4.5 Immunization of Children with Cancer

General Issues

When using vaccines in immunosuppressed patients, one needs to be concerned about safety as well as efficacy. The following document contains guidance for immunization of children with cancer both at the time of immunosuppressive therapy and following the end of their immunosuppressive therapy. It is based in part on existing guidelines or major reports wherever possible.[1-11]

In general, all live virus vaccines should be avoided in the immunocompromised patient, and should not be given until at least three months following the end of immunosuppressive therapy. In the case of children receiving bone marrow transplantation, this period should be extended to at least 24 months (please see below for guidelines for immunization post-bone marrow transplantation).

In the cases of the non-live vaccines, the major concern is not safety but rather efficacy. Thus, in general, it is advisable to give even inactivated vaccines at times of maintenance chemotherapy rather than during periods of intensive treatment as the antibody responses are likely to be better.

Considerations for Specific Vaccines

Vaccines That Are Contraindicated

In cancer patients, the possibility of complications from live vaccines is well recognized.[12-14] The oral polio (which is not recommended in Canada), yellow fever and oral typhoid vaccines are live and are contraindicated in the cancer patient. The live attenuated intranasal influenza vaccine is also contraindicated.

Measles, Mumps and Rubella

Measles, mumps and rubella (MMR) vaccines are relatively contraindicated, with the provisos as discussed above.

Varicella

The varicella vaccine is also relatively contraindicated and is not approved for use in children with cancer. While accumulating data[15-17] has resulted in recommendations from the American Academy of Pediatrics that suggest immunization should be considered in susceptible children who have been in continuous remission from acute lymphoblastic leukemia for at least 1 year, this should not be considered routine and should be done only in discussion with the patient's specialized childhood cancer program. Two doses of vaccine are required to be considered immune.

Vaccines That Are Not Contraindicated

As indicated above, the non-live vaccines are not contraindicated in the cancer patient. Recommendations are based on limited data, expert opinion and consensus.[7, 8, 18-23] The section below summarizes these vaccines and specific relevant issues.

Diphtheria, Tetanus, Acellular Pertussis / Inactivated Polio/ Haemophilus Influenzae Type B Vaccine
Children with cancer should receive Hib-containing vaccine (such as Pediacel®) according to routine vaccination schedules. Individuals aged 5 years and older should receive one dose of Hib vaccine, regardless of prior history of Hib vaccination, and at least 1 year after any previous dose.

Pneumococcal Vaccine
Children with Hodgkin lymphoma are known to be at high risk of invasive pneumococcal disease.[24-26] Those with other hematologic malignancies are presumed to be at high risk of invasive pneumococcal disease and they require an alternative treatment schedule. There is a paucity of data on the use of the conjugate pneumococcal vaccine in immunosuppressed patients. Infants and children <2 years of age should receive the regular childhood schedule for the conjugate vaccine. For previously unvaccinated children 24–59 months of age, most experts recommend 2 doses of the 13-valent conjugate vaccine 8 weeks apart followed 8 weeks later by a dose of the 23-valent pneumococcal vaccine. The 23-valent vaccine is not effective in children less than 24 months of age.

Children with cancer or those who are either asplenic, functionally asplenic or anticipated to probably need splenectomy should receive the appropriate schedule of 13-valent conjugate vaccine followed 8 weeks later by the 23-valent polysaccharide vaccine.

Meningococcal Vaccine
Theoretically, cancer patients are at increased risk of meningococcal disease. Patients with Hodgkin lymphoma are known to be at increased risk for serious bacterial infections with encapsulated organisms.[24-26] Conjugated vaccine is better than polysaccharide vaccine and should always be the product of choice for immunocompromised patients.

All Canadian provinces have universal, provincially funded programs, with somewhat different schedules. In Ontario, currently all infants are offered one conjugate meningococcal C vaccine dose at 12 months of age. A quadrivalent (ACYW135) vaccine is offered to 12-year-olds. Patients who are asplenic, functionally asplenic or anticipated to probably need splenectomy should have conjugate quadrivalent vaccine. If less than 2 years of age, the vaccine should be Menveo™ and any quadrivalent conjugate meningococcal ACYW135 (Menveo™, Menactra®, Nimenrix™) should be given if over 2 years of age. The use of conjugate quadrivalent meningococcal vaccine should replace the polysaccharide vaccine (Menomune) in all patients. Conjugate quadrivalent meningococcal vaccine is required every 5 years.

All people with asplenia or hyposplenism should receive quadrivalent conjugate meningococcal vaccine (Men-C-ACYW-135). The schedule for those who are previously unimmunized is as follows:

- Children aged 2 to 11 months should receive 2 or 3 doses of Menveo™ given 8 weeks apart (with another dose given between 12 to 23 months of age and at least 8 weeks from the previous dose) and booster doses as outlined below.
- Children aged 12 to 23 months should receive 2 doses of Menveo™ vaccine given at least 8 weeks apart and booster doses as outlined below.
- People aged 2 to 55 years should receive 2 doses of a Men-C-ACYW-135 vaccine (either Menactra®, Menveo™ or Nimenrix™) 8 weeks apart and booster doses as outlined below.

- Adults aged 56 years and over should receive 2 doses of a Men-C-ACYW-135 vaccine (either Menactra® ,Menveo™ or Nimenrix™) 8 weeks apart and booster doses as outlined below. If only one dose of Men-C-ACYW-135 vaccine was previously given, give another dose at the earliest opportunity and proceed with booster doses as outlined based on the interval from the second dose.

Booster Doses: A booster dose of Men-C-ACYW-135 vaccine should be given every 5 years.

Killed Influenza Vaccines
Immunocompromised patients are at risk of adverse outcomes from influenza infections. Such patients, including those with cancer, are candidates for the yearly killed influenza vaccines during the autumn season. Children receiving immunosuppressive chemotherapeutic agents may have less of an immune response compared with healthy children. Current recommendations suggest that the optimal timing of influenza vaccination is >3 weeks after discontinuation of chemotherapy or in maintenance and when the granulocyte and lymphocytes counts are 1.0 x 10^9/L or greater.[7] In practice, these conditions may be difficult to obtain but vaccination should still be done. Ensure the child gets two doses, 4 weeks apart, if they have never received influenza vaccination before. Everyone with whom they live should also get influenza vaccination.

Travel-Related Vaccination (Including Hepatitis A and B)
Travel is a good opportunity for healthcare providers to review and update the immunization status of children and those with whom they travel. The hepatitis A and B vaccines as well as the injectable typhoid vaccine should be considered if patients are visiting resource-poor regions. Children with cancer should be fully vaccinated with hepatitis B vaccine and have demonstrated protective titres. Hepatitis A vaccine is recommended if they are going to any resource-poor country. Due to the incubation period of hepatitis A, the vaccine might be effective even if it is administered on the day of departure (as a last resort).

In addition to the above, cancer patients are candidates for hepatitis A and B vaccines if they have similar risk factors as healthy children (e.g., high-risk households, chronic liver disease, etc.).

Varicella and Measles Exposures

Varicella / Zoster

While the varicella vaccine is relatively contraindicated in cancer patients, their siblings and susceptible household members should be vaccinated. In this regard, there is a small risk of transmission of vaccine virus from siblings to the cancer patient. However, the disease that is associated with vaccine virus tends to be mild, while the risk associated with natural varicella virus is more significant.

Cancer patients without a history of varicella AND without two confirmed doses of varicella vaccine should receive post-exposure prophylaxis with Varicella-Zoster Immune Globulin (VariZIG) or acyclovir (if the VariZIG window is missed).[7, 29] Please see Section 4.4 Treatment of Varicella-Zoster Infections for guidance on varicella exposure and use of VariZIG.

Pending additional data, if a patient has received immune globulin or blood products, it is recommended that the varicella vaccine be withheld for the same interval as the measles vaccine. **Immune globulin**

should not be administered within 2 weeks after measles or varicella vaccines are given. (https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-5-passive-immunization.html).

Measles

The consequences of measles can be devastating for immunocompromised patients.[30] Cancer patients who have been exposed to measles should receive immune globulin (IG) 0.5 mL/kg IM (maximum 15 mL) as soon as possible. It is most effective within 3 days, but can be given up to 6 days after exposure regardless of their immunization status. Current lots of IVIG are likely to contain enough measles antibodies to offer protection. Patients who regularly receive IVIG (100 to 400 mg/kg) do not need additional prophylaxis if their last dose of IVIG was within 21 days of exposure to measles.

The use of immune globulin does alter the effectiveness of the measles vaccine if it is administered in close proximity to the dose of immune globulin. Please refer to the NACI table for the suggested intervals between the administration of such vaccines and receipt of immune globulin and other blood products https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-5-passive-immunization.html. It is unknown if the same approach applies to the varicella vaccine.

Pending additional data, if a patient has received immune globulin or blood products, it is recommended that the measles vaccine be withheld for the same intervals as the varicella vaccine. Immune globulin should not be administered within 2 weeks after measles or varicella vaccines are given.

Household and Healthcare Team Members

It is important for clinicians to be acutely aware that the vaccination of siblings and family members is an important strategy in the prevention of vaccine-preventable diseases in immunosuppressed patients. Family members need to ensure their immunizations are up to date. Yearly influenza vaccination of family members is important in minimizing the potential for exposure to influenza within the home.

The role of varicella vaccine for family members is discussed above. The MMR vaccine can be safely administered to siblings and family members. While inactivated polio vaccine can be safely administered to family members, the oral polio vaccine (OPV) should not be administered. If OPV is inadvertently given to a household member, close contact between the immunocompromised patient and the OPV recipient should be minimized or avoided for 4–6 weeks. Oral polio vaccine is no longer available in Canada. Immunocompetent family members of immunosuppressed individuals can receive the live-attenuated yellow fever vaccine. There are no data to suggest that the use of the oral typhoid vaccine Ty21a in immunocompetent family members poses a risk of transmission to immunocompromised household members. Indeed, the concerns regarding the use of the vaccine in immunocompromised persons are theoretical and not based on any case of disseminated vaccine-associated disease.

Healthcare workers who care for immunocompromised patients need to ensure that their immunizations are up to date. In this context, while all recommended vaccines are important, special attention to varicella, influenza, pertussis and hepatitis B vaccines is required.

See Also

Vaccination of Immunocompromised Persons with Acquired (Secondary) Immunodeficiency
https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a13

Ontario's Publicly Funded Immunization Schedules

This guidance was developed by Dr. Marina Salvadori, Children's Hospital, London Health Sciences Centre, London and Dr. Nisha Thampi, Children's Hospital, London Health Sciences Centre, London based on the sources below.

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