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Ensure proper immunization for patients who received chemotherapy or transplantation

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With improvements in survival rates after pediatric cancer, long-term management of children and adolescents with cancer has come to the forefront of pediatric oncology and post-transplantation care. Vaccinations are an integral part of this care.

Patients and families rely on recommendations from their primary care providers (PCP) and pediatric oncology and infectious disease specialists, who share the responsibility to ensure appropriate and optimal vaccinations.

Pediatricians can provide families with clear recommendations and education on the timeline of age-appropriate vaccinations to optimize protection against vaccine-preventable infections (VPI) and ensure healthy survivorship. In addition, age-appropriate vaccination of household and close contacts of pediatric cancer patients, survivors, hematopoietic cell transplantation (HCT) candidates and recipients remains critical.

Vaccinations after completion of chemotherapy

The Centers for Disease Control and Prevention's (CDC's) Advisory Committee on Immunization Practices, the AAP and Infectious Diseases Society of America recommend providing inactivated vaccines as early as three months following completion of chemotherapy to optimize vaccine immunogenicity (Rubin LG, et al. *Clin Infect Dis.* 2014;58:309-318; AAP *Red Book*).

Live-attenuated vaccines for varicella and measles, mumps and rubella (MMR) are considered safe and effective when administered at least three months after completion of chemotherapy. An exception to this timing are children who received anti-B cell therapies such as rituximab or blinatumomab. Vaccination candidacy for these children should be assessed six to nine months after completion of biologic therapy and vaccines provided when there is evidence of B cell recovery.

Vaccinations after HCT

In HCT recipients, there are additional complexities to consider when determining the type and timing of vaccinations, including ongoing maintenance immunotherapy, presence of chronic graft vs. host disease (GVHD) and dynamics of immune reconstitution post-HCT (Haynes AS, et al. *Transplant Cell Ther.* 2021;27:317-326).

Considering vaccination rates are suboptimal in this population, influenza, varicella and invasive pneumococcus are the most frequent causes of VPI-associated hospitalizations in HCT recipients within five years of transplantation (Danino D, et al. *Bone Marrow Transplant.* 2021;56:2656-2663).

In general, guidelines recommend that for most allogeneic and autologous HCT recipients, inactivated vaccines can be given safely three to six months post-HCT. In addition, meningococcal vaccines (meningococcal conjugate A,C,W,Y and meningococcal B vaccines) may be appropriate for certain HCT recipients at high-risk for invasive disease (e.g., asplenia, chronic GVHD).

The table below summarizes *general* recommendations (excluding primary immunodeficiencies as indication for transplantation) and timing of vaccinations for pediatric HCT recipients.

Timing of vaccination after pediatric hematopoietic cell transplantation (HCT)

Vaccine	Time after HCT (in months)	Number of doses	Considerations
Inactivated			
Inactivated influenza vaccine	1-6	1 or 2	• Minimum age: 6 months • Children <9 years old should receive 2 doses 4 weeks apart • Can be administered during chemotherapy • Administer 4-6 months following HCT; can be provided as early as 1 month post-HCT during influenza season
Pneumococcal conjugate vaccine-13 valent (PCV-13)	3-6	1-4	• Interchangeable with PCV-15 • Number of doses dependent on age at first dose and presence of GVHD
Pneumococcal conjugate vaccine-15 valent (PCV-15)	3-6	1-4	Interchangeable with PCV-13
Pneumococcal polysaccharide vaccine-23 valent	8 weeks after last dose of PCV-13/PCV-15	1-2	• Minimum age: 2 years • Minimum interval between doses: 5 years
Haemophilus influenzae type B	3-6	3	
Diphtheria-tetanus-acellular pertussis	3-6	3	
Inactivated polio vaccine	3-6	3	
Meningococcal serogroup A,C,W,Y	6	2-4	• Minimum age: 2 months to 2 years, depending on vaccine formulation • Number of doses dependent on age at first dose and formulation. • Booster doses may be needed in patients with ongoing increased risk of meningococcal disease.
Meningococcal serogroup B	6	2 or 3	• Minimum age: 10 years • Number of doses dependent on vaccine formulation. • Booster doses may be needed in patients with ongoing increased risk of meningococcal disease.
Hepatitis A	6-12	2	Minimum age: 12 months
Hepatitis B	6-12	3	Consider obtaining post-vaccination quantitative hepatitis B surface antibody (HBsAb) titer 1-2 months after last dose. If HBsAb <10 mIU/mL, provide a second, 3-dose vaccine series.
Human papillomavirus-9 valent	6-12	3	Minimum age: 9 years
Live-attenuated viral			
Measles, mumps rubella*	24	2	Minimum age: 12 months
Varicella*	24	2	Minimum age: 12 months

*HCT recipients should meet all of the following criteria to receive live-attenuated virus vaccination: 2 years after HCT *and* minimum of 8 months after last intravenous immunoglobulin dose *and* 12 months after completing systemic immunosuppression (e.g., calcineurin inhibitors)

Find additional details about vaccination in immunocompromised individuals, including timing, minimum dosing intervals, vaccine formulations and risk factors, at https://www.cdc.gov/vaccines/schedules/ and http://bit.ly/3GLP2sk.

COVID-19 vaccination following chemotherapy and HCT

The AAP, American Society of Hematology and American Society for Transplantation and Cellular Therapy provide concise recommendations for the administration of COVID-19 mRNA vaccines in immunocompromised children based on the schedule approved by the CDC.

The CDC recommends COVID-19 mRNA vaccination as a three-dose primary series in moderately to severely immunocompromised patients ages 6 months and older. Based on current evidence of efficacy and safety, current mRNA vaccines can be offered to eligible children two to four weeks before planned

immunosuppressive therapy, during chemotherapy (optimally, between treatment cycles or when immunosuppression is minimized) and three to six months after HCT or CAR-T therapies. Type, number and timing of booster doses will depend on the child's age.

Given the expected changes in the dynamics of the pandemic, emergence of variants and new vaccine formulations, pediatricians should refer to the most recent CDC COVID-19 vaccine recommendations and schedule at https://www.cdc.gov/vaccines/schedules/index.html.

Through multidisciplinary communication, education and assessment of immunization needs at each visit, PCPs, oncologists and infectious disease specialists can guide the optimal vaccination of patients following the completion of chemotherapy or HCT (Choi DK, et al. *Pediatr Blood Cancer.* 2020;67:e28565). Vaccination against SARS-CoV-2 along with other age-appropriate childhood immunizations is vital to ensure that pediatric cancer survivors and HCT recipients avoid the morbidity and mortality associated with vaccine-preventable infections.

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Resources

- Critical updates on COVID-19 from the AAP
- AAP pediatric COVID-19 vaccine dosing quick reference guide