Principles of Vaccination

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Immunity

- Self vs. “nonself”
- Protection from infectious diseases
- Usually indicated by the presence of antibody
- Generally specific to a single organism
Antigen

- Live or inactivated substances (e.g., viruses, bacteria, toxins)
  - Capable of stimulating an immune response

- Anti + gen = antibody generator
Antibody

- Protein molecules (immunoglobulins)
  - Produced by B cells (lymphocytes) to bind to a corresponding antigen (lock and key mechanism)
  - Helps neutralize antigen and prepare it for destruction
  - B cells develop in the bone marrow
Arms of the Immune System

- **Humoral**
  - Production of antibodies that are specific to a certain antigen or group of antigens
  - Antibodies attach to invading organism and interfere with its ability to produce more invading organisms
Arms of the Immune System

- **Cell-mediated – T lymphocytes (T-cells)**
  - Involves the activation of T-cells, macrophages, and other substances that eliminate the antigen
  - T-cells mature in the thymus gland
Types of Immunity: Active and Passive
Passive Immunity

- Transfer of antibody produced by one human or animal to another
- Temporary protection that wanes with time
- Transfer of antibody through placenta – important to protect infants
Passive Immunity Video

- The video will start shortly.
Sources of Passive Immunity

- Many types of blood or blood products

- Homologous pooled human antibody (immune globulin or IG)
  - IgG antibody from the blood of thousands of American adult donors
  - Hepatitis A and measles postexposure prophylaxis (PEP)
Sources of Passive Immunity

- **Homologous human hyperimmune globulin (e.g., HBIG)**
  - Taken from donors with high concentrations of a specific antibody
  - HBIG, RIG, TIG, VariZIG, VIG

- **Heterologous hyperimmune serum**
  - Antitoxin (e.g., diphtheria antitoxin)
  - Serum sickness
Sources of Passive Immunity

- Monoclonal antibodies
  - Derived from a single type, or clone, of antibody-producing cells (B cells)
    - Immune globulin from human sources is polyclonal (contains many different kinds of antibodies)
  - Antibody is specific to a single antigen or closely related group of antigens
  - Used for diagnosis of and therapy for certain cancers and autoimmune and infectious diseases, as well as prevention of transplant rejection
  - Monoclonal-antibody-derived drugs end in –mab (i.e., Palivizumab)
Antibody for Prevention of RSV

- Palivizumab (Synagis)
  - Monoclonal
  - Contains only RSV antibody
  - Will not interfere with the response to a live-virus vaccine
Active Immunity

- Protection produced by a person's own immune system
- Lasts for many years, often lifetime
Active Immunity Video

- The video will start shortly.
Sources of Active Immunity

- Infection with disease-causing form of organism
- Vaccination
Vaccination

- Active immunity produced by vaccine
  - Vaccine delivers a dead or attenuated (weakened, nonpathogenic) form of the pathogen

- Immunity and immunologic memory similar to natural infection but without risk of disease
  - Immunologic memory allows for an anamnestic response after the primary immune response, so that antibody reappears when the antigen is introduced
Factors that Affect Immune Response to Vaccines

- Presence of maternal antibodies
- Nature and amount of antigen in vaccine
- Route of administration
- Presence of an adjuvant (ingredient that promotes a stronger immune response)
- Storage and handling of vaccine
- Vaccinee
  - Age
  - Nutritional status
  - Genetics
  - Coexisting disease
Classification of Vaccines
Classification of Vaccines

- Live, attenuated (weakened form of the organism)
  - Viral
  - Bacterial

- Inactivated (non-live or fraction of the organism)
  - Viral
  - Bacterial
Principles of Vaccination

- General rule: The more similar a vaccine is to the natural disease, the better the immune response to the vaccine
Live Attenuated Vaccine Video

- The video will start shortly.
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

- Usually produce immunity with 1 dose*

*Except those administered orally
Individual Response to Live Vaccine

The graph shows the antibody levels before and after receiving doses of a live vaccine. The x-axis represents different time points: Pre, Post 1, Post 2, Post 3, and 5 years. The y-axis represents the antibody level. The protective level is indicated by a pink line.

- Pre: Antibody level is very low.
- Post 1: Antibody level increases significantly.
- Post 2: Antibody level remains high.
- Post 3: Antibody level decreases but remains above protective level.
- 5 yrs: Antibody level is still above the protective level.

The graph indicates a positive immune response to the live vaccine, with protective levels maintained over time.
Population Response to Live Vaccine

- Pre
- Post 1
- Post 2
- Post 3

Percent Immune vs. Dose
**Herd Immunity/Community Immunity**

- When a significant portion of the population is immune and provides protection for individuals who are not immune.
Live, Attenuated Vaccines

- Severe reactions possible

- Interference from circulating antibody

- Fragile – must be stored and handled carefully
Live, Attenuated Vaccines

- **Viral**
  - MMR, varicella, zoster vaccine live (ZVL), yellow fever, rotavirus, LAIV (intranasal influenza), smallpox (vaccinia), oral adenovirus, oral polio*

- **Bacterial**
  - BCG**, oral typhoid, oral cholera

* Not used in the United States

**Not used in the United States for routine TB protection
Inactivated Vaccines

- **Whole**
  - Viruses
  - Bacteria

- **Fractional**
  - Protein-based
    - Toxoid
    - Subunit
  - Polysaccharide-based
    - Pure
    - Conjugate
Inactivated Vaccine Vaccine Video

- The video will start shortly.
Inactivated Vaccines

- Cannot replicate

- Less affected by circulating antibody than live vaccines
  - Example: HepB vaccine and HBIG for perinatal hepatitis B PEP

- Always require multiple doses

- Immune response mostly humoral

- Antibody titer diminishes with time

- May require periodic supplemental doses
Individual Response to Inactivated Vaccine

Protective level

Antibody level

Dose

Pre Post 1 Post 2 Post 3 Post 4 5 yrs
Population Response to Inactivated Vaccine

![Graph showing the percentage immune over doses](image-url)
Inactivated Vaccines

- **Whole**
  - **Viral**
    - Polio, hepatitis A, rabies, Japanese encephalitis, and influenza*
  - **Bacterial**
    - Pertussis*, typhoid*, cholera*, plague*

*Not available in the United States
Inactivated Vaccines

- Fractional
  - Subunit
    - Hepatitis B, influenza, acellular pertussis, human papillomavirus, and anthrax
    - Polysaccharide vaccines
  - Toxoid
    - Diphtheria, tetanus
Capsular Polysaccharide
Capsular Polysaccharide
Pure Polysaccharide Vaccines

- Immune response typically T-cell-independent
- Not consistently immunogenic in children younger than 2 years of age
- No booster response
- Antibody with less functional activity (IgM rather than IgG)
- Immunogenicity improved by conjugation
Polysaccharide Vaccines

- **Pure polysaccharide**
  - Pneumococcal (PPSV23)
  - *Salmonella Typhi* (Vi)

- **Conjugate polysaccharide**
  - *Haemophilus influenzae* type b (Hib)
  - Pneumococcal (PCV13)
  - Meningococcal
Genetically Engineered Vaccines

- Viral: hepatitis B, human papillomavirus, influenza (RIV), influenza (LAIV), and rotavirus (RV5)

- Bacterial: meningococcal B
Figure 1. Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger—United States, 2018.

(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.

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<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>18-33 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16 yrs</th>
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<td>Hemophilus influenza type b (HiB)</td>
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<td>Annual vaccination (IV)</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis</td>
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<td>Human papillomavirus (HPV)</td>
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<td>Meningococcal B (MenB)</td>
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<td>Pneumococcal polysaccharide (PPV23)</td>
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Range of recommended ages for all children
Range of recommended ages for catch-up immunization
Range of recommended ages for certain high-risk groups
Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision making
No recommendation

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—18 years who start late or who are more than 1 month behind—United States, 2018.

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.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Minimum Age for Dose 1</th>
<th>Minimum Interval Between Doses</th>
<th>Minimum Interval for Dose 2</th>
<th>Dose 3 to Dose 2</th>
<th>Dose 3 to Dose 4</th>
<th>Dose 4 to Dose 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B1</td>
<td>Birth</td>
<td>8 weeks and at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks.</td>
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<tr>
<td>Rotavirus2</td>
<td>6 weeks maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Diphtheria, tetanus, and acellular pertussis</td>
<td>6 weeks maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Haemophilus influenza type b1</td>
<td>6 weeks maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Haemophilus influenza type b1</td>
<td>6 weeks maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Inactivated poliovirus2</td>
<td>6 weeks maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Measles, mumps, rubella</td>
<td>12 months maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<td>Meningococcal (MenA,C,Y,W13) vaccine</td>
<td>12 months maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<td>Meningococcal (MenA,C,Y,W13) vaccine</td>
<td>12 months maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Hepatitis A</td>
<td>12 months maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Meningococcal (MenA,C,Y,W13) vaccine</td>
<td>12 months maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<td>Tetanus, diphtheria, tetanus, and acellular pertussis</td>
<td>7 years maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Human papillomavirus</td>
<td>9 years maximum age for first dose 4 weeks</td>
<td>4 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Hepatitis B</td>
<td>N/A</td>
<td>6 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Inactivated poliovirus2</td>
<td>N/A</td>
<td>6 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Measles, mumps, rubella</td>
<td>N/A</td>
<td>6 weeks maximum age for final dose is 8 months, 0 days</td>
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<tr>
<td>Vancella</td>
<td>N/A</td>
<td>6 weeks maximum age for final dose is 8 months, 0 days</td>
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</tbody>
</table>

NOTE: The above recommendations must be read along with the footnotes of this schedule.
Figure 3. Vaccines that might be indicated for children and adolescents aged 18 years or younger based on medical indications

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>INDICATION</th>
<th>Pregnancy</th>
<th>Immunocompromised status (excluding HIV infection)</th>
<th>HIV infection (CD4+ count)</th>
<th>Kidney failure, end-stage renal disease, on hemodialysis</th>
<th>Heart disease, chronic lung disease</th>
<th>CSF leaks/cochlear implants</th>
<th>Asplenia and persistent complement deficiencies</th>
<th>Chronic liver disease</th>
<th>Diabetes</th>
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<tr>
<td><strong>Hepatitis B</strong></td>
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<td><strong>Diphtheria, tetanus, &amp; acellular pertussis</strong> (DTaP)</td>
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<td><strong>Haemophilus influenzae type b</strong></td>
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<td><strong>Measles, mumps, rubella</strong></td>
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<td><strong>Varicella</strong></td>
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<td><strong>Hepatitis A</strong></td>
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<td><strong>Tetanus, diphtheria, &amp; acellular pertussis</strong> (Tdap)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Human papillomavirus</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>Meningococcal B</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Pneumococcal polysaccharide</strong></td>
<td></td>
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</tr>
</tbody>
</table>

*Severe combined immunodeficiency

**Precaution for vaccination**

NOTE: The above recommendations must be read along with the footnotes of this schedule.
Figure 1. Recommended Immunization schedule for adults aged 19 years or older by age group, United States, 2018

This figure should be reviewed with the accompanying footnotes. This figure and the footnotes describe indications for which vaccines, if not previously administered, should be administered unless noted otherwise.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19–21 years</th>
<th>22–26 years</th>
<th>27–49 years</th>
<th>50–64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza¹</td>
<td></td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tdap³ or Td²</td>
<td></td>
<td></td>
<td>1 dose Tdap, then Td booster every 10 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAR⁴</td>
<td></td>
<td></td>
<td></td>
<td>2 doses</td>
<td></td>
</tr>
<tr>
<td>RZV⁵ (preferred)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 doses RZV (preferred)</td>
</tr>
<tr>
<td>Or ZVL⁶</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV–Female²</td>
<td></td>
<td></td>
<td>2 or 3 doses depending on age at series initiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV–Male³</td>
<td></td>
<td></td>
<td></td>
<td>2 or 3 doses depending on age at series initiation</td>
<td></td>
</tr>
<tr>
<td>PCV13⁷</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
</tr>
<tr>
<td>PPSV23⁷</td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
<td></td>
</tr>
<tr>
<td>HepA⁸</td>
<td></td>
<td></td>
<td></td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
</tr>
<tr>
<td>HepB⁸</td>
<td></td>
<td></td>
<td></td>
<td>3 doses</td>
<td></td>
</tr>
<tr>
<td>MenACWY¹⁰</td>
<td></td>
<td></td>
<td>1 or 2 doses depending on indication, then booster every 5 yrs if risk remains</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MenB¹⁰</td>
<td></td>
<td></td>
<td></td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
</tr>
<tr>
<td>Hib¹¹</td>
<td></td>
<td></td>
<td></td>
<td>1 or 3 doses depending on Indication</td>
<td></td>
</tr>
</tbody>
</table>

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

Recommended for adults with other indications

No recommendation
### Figure 2. Recommended Immunization Schedule for Adults Aged 19 Years or Older by Medical Condition and Other Indications, United States, 2018

This figure should be reviewed with the accompanying footnotes. This figure and the footnotes describe indications for which vaccines, if not previously administered, should be administered unless noted otherwise.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Pregnancy</th>
<th>Immuno-compromised (excluding HIV infection)</th>
<th>HIV infection CD4+ count (cells/µL)</th>
<th>Asplenia, complement deficiencies</th>
<th>End-stage renal disease, on hemodialysis</th>
<th>Heart or lung disease, alcoholism</th>
<th>Chronic liver disease</th>
<th>Diabetes</th>
<th>Health care personnel</th>
<th>Men who have sex with men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza¹</td>
<td>1 dose annually</td>
<td>1 dose Tdap, then Td booster every 10 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tdap or Td²</td>
<td>contraindicated</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>MMR³</td>
<td>contraindicated</td>
<td>1 or 2 doses depending on indication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAR⁴</td>
<td>contraindicated</td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>RZV (preferred) or ZVL²</td>
<td>2 doses RZV at age ≥50 yrs (preferred)</td>
<td>1 dose ZVL at age ≥60 yrs</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>HPV—Female*</td>
<td>3 doses through age 26 yrs</td>
<td>2 or 3 doses through age 26 yrs</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>HPV—Male*</td>
<td>3 doses through age 26 yrs</td>
<td>2 or 3 doses through age 21 yrs</td>
<td>2 or 3 doses through age 26 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>PCV13³</td>
<td>1 dose</td>
<td></td>
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<tr>
<td>PPSV23³</td>
<td>1, 2, or 3 doses depending on indication</td>
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<td></td>
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<tr>
<td>HepA⁴</td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>HepB⁵</td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MenACWY⁶⁷</td>
<td>1 or 2 doses depending on indication, then booster every 5 yrs if risk remains</td>
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<td></td>
</tr>
<tr>
<td>MenB⁸⁹</td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hib¹¹</td>
<td>3 doses HSCT recipients only</td>
<td>1 dose</td>
<td></td>
<td></td>
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</tbody>
</table>

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**Legend:**
- Yellow: Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection
- Purple: Recommended for adults with other indications
- Red: Contraindicated
- White: No recommendation

---

¹ For patients ≥65 years of age, a single dose of influenza vaccine is recommended annually.
² Tdap is preferred over Td for adults ≥11 years. Td every 10 years is recommended for adults aged 65 years and older.
³ MMR vaccine is contraindicated for pregnancy. PEP (post-exposure prophylaxis) is recommended until measles has been ruled out.
⁴ VAR vaccine is contraindicated for pregnancy. PEP is recommended until varicella has been ruled out.
⁵ RZV vaccine is contraindicated for pregnancy.
⁶ PPSV23 vaccine is contraindicated for pregnancy.
⁻ HPV vaccine is contraindicated for pregnancy.
¹¹ Hib vaccine is contraindicated for pregnancy.
What Do You Think?

- Because pure polysaccharide vaccines (e.g., PPSV23) are T-cell-independent, they provide good booster responses with subsequent doses.
  - True
  - False