vaccines/acip/about.html

How are vaccines chosen for the schedule?

- Latest research is reviewed year-round by working groups
- Research on specific vaccines includes:
  - Safety, immunogenicity, effectiveness of a vaccine at a given age
  - Severity of disease being prevented
  - Number of children affected if no vaccine exists

The Advisory Committee on Immunization Practices (ACIP): Questions and Answers

How is the timing of vaccines determined?

- Research on timing of administration primarily focuses on **morbidity and mortality at different ages**
  - ACIP studies the ages at which disease rates peak
  - Balances risks of disease exposure to vaccine safety and effectiveness
  - Goal is to vaccinate as early and safely as is beneficial

The Advisory Committee on Immunization Practices (ACIP): Questions and Answers

Is it safe to give so many vaccines at once?!

- YES.
- Giving multiple vaccines at a single visit
  - Improves coverage rates and individual protection
  - More convenient/cost-effective for patient
  - Does not change safety or efficacy of vaccines

CDC Pinkbook p. 27

Exceptions to multi-vaccine administration

- In general, any vaccine can be co-administered with any other vaccine except…
- AVOID co-administering the following:
  - PCV-13 and Menactra
    - Especially in asplenic patients
  - Combo MMRV vaccine (age <4 y or first dose)
    - Ok to give MMR and VZV at the same time but separately

http://www.immunize.org/askexperts/experts_meningococcal_acwy.asp
CDC Pinkbook p. 12

Adverse Events

Adverse Events Following Immunization (AEFI)

- What is an AEFI?
  - "An untoward effect caused by a vaccine that is extraneous to the vaccine's primary purpose of producing immunity"
  - aka Side Effect
- Three primary types
  - Localized
  - Systemic
  - Allergic

CDC Pinkbook p. 15

Localized Reactions

- Most common type (up to 80% of vaccine doses)
- Examples: pain, swelling, redness at injection site, etc
- Occurs within hours of vaccine administration
- Usually mild, self-limited
- Rarely more severe—Arthus reaction

CDC Pinkbook pp. 15-16

Systemic Reactions

- Generalized, relatively mild symptoms
- Examples: fever, myalgias, headache, etc
- Non-specific symptoms; not always related to vaccine itself
- Somewhat more common with live-vaccines
  - Virus needs to replicate
- Occurs days to weeks after vaccination

CDC Pinkbook p. 16

Allergic Reactions

- Rare, require medical attention
- Occur within minutes to hours of receiving vaccine
- Examples: diffuse urticaria, wheezing, anaphylaxis, etc
- Reaction may be to any vaccine component: antigen, preservative, cell culture medium, etc
- Risk can be reduced with pre-vaccine screening

CDC Pinkbook pp. 16-18

AEFI and Causality

- AEFI can fit into multiple other categories besides extent of effects
  - Severity, frequency, disease, age
  - Vaccine-induced, programmatic, idiosyncratic, coincidental
- Difficult to assess causality
  - More likely if: occurs on repeat administration, observed in prior studies, timing plausible,* biologically plausible
  - *Note: timing does NOT necessarily indicate causality

CDC Pinkbook pp. 49-50

The Provider's Responsibility

- Product Management (storage, handling, administration)
- Patient Care
  - Screening for precautions and contraindications
  - Timing and spacing of vaccines
  - Managing AEFI
  - Reporting AEFI to Vaccine Adverse Events Reporting System
  - Communicating risks/benefits to patients

CDC Pinkbook p. 55

National Vaccine Safety Regulations

Vaccine Safety & Monitoring

- National Childhood Vaccine Injury Act (NCVIA) (1986)
  - Spurred by increase in lawsuits against manufacturers
  - Mandated providers, manufacturers to report adverse events after vaccination
- **Vaccine Adverse Event Reporting System (VAERS) (1990)**
  - Administered by the CDC and FDA
  - May be confirmed adverse reactions or coincidental events
  - Receives 30,000 reports/year (41% providers, 29% manufacturers, 14% patients/parents)

CDC Pinkbook pp. 51-52

Vaccine Adverse Effects Monitoring System

- VAERS is able to detect
  - New or rare adverse events
  - Increase in rates of AEFIs
  - Patient risk factors for AEFIs
- Further studies needed to clarify adverse event signals
- Not all reported adverse events are causal effects

CDC Pinkbook pp. 52

Vaccine Adverse Effects Monitoring System

- Providers are required to report some adverse events following specific vaccinations to VAERS
- Encouraged to report any clinically significant event after vaccination if unsure about causality
- Manufacturers required to submit any adverse effects of which they become aware

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Vaccine Information Statements

- Vaccine information statements (VIS) must be given to patients prior to vaccination
- Mandated by National Childhood Vaccine Injury Act
- Available from CDC website, multiple languages
- Can use as a starting point in addressing patient concerns or screening for contraindications

CDC Pinkbook pp. 59

VAERS Reportable Events Following Vaccination

- Table of mandated reportable events available online

Measles, mumps and rubella in any combination; MMR, MR, M, MMRV, R	A. Anaphylaxis or anaphylactic shock (7 days) B. Encephalopathy or encephalitis (15 days) C. Any acute complications or sequelae (including death) of above events (interval - not applicable) D. Events described in manufacturer's package insert as contraindications to additional doses of vaccine (interval - see package insert)
Rubella in any combination; MMR, MMRV, MR, R	A. Chronic arthritis (42 days) B. Any acute complications or sequelae (including death) of above event (interval - not applicable) C. Events described in manufacturer's package insert as contraindications to additional doses of vaccine (interval - see package insert)
Measles in any combination; MMR, MMRV, MR, M	A. Thrombocytopenic purpura (7-30 days) B. Vaccine-strain measles viral infection in an immunodeficient recipient (6 months) C. Any acute complications or sequelae (including death) of above events (interval - not applicable) D. Events described in manufacturer's package insert as contraindications to additional doses of vaccine (interval - see package insert)

https://vaers.hhs.gov/resources/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf

More Vaccine Safety & Monitoring

- Vaccine Safety Datalink (VSD) (1990)
  - Partnership between CDC and large health plans to monitor rare and serious adverse events
  - Allows rapid cycle analysis of events in close to real time
- Vaccine Injury Compensation Program (VICP) (1986)
  - “No fault” program
  - Covers routine childhood vaccines (adults can file claims too)
  - Uses vaccine injury table

CDC Pinkbook p. 53
CDC Pinkbook pp. 54-55

CISA Program

- Clinical Immunization Safety Assessment Program (CISA)
  - CDC-supported program focusing on vaccine safety at individual patient level
  - Works on strategies to detect and prevent adverse events especially in special populations
  - Provides free consult service to providers
    - Phone: 1-800-CDC-INFO
    - Email: CISAeval@cdc.gov

CDC Pinkbook p. 54

Contraindications and Precautions

When NOT to Vaccinate

- Contraindication
  - A condition that increases the risk of a patient developing a serious AEFI
  - Do not administer the vaccine
- Precaution
  - A condition that might increase the risk or severity of an AEFI or compromise vaccine's effectiveness
  - Avoid administering unless benefits >> risks

CDC Pinkbook p. 57

Screening for Contraindications/Precautions

- May be temporary or permanent
  - Temporary: Moderate-severe illness, pregnant, etc
  - Permanent: Prior history of anaphylaxis after receiving vaccine, Guillain-Barre, etc
- Screening is important tool in reducing risk of AEFI
  - Immunization Action Coalition has standardized screening forms for children and adults

CDC Pinkbook p. 30

General Contraindications

- All vaccines
  - Allergy to vaccine component
  - Encephalopathy
- Live-attenuated vaccines (MMR, VZV, LAIV, typhoid)
  - Pregnancy
  - Immunosuppression

CDC Pinkbook p. 17

General Precautions

- All vaccines
  - Moderate to severe illness
  - Acutely febrile
- Live-attenuated vaccines (MMR, VZV, LAIV, typhoid)
  - Recently received blood products (MMR, VZV)

CDC Pinkbook pp. 17

Specific Contraindications

- Rotavirus
  - SCID, Intussusception
- Tdap
  - Encephalopathy within 7 days without other clear cause
- HPV
  - Pregnancy
- Live vaccines
  - Immunosuppression, pregnancy

CDC Pinkbook pp. 17

Specific Precautions

- Guillain-Barré Syndrome
  - Tetanus, influenza
- DTaP
  - Inconsolable crying, seizure, limp/pale episode, high fevers within 48 h of administration without other known cause

CDC Pinkbook pp. 28-29

NOT a Contraindication to Vaccination

- Mild illness
- Mild self-limited localized reaction to previous dose
- Living with immunocompromised or pregnant person
- Potential exposure to infectious disease
- Current antibiotic use
- Breastfeeding
- Premature birth

CDC Pinkbook p. 24

Special Considerations

Timing/Spacing Between Doses

- Vaccines can be given up to **4 days before** minimum interval to be counted as valid per ACIP recommendations
  - Rules may vary by organization
- Interval between doses
  - Typically about 4 weeks
  - Increasing interval does not reduce effectiveness
  - Decreasing interval may interfere with antibody response to previous dose

Source: CDC Pink book, pp. 9-14

Egg Allergy

- General rule: If patient can eat eggs and egg-containing products without difficulty, they can get egg-prepared vaccines (flu, yellow fever, MMR)
  - MMR ok to give with egg allergies
- If patient has history of anaphylaxis with egg products, avoid or “refer for further evaluation”

CDC Pinkbook pp. 18

Pregnancy

- ACOG Committee Opinion 741
  - No evidence of adverse fetal effects from inactivated vaccines
  - Growing evidence of safety of vaccination in pregnancy
- DO NOT administer
  - Live vaccines (MMR, VZV, intranasal flu, typhoid)→avoid pregnancy for 4 weeks following administration
  - HPV (not enough data yet)

ACOG Committee Opinion 741, June 2018
CDC Pinkbook pp. 17-19

Pregnancy

- Can give >1 vaccine at a time
- Tdap
  - Safe to give anytime
  - Preferably administer weeks 27-36 for highest chance of intrapartum transfer of passive immunity
  - Close family and caregivers should be vaccinated within 2 weeks of anticipated due date (“cocooning”)

CDC Pinkbook pp. 17-19

Thimerosal

- Mercury-based antimicrobial additive used in many vaccines
  - NOT the same as toxic mercury found in fish
- Has been safely used in vaccines since the 1930s
- No longer used in childhood vaccines
  - Exception: multi-dose flu given to adults and kids
- Does NOT cause toxicity or autism

https://www.cdc.gov/vaccinesafety/concerns/thimerosal/faqs.html

Do Vaccines Cause Autism?

- **NO.**
  - Neither do any known additives or adjuvants (e.g. thimerosal)
- MULTIPLE peer-reviewed studies have shown that there is NO link between autism and any vaccine, including MMR
  - See CDC website and PubMed for full papers
  - Studies include comparisons of vaccinated to unvaccinated children and those with autism compared to those without

https://www.cdc.gov/vaccinesafety/concerns/autism.html

Great Resources on Vaccines

- CDC's Epidemiology and Prevention of Vaccine Preventable Diseases, 13th edition
  - Available for free online at cdc.gov
- Immunization Action Coalition
  - Great provider and parent resources including vaccine screening sheets free at immunize.org
- The History of Vaccines
  - Interactive educational tool for providers, parents, kids at historyofvaccines.org
- Naro, Maki. Vaccines Work: Here are the Facts.
  - http://deadstate.org/this-comic-strip-is-the-definitive-smackdown-to-anti-vaxxers-everywhere/

The End

THANK YOU!

Sources

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