

# Immunization of Children Receiving Immunosuppressive Therapy for Cancer or Hematopoietic Stem Cell Transplantation

Avinash K. Shetty, MD,\* Mary A. Winter, PharmD†

\*Department of Pediatrics and †Department of Pharmacy  
Wake Forest University School of Medicine, Winston-Salem, NC

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## ABSTRACT

In the past 3 decades, the number of immunocompromised children has increased steadily because of dramatic improvement in survival rates in certain malignancies as a result of intensive curative treatment regimens and an increase in the number of children undergoing life-saving hematopoietic stem cell transplantation (HSCT). Children receiving immunosuppressive therapy for cancer, as well as HSCT recipients, will benefit from vaccination but warrant close evaluation for a variety of reasons, such as the risk of developing severe infections, serious adverse events following certain vaccines, and decreased vaccine efficacy caused by poor immune response to vaccination. Various professional organizations have published vaccination guidelines for immunocompromised patients. Given their heterogeneity, recommendations for the immunization of immunocompromised patients may not be universally applicable. The safety of many commonly used vaccines has not been established in immunocompromised children. In addition, no large-scale vaccine studies have evaluated the clinical outcome of disease prevention in this population. All killed vaccines are generally safe, while live vaccines may be administered to immunocompromised children in select circumstances, depending on the degree of altered immunocompetence and the underlying primary condition. Healthcare providers should be knowledgeable about the indications, contraindications, and precautions for vaccine administration in immunocompromised patients. To protect immunocompromised patients, all family, household

contacts, and healthcare workers should also be immunized with all routinely recommended vaccines. Pediatricians play a crucial role in identifying and effectively communicating the risks and benefits of vaccines to immunocompromised patients and their parents.

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## INTRODUCTION

Vaccines represent one of the most successful public health advances of the 20th century.<sup>1</sup> The vaccination of immunocompromised pediatric patients merits careful consideration because these children are at increased risk for exposure to microbes from frequent association with healthcare settings and for the development of life-threatening vaccine-preventable infections compared to patients with normal immune function.<sup>2–15</sup> The 2009 H1N1 influenza pandemic, the rise in the incidence of pertussis and antibiotic-resistant *Pneumococcus*, and recent outbreaks of measles and mumps in individuals with normal immune function further highlight the need for effective revaccination of immunocompromised patients.<sup>2–6</sup> Other important considerations include safety concerns and the ability of immunocompromised individuals to generate a protective and sustained immune response.<sup>4</sup>

In the past 3 decades, the number of immunocompromised children has increased steadily in the United States. Dramatic improvement in survival rates in certain childhood malignancies has occurred. For example, acute lymphocytic leukemia (ALL) currently has a 5-year survival rate greater than 90%. This improvement is a result of more intensive and potentially curative treatment regimens and an increase in children undergoing life-saving hematopoietic stem cell transplantation (HSCT) and solid organ transplantation (SOT).<sup>16,17</sup> Likewise, in resource-rich settings such as the United States and Europe, dramatic decreases in morbidity and mortality and improved quality of life have occurred in children and adolescents infected with the human immunodeficiency virus (HIV) because of widespread access to highly active antiretroviral therapy, care, and support.<sup>18,19</sup>

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Address correspondence to  
Avinash K. Shetty, MD  
Department of Pediatrics  
Wake Forest University School of Medicine  
Medical Center Blvd.  
Winston Salem, NC 27157-1089  
Tel: (336) 716-2740  
Fax: (336) 716-9699  
Email: ashetty@wakehealth.edu

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The increased intensity of complex chemotherapy regimens for childhood cancer and aggressive immunosuppressive therapy to prevent rejection in pediatric HSCT and SOT recipients often result in prolonged and severe immune suppression that causes an increased risk for morbidity and mortality from certain infections (eg, invasive disease caused by *Streptococcus pneumoniae*, varicella, and influenza).<sup>13-15</sup> Therefore, the administration of appropriate vaccines to immunocompromised children is an important consideration for pediatricians and oncologists.<sup>6,9</sup> Healthcare providers must be aware of the indications, contraindications, and precautions for the use of vaccines in individuals with altered immune competence.<sup>9</sup>

In this article, we review the basic concepts, strategies, and challenges related to vaccinations of immunocompromised individuals, discuss the indications and safety of specific vaccines in children with cancer and in HSCT recipients, summarize vaccine recommendations of the American Academy of Pediatrics (AAP) and the Advisory Committee on Infectious Diseases (ACIP), and review immunizations of healthcare workers and household contacts of immunocompromised children.<sup>9,20</sup> Vaccine recommendations for HIV-infected children and adolescents are beyond the scope of this article, but professional societies have published comprehensive guidelines.<sup>19,20</sup>

## PRINCIPLES AND CHALLENGES FOR VACCINATING IMMUNOCOMPROMISED CHILDREN

Table 1 summarizes the basic principles of vaccinating immunocompromised children.

Categories of altered immune competence include patients with primary immune deficiency or, more commonly, secondary (acquired) immune deficiency as a result of conditions such as HIV infection, solid organ or hematologic malignancies, SOT, or HSCT.<sup>13,19</sup> Immune deficiencies can also result from radiation or immunosuppressive medication therapy, such as chemotherapy, corticosteroids, immunomodulators (such as 6-mercaptopurine, azathioprine, or methotrexate), calcineurin inhibitors (such as cyclosporine or tacrolimus), and the newer biological agents such as anti-tumor necrosis factor antibodies (infliximab, adalimumab, and certolizumab), anti-integrin antibodies (natalizumab), anti-cytotoxic T-lymphocyte antigen-4 agonists (abatacept), and anti-CD20 (rituximab).<sup>4,5</sup> Other categories of secondary immune deficiency include chronic disorders such as diabetes, autoimmune disorders, severe malnutrition, protein loss, uremia, and splenectomy.<sup>9</sup>

Oral corticosteroids are a commonly prescribed form of systemic therapy. The immunosuppressive dose of oral corticosteroids is defined as a dose >20 mg/d in

**Table 1. Basic Principles of Vaccinating Immunocompromised Children<sup>9</sup>**

- 
- Determine immune status.
  - Carefully assess risks versus benefits.
  - Understand that inactivated vaccines are generally safe and play an important role and that live vaccines are generally contraindicated, except in select circumstances for which safety and efficacy data are available.
  - Vaccinate contacts and healthcare workers.
  - Follow current vaccine recommendations.
  - Administer vaccines before immunosuppression when possible.
  - Consider antibody testing to evaluate vaccine response.
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children weighing  $\geq 10$  kg or >2 mg/kg/d in children weighing <10 kg.<sup>20</sup> Treatment with high-dose steroids for more than 2 weeks' duration will decrease immune function. The local administration of corticosteroids via the skin, the lungs, or the upper respiratory tract or by intraarticular injection will not be immunosuppressive.

Immunocompromised children benefit from vaccination but warrant unique considerations for reasons such as the risk of developing severe infections, serious adverse events after certain vaccines, and decreased efficacy from a poor immune response to vaccination compared to normal hosts.<sup>2-8</sup> The determination of immune status depends on the underlying diagnosis. Not all immune deficiency states are comparable because individuals with altered immune competence often vary in their degree of immunosuppression and susceptibility to infection.<sup>13</sup> The safety of many commonly used vaccines has not been established in immunocompromised children, especially HSCT recipients. In addition, no large-scale vaccine studies have evaluated clinical outcome (disease prevention) in individuals with altered immune competence. Table 2 lists the various challenges in vaccinating immunocompromised children. Given their heterogeneity, recommendations for the immunization of patients with altered immune competence may not be universally applicable.<sup>11</sup> All killed vaccines are generally safe, while the live vaccines may be administered to immunocompromised children in select circumstances, depending on the degree of altered immunocompetence and underlying primary condition.<sup>7</sup>

## IMMUNOSUPPRESSION AND IMMUNE RECONSTITUTION

### Children With Cancer Receiving Chemotherapy

At the time of diagnosis, most children with cancer have normal immune function characterized by normal levels of total immunoglobulins and antibodies

**Table 2. Challenges of Vaccinating Immunocompromised Children<sup>7</sup>**

- 
- Safety issues
  - Immunogenicity
  - Decreased vaccine efficacy
  - Changing immune status
  - Heterogeneous patient groups with variable immune deficits
  - Increasing use of potent immunosuppressive regimens
  - Preimmunosuppression immunization
  - Vaccination of contacts to reduce exposure of the immunocompromised child
  - Compliance
- 

to specific vaccine antigens, although peripheral blood T lymphocytes may be reduced in a small proportion of patients; significant lymphopenia is noted in untreated Hodgkin disease or Burkitt lymphoma.<sup>21,22</sup>

Immunosuppressive effects of malignant disease and chemotherapy include loss of cell-mediated immunity and humoral immunity.<sup>23</sup> Although B cells, plasma cells, natural killer (NK) cells, and immunoglobulins (Igs) return to normal by 6 months after the cessation of therapy, the recovery of the T-lymphocyte population is relatively slow. CD4<sup>+</sup> T lymphocytes are persistently low for more than 9-12 months at the end of therapy in 20%-50% of pediatric patients with cancer.<sup>24-26</sup>

In cancer patients receiving chemotherapy, all T-cell subsets decline but without the complete inversion of the CD4:CD8 ratio as reported after bone marrow transplantation.<sup>27</sup> The low levels of naïve T cells are replaced by memory T cells. Antigen-specific T-cell memory is preserved in a majority of treated children with ALL, consistent with studies demonstrating a low infectious disease mortality in these children.<sup>28</sup> In addition, the regeneration of naïve T cells occurs readily in children because of residual thymic function.<sup>29,30</sup> Eventually, both pathways of T-cell regenerative capacity are restored in childhood ALL patients after remission induction therapy, explaining the low occurrence of severe opportunistic infections in ALL patients outside periods of neutropenia.<sup>3,31</sup>

Low levels of IgG, IgM, and IgA have been noted in cancer patients receiving chemotherapy.<sup>25</sup> Studies have also shown that current ALL protocols induce a loss of humoral immunity to viral vaccination antigens in a high proportion of children, especially younger infants. These findings suggest that revaccinating immunocompromised children at the end of therapy is prudent.<sup>23</sup>

**Table 3. Heterogeneity in Hematopoietic Stem Cell Transplant Recipients<sup>5</sup>**

- 
- Degree of functional immune deficit
  - Recipient age
  - Underlying disease
  - Previous treatment
  - Conditioning regimen
  - Source of stem cells
  - Degree of human leukocyte antigen mismatch
  - Graft-versus-host disease
  - Concomitant infections
  - Preexisting immunity in the donor and recipient
- 

### HSCT Recipients

HSCT is the standard of care for defined hematological malignancies, and most patients become long-term survivors. HSCT recipients represent a heterogeneous group, and their degree of immunosuppression varies by underlying disease, type of transplant, conditioning regimen, presence of graft-versus-host disease (GVHD), and several other factors (Table 3).<sup>32,33</sup> HSCT recipients typically receive high doses of immunosuppressive regimens to prevent rejection, resulting in a high susceptibility to life-threatening infections.<sup>34</sup>

Several studies indicate that patients who receive HSCT lose the protective immunity to vaccine-preventable infectious diseases that was achieved after childhood immunization.<sup>35</sup> In the absence of reimmunization, antibody titers to pathogens such as tetanus, polio, measles, mumps, and rubella decrease during the 1-10 years after HSCT.<sup>6</sup> Functional neutrophils, monocytes, and NK cells recover by 2-3 weeks after transplantation.<sup>5</sup> However, the reconstitution of B-cell counts and T cells is slow. B lymphocytes remain very low (typically zero or near zero) in the first 1-3 months after HSCT and recover 3-12 months after transplant.<sup>6</sup> CD4<sup>+</sup> T lymphocytes remain low (typically <200 cells/ $\mu$ L) in the first 1-3 months after transplant and recover by 6-9 months in pediatric HSCT recipients (<18 years of age) without chronic GVHD. In contrast, the recovery of T cells may be delayed more than 2 years in adult HSCT recipients with chronic GVHD.<sup>6</sup>

Regardless of the interval to recovery, posttransplant recipients, especially those with chronic GVHD, exhibit persistent functional deficits with impaired T-cell and antibody responses, and immune reconstitution can be delayed for months to years.<sup>5,6</sup> Impaired antigen-specific responses have been noted in newly regenerated B cells in the first year after transplant.

The maintenance of immune memory is impaired in immunosuppressed transplant recipients.<sup>35</sup>

Memory/effector T cells are the predominant T cells circulating in adult HSCT recipients, likely originating from the T cells infused with the graft.<sup>6</sup> In young children, newly generated naïve T cells can respond to new antigens as early as 6-12 months after transplantation.<sup>6</sup> In general, autologous HSCT recipients have a lesser degree of altered immune function compared to allogeneic HSCT recipients and experience immune reconstitution within several months. In contrast, immune reconstitution may take up to a year or longer in allogeneic HSCT recipients.<sup>32</sup> However, autologous HSCT recipients who were treated with multiple courses of chemotherapy before transplant have vaccine responses similar to those that occur after allogeneic HSCT.<sup>6</sup>

Vaccine studies show that T-cell responses to vaccines for exposed pathogens before transplant (such as the varicella zoster virus) are detected as soon as 1-6 months after transplant. In contrast, antibody responses to vaccines for exposed pathogens after transplant (such as hepatitis B virus) are often detected 6-12 months after transplant. Allogeneic HSCT recipients respond poorly to polysaccharide vaccines, likely because of the predominance of immature B cells and deficits in CD27+ memory cells.<sup>36-38</sup> However, these patients' response to protein conjugate vaccines is significantly better than their response to polysaccharide vaccines.<sup>32,39,40</sup>

## **VACCINATION, TIMING OF IMMUNIZATION, AND CURRENT RECOMMENDATIONS**

### **Children With Cancer Receiving Chemotherapy**

Studies of vaccine responses in immunocompromised children are needed to assess functional immune reconstitution and to guide rational vaccination strategies.<sup>5</sup> The safety and effectiveness of any administered vaccine depends on the patient's degree of immunosuppression.<sup>9</sup> Studies have reported inconsistent results regarding the loss of preexisting antibodies and responses to immunization after receiving chemotherapy.<sup>41-43</sup> Given the paucity of data on which to base firm recommendations, no universal guidelines exist. Therefore, different approaches have been proposed to manage vaccinations in children with cancer who are off therapy, including the administration of a new complete vaccine series, the administration of a booster dose without measuring possible residual immunity, or the measuring of serum levels of antibodies against vaccine antigens followed by the administration of a booster dose if no evidence of protective levels

exists.<sup>2,44-46</sup> Testing of residual immunity is complicated by the absence of correlates of protection for some vaccines and an inability to determine the antibody titer for each vaccine antigen. In addition, low serum antibody concentrations do not always indicate a loss of protective immunity.

To protect cancer patients against vaccine-preventable infectious diseases, physicians must ensure that patients have received all universally recommended vaccines, including the seasonal influenza vaccine.<sup>9</sup> Patients who have not been fully vaccinated should receive the indicated vaccines soon after their cancer is diagnosed. In general, live attenuated vaccines are contraindicated during treatment or within 3-6 months from the end of immunosuppressant chemotherapy or radiotherapy because of the documented and theoretical risks of disseminated infection caused by the vaccine virus (Table 4).<sup>6,9,13,14,20</sup> The recommended timing of live vaccines in relation to poststeroid and postimmunoablative therapy varies among different countries (Table 5). Although safe, the administration of inactivated or recombinant vaccines is not recommended within 3-6 months of the completion of therapy because of a possible poor immune response, although the physician should make this decision on an individual basis after careful evaluation of the patient's social or epidemiologic risks of acquiring vaccine-preventable infectious diseases (Table 6).<sup>3</sup> Given the seasonality of influenza outbreaks, the AAP recommends administration of the influenza vaccine annually; optimal immune responses are achieved when the vaccine is given at least 3-4 weeks after the interruption of chemotherapy.<sup>20,38</sup> Passive immunization may also be indicated in select circumstances (eg, exposure to hepatitis B virus or varicella).<sup>3</sup>

### **HSCT Recipients**

Because HSCT recipients lose their previously acquired immunity from vaccines, repeating the primary vaccine series at fixed times posttransplant is critical to prevent infectious disease morbidity and mortality.<sup>6,39</sup> Limited controlled data are available on the safety and efficacy of vaccines in this population. In general, indicated vaccines should be administered despite the possibility of reduced efficacy. However, live vaccines should be deferred for safety concerns. Data are also limited on the immunogenicity of vaccines in transplant patients who have received umbilical cord blood, haploidentical grafts, or less-intensive conditioning regimens.<sup>6</sup> Various professional organizations and groups—including the Centers for Disease Control and Prevention (CDC), the Infectious Diseases Society of America, the American Society for Blood and Bone Marrow Transplantation,

**Table 4. Contraindicated Vaccines in Immunosuppressed Children With Cancer and Hematopoietic Stem Cell Transplant (HSCT) Recipients**

Category	Vaccine Type	Contraindicated Vaccines
Cancer patients receiving chemotherapy	Live bacteria	BCG, Ty21a <i>Salmonella typhi</i>
	Live virus	LAIV, MMR, varicella, OPV, yellow fever, rotavirus (RV1, RV5)
HSCT recipients	Live bacteria	BCG, Ty21a <i>S typhi</i> vaccine <sup>a</sup>
	Live virus	LAIV, MMR, varicella, OPV, yellow fever, rotavirus (RV1, RV5)

BCG, Bacillus Calmette-Guérin; LAIV, live attenuated influenza vaccine; MMR, measles-mumps-rubella; OPV, oral polio vaccine; RV1, monovalent rotavirus vaccine; RV5, pentavalent rotavirus vaccine.

<sup>a</sup> Contraindicated in subacute combined immunodeficiency patients; the safety and efficacy of rotavirus vaccines have not been studied in immunocompromised patients.

the European Blood and Marrow Transplantation group, and the German-Austrian-Swiss-Consensus Conference on clinical practice in chronic GVHD—have published vaccination guidelines for HSCT recipients.<sup>6,9,33,40</sup>

In general, transplant recipients should receive all recommended immunizations, preferably prior to transplantation and on accelerated schedules if indicated. Transplant recipients should be vaccinated at least 2 weeks, but ideally more than 1 month, before the onset of immunosuppression. In general, live attenuated vaccines are contraindicated during treatment.<sup>33</sup> In HSCT patients not receiving immunosuppressive therapy and free of ongoing GVHD, the recommendation is to withhold live-virus vaccinations—such as the measles-mumps-rubella (MMR) and varicella vaccines—for 2 years after transplant.<sup>6,33</sup> Inactivated or recombinant vaccines are not recommended within 6 months of completion of therapy (Table 7). HSCT recipients are at high risk for infections caused by encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b. Therefore, the administration of conjugate vaccines against these encapsulated pathogens is a priority for allogeneic HSCT recipients because of their poor immune responses to polysaccharide vaccines.<sup>33</sup>

Although early vaccination to protect against vaccine-preventable diseases is desirable, limited data exist regarding whether this approach is efficacious in patient groups whose immune recovery differs from recipients of an unmodified human leukocyte antigen–matched sibling transplant. In the absence of such data, prospective trials are needed to better define the optimal timing for immunizing recipients of alternative donor cells. Ideally, such trials should identify biological markers that will predict an optimal and durable vaccine response. However, recent data from the German-Austrian-Swiss Pediatric Working Group on Bone Marrow and Blood Stem Cell

Transplantation recommend early revaccination of pediatric HSCT recipients starting at 6 months posttransplant followed by a booster dose at 18 months.<sup>40</sup> Because children remain at high risk of exposure to infectious agents in day care centers and schools and experience relatively more rapid immune reconstitution compared to adult HSCT transplant patients, the recent guidelines also emphasize that immunizations should not be delayed in pediatric HSCT recipients with ongoing active or resolved chronic GVHD regardless of immunosuppressive therapy.<sup>33</sup>

Most experts recommend the measurement of specific antibody levels before and after HSCT in patients with chronic GVHD because immune reconstitution can be delayed considerably and vaccine

**Table 5. Timing of Live Vaccines After Steroid Therapy and Chemotherapy<sup>4</sup>**

Therapy	Duration of Delay
<b>Immunoablative therapy</b>	
AAP Red Book	At least 3 months
United Kingdom <sup>a</sup>	6-12 months
Australia	12 months
Canada	12 months
<b>Steroid dose</b>	
Topical (skin or respiratory tract)	None
Local injection	None
Physiologic	None
Systemic steroids (low or moderate dose)	None
Systemic steroids (high dose <sup>b</sup> ) for <2 weeks	2 weeks
Systemic steroids (high dose) for ≥2 weeks	1 month

AAP, American Academy of Pediatrics.

<sup>a</sup> Data based on survey.

<sup>b</sup> High-dose steroids are defined as ≥2 mg/kg/d of prednisone or the equivalent of ≥20 mg/kg/d for a child weighing >10 kg.

**Table 6. Vaccination Schedule in Children With Cancer After Completion of Chemotherapy<sup>2,3</sup>**

Vaccine	Timing of Immunization Postchemotherapy
<b>Infants and children not vaccinated or only partially vaccinated at the time of cancer diagnosis</b>	
Live Attenuated	
MMR	Give 2 doses at 3-month intervals at least 6 months off therapy.
VZV	Give 2 doses at 3-month intervals in patients in continuous remission for at least 1 year, with a lymphocyte count of >700/ $\mu$ L and a platelet count of >100,000/ $\mu$ L.
Inactivated or Recombinant	
TIV <sup>a</sup>	Recommended for all patients, including those receiving chemotherapy; administer >3-4 weeks after the last chemotherapy treatment.
DTaP	Start primary vaccine series in patients who are 3 months off therapy.
IPV	Start primary vaccine series in patients who are 3 months off therapy.
HBV	Start primary vaccine series in patients who are 3 months off therapy.
Hib	Start primary vaccine series in patients who are 3 months off therapy.
PCV	Start primary vaccine series in patients who are 3 months off therapy.
MCV4	Start primary vaccine series in patients who are 3 months off therapy.
HAV	Give 2 doses at 6-month intervals regardless of chemotherapy in the presence of epidemiological risk factors.
<b>Infants and children fully vaccinated at the time of cancer diagnosis</b>	
Live Attenuated	
MMR	Give a booster dose to patients who have been off therapy for 6 months.
VZV	Give a booster dose to patients in continuous remission for at least 1 year, with a lymphocyte count of >700/ $\mu$ L and a platelet count of >100,000/ $\mu$ L.
Inactivated or Recombinant	
TIV	Give a booster dose to all patients regardless of chemotherapy.
DTaP	Give a booster dose to patients who are 3 months off therapy.
IPV	Give a booster dose to patients who are 3 months off therapy.
HBV	Give 2 booster doses at 3-month intervals regardless of chemotherapy in the presence of epidemiologic risk factors.
Hib	Give a booster dose to patients who are 3 months off therapy.
PCV	Give a booster dose to patients who are 3 months off therapy. <sup>a</sup>
MCV4	Give a booster dose to patients who are 3 months off therapy. <sup>a</sup>
HAV	Give a booster dose regardless of chemotherapy in the presence of epidemiological risk factors.

MMR, measles-mumps-rubella vaccine; VZV, varicella-zoster vaccine; TIV, trivalent inactivated influenza vaccine; DTaP, diphtheria-tetanus-pertussis vaccine; IPV, inactivated polio vaccine; HBV, hepatitis B virus vaccine; Hib, *Haemophilus influenzae* type b vaccine; PCV, pneumococcal conjugate vaccine; MCV4, meningococcal conjugate vaccine quadrivalent; HAV, hepatitis A virus vaccine.

<sup>a</sup> Additional studies are needed.

responses cannot be reliably predicted in this population.<sup>6,33</sup> Serologic testing prior to vaccination and 1 month after the primary series and/or booster dose is useful to determine if additional doses are needed because a number of immunogens have demonstrated considerable variability in the magnitude of immune responses (eg, hepatitis B, measles, varicella, and pneumococcal polysaccharide vaccines). Donor vaccination before harvest may improve the posttransplant immunity of the allogeneic HSCT recipient against certain vaccines such as the tetanus toxoid vaccine, the 7-valent pneumococcal conjugate vaccine (PCV), and the *H influenzae* type b conjugate

vaccine, although this approach is limited by ethical and practical concerns.<sup>6</sup>

## ACTIVE IMMUNIZATION

### Live Vaccines

Both bacterial and viral live vaccines are generally contraindicated for severely immunocompromised individuals because of the risk of disease caused by vaccine strains.

**Oral Poliovirus Vaccine.** Use of the oral poliovirus vaccine (OPV) is contraindicated in patients with acquired immunodeficiency and their household contacts because of the risk of vaccine-associated

**Table 7. Vaccination Schedule After Allogeneic Hematopoietic Stem Cell Transplant for Children and Adolescents<sup>6,33</sup>**

Vaccine	Timing of Immunization Post-HSCT						
	4-6 mo	6 mo	7 mo	8 mo	18 mo	24 mo	26 mo
<b>Indicated Vaccines</b>							
TIV	Yes <sup>a</sup>						
DTaP	Yes	Yes	Yes	Yes	Yes		
IPV	Yes	Yes	Yes	Yes	Yes		
HBV	Yes	Yes	Yes	Yes	Yes		
Hib	Yes	Yes	Yes	Yes	Yes		
PCV	Yes	Yes	Yes	Yes	Yes		
MMR						Yes	Yes
<b>Optional Vaccines<sup>b</sup></b>							
VZV <sup>c</sup>						≥24 mo	
HAV <sup>d</sup>						≥24 mo	
HPV <sup>d</sup>						≥24 mo	
MCV						≥24 mo	

<sup>a</sup> Children aged <9 years of age should receive 2 doses of TIV annually.

<sup>b</sup> Limited or no data are available on safety and efficacy.

<sup>c</sup> Administer only to immunocompetent patients.

<sup>d</sup> Follow ACIP/AAP Red Book general recommendation.

HSCT, hematopoietic stem cell transplant; TIV, trivalent inactivated influenza vaccine; DTaP, diphtheria-tetanus-pertussis vaccine; IPV, inactivated polio vaccine; HBV, hepatitis B virus vaccine; Hib, *Haemophilus influenzae* type b vaccine; PCV, pneumococcal conjugate vaccine; MMR, measles-mumps-rubella vaccine; VZV, varicella-zoster vaccine; HAV, hepatitis A virus vaccine; ACIP, Advisory Committee on Infectious Diseases; AAP, American Academy of Pediatrics; HPV, human papillomavirus vaccine; MCV, meningococcal conjugate vaccine.

polio in immunocompromised children.<sup>47,48</sup> Viral shedding may occur in OPV recipients for 8-12 weeks after vaccine administration. Inactivated poliovirus vaccine is recommended when immunization is appropriate in both immunocompromised patients and their contacts. If OPV is introduced into the household of an immunosuppressed child, to minimize exposure to OPV, shedding household members should practice proper hand hygiene after contact with the child and the person who received the OPV should avoid changing diapers.

**Varicella Vaccine.** Immunosuppressed patients are at a higher risk of complications from varicella infection than immunocompetent patients.<sup>49</sup> Although effective antiviral therapy against varicella infections exists and the incidence of varicella immunization is increasing, infectious complications remain a relevant concern because antiviral therapy can fail and not all contacts are likely to be immunized.<sup>50</sup> The varicella vaccine should not be routinely administered to children who have T-lymphocyte immunodeficiency,

including those with leukemia, lymphoma, and other malignant neoplasms affecting the bone marrow or lymphatic systems, as well as children receiving long-term immunosuppressive therapy.<sup>20,51</sup> Patients who have received high-dose steroids for ≥14 days should not receive a varicella vaccine for at least 1 month after the discontinuation of steroid therapy.

The timing of the varicella vaccine is controversial in leukemic patients in remission, but administration is prudent because the risk of natural varicella infection outweighs the risk of acquiring the disease via the live-attenuated vaccine virus.<sup>4,51</sup> The varicella vaccine should be given as either a primary immunization or a booster dose in patients fully immunized at the time of cancer diagnosis if the patient is in continuous remission for at least 1 year with lymphocyte counts >0.7 × 10<sup>9</sup>/L and platelet counts >100 × 10<sup>9</sup>/L 24 hours before the immunization.<sup>46,47</sup> If a patient requires multiple doses of the varicella vaccine, the doses should be scheduled 3 months apart.

In HSCT recipients, the administration of an Oka strain vaccine 12-18 months after transplantation in patients not receiving immunosuppressive therapy did not result in adverse events.<sup>52</sup> Seroconversion occurred in all recipients after 2 doses, and antibodies lasted for at least 2 years in 6 respondents. The optimal time to administer the varicella vaccine after HSCT has not been determined.<sup>20</sup>

**MMR Vaccine.** The severity of both measles and mumps is increased in severely immunosuppressed patients.<sup>53,54</sup> Because the greatest morbidity from rubella infections is likely to be from vertically acquired infections causing congenital rubella syndrome, unvaccinated and immunocompromised pediatric patients are not likely to suffer adversely from exposure to rubella. Because MMR is a live vaccine formulation, this vaccine should not be administered in patients with pharmacologically induced immunosuppression for a malignancy or HSCT.<sup>55</sup>

In children who will be receiving immunosuppressing therapy for a malignancy and have not received an MMR vaccine, the MMR vaccine should be withheld until at least 3 months after therapy is complete.<sup>42,56,57</sup> Already-administered doses do not need to be repeated, but some experts recommend giving a booster dose to patients who have been off therapy for 6 months.<sup>2,3</sup> Most studies have shown that the immune response 3-6 months after the completion of chemotherapy is similar to that of age-matched healthy children, with no risk of severe adverse events.<sup>42,56,57</sup> However, some evidence indicates that in children (average 3 years old, range 1.5-10 years) who had completely lost immune response, only low-avidity antibodies were generated.<sup>23</sup> If the child is exposed to measles before the MMR vaccine can be safely administered, prophylaxis can be given with Ig.<sup>55</sup>

Revaccination with MMR should be delayed for at least 24 months after HSCT in children who no longer have a need for pharmacologic immunosuppression and do not have GVHD.<sup>58</sup> After HSCT, the decision to reimmunize with MMR should be evaluated with consideration of serum antibody titers for MMR and in conjunction with the bone marrow transplant team. The need for a booster dose of MMR should be evaluated in conjunction with titers and given at least 28 days after the first dose of MMR.<sup>20</sup>

**Rotavirus Vaccine.** Because it is a live virus vaccine, the use of rotavirus vaccine is contraindicated in patients with severe immune suppression such as severe combined immunodeficiency syndrome.<sup>59</sup> Rotavirus vaccines are of unproven safety in infants with immune deficiencies, and the ACIP notes that rotavirus vaccine should be used with caution. Physicians should carefully weigh the risks and benefits before recommending rotavirus vaccine in infants. Household contacts of immunocompromised patients should receive the rotavirus vaccine to minimize risk because the benefits of protection outweigh the small risks of transmission. Because horizontal transmission has occurred in clinical trials from rotavirus-positive diarrhea, precautions should be implemented if household contacts who have been immunized with rotavirus develop diarrhea.<sup>60</sup> Immunocompromised patients should be instructed to avoid stools from rotavirus-immunized contacts, and all members of the family should practice good hand hygiene for at least 1 week after vaccination.<sup>20</sup>

**Bacillus Calmette-Guérin (BCG) Vaccine.** The BCG live vaccine is recommended only in rare circumstances in the United States, including for patients with an unavoidable risk of being exposed to tuberculosis and in whom other control measures have failed or are not feasible.<sup>61</sup> However, any patient with a primary or secondary immune deficiency should not receive the BCG virus because cases of localized and disseminated BCG have been described in infants and children with HIV infection.<sup>61,62</sup>

### Killed and Component Vaccines

Killed and component vaccines should not present a risk to immunocompromised patients, and these vaccines are not generally contraindicated. However, the immunocompromised patient's ability to develop an adequate immune response is a significant clinical consideration that the physician should weigh against the risk of contracting a vaccine-preventable disease when making clinical decisions about when to immunize.

**Diphtheria-Tetanus-Pertussis Vaccine.** The risk of contracting diphtheria or tetanus within 1 year of HSCT is low. However, increased reports of pertussis

in adolescents and young adults have led to the recommendation to administer Tdap to all 11- to 12-year-old patients routinely. Data do not exist regarding the safety or immunogenicity of pertussis immunization for HSCT recipients.<sup>20</sup> Children with intense immunosuppressing therapy, either to treat malignancy or from HSCT, should not receive vaccines because their immunity is unlikely to be developed.

After 3 months have passed from the last dose of immunosuppressant chemotherapy, the vaccination schedule should be continued where it left off prior to the initiation of chemotherapy. Some evidence suggests that antineoplastic treatment may decrease serologic immunity to diphtheria-tetanus-pertussis.<sup>63</sup> Patients who have received immunosuppressing therapy should be assessed to identify who could benefit from a booster dose of DTaP or Tdap. A booster dose of the diphtheria-tetanus-pertussis vaccine 3 months after the completion of chemotherapy has resulted in protective antibody titers.<sup>56,64-66</sup>

Revaccinating children with a 3-dose series of diphtheria-tetanus-pertussis 12 months after stem cell transplant is reasonable because an adequate immune response may be generated at this time.<sup>67</sup> This patient population should be classified as never vaccinated, so the full toxoid vaccine, DTaP, should be given if possible to generate an adequate immune response.<sup>6,68</sup> Some evidence suggests that using reduced-dose pertussis in Tdap results in a poor immune response.<sup>68</sup> Serum titers may be used to determine the number of doses needed to achieve an adequate immune response because patients may have heterogeneous responses to vaccinations.

**H influenzae (Hib) Vaccine.** Children with immunologic impairment are at an increased risk of Hib disease and may have an impaired anti-polyribosylribitol phosphate antibody response to conjugate vaccines.<sup>69-72</sup> Although these children may benefit from an additional dose of Hib vaccine, studies have not been conducted to evaluate this practice.

Waiting to resume vaccination until immune function has returned after immunosuppressant chemotherapy would optimize an immune response to the vaccine. Starting or resuming vaccination with Hib 3 months after the completion of chemotherapy has resulted in protective antibody levels.<sup>73,74</sup>

More than 80% of adult HSCT patients who received Hib vaccines at 12 and 24 months after HSCT achieved protective antibody concentrations.<sup>67</sup> Starting or resuming Hib vaccination 6 months after an allogeneic HSCT is recommended.<sup>6,33</sup>

**Hepatitis A Vaccine.** Hepatitis A is generally an acute self-limiting illness, but prolonged hepatic impairment and fulminant hepatitis can occur. Patients with malignancies have a high prevalence of



antibodies to the hepatitis A antigen and a high incidence of hepatitis B virus infection.<sup>75,76</sup> The vaccine is recommended at 12 and 23 months of age and for those at risk of developing chronic conditions. The immune response to the hepatitis A vaccine in immunocompromised patients may be suboptimal.<sup>20</sup> Vaccinating after immune function has reconstituted is prudent and would likely provide the most benefit.

If risk factors are present, the hepatitis A vaccine may be administered as either a primary vaccine or as a booster 3 months after patients have completed chemotherapy.<sup>2,3</sup> Combining the hepatitis A vaccine with the hepatitis B vaccine resulted in an immunogenic response in children with solid tumors.<sup>77</sup> Patients who have not received the full course should receive 2 doses given 6 months apart, and a single dose should be administered to patients who have received a full course of the hepatitis A vaccine.

HSCT patients with risk factors for hepatitis A may benefit from a hepatitis A series.<sup>6,33</sup> Recommendations on when to administer the hepatitis A vaccine had not been made at the time of writing, but practitioners should consider the return of immune function when making a clinical decision.

**Hepatitis B Vaccine.** Because the risk of chronic infection with hepatitis B is inversely related to age at the time of infection, universal vaccination is recommended for all infants, children, and adolescents.<sup>78</sup> The physician should use clinical judgment to determine the optimal time to resume vaccination in immunosuppressed patients who have not completed a full course of hepatitis B. Serologic testing for the antibody to the hepatitis B surface antigen is recommended for immunosuppressed patients who are at risk of exposure to the hepatitis B virus.<sup>78</sup>

Starting or completing a primary vaccination schedule 3 months after the end of chemotherapy is recommended.<sup>2,3,77</sup> If epidemiological risk factors are present in patients who have received a full course of the hepatitis B vaccine, a booster dose should be administered 3 months after chemotherapy.<sup>2,3</sup>

The hepatitis B vaccine series should be administered 6 months after an allogeneic HSCT.<sup>6,33</sup>

**Pneumococcal Vaccines.** Patients are at a high risk of invasive pneumococcal infections when a condition associated with immunosuppressive therapy such as HSCT or cancer is present.<sup>79,80</sup> The 13-valent pneumococcal conjugate vaccine (PCV13) provides protection against 13 pneumococcal serotypes and should be used instead of the older 7-valent pneumococcal conjugate vaccine (PCV7) formulation. Patients who have been immunized with a course of PCV7 should receive 1 supplemental dose of PCV13. Courses that have been started with PCV7

should be completed with PCV13. Vaccination with a 23-valent pneumococcal polysaccharide vaccine (PPSV23) in addition to a full course of PCV13 is recommended to provide additional protection in immunosuppressed patients. PPSV23 should be administered 8 weeks after the last dose of PCV13. In patients eligible for PPSV23 and younger than 5 years, an additional dose of PPSV23 should be given 5 years after the previous dose because the polysaccharide formulation is less immunogenic than the conjugate vaccine, particularly in the first years of life.<sup>81</sup> As with other inactivated vaccines in immunosuppressed patients, clinical judgment is important in determining the optimal time to resume immunization with the pneumococcal vaccine.

Starting or completing a primary vaccination series with PCV13 should occur 3 months after chemotherapy.<sup>2,3,82</sup> Patients who have received a full course of PCV7 or PCV13 should receive a booster dose 3 months after chemotherapy. A 1- or 2-dose course of PCV23 is recommended in patients after the PCV13 series is complete.

Administration of a PCV13 and PPSV23 series should occur beginning 6 months after HSCT.<sup>6,33</sup> The PCV formulation has been found to have better immune responses than the PPSV formulation, and a PCV13 series should be given first.<sup>40,83-85</sup> A fourth dose of PPSV23 is likely beneficial because it affords protection against additional pneumococcal strains.<sup>39</sup>

**Meningococcal Conjugate Vaccine.** The tetravalent meningococcal conjugate vaccine (MCV4) is recommended for children ages 11-12 years. MCV4 is approved in infants as young as 9 months of age. This inactivated vaccine should be administered to immunosuppressed patients who are eligible to receive it at a time when adequate immunity is most likely to develop.<sup>86</sup>

The MCV4 was studied in 35 children ranging from 2-18 years old.<sup>87</sup> A majority of these patients had ALL and had completed chemotherapy 3-18 months prior to vaccination or were on maintenance therapy. The vaccine was found to be safe and well tolerated, and a majority of the children generated either a positive serological response or a complement-mediated bactericidal response. Starting or completing a primary vaccination series with MCV4 should occur at least 3 months after chemotherapy.<sup>2,3,87</sup> Some experts recommend the administration of a booster dose in patients who received a full course of MCV4 3 months after chemotherapy.

Both polysaccharide-based and conjugate-type vaccines for meningococcal infections exist. Although no studies have compared the 2 types of meningococcal vaccines, it is reasonable to assume that a more stable immune response will result from a

meningococcal conjugate vaccine because studies have shown this result for pneumococcal and Hib vaccines.<sup>88,89</sup> The German-Austrian-Swiss-Consensus Conference on clinical practice in chronic GVHD recommends administration of 3 monthly doses of a meningococcal type C conjugate vaccine starting at 6-12 months after an allogeneic HSCT.<sup>6,33</sup> No data are currently available on the immunogenicity and safety of MCV4 in pediatric allogeneic HSCT recipients.

*Inactivated Poliovirus Vaccine (IPV).* The IPV vaccine can be given to immunosuppressed patients and their household contacts. In patients receiving high-dose steroids or immunosuppressant chemotherapy, the administration of incomplete courses of IPV vaccines should be resumed after the immune system has recovered.<sup>47</sup>

Starting or completing a primary vaccination series with IPV should occur 3 months after chemotherapy.<sup>2,3,90</sup> For patients who have received a full course of IPV, a booster dose 3 months after chemotherapy is recommended because up to 38% of children no longer have protective antibody levels by then.<sup>90</sup>

A 4-dose IPV series (3 + 1) should be administered 6 months after HSCT.<sup>6,33</sup> Three doses of IPV should be administered at monthly intervals, followed by a booster dose at 18 months after allogeneic HSCT.<sup>33</sup>

*Human Papillomavirus (HPV) Vaccine.* The HPV vaccine has been shown to prevent the majority of HPV strains that cause cervical cancer and genital warts. Rates of HPV-related warts, neoplasia, and anogenital cancers are increased in SOT recipients.<sup>91</sup> Patients with other causes of immune suppression are expected to have similar rates of increased HPV effects. Guidelines recommend the routine vaccination of females and males at age 11-12 years in a 3-dose series with a quadrivalent Gardasil (Merck & Co., Whitehouse Station, NJ) vaccine or female patients only with a bivalent Cervarix (GlaxoSmithKline, Brentford, UK) vaccine. The HPV vaccine may be administered to immunocompromised female and male patients, but immune response and vaccine efficacy may be reduced in such recipients.<sup>92</sup>

Patients with a malignancy may benefit from a HPV vaccine series or booster. Recommendations about when to administer the HPV vaccine have not been made in cancer patients, but administering other inactivated vaccines is recommended 3 months after chemotherapy.<sup>2,3</sup>

Many HSCT patients may benefit from the HPV vaccine. Although specific recommendations about when to administer the HPV vaccine have not been made for HSCT patients, recommendations for other

inactivated vaccines suggest administering them 6 months after HSCT.<sup>6,33</sup>

*Influenza Vaccine.* Patients and close contacts of immunosuppressed patients who are  $\geq 6$  months old should receive an annual dose of the inactivated influenza vaccine. Immunosuppressed patients are at a higher risk of complications from influenza, including prolonged hospitalization and intensive care stays, than the general population.<sup>20,93,94</sup> The live influenza vaccine is contraindicated in patients with immune suppression because of the risk of disease from the vaccine strain.

In addition to the increased risk of complications, delays in the administration of life-saving chemotherapy can result when patients who have a malignancy contract influenza—an additional incentive to administer an annual influenza vaccine to these patients. In children with malignant neoplasms, inactivated influenza immunizations should be given no sooner than 3 to 4 weeks after a course of chemotherapy has been discontinued and when peripheral granulocyte and lymphocyte counts  $>1,000$  cells/ $\mu\text{L}$  ( $1 \times 10^9$ ) are achieved.<sup>20</sup> Evaluations of the immune responses in oncology patients have found the influenza vaccine to be modestly immunogenic, safe, and well tolerated.<sup>95-100</sup>

Lifelong seasonal influenza vaccination is recommended for all HSCT candidates and recipients. Vaccination must be administered before the influenza season, starting at 6 months after HSCT and continued annually.<sup>33</sup> Two vaccine doses must be administered in children younger than 9 years who have not been previously immunized against influenza.<sup>20,33</sup> However, because the immune response may be suboptimal in patients with recent immunosuppression from HSCT or malignancy, vaccinating close contacts and healthcare workers in transplant units should be encouraged to prevent exposure and contraction of influenza.<sup>33</sup>

## PASSIVE IMMUNIZATION

Passive immunization occurs when a preformed antibody is administered to a recipient. It is indicated in certain situations with several types of products. The prototypical example in an immunocompromised patient is exposure to a vaccine-preventable disease in a person without immunity to that disease. Ig, administered intramuscularly, can be given for hepatitis A, measles, or rubella prophylaxis. Specific Ig preparations include hepatitis B Ig, rabies Ig, tetanus Ig, investigational varicella-zoster Ig (VariZIG), cytomegalovirus Ig intravenous, and botulism Ig intravenous. If VariZIG is not available, intravenous Ig can be administered for varicella prophylaxis. Intravenous Ig can be given up to 96 hours after exposure but has maximum benefit if administered as soon as possible

after exposure. After passive immunization occurs with Ig, a washout period of 3 to 6 months should occur before other active vaccinations are administered.<sup>101</sup> Detailed passive immunization recommendations for specific diseases are beyond the scope of this article, but the AAP provides comprehensive guidelines.<sup>20</sup>

### Palivizumab

Administration of 5 monthly doses of the monoclonal antibody palivizumab during the respiratory syncytial virus season is recommended for certain infants and children with chronic lung disease of prematurity, a history of prematurity ( $\leq 35$ -week gestation), or congenital heart disease. Prophylaxis with palivizumab has not been evaluated in randomized controlled trials in immunocompromised children, but children with immunodeficiencies may benefit from prophylaxis.<sup>102</sup> Some experts routinely recommend the use of palivizumab prophylaxis for SOT recipients and candidates younger than 2 years.<sup>103</sup>

### IMMUNOCOMPROMISED TRAVELERS

There is a paucity of data regarding the administration of travel vaccines in immunocompromised patients.<sup>104</sup> Timely pretravel advice is recommended 4-6 weeks before departure. Immunocompromised patients should be routinely immunized against hepatitis B and hepatitis A. Live attenuated travel vaccines such as the yellow fever vaccine and the oral typhoid vaccine are contraindicated in patients receiving immunosuppressive and immunomodulatory therapies.<sup>105</sup> Likewise, the cholera and tick-borne encephalitis vaccines are not recommended in immunocompromised individuals because of a lack of data in HSCT recipients.<sup>25,104</sup> The rabies vaccine may be indicated for use in HSCT recipients with potential exposure to rabies. Expert guidelines suggest delaying the preexposure rabies vaccination until 12-24 months after HSCT.<sup>6</sup> Postexposure prophylaxis with rabies vaccine in conjunction with human rabies Ig can be given any time after HSCT, as indicated.<sup>6</sup>

### Typhoid Vaccine

In the United States, travelers to areas where risk of exposure to the *Salmonella* serotype Typhi is recognized, people with intimate exposure to a documented typhoid fever carrier, or laboratory workers who have frequent contact with *Salmonella* serotype Typhi are candidates to receive a typhoid vaccine. However, the live attenuated oral vaccine Ty21a is contraindicated in immunosuppressed patients.<sup>25</sup> The parenteral vaccine against typhoid, Vi capsular polysaccharide, can be administered to patients who are traveling to endemic areas and those who are at risk of contracting *Salmonella* serotype Typhi.<sup>29</sup>

### Japanese Encephalitis Vaccines

Licensed Japanese encephalitis (JE) vaccines include JE-MB, an inactivated mouse brain-derived vaccine and the JE-VC, a Vero cell culture-derived vaccine. No data exist regarding the safety and immunogenicity of the JE vaccine in HSCT recipients.<sup>6</sup> Some expert reviews suggest that the JE vaccine may be considered in SOT recipients, but the ACIP does not offer guidance because data are very limited regarding the use of JE-VC in immunocompromised hosts.<sup>104</sup> The limited information in pediatrics indicates that the JE-MB vaccine is safe and well tolerated in HIV-infected patients and those with cancer.<sup>105</sup> In limited studies, JE-MB has shown an acceptable safety profile in children with HIV and neoplastic diseases.<sup>106</sup>

### FAMILY, HOUSEHOLD CONTACTS, AND HEALTHCARE WORKERS

All close contacts who live in the same household as the immunocompromised patient should be immunized with all routinely recommended vaccines, including the live attenuated MMR, varicella, and rotavirus vaccines because the transmission of the live vaccine virus is rare (Table 8).<sup>8,25,107</sup> The transmission of the live varicella vaccine virus from vaccine recipients to close contacts who are not immunosuppressed has occurred, but only from vaccine recipients who developed a rash.<sup>23</sup> Household contacts who develop a vesicular rash after varicella vaccination should avoid contact with immunosuppressed individuals until the rash resolves. Immunocompromised patients should be instructed to avoid stools from rotavirus-immunized contacts, and all members of the family should practice good hand hygiene for at least 1 week after vaccination.<sup>15</sup> In addition, the trivalent inactivated influenza vaccine should be administered annually to all close contacts of immunocompromised individuals.<sup>25</sup> Vaccinating siblings, family members, and other close contacts is an important strategy to protect immunocompromised patients against vaccine-preventable diseases, especially those transmitted in households, such as pertussis and influenza.<sup>12</sup> Data are limited related to the transmission of the live attenuated influenza vaccine virus from vaccinated individuals to immunocompromised patients, but transmission may occur in rare instances.<sup>7</sup> Live attenuated vaccines such as the oral polio, BCG, and oral typhoid Ty21a vaccines are contraindicated in household contacts.<sup>8</sup>

### ROLE OF THE CLINICIAN AND INFORMATION RESOURCES

Healthcare providers who care for immunocompromised children should be knowledgeable about

**Table 8. Immunization of Caregivers and Household Contacts of Immunocompromised Children<sup>9</sup>**

Vaccine Type	Specific Vaccine	Comments
Live bacteria	BCG	Contraindicated
	Ty21a <i>Salmonella typhi</i> vaccine	Contraindicated
Live virus	OPV	Contraindicated
	MMR	Indicated
	Varicella	Indicated; if a vesicular rash develops after vaccination, avoid contact with immunosuppressed individual until rash resolves.
	Rotavirus (RV1, RV5)	Indicated; avoid contact with stools by the immunocompromised patient. All family members should practice good hand hygiene for at least 1 week after vaccination.
Inactivated	IPV, TIV	Immunize all household contacts to minimize exposure of immunocompromised patients to vaccine-preventable diseases

BCG, Bacillus Calmette-Guérin; OPV, oral polio vaccine; MMR, measles-mumps-rubella vaccine; RV1, monovalent rotavirus vaccine; RV5, pentavalent rotavirus vaccine; IPV, inactivated polio vaccine; TIV, trivalent inactivated influenza vaccine.

the indications, contraindications, and precautions for vaccine administration in patients with altered immunocompetence.<sup>5</sup> Pediatricians play a crucial role in identifying and effectively communicating the risks and benefits of vaccines to immunocompromised patients and their parents.<sup>108</sup> Parents should also be educated about trustworthy websites where they can find reliable health information about vaccines and vaccine-preventable diseases (Table 9).<sup>109,110</sup> Examples include the AAP, CDC, National Institutes of Health, World Health Organization, National Network for Immunization Information, and Immunization Action Coalition.<sup>111</sup> In addition to education, physicians should ensure proper storage and administration of

vaccines by following ACIP recommendations, identify contraindications, report and treat adverse reactions, and refer and follow up as appropriate.

#### FUTURE RESEARCH NEEDS

Given the paucity of data on the safety and efficacy of several newly introduced vaccines and the growing population of immunocompromised children and adolescents, additional research is a priority to guide rational guidelines and vaccine policy recommendations.<sup>35</sup> Understanding the degree of immune reconstitution and identifying specific host immune responses and their clinical implications are important.<sup>8</sup> Research must use rigorous study designs that will evaluate the

**Table 9. Selected Online Resources Regarding Vaccines**

Agency	Website Address
American Academy of Pediatrics	<a href="http://www.aap.org">www.aap.org</a>
Centers for Disease Control and Prevention	<a href="http://www.cdc.gov/vaccines">www.cdc.gov/vaccines</a>
Immunization Action Coalition	<a href="http://www.immunize.org">www.immunize.org</a>
Infectious Diseases Society of America	<a href="http://www.idsociety.org">www.idsociety.org</a>
Institute of Medicine	<a href="http://www.iom.edu">www.iom.edu</a>
Institute for Vaccine Safety	<a href="http://www.vaccinesafety.edu">www.vaccinesafety.edu</a>
Global Alliance Vaccines and Immunization	<a href="http://www.gavialliance.org">www.gavialliance.org</a>
National Foundation for Infectious Diseases	<a href="http://www.nfid.org">www.nfid.org</a>
National Institute of Allergy and Infectious Diseases	<a href="http://www.niaid.org">www.niaid.org</a>
National Institutes of Health	<a href="http://www.nih.gov">www.nih.gov</a>
National Network for Immunization Information	<a href="http://www.immunizationinfo.org">www.immunizationinfo.org</a>
Sabin Vaccine Institute	<a href="http://www.sabin.org">www.sabin.org</a>
Food and Drug Administration	<a href="http://www.fda.gov/cber/vaccines.htm">www.fda.gov/cber/vaccines.htm</a>
Vaccine Education Center at Children's Hospital of Philadelphia	<a href="http://www.vaccine.chop.edu">www.vaccine.chop.edu</a>
World Health Organization	<a href="http://www.who.int/topics/immunization/en">www.who.int/topics/immunization/en</a>

outcome of natural infections and immunization in populations receiving varying immunosuppressive regimens.

## CONCLUSIONS

Children who are diagnosed with cancer and receive chemotherapy or HSCT are at increased risk for vaccine-preventable infectious diseases. Therefore, the immunization of immunocompromised patients is an important priority. Physicians must be aware of current immunization policy guidelines from the ACIP and AAP and should consider the risks and benefits of vaccines when recommending vaccination in compromised hosts. Further, all household contacts should be immunized with all routinely recommended vaccines to protect compromised patients against common vaccine-preventable infections, such as influenza and pertussis.

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