OPTIMIZING VACCINE IMMUNITY IN THE IMMUNOCOMPROMISED PEDIATRIC PATIENT

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Disclosures

- I do not have relevant financial relationships with commercial interests related to the content of this presentation.
Learning Objectives

- Delineate guiding principles for immunization of immunocompromised children
- Implement specific immunization recommendations into practice
- Improve systems for vaccine delivery in immunocompromised pediatric patients
Learning Objectives

- Delineate guiding principles for immunization of immunocompromised children
Tommy

- 12 yo male with history of hypoplastic left heart syndrome
- Underwent orthotopic heart transplant at 10 years of age
- Remains on Immunosuppression
- New to the area
Tommy
Vaccine-Preventable Diseases Timeline

- Smallpox
- Rabies
- Cholera
- Typhoid
- Diphtheria
- Pertussis
- Tetanus
- Tuberculosis
- Measles
- Mumps
- Rubella
- N. meningitidis
- S. pneumoniae
- Yellow Fever
- Influenza
- Hepatitis A
- Varicella
- Rotavirus
- Cervical cancer
- Herpes zoster
- Polio
- Hepatitis B
- H. influenzae

Marshall, The Vaccine Handbook, 2017
<table>
<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>19-23 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>
<th>17-18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B&lt;sup&gt;1&lt;/sup&gt; (HepB)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
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<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
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<tr>
<td>Rotavirus&lt;sup&gt;1&lt;/sup&gt; (R) (2-dose series); RSV (3-dose series)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
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<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis&lt;sup&gt;1&lt;/sup&gt; (DTaP&lt;sup&gt;1&lt;/sup&gt;; &lt;7 yrs)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
<td>4&lt;sup&gt;th&lt;/sup&gt; dose</td>
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<td>5&lt;sup&gt;th&lt;/sup&gt; dose</td>
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<tr>
<td>Haemophilus influenzae type b&lt;sup&gt;1&lt;/sup&gt; (Hib)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
<td>4&lt;sup&gt;th&lt;/sup&gt; dose</td>
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<td>5&lt;sup&gt;th&lt;/sup&gt; dose</td>
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<tr>
<td>Pneumococcal conjugate&lt;sup&gt;1&lt;/sup&gt; (PCV13)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
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<tr>
<td>Inactivated poliovirus&lt;sup&gt;1&lt;/sup&gt; (IPV; &lt;18 yrs)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt; dose</td>
<td>4&lt;sup&gt;th&lt;/sup&gt; dose</td>
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<tr>
<td>Influenza&lt;sup&gt;1&lt;/sup&gt; (IV)</td>
<td>\text{Annual vaccination (IV) 1 or 2 doses}</td>
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<td>\text{Annual vaccination (IV) 1 dose only}</td>
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<tr>
<td>Measles, mumps, rubella&lt;sup&gt;1&lt;/sup&gt; (MMR)</td>
<td>See footnote 8</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
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<tr>
<td>Varicella&lt;sup&gt;1&lt;/sup&gt; (VAR)</td>
<td>\text{See footnote 8}</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
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<tr>
<td>Hepatitis A&lt;sup&gt;1&lt;/sup&gt; (HepA)</td>
<td>\text{2-dose series, See footnote 10}</td>
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<tr>
<td>Meningococcal&lt;sup&gt;1&lt;/sup&gt; (Hib-MenCY ≥6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)</td>
<td>\text{See footnote 11}</td>
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<td>1&lt;sup&gt;st&lt;/sup&gt; dose</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt; dose</td>
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<td>Tetanus, diphtheria, &amp; acellular pertussis&lt;sup&gt;1&lt;/sup&gt; (Tdap ≥7 yrs)</td>
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<tr>
<td>Human papillomavirus&lt;sup&gt;1&lt;/sup&gt; (HPV)</td>
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<tr>
<td>Meningococcal B&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>Pneumococcal polysaccharide&lt;sup&gt;1&lt;/sup&gt; (PPSV23)</td>
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</tbody>
</table>

\text{Range of recommended ages for all children} \hspace{1cm} \text{Range of recommended ages for catch-up immunization} \hspace{1cm} \text{Range of recommended ages for certain high-risk groups} \hspace{1cm} \text{Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical judgement} \hspace{1cm} \text{No recommendation}

The Players

Tommy
The Players

Primary care provider

Tommy

Tommy’s family
The Players

Primary care provider

Subspecialist

Tommy

ID doctor

Tommy’s family
The Players

Local Health Department

Subspecialist

Primary care provider

Tommy

Tertiary Children’s Hospital

ID doctor

Tommy’s family
General Considerations

1. Vaccination is a shared responsibility
SPECIAL ARTICLE

Standards for Child and Adolescent Immunization Practices

National Vaccine Advisory Committee

ABBREVIATIONS. NVAC, National Vaccine Advisory Committee; ACIP, Advisory Committee on Immunization Practices; AAP, American Academy of Pediatrics; AAFP, American Academy of Family Physicians; VFC, Vaccines for Children Program; CDC, Centers for Disease Control and Prevention; VIS, Vaccine Information Statement; VAERS, Vaccine Adverse Events Reporting System; VICP, Vaccine Injury Compensation Program.

In 1992, the National Vaccine Advisory Committee (NVAC), in collaboration with the Ad Hoc Working Group for the Development of Standards for Pediatric Immunization Practices, a working group representing public and private agencies with input from state and local health departments, physicians and nursing organizations, and public and private providers, developed a set of standards as to what constitutes the most essential and desirable immunization policies and practices. These standards were endorsed by a variety of medical and public health organizations and represented an important element in our national strategy to protect America’s children against vaccine-preventable diseases.

Since that time, vaccine delivery in the United States has changed in several important ways. First, vaccination coverage rates among preschool children have increased substantially and are now monitored by the National Immunization Survey. Second, vaccination of children has shifted markedly from the public to the private sector with an emphasis on vaccination in the context of primary care and the medical home. The Vaccines for Children Program has provided critical support to this shift by covering the cost of vaccines for the most economically disadvantaged children and adolescents. Third, the development and introduction of performance measures, such as the National Committee for Quality Assurance’s Health Plan Employer Data and Information Set, have focused national attention on the quality of preventive care, including vaccination. Finally, high-quality research in health services has helped to refine strategies for raising and sustaining vaccination coverage levels among children, adolescents, and adults.

Health care professionals who vaccinate children and adolescents continue to face important challenges. These challenges include a diminishing level of experience among patients, parents, and physicians—with the diseases that vaccines prevent, the ready availability of vaccine-related information that may be inaccurate or misleading, the increasing complexity of the vaccination schedule, and the failure of many health plans to pay the costs associated with vaccination. In addition, recommendations from the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American Medical Association in 1996 underscored the need to focus on adolescent vaccination.

In this context, NVAC, along with partners representing the federal agencies, state and local health departments, and professional organizations, revised and updated the standards during 2001–2002 to reflect these changes and challenges in vaccine delivery. The revision was approved by NVAC on February 8, 2002 (Table 1), and distributed widely among a variety of medical and public health organizations for review and endorsement. Table 2 lists those organizations that have formally endorsed the Standards for Child and Adolescent Immunization Practices.

The standards are directed toward “health care professionals,” an inclusive term for the many people in clinical settings who share in the responsibility for vaccination of children and adolescents: physicians, nurses, midlevel practitioners (e.g., nurse practitioners, physician assistants), medical assistants, and clerical staff. In addition to this primary audience, the standards are intended to be useful to public health professionals, policy makers, health plan administrators, employers who purchase health care coverage, and others whose efforts shape and support the delivery of vaccination services.

Of note, the use of the term “standards” should not be confused with a minimum standard of care. Rather, these standards represent the most desirable immunization practices, which health care professionals should strive to achieve. Given current resource limitations, some health care professionals may find it difficult to implement all of the standards, because of circumstances over which they have little control. The expectation is that, by summarizing best immunization practices in a clear and concise format, the standards will assist these providers in securing the resources necessary to implement this set of recommendations.
### TABLE 1. Standards for Child and Adolescent Immunization Practices

<table>
<thead>
<tr>
<th>Availability of vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Vaccination services are readily available.</td>
</tr>
<tr>
<td>2. Vaccinations are coordinated with other health care services and provided in a medical home when possible.</td>
</tr>
<tr>
<td>3. Barriers to vaccination are identified and minimized.</td>
</tr>
<tr>
<td>4. Patient costs are minimized.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessment of vaccination status</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Health care professionals review the vaccination and health status of patients at every encounter to determine which vaccines are indicated.</td>
</tr>
<tr>
<td>6. Health care professionals assess for and follow only medically accepted contraindications.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effective communication about vaccine benefits and risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Parents/guardians and patients are educated about the benefits and risks of vaccination in a culturally appropriate manner and in easy-to-understand language.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Proper storage and administration of vaccines and documentation of vaccinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Health care professionals follow appropriate procedures for vaccine storage and handling.</td>
</tr>
<tr>
<td>9. Up-to-date, written vaccination protocols are accessible at all locations where vaccines are administered.</td>
</tr>
<tr>
<td>10. People who administer vaccines and staff who manage or support vaccine administration are knowledgeable and receive ongoing education.</td>
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<tr>
<td>11. Health care professionals simultaneously administer as many indicated vaccine doses as possible.</td>
</tr>
<tr>
<td>12. Vaccination records for patients are accurate, complete, and easily accessible.</td>
</tr>
<tr>
<td>13. Health care professionals report adverse events after vaccination promptly and accurately to the Vaccine Adverse Events Reporting System (VAERS) and are aware of a separate program, the Vaccine Injury Compensation Program (VICP).</td>
</tr>
<tr>
<td>14. All personnel who have contact with patients are appropriately vaccinated.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Implementation of strategies to improve vaccination coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>15. Systems are used to remind parents/guardians, patients, and health care professionals when vaccinations are due and to recall those who are overdue.</td>
</tr>
<tr>
<td>16. Office- or clinic-based patient record reviews and vaccination coverage assessments are performed annually.</td>
</tr>
</tbody>
</table>
Shared Responsibility

“Specialists who care for immunocompromised patients share responsibility with the primary care provider for ensuring that appropriate vaccinations are administered to immunocompromised patients.”

Rubin, CID 2013.
Shared Responsibility

“ Specialists who care for immunocompromised patients *share responsibility* with the primary care provider for ensuring that appropriate vaccinations are administered to immunocompromised patients. ”

Rubin, CID 2013.
Multidisciplinary Approach

- Frequent visits to specialists
- Opportunities for education +/- vaccination
- Information sharing among institutions
- Coverage rates higher among those whose specialists administer vaccines

CDC, MMWR, 2011
Tommy

You review the immunization record
You discuss immunizations and expectations with the family
General Considerations

1. Vaccination is a shared responsibility
2. The balance between risks and benefits is complex
Healthy Child

Costs and side effects of vaccination

RISKS

BENEFITS

Morbidity from vaccine-preventable disease
Immunocompromised Patient

Costs and side effects of vaccination

Severe morbidity and mortality from vaccine-preventable disease

RISKS

BENEFITS
Immunocompromised Patient

Will the vaccines work?

Costs and side effects of vaccination

RISKS

BENEFITS

Severe morbidity and mortality from vaccine-preventable disease
Immunocompromised Patient

Costs and side effects of vaccination

Will the vaccines work?

Severe morbidity and mortality from vaccine-preventable disease

Are there special or unknown adverse effects?
Risks and Benefits

- Prevalence
- Chance of exposure
- Degree of immune compromise
- Type of vaccine
- Efficacy of the vaccine in person with impaired immunity
Vaccines and Worsening of Condition?

- Worsen inflammatory condition?
- Induce allograft rejection?

- Non-specific immune activation/antigenic stimulation
- Difficult to establish causal relationship due to confounding
- No current data indicate vaccination causes acute rejection
- Overall vaccines not important triggers of disease flares
- Do not withhold vaccines due to these fears

Dos Santos, Vaccine, 2016.
Tommy

- Mom asks how you determine which vaccines Tommy might need
General Considerations

1. Vaccination is a shared responsibility
2. The balance between risks and benefits is complex
3. Immunocompromised states are different
B-cells  T-cells  Phagocytes  Complement
B-cells  T-cells  Phagocytes  Complement

XLA

Rituximab

Recurrent respiratory tract infections with encapsulated organisms
B-cells  T-cells  Phagocytes  Complement

XLA  DiGeorge Syndrome

Rituximab  ATG

Recurrent respiratory tract infections with encapsulated organisms  Severe viral and fungal infections
<table>
<thead>
<tr>
<th>B-cells</th>
<th>T-cells</th>
<th>Phagocytes</th>
<th>Complement</th>
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</thead>
<tbody>
<tr>
<td>XLA</td>
<td>DiGeorge Syndrome</td>
<td>Chronic Granulomatous Disease</td>
<td>Neutropenia</td>
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<tr>
<td>Rituximab</td>
<td>ATG</td>
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</tbody>
</table>

- **B-cells**: XLA
- **T-cells**: DiGeorge Syndrome
- **Phagocytes**: Chronic Granulomatous Disease
- **Complement**: Neutropenia

- **Rituximab**
  - Recurrent respiratory tract infections with encapsulated organisms

- **ATG**
  - Severe viral and fungal infections

- **Neutropenia**
  - Skin abscesses, pneumonia, catalase+ organisms
<table>
<thead>
<tr>
<th>B-cells</th>
<th>T-cells</th>
<th>Phagocytes</th>
<th>Complement</th>
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<tbody>
<tr>
<td>XLA</td>
<td>DiGeorge Syndrome</td>
<td>Chronic Granulomatous Disease</td>
<td>Complement deficiency</td>
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<td>Rituximab</td>
<td>ATG</td>
<td>Neutropenia</td>
<td>Eculizumab</td>
</tr>
</tbody>
</table>

**Recurrent respiratory tract infections with encapsulated organisms**

**Severe viral and fungal infections**

**Skin abscesses, pneumonia, catalase+ organisms**

**Infections with encapsulated bacteria and *Neisseria* infections**
Immunocompromised States

- HIV
- Solid organ transplant
- Cancer chemotherapy
- Stem cell transplant
- Chemotherapy
- Immunosuppressive medications
- Asplenia
At-Risk Children

- Pneumococcal infection
  - Cochlear implant
  - CSF leak
  - Heart disease
  - Chronic lung disease
  - Kidney failure
  - ESRD
  - Hemodialysis
  - Diabetes
<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of Person-Years</th>
<th>Invasive Pneumococcal Disease</th>
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<tbody>
<tr>
<td></td>
<td>Age &lt;5 y</td>
<td>Age 5–17 y</td>
<td>Rate per 100 000</td>
<td>Rate Ratio&lt;sup&gt;a&lt;/sup&gt; (95% CI)</td>
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<tr>
<td>Risk group</td>
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<tr>
<td>No at-risk/high-risk conditions</td>
<td>5,494,451</td>
<td>18,911,630</td>
<td>7.3</td>
<td>1.8 (1.4–2.3)</td>
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<tr>
<td>At-risk conditions</td>
<td>532,172</td>
<td>1,469,970</td>
<td>12.8</td>
<td>2.4 (1.3–4.2)</td>
</tr>
<tr>
<td>Asthma</td>
<td>190,281</td>
<td>1,062,121</td>
<td>11.6</td>
<td>2.0 (1.0–2.4)</td>
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<tr>
<td>Chronic heart disease</td>
<td>69,942</td>
<td>66,234</td>
<td>17.2</td>
<td>2.4 (1.3–4.2)</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>746</td>
<td>2,989</td>
<td>134.1</td>
<td>18.5 (2.6–131.4)</td>
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<tr>
<td>Chronic lung disease</td>
<td>61,722</td>
<td>130,992</td>
<td>17.8</td>
<td>2.5 (1.3–4.5)</td>
</tr>
<tr>
<td>Chronic use of oral steroids</td>
<td>5,878</td>
<td>16,561</td>
<td>34.0</td>
<td>4.7 (1.2–18.8)</td>
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<tr>
<td>Diabetes</td>
<td>2,346</td>
<td>86,485</td>
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<tr>
<td>Trisomy 21</td>
<td>6,933</td>
<td>13,720</td>
<td>28.8</td>
<td>4.0 (1.0–15.9)</td>
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<tr>
<td>Neuromuscular/seizure disorders</td>
<td>36,239</td>
<td>157,396</td>
<td>22.1</td>
<td>3.0 (1.5–6.1)</td>
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<tr>
<td>Prematurity/low birthweight</td>
<td>242,192</td>
<td>7,378</td>
<td>12.0</td>
<td>1.6 (1.1–2.4)</td>
</tr>
<tr>
<td>High-risk conditions</td>
<td>22,167</td>
<td>98,436</td>
<td>81.2</td>
<td>11.2 (7.0–17.9)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>36,24</td>
<td>13,491</td>
<td>27.6</td>
<td>3.8 (5.5–27.0)</td>
</tr>
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<td>Cochlear implant</td>
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<td>Congenital immunodeficiency</td>
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<td>16,861</td>
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<td>Diseases of white blood cells</td>
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<td>Functional/anatomic asplenia</td>
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<td>HIV</td>
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<td>Immunosuppressive drugs/conditions</td>
<td>64,47</td>
<td>58,319</td>
<td>186.1</td>
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</table>
Tommy

- You inform Mom that the vaccine recommendations depend on Tommy’s type and degree of immunocompromise
- Mom asks how you know that the vaccines will work
General Considerations

1. Vaccination is a shared responsibility
2. The balance between risks and benefits is complex
3. Immunocompromised states are different
4. Immune responses may be suboptimal
Inability To Respond to All Vaccines

- X-linked agammaglobulinemia
  - Unable to make antibody
  - T-cells cannot respond to live viral vaccines because these patients receive IVIG, which inactivates the vaccines
  - Some T-cell immunity when given influenza vaccine?
Inability To Respond to Some Vaccines

- Specific antibody deficiency
  - Unable to make antibody to pneumococcus
  - Unable to respond to pneumococcal vaccination
Inability To Respond Well to Vaccines

- T-cell deficiencies (i.e. HIV or children on anti-T-cell therapies)
  - Suboptimal responses to one dose of a vaccine
  - May respond better if given additional doses
Once Immune... Always Immune?

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>Date Given</th>
<th>Vaccine Manufacturer</th>
<th>Vaccine lot Number</th>
<th>Site Given</th>
<th>Vaccine Administrator</th>
<th>Signature of Parent or Guardian</th>
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<tbody>
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<td>8/1/81</td>
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<tr>
<td>OPV</td>
<td>10/2/81</td>
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<tr>
<td>OPV80</td>
<td>1/28/82</td>
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<td>IPV</td>
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**Notes:**
- Chicken Pox Disease 3/11
- Signed: [Handwritten Signature]

UNIVERSITY OF LOUISVILLE
SCHOOL OF MEDICINE
Vaccine Efficacy and Immunogenicity

- Vaccines studied in RCTs
- EFFICACY: ability to prevent disease
- IMMUNOGENICITY: ability to generate immune response
Proof of Protection

- Paucity of RCTs in immunocompromised populations
- Correlates of protection
## Correlates of Protection

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Test</th>
<th>Correlate</th>
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</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>Toxin neutralization</td>
<td>0.01-0.1 IU/mL</td>
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<tr>
<td>HepA</td>
<td>ELISA</td>
<td>10 mIU/mL</td>
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<tr>
<td>HepB</td>
<td>ELISA</td>
<td>10 mIU/mL</td>
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<tr>
<td>Hib polysaccharide</td>
<td>ELISA</td>
<td>1 mcg/mL</td>
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<tr>
<td>Hib conjugate</td>
<td>ELISA</td>
<td>0.15 mcg/mL</td>
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<tr>
<td>Influenza</td>
<td>HAI</td>
<td>1:40 dilution</td>
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<tr>
<td>Lyme</td>
<td>ELISA</td>
<td>1100 EIA U/mL</td>
</tr>
<tr>
<td>Measles</td>
<td>Microneutralization</td>
<td>120 mIU/mL</td>
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<tr>
<td>Pneumococcus</td>
<td>ELISA</td>
<td>0.2-0.35 mcg/mL</td>
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<tr>
<td></td>
<td>Opsonophagocytosis</td>
<td>1:8 dilution</td>
</tr>
<tr>
<td>Polio</td>
<td>Serum neutralization</td>
<td>1:4 to 1:8 dilution</td>
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<tr>
<td>Rabies</td>
<td>Serum neutralization</td>
<td>0.5 IU/mL</td>
</tr>
<tr>
<td>Rubella</td>
<td>Immunoprecipitation</td>
<td>10-15 mIU/mL</td>
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<tr>
<td>Tetanus</td>
<td>Toxin neutralization</td>
<td>0.1 IU/mL</td>
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<td>Varicella</td>
<td>Serum neutralization</td>
<td>≥1:64 dilution</td>
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<tr>
<td></td>
<td>gpELISA</td>
<td>≥5 IU/mL</td>
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</table>

Limitations of Measuring Antibody

- Assays may lack sensitivity to detect vaccine-induced immunity
- Seroconversion ≠ full protection
- Seroreversion ≠ loss of protection
- Cell-mediated immunity plays an important role in long-term protection
- May be reasonable to monitor antibody against some vaccine-preventable diseases

Rubin, CID 2013.
Tommy

- Let’s talk about timing of vaccination
General Considerations

1. Vaccination is a shared responsibility
2. The balance between risks and benefits is complex
3. Immunocompromised states are different
4. Immune responses may be suboptimal
5. Immunization before immunosuppression is ideal
Window of Opportunity
Transplantation

- Months to years
- 4 weeks
- 2 to 6 months
- Months to years
Transplantation

Months to years

4 weeks

2 to 6 months

Months to years

Live vaccines are contraindicated and responses to inactivated vaccines may be suboptimal

Consider IIV and other inactivated vaccines

Resumption of routine vaccination

2 to 6 months

Months to years
Transplantation

Routine and special vaccines based on age and underlying medical condition

Live vaccines are contraindicated and responses to inactivated vaccines may be suboptimal

Resumption of routine vaccination

Consider IIV and other inactivated vaccines

Months to years

4 weeks

2 to 6 months

Months to years

Routine and special vaccines based on age and underlying medical condition

Live vaccines are contraindicated and responses to inactivated vaccines may be suboptimal

Consider IIV and other inactivated vaccines

Resumption of routine vaccination

Months to years
Transplantation

Inactivated vaccines

Years

2 to 6 months

Live vaccines are contraindicated and responses to inactivated vaccines may be suboptimal

Routine and special vaccines based on age and underlying medical condition

Months to years

4 weeks

2 to 6 months

Live vaccines deadline

Consider IIV and other inactivated vaccines

Inactivated vaccines deadline

Resumption of routine vaccination
Tommy

- Mom asks about Tommy’s 4-yr-old sister
- She’s supposed to get MMR and varicella vaccines
- Mom is worried because these are live-attenuated vaccines
General Considerations

1. Vaccination is a shared responsibility
2. The balance between risks and benefits is complex
3. Immunocompromised states are different
4. Immune responses may be suboptimal
5. Immunization before immunosuppression is ideal
6. Immunization of close contacts is important
Circle of Protection
Circle of Protection

Healthcare workers
Circle of Protection

Healthcare workers

Household members
Circle of Protection

- Healthcare workers
- Household members
- Teachers
Circle of Protection

- Healthcare workers
- Household members
- Teachers
- Co-workers and classmates
Circle of Protection

- Healthcare workers
- Household members
- Teachers
- Co-workers and classmates
- Grandparents
Circle of Protection

Healthcare workers

Household members

Teachers

Co-workers and classmates

Grandparents

Community at large
Immunize Close Contacts

- All recommended inactivated vaccines
- All routinely recommended live attenuated vaccines
Contacts May Receive All Routine Vaccines

- Rotavirus: shed in stool
- Varicella: rash
- MMR: not transmitted
- LAIV: not severely compromised
Contacts May Receive All Routine Vaccines

- Rotavirus: shed in stool
- Varicella: rash
- MMR: not transmitted
- LAIV: not severely compromised

Smallpox vaccine
Oral polio vaccine

*Rubin, CID 2013.*
Learning Objectives

- Delineate guiding principles for immunization of immunocompromised children
- Implement specific immunization recommendations into practice
<table>
<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>19-23 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>
<th>17-18 yrs</th>
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<tbody>
<tr>
<td>Hepatitis B (HepB)</td>
<td>1st</td>
<td>2nd</td>
<td></td>
<td>3rd</td>
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<tr>
<td>Rotavirus (RV) (RV1) (2-dose series); RV5 (3-dose series)</td>
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<td>2nd</td>
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</tr>
<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis (DTaP; &lt;7 yrs)</td>
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<td>2nd</td>
<td>3rd</td>
<td>4th</td>
<td></td>
<td>5th</td>
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<td>1st</td>
<td>2nd</td>
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<td></td>
<td>3rd</td>
<td>or 4th</td>
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<td>2nd</td>
<td>3rd</td>
<td>4th</td>
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<td>5th</td>
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<tr>
<td>Inactivated poliovirus (IPV; &lt;18 yrs)</td>
<td>1st</td>
<td>2nd</td>
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<td>3rd</td>
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<td>4th</td>
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<td>Influenza (IIV)</td>
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<td>Annual vaccination (IIV) 1 or 2 doses</td>
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</table>

- **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**

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 (cells/μL)</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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<tbody>
<tr>
<td>Hepatitis B</td>
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<td>Pneumococcal polysaccharide</td>
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Legend:
- **Yellow**: Vaccination according to the routine schedule recommended
- **Purple**: Recommended for persons with an additional risk factor for which the vaccine would be indicated
- **Orange**: Vaccination is recommended, and additional doses may be necessary based on medical condition. See footnotes.
- **Red**: Contraindicated
- **Orange**: Precaution for vaccination

No recommendation

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2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

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An international panel of experts prepared an evidenced-based guideline for vaccination of immunocompromised adults and children. These guidelines are intended for use by primary care and subspecialty providers who care for immunocompromised patients. Evidence was often limited. Areas that warrant future investigation are highlighted.

Keywords: vaccination; immunization; immunocompromised patients; immunosuppression; asplenic patients; immunodeficiency patients

EXECUTIVE SUMMARY

These guidelines were created to provide primary care and specialty clinicians with evidence-based guidelines for active immunization of patients with altered immunocompetence and their household contacts in order to safely prevent vaccine-preventable infections. They do not represent the only approach to vaccination.

Received 4 October 2013; accepted 5 October 2013; electronically published 4 December 2013.

It is important to realize that guidelines cannot always account for individual variation among patients. The guidelines are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The Infectious Diseases Society of America considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient’s individual circumstances.

An asterisk (*) indicates recommendation for a course of action that deviates from recommendations of the Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention.

Correspondence: Larry G. Rubin (lrubin@nihs.edu)

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Recommended immunization schedules for normal adults and children as well as certain adults and children at high risk for vaccine-preventable infections are updated and published annually by the Centers for Disease Control and Prevention (CDC) and partner organizations. Some recommendations have not been addressed by the Advisory Committee on Immunization Practices (ACIP) to the CDC or they deviate from recommendations. The goal of presenting these guidelines is to decrease morbidity and mortality from vaccine-preventable infections in immunocompromised patients. Summarized below are the recommendations made by the panel. Supporting tables that provide additional information are available in the electronic version. The panel followed a process used in the development of other Infectious Diseases Society of America guidelines, which included a systematic weighting of the quality of the evidence and the grade of the recommendation (Table I). The key clinical questions and recommendations are summarized in this executive summary. A detailed description of the methods,
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendation</th>
<th>Strength, Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. influenzae</em></td>
<td>U</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>U, R</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>U, R</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Diphtheria toxoid, tetanus toxoid, acellular pertussis</td>
<td>U</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>U: 11-26 y</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Influenza-inactivated</td>
<td>U</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Influenza-live attenuated</td>
<td>X</td>
<td>Weak, low</td>
</tr>
<tr>
<td>Measles, mumps, rubella-live</td>
<td>R: 6-11 mo</td>
<td>Weak, very low</td>
</tr>
<tr>
<td></td>
<td>U: age ≥12 mo</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Meningococcal conjugate</td>
<td>U</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Pneumococcal conjugate (PCV13)</td>
<td>U: age ≤5 yr</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td></td>
<td>R: age ≥6 yr</td>
<td>Strong, very low</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>R: age ≥ 2 y</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Polio-inactivated</td>
<td>U</td>
<td>Strong, moderate</td>
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<tr>
<td>Rotavirus-live</td>
<td>U</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Rotavirus-live</td>
<td>U</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Varicella-live</td>
<td>R: 6-11 mo</td>
<td>Weak, very low</td>
</tr>
<tr>
<td></td>
<td>U: age ≥12 mo</td>
<td>Strong, low</td>
</tr>
<tr>
<td>Zoster-live</td>
<td>R: age 50-59 yr</td>
<td>Weak, low</td>
</tr>
<tr>
<td></td>
<td>U: age ≥60 yr</td>
<td>Strong, moderate</td>
</tr>
</tbody>
</table>

**R:** Recommended  
**U:** Usual  
**X:** Contraindicated

Adapted from Rubin, CID 2013.
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</tr>
<tr>
<td>Pneumococcal conjugate (PCV13)</td>
<td>U: age 2-5 yr R: age ≥6 yr</td>
<td>Strong, moderate Strong, very low</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>R: age ≥ 2 y</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Polio-inactivated</td>
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</tr>
</tbody>
</table>

R: Recommended  
U: Usual  
X: Contraindicated

Adapted from Rubin, CID 2013.
Inactivated Influenza Vaccine

- Everyone ≥6 months of age
- May consider not giving to those unlikely to respond
  - Intensive chemotherapy
  - Within 1 month of solid organ transplant
  - Within 6 months of rituximab therapy
Pneumococcal Vaccines

- Pneumococcal conjugate vaccine (PCV13)
- Pneumococcal polysaccharide vaccine (PPSV23)
Pneumococcal Vaccine

- **Ages 2-5 years: Based on previous PCV administration**
  - Incomplete schedule of 3 doses: Give 1 dose PCV13
  - Unvaccinated or incomplete schedule <3 doses: Give 2 doses PCV13 8 weeks apart
  - Give 1 dose of PPSV23 at least 8 weeks after last PCV13

- **Ages 6-18 years**
  - At least 1 dose PCV13
  - At least 1 dose PPSV23

- **Second dose of PPSV23 in 5 years**

Meningococcal Vaccines

- Serogroups A, C, W135, Y: MCV4-D or MCV4-CRM
  - First dose at 11-12 years, booster dose at 16 years

- Serogroup B: MenB-FHbp or MenB-4C
  - Category A recommendation: asplenia, complement deficiency
  - Category B recommendation: 16-23 years of age

# Meningococcal Vaccines in At-Risk Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Complement deficiency</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asplenia</td>
<td></td>
</tr>
<tr>
<td>2-23 months</td>
<td>MCV4-CRM (4 doses)</td>
<td>MCV4-CRM (4 doses)</td>
</tr>
<tr>
<td>2-55 years</td>
<td>MCV4-CRM (2 doses)</td>
<td>MCV4-CRM (2 doses)</td>
</tr>
<tr>
<td></td>
<td>MCV4-D (2 doses)</td>
<td>MCV4-D (2 doses)</td>
</tr>
<tr>
<td>≥ 10 years</td>
<td>MenB-FHbp (3 doses)</td>
<td>Category B</td>
</tr>
<tr>
<td></td>
<td>MenB-4C (2 doses)</td>
<td>recommendation</td>
</tr>
</tbody>
</table>

Those with ongoing complement deficiency should receive a booster dose of MCV4 every 5 years.

MCV4-D may be used between 9-23 months, but interferes with DTaP and can interfere with PCV13.


Immunocompromised States

- Complement deficiency
- Anatomic and functional asplenia
- HIV
- Children on steroids
- Children receiving cancer chemotherapy
- Solid organ transplant recipients
- HSCT recipients
Complement Deficiencies

- At risk for infections caused by encapsulated bacteria
- Congenital complement deficiency
- Systemic lupus erythematosus
- Eculizumab (monoclonal antibody to C5) therapy
Complement Deficiencies

- All routine immunizations
- *Haemophilus influenzae* Type B
- PCV13

- PPSV23 at 2 years of age, repeat 5 years later
- Meningococcal conjugate vaccine series, repeat one every 5 years
- Meningococcal B vaccine series at 10 years of age
Anatomic and Functional Asplenia

- At risk for infections caused by encapsulated bacteria because of impaired clearance of opsonized bacteria
- Congenital asplenia, surgical asplenia
- Polysplenia resulting in dysfunction
- Sickle cell disease
Anatomic and Functional Asplenia

- All routine immunizations
- *Haemophilus influenzae* Type B
- PCV13

- PPSV23 at 2 years of age, repeat 5 years later
- Meningococcal conjugate vaccine series, repeat one every 5 years
- Meningococcal B vaccine series at 10 years of age
HIV

- If on combination anti-retroviral therapy with good response, may receive routine vaccinations
  - Response in general is good
  - Persistence of immunity and long-term memory may not be as good
HIV

- All routine immunizations
- *Haemophilus influenzae* Type B
- PCV13

- PPSV23 at 2 years of age, repeat 5 years later
- Meningococcal conjugate vaccine series, repeat one every 5 years
HIV

- **Hepatitis B**
  - HBSAb titer 1 month after last dose of series
  - If < 10 mIU/mL, give another 3-dose series

- **MMR and varicella vaccines**
  - Do not give if severe immunosuppression
  - CD4% < 15% sustained for ≥6 months at any age
  - CD4 count < 200 cells/mcL sustained for ≥6 months for those ≥6 years of age
  - Do not give MMRV (higher varicella concentration)
Steroids

- Live viral vaccines may be given at the same time as
  - Topical or inhaled steroids
  - Physiologic replacement
  - $< 2 \text{ mg/kg/day} \text{ (or } < 20 \text{ mg/day if } > 10 \text{ kg})$ prednisone or equivalent
- Live viral vaccines can be given after stopping steroids
  - $> 2 \text{ mg/kg/day} \text{ (or } > \text{ mg/day if } > 10 \text{ kg})$ prednisone or equivalent for $< 14 \text{ days}$
- Live viral vaccines can be given after $> 1 \text{ month} after stopping steroids$
  - $> 2 \text{ mg/kg/day} \text{ (or } > \text{ mg/day if } > 10 \text{ kg})$ prednisone or equivalent for $> 14 \text{ days}$
Solid Organ Transplant Recipients

- Pneumococcal vaccination, including PPSV23
- Hepatitis B vaccination with monitoring of titers
- HPV vaccination

- Accelerated schedule of MMR and varicella vaccines if needed pre-transplant
- Live viral vaccines contraindicated post transplant
Cancer Chemotherapy

- Live viral vaccines withheld until $\geq 3$ months post therapy (interval may vary)
- Inactivated vaccines
  - Not harmful
  - Suboptimal responses
  - Not valid unless documentation of antibody response
Hematopoietic Stem Cell Transplant Recipients

- Vaccine immunity may be lost after HSCT
- Full re-vaccination post-transplant is recommended
Learning Objectives

- Delineate guiding principles for immunization of immunocompromised children
- Implement specific immunization recommendations into practice
- Improve systems for vaccine delivery in immunocompromised patients
Identifying Barriers
Identifying Barriers

Fragmented records
Identifying Barriers

Fragmented records

Multiple providers
Identifying Barriers

- Fragmented records
- Multiple providers
- Lack of immunization registries
Identifying Barriers

- Fragmented records
- Multiple providers
- Lack of immunization registries
- Lack of vaccine hero

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Identifying Barriers

- Fragmented records
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- Inability of subspecialist to give vaccines

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Identifying Barriers

- Fragmented records
- Multiple providers
- Lack of immunization registries
- Lack of vaccine hero
- Inability of subspecialist to give vaccines
- Urgent transplant/immunosuppression
Improving Systems for Vaccine Delivery

- Appoint a vaccine superhero
  - Infectious Disease
  - Clinic or transplant coordinator
  - Nurse
  - Pharmacist
- Improve vaccine knowledge
Operationalize and Execute

- Add vaccinations to checklists
- Request records
  - Referring center
  - Primary care physician
  - Health department
  - Hospital
  - Registries
Operationalize

- Review records
- Add vaccinations to checklists
- Make recommendations
  - Vaccinate early in disease process
  - Special cases
  - Household members
- Immunize!
  - Immunize in office
  - Immunize in hospital
  - Centralized vaccination station
  - Educate families where to get vaccines
Operationalize

- Follow-up: obtain documentation of vaccination
UofL Pediatric Heart Transplant Recipients

- UTD
- PCV13
- PPSV23
Summary

- Multidisciplinary approach to immunization
- Recognize differences in immune deficiencies
- Immunize early in end-stage organ disease and prior to immunosuppression or transplant
- Immunize close contacts
- Know specific vaccine recommendations for immunocompromised patients
- Develop a system