PNEUMOCOCCAL IMMUNIZATION IN ADULT AND PEDIATRIC PATIENTS UNDERGOING CANCER TREATMENT

Effective Date: August, 2016

The recommendations contained in this guideline are a consensus of the Alberta Provincial Tumour Council and members of the Alberta Health Services Province-wide Immunization Program Standards and Quality, and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.
BACKGROUND

*Streptococcus pneumoniae* is a frequent cause of pneumococcal bacteremia, and often attacks individuals with influenza as a secondary infection. There is evidence to suggest that asymptomatic pneumococcal carriage may also affect subsequent influenza virus infections and clinical outcomes. Individuals over 65 years of age are at greatest risk of fatality from pneumonia combined with influenza, as well as from pneumonia alone; in 2010, the American Lung Association reported that the mortality rate increases three-fold from age 55-64 years (10 deaths per 100,000) to 65-74 years (32 deaths per 100,000), and then increases four-fold at 75-84 years (127 deaths per 100,000), and another four-fold at 85 years and older (500 deaths per 100,000). Moreover, individuals with underlying medical conditions who are immunosuppressed as a result of their disease or treatments are also at increased risk of complications and death from pneumonia. In particular, pneumococcal infections are an important cause of morbidity and mortality in adult and pediatric patients with cancer. Therefore, immunization of cancer patients with the pneumococcal vaccine may be important in preventing pneumonia. Although the pneumococcal vaccine is provided throughout the year by Public Health and community providers, the influenza season presents an excellent opportunity to assess and immunize eligible persons who have not previously received this immunization or those eligible for a one-time single reinforcing dose. The purpose of this guideline is to describe the use of the pneumococcal vaccine in adult and pediatric patients with solid tumours or hematologic cancers such as leukemia, Hodgkin and non-Hodgkin lymphoma, multiple myeloma, and other malignancies.

GUIDELINE QUESTIONS

- What are the recommendations for pneumococcal immunization for adult and pediatric patients with solid tumours or hematologic cancers in Alberta?
- What is the current evidence for response to the pneumococcal vaccine among adult and pediatric patients with cancer receiving chemotherapy or other systemic therapy?
- What is the best timing for administering the pneumococcal vaccine in relation to the therapy cycle?

DEVELOPMENT AND REVISION HISTORY

The 2016 update of this guideline was reviewed and endorsed by members the Alberta Provincial Tumour Team Council, which includes medical and radiation oncologists, surgeons, nurses, hematologists, and allied health care providers, as well as content experts from the Alberta Health Services Province-wide Immunization Program Standards and Quality, Communicable Disease Control. Updated evidence was selected and reviewed by the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Resource Unit Handbook](#).

This guideline was originally developed and posted to the website in November 2012. The guideline was revised and reposted in August 2016.

SEARCH STRATEGY

For the original guideline published in 2012, the MEDLINE, PubMed, Cochrane, CINAHL, and EMBASE databases were searched. The search included practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, and clinical trials published between 1965 and October 2012. Websites from health organizations including the World Health Organization, Health Canada, the Public Health Agency of
Canada, Alberta Health Services, Alberta Health, the BC Cancer Agency, the National Comprehensive Cancer Network, the American Academy of Pediatrics, and the Centers for Disease Control and Prevention were also searched for relevant guidance. The search terms included pneumococcal vaccine and neoplasm.

For the 2016 update, the PubMed and Cochrane databases were searched using the search terms “cancer” OR “neoplasm” OR “oncology” AND “pneumococcal vaccination”. Limits for the literature search included publication date (January 2012 – October 2015), language (English) and species (human).

TARGET POPULATION

The recommendations outlined in this guideline apply to children and adults with solid tumours or hematologic malignancies. For current information on immunizations for the general population please refer to the Alberta Health Services Immunization Program Standards Manual at http://www.albertahealthservices.ca/info/Page10802.aspx

RECOMMENDATIONS

The following recommendations have been adapted from existing practice guidelines, policy documents, and consensus statements, including those from the Alberta Health Services Immunization Program Standards Manual, the Public Health Agency of Canada,7 and the Centers for Disease Control and Prevention.8,9 Evidence from published clinical trials, retrospective reviews, and case study reports was also reviewed and considered.

1. Immunization against Streptococcus pneumoniae using pneumococcal vaccine is very important for patients who may be immunosuppressed as a result of their cancer or treatment of their cancer. This includes patients with solid tumours, leukemia, lymphoma, multiple myeloma, and hematopoietic stem cell transplant (HSCT) recipients.

2. Adult and pediatric patients who may be immunosuppressed as a result of their cancer or treatment of their cancer should consult with Public Health Services regarding an immunization schedule for the pneumococcal vaccine.

3. Adult and pediatric patients undergoing HSCT should consult with Public Health Services regarding an immunization schedule for the pneumococcal vaccine starting at six months post-transplant. When the recipient is at high risk of chronic graft-versus-host disease (GVHD), vaccine response may be improved by donor immunization.

4. Patients who are treated with rituximab or other B-cell depleting antibodies should have all immunizations postponed until at least six months after the last dose of rituximab.10-13

5. Pneumococcal Conjugate Vaccine (PNEU-C13; Prevnar ®13):
   • PNEU-C13 is provided routinely to all children and adults who are candidates/ recipients of solid organ transplants, and HSCT.
   • When both PNEU-C13 and PNEUMO-P vaccines are indicated, it is recommended that the conjugate series/dose be completed prior to administering the PNEUMO-P vaccine:
6. Pneumococcal Polysaccharide Vaccine (PNEUMO-P; Pneumovax ® 23):
   - Immunization with PNEUMO-P is recommended for all adult and pediatric patients with solid
tumours and hematologic malignancies who have not previously been immunized.
   - A **one-time** reinforcing dose of PNEUMO-P is recommended only for those individuals at
   highest risk of invasive pneumococcal disease, including patients who are immunosuppressed
   as a result of their cancer or treatment of their cancer. This **one-time** reinforcing dose of
   PNEUMO-P should be given:
     - Five years after the initial dose (HSCT recipients follow specific spacing
       recommendations. Refer to the Alberta Health Services Immunization Program
       Standards Manual, Immunization of Special Populations at the following links:
       - Internal AHS Link: [http://insite.albertahealthservices.ca/11322.asp](http://insite.albertahealthservices.ca/11322.asp)
       - External AHS Link: [http://www.albertahealthservices.ca/info/Page10802.aspx](http://www.albertahealthservices.ca/info/Page10802.aspx)
     - Exception: Individuals will be eligible for a dose of PNEUMO-P vaccine at 65 years of
       age and older (as long as five years have passed since a previous dose of this
       vaccine), regardless of the number of doses received prior to 65 years of age.
   - The timing of PNEUMO-P immunization should ideally occur four to six weeks (and at least 14
days) prior to initiation of immunosuppressive therapies such as chemotherapy or radiation. If this
   is not possible and delay of treatment would result in an increased risk of cancer-related
   complications or death, it is recommended that immunization be delayed for three months after
   completing immunosuppressive chemotherapy (at least one month after stopping high dose
   steroids).

7. Patients immunized while on immunosuppressive therapy or less than two weeks before starting
   therapy should be considered un-immunized and should be re-immunized at least three months after
   discontinuation of therapy. Further discussion with Public Health Services may be appropriate before
   the patient is re-immunized.

8. Pneumococcal immunizations should not be administered to individuals who:
   - have had an anaphylactic reaction to a previous dose of the vaccine.
   - have a known hypersensitivity to any component of the vaccine.
   - are less than two years of age (for PNEUMO-P vaccine) or less than two months of age (for
   PNEU-C13 vaccine).
   - present with a serious acute febrile illness; recommendations should be provided for these
   individuals to be immunized when their symptoms have resolved. Individuals with non-serious
   febrile illness may be immunized.
DISCUSSION

Although cancer patients are especially susceptible to severe pneumococcal infections, evidence from controlled studies addressing pneumococcal immunization in adult and pediatric patients with solid tumours and hematologic malignancies cancer is limited. Existing national and international guidelines and policy statements support pneumococcal immunization in adult and pediatric immunocompromised populations. The Advisory Committee on Immunization Practices (ACIP) from the Centers for Disease Control and Prevention recommends that children younger than five years old, adults 65 years or older, and people six years or older with immunocompromising conditions should be immunized with the PNEU-C13 vaccine. The committee also recommends immunization with the PNEUMO-P vaccine for adults 65 years or older and for people aged two to 64 years old with immunocompromising conditions.8,9 Similarly, the Public Health Agency of Canada’s Canadian Immunization Guide states that there is no contraindication to the use of any inactivated vaccine in immunosuppressed individuals and that particular attention should be paid to the completion of childhood immunizations, annual influenza immunization, and pneumococcal immunization.14 However, because of the impact of therapy on immunogenicity, timing of immunization is an important factor for this population.

The National Comprehensive Cancer Network’s guideline, Prevention and Treatment of Cancer-Related Infections, recommends that patients should ideally be immunized against S. pneumoniae at least two weeks before starting chemotherapy or other immunosuppressive therapies. Further, patients should be considered unprotected if they are immunized less than two weeks before starting therapy, and should be re-immunized at least three months after therapy has stopped.15 The Canadian Immunization Guide is in line with these consensus recommendations, noting that all immunizations should be administered a minimum of two weeks before the initiation of therapy or a minimum of three months after the completion of therapy. This guide also suggests that the immunization schedule may vary with the intensity of the immunosuppressive therapy, underlying disease, and other factors; if treatment is ongoing, immunizations should be administered when the therapy is at the lowest possible level.7

In the general pediatric population, there are no efficacy data available for other pneumococcal conjugate vaccines, including PNEU-C13. The efficacy of the PNEUMO-P vaccine is estimated to be between 50 and 80% among the elderly and high-risk groups,14 and efficacy in patients with solid tumours and malignant lymphoma undergoing mild to moderate immunosuppressive chemotherapy has also been reported as good.16 However, the polysaccharide vaccine is less effective than the conjugate vaccine in this group of patients, particularly during treatment.16-21 Treatment with medications such as methotrexate has also been shown to decrease the immune response to the pneumococcal vaccine.22,23

Pediatric and adult cancer patients undergoing hematopoietic stem cell transplantation (HSCT) are immunosuppressed for several months post-transplant, and antibody responses are low post-transplant.24-32 The Alberta Immunization Policy recommends that both pediatric and adult HSCT recipients be completely re-immunized post-transplant. The PNEU-C13 vaccine is recommended at six, seven, and eight months post-transplant, while the PNEUMO-P vaccine is recommended at 14 and 24 months post-transplant. Patients with chronic graft-versus-host-disease (GVHD) treated with immunosuppressive drugs should receive PNEU-C13 instead of PNEUMO-P at the 14 and 24 month post-transplant immunizations.11,33,34 In addition, when the recipient is at high risk of GVHD, vaccine response may be improved by donor vaccination.35 The minimum acceptable interval between PNEU-C13 doses is four weeks and the minimum interval between PNEU-C13 and PNEUMO-P doses is six months.33,34
Berglund and colleagues recently reported the results of a subgroup analysis of rituximab-treated patients among adult outpatients with cancer who were undergoing treatment. Patients treated with rituximab had almost no response to the pneumococcal, influenza A (H1N1), and seasonal influenza vaccines. Specifically, the mean number of serotype-specific protective pneumococcal antibodies (SPP) was not significantly different between the 8 rituximab-treated and 55 non-treated patients before immunization whereas it was significantly increased after immunization for those patients who did not receive rituximab. Patients who are treated with maintenance rituximab or other B cell depleting antibodies following HSCT should have all immunizations postponed until at least 6 months after the last dose of rituximab or other B cell depleting therapies.

GLOSSARY OF ABBREVIATIONS

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<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<td>GVHD</td>
<td>graft-versus-host disease</td>
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<td>hematopoietic stem cell transplant</td>
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<td>PHAC</td>
<td>Public Health Agency of Canada</td>
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<tr>
<td>PNEU-C13</td>
<td>13-valent pneumococcal conjugate vaccine</td>
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<td>PNEUMO-P</td>
<td>23-valent pneumococcal polysaccharide vaccine</td>
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DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

MAINTENANCE

A formal review of the guideline will be conducted in September 2017. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

CONFLICT OF INTEREST

Participation of members of the Alberta Provincial Tumour Council and the Alberta Health Services Province-wide Immunization Program Standards and Quality in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. While some members may be involved in research funded by industry or have other such potential conflicts of interest, the developers of this guideline are satisfied it was developed in an unbiased manner.
REFERENCES


APPENDIX A: Additional Resources

Alberta Bone Marrow and Blood Cell Transplant Program. Standard Practice Manual:

Alberta Health. Manuals and Guidelines for Health Professionals.
http://www.health.alberta.ca/professionals/manuals.html

Alberta Health Services. Immunization Program Standards Manual:
http://www.albertahealthservices.ca/info/Page10802.aspx

Alberta Health Services. Immunization for Adult HSCT Transplant Recipients *(available to AHS staff on intranet).*

Alberta Health Services. Immunization for Child HSCT Transplant Recipients *(available to AHS staff on intranet).*

Centers for Disease Control and Prevention. Vaccines and Immunizations – Pneumococcal Vaccination (June, 2015):
http://www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm

Centers for Disease Control and Prevention. Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP) – Pneumococcal Disease:
http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/pneumo.html

www.nccn.org/professionals/physician_gls/f_guidelines.asp

Public Health Agency of Canada. Canadian Immunization Guide:

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