Guidelines for the prevention and therapy of bacterial infections for children with asplenia and hyposplenia

Question

Children with asplenia and hyposplenia are at increased risk of bacterial infections. What are the most appropriate preventative measures and treatments for children with asplenia and hyposplenia to decrease the risk of sepsis and death?

Target Population

All children with asplenia and hyposplenia.

Target Users

All health professionals within the Atlantic Provinces caring for asplenic or hyposplenic children and youth.
Recommendations

There is a lack of randomized controlled trial evidence related to the clinical question. Based on evidence from well conducted clinical trials and the interpretation of evidence from retrospective studies and expert consensus opinion, the Atlantic Provinces Pediatric Hematology Oncology Network recommends the following for all children who are asplenic and hyposplenic or have undergone a subtotal splenectomy:

1. Families and patients should be well educated about the potential signs of infection, associated risks, management and prevention of overwhelming postsplenectomy infections (Grade C).
   - Potential signs of infection can include, but are not limited to, fever, malaise, myalgias, headache, vomiting, diarrhea, and abdominal pain.
   - An asplenic or hyposplenic child with a fever is at risk of dying if they do not seek immediate medical attention.

2. Families of children with a fever should be instructed to immediately take an age appropriate amount of their prophylactic antibiotic if they haven’t already and seek immediate medical attention, because early recognition and aggressive treatment with antibiotics are critical for management of infections (Grade C).

3. Medical attention for a child with fever would include a blood culture followed by the immediate administration of appropriate parenteral antibiotics (Grade C).

4. Parenteral antibiotics for all groups includes a cephalosporin effective against Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitides.
   - Cefotaxime is recommended over Ceftriaxone due to a decreased risk of immune hemolysis and encephalopathy in hyperbilirubinemic neonates (Grade C).
   - Ampicillin is recommended in children less than 2 months of age due to the increased risk of E.coli infections (Grade C).
   - Vancomycin is recommended in those suspected of having meningitis for treatment of penicillin resistant S.pneumoniae organisms (Grade C).
   - Cefuroxime is recommended as single agent for those with less severe symptoms to maximize safety and minimize toxicity (Grade C).

5. There is no clear definition of a protective level of antibodies to prevent postsplenectomy sepsis. Even though the response rates to vaccines are generally lower in asplenic and hyposplenic patients, it is felt that the response is adequate and does decrease the incidence of bacteremic disease (Grade B, C) (Ammann 1977). For this reason the following vaccinations are recommended in addition to all routine immunizations:
   - All children less than 2 years should receive the pneumococcal conjugate vaccine (Prevnar®) (Grade C).
   - The pneumococcal conjugate vaccine should be followed by the pneumococcal polysaccharide vaccine (Pneumovax®) in children 2 years and greater (Grade B, C) (Smets 2007, Stoehr 2006).
   - The conjugate vaccine is thought to act to prime the immune system and provide a better response to the polysaccharide vaccine (Grade C).
   - The Haemophilus Influenzae Type B vaccine (Grade C).
• The Meningococcal conjugate C vaccine (MenC®) (Grade B, C) (Balmer 2004, Stoehr 2008) followed by the Meningococcal conjugate ACYW vaccine (Menactra®) (Grade C). Both vaccines are being recommended at this time as it is not known if the C component of the conjugate ACYW vaccine provides sufficient protection.

6. Vaccinations should be given at least two to four weeks prior to splenectomy, in order to ensure an optimal antibody response, and decrease the risk of overwhelming infection (Grade C).

7. In the case of emergency splenectomy vaccinations should be given two weeks after splenectomy for those not previously vaccinated (Grade A) (Shatz 1998, 2002). If compliance after discharge is not assured then vaccines should be given before discharge from the hospital even if less than 14 days has elapsed since splenectomy (Grade C).

8. The influenza vaccine and all childhood vaccine are recommended at this time (Grade C).

9. Booster doses of pneumococcal vaccine are recommended (Grade B, C). (Stoehr 2006, Smets 2007). Pneumococcal polysaccharide vaccine should be used for booster doses as this vaccine has a wider coverage of serotypes(Grade C):
   • A single booster after 5 years in those aged greater than 10 years at the time of initial immunization.
   • A single booster after 3 years in those aged 10 years and younger at the time of initial immunization.

10. Life long antibiotic prophylaxis is still recommended to be given to decrease the risk of overwhelming infection (Grade C)
    • Cefixime is recommended in children less than two months of age to provide sufficient coverage for *E.coli* (Grade C). Sulfamethoxazole and Trimethoprim (Septra®) is not recommended due to the risk of Kernicterus.

11. For non-compliant patients Stand-by antibiotics should be available (with instructions) if the patient feels unwell, or for the following symptoms: fever, malaise, myalgias, headache, vomiting, diarrhea, and abdominal pain (Grade C).

12. Children and families should be educated as to the potential risk of overseas travel, with special emphasis on malaria and unusual infections, for example resulting from tick and animal bites (Grade C).

13. Children should wear a medical alert bracelet (Grade C).

**Key Evidence**

Although randomized controlled trials can theoretically provide the best estimate of vaccine efficacy, the large sample size required to have adequate statistical power and the ethical concerns of withholding a licensed vaccine make such trials difficult in high-risk groups.
A small, nonrandomized study of children and young adults who had sickle cell disease or elective splenectomy demonstrated that the vaccinated group experienced significantly less bacteremic disease than the nonvaccinated group (Ammann 1977).

A small randomized study of asplenic children determined revaccination with pneumococcal conjugate vaccine is safe and immunogenic in asplenic children and could provide appropriate booster response in this high-risk population (Smets 2007).

An open multi-centre study of 39 splenectomized children determined that pneumococcal antibodies against 5 of 7 serotypes were significantly higher after vaccination with the pneumococcal conjugate vaccine followed by the pneumococcal polysaccharide vaccine (Stoehr 2005).

A nonrandomized study of 120 splenectomized patients showed that vaccination with Meningococcal conjugate C vaccine showed that 80% of asplenic individuals achieved the proposed protective bactericidal antibody in serum titer (Balmer 2004).

An open multicentre study of 16 splenectomized patients and 25 near-total splenectomized patients vaccinated with meningococcal conjugate C followed 8 weeks later with conjugate ACYW showed significant increases in serum bactericidal activity geometric mean titres for serogroup C. In the splenectomized group 14 of 16 patients achieved seroprotection for serogroup A 4 weeks after vaccination (Stoehr 2008).

A randomized controlled trial of 59 patients undergoing splenectomy were randomized to receive pneumococcal polysaccharide vaccine (Pneumovax®) postoperatively at 1 (n18), 7 (n20) or 14 (n21) days compared with a control group. With the exception of one serotype 19F all titers for the 14 day group approached those of the control subjects. Postvaccination titers were significantly reduced in early vaccination groups (Shatz 1998).

A randomized controlled trial of 38 patients undergoing splenectomy were randomized to receive pneumococcal polysaccharide vaccine (Pneumovax®) at 14 or 28 days after splenectomy. There were no statistically significant differences in the titers (Shatz 2002).

Grades of Evidence

A. Requires at least one randomized controlled trial, as part of the body of literature of overall good quality and consistency addressing the specific recommendations.

B. Requires the availability of well conducted clinical studies, but no randomized clinical trials on the topic of the recommendation.

C. Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality.

These grades of recommendation have been widely adopted, but originate from the US Agency for Health Care Policy and Research.
Introduction

Overwhelming bacterial infection is a significant risk in patients with no spleen (asplenia) or a dysfunctional spleen (functional asplenia/hyposplenia). The incidence of overwhelming postsplenectomy infection (OPSI) is controversial as most of the data comes from retrospective studies that do not have adequate follow-up, as death from sepsis can occur 65 years after a splenectomy. The incidence also varies with the age of the patient and the underlying disease, asplenia/hyposplenia and OPSI are rare which means large numbers of patients would be needed to appropriately determine incidence of OPSI (Price, 2005). The literature reports a 3.3 to 4.25% incidence of sepsis in children with this number decreasing to around 0.8% in adults (Montalembert 2004, Melles 2004, Brigden 1999). The incidence of death from sepsis is 50-70% in asplenic/hyposplenic children (Omlin 2005, Price 2007, Stoehr 2008).

This risk is highest in children with underlying hematologic conditions including, sickle cell anemia or thalassemia, in those that are immunosuppressed and in the child less than 5 years of age (Brigden 1999). Despite medical attention 50% die in the first 48 hours after presentation. Incidence of death from OPSI has been shown to be decreased to 10% in those patients who seek medical attention immediately on feeling unwell (Brigden 1999). Although there is a 5% lifelong risk of severe sepsis in asplenic/hyposplenic patients, the risk is higher in the first 2 years following splenectomy or the development of a dysfunctional spleen (Brigden 1999, Waghorn 2001, Price 2007, Omlin 2005, Castagnola 2003). An annual mortality rate of 1-3.8% is reported despite education of patients/families (Landgren 2004, Cherif 2006). It is not clear whether this is due to a lack of comprehensive education for patients and families; and/or adherence to guidelines for management of aplenic/hyposplenic children.

The overwhelming bacteremia or meningitis in these children is usually caused by polysaccharide encapsulated bacteria. *Streptococcus pneumoniae* is the most common pathogen seen in greater than 50% of cases in older infants and children (*Escherichia coli* is more prevalent in infants less than 3 months of age). In addition, *Haemophilus influenzae* type b, *Neisseria meningitidis*, and *Escherichia coli* are common causes of infection in these children. Less common causes of sepsis include, *Staphylococcus aureus, Streptococcus pyogenes, Pseudomonas, Klebsiella* and *Salmonella* (especially in children with sickle cell disease) (Price 2007, William 2007). Asplenic and hyposplenic patients are at increased risk of *Capnocytophaga* infection following dog, cat and rodent bites, protozoan infections caused by *Babesia* species that are contracted by tick bites and *Falciparum malaria* (Price 2007, Spelman 2008). It is therefore of great importance to education these patients/families on their increased risk for these infections and to seek medical attention as soon as they feel unwell, are exposed to an animal, tick or mosquito bite (in an area where malaria is endemic).

Methods

The guideline development group consisted of experts in pediatrics, hematology and infectious diseases. The formal consensus of the guideline development group was
integrated with the findings of systematic review of published evidence to formulate the ensuing recommendations.

**Literature Search Strategy**

A search in PubMed and Embase (1970-2008) was under-taken to identify studies reporting data on management for asplenic or hyposplenic patients. The key words used were ‘splenectomy / asplenia / hyposplenism’ combined with ‘fever /antibiotic/prophylaxis’ and ‘vaccination / immunization’ and ‘Streptococcus pneumoniae, Neisseria meningitides, or Haemophilus influenzae’. In addition, a search of the National Guideline Clearinghouse, Cochrane, all relevant guideline development groups and Google was done further searching for relevant guidelines, using the terms ‘guidelines and asplenia and management’.

**Study Selection Criteria**

The complete texts of relevant original articles were read. Reviewed studies were limited to those dealing with humans and published in English.

Preference was given to information obtained from randomized controlled trials where available and where not evidence based and best practice information were used to determine the intervention recommendations contained in this guideline.

**Supportive Care**

Children and families, who have supportive care needs that are not addressed in the APPHON/ROHPPA guidelines for the prevention and therapy of bacterial infections for children with asplenia and hyposplenia (e.g., access to immunizations; difficulty coping with the stresses and worries of this condition), can contact the hematology family care coordinators at the tertiary care centres for assistance. Supportive care consists of the provision of services to meet children and families' physical, social, emotional, nutritional, informational, psychological, spiritual and practical needs throughout the illness experience (Fitch 1994, 2000).
Algorithm for the Management of Asplenia Patients with Fever or Acute Illness

- Immediate assessment to determine if patient has focal point of infection, ex. meningitis etc.
- Appropriate cultures, including a blood culture before antibiotics if possible.
- Usual organisms include: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Salmonella* and *Escherichia coli*.
- Early administration of parenteral antibiotics (within 30 minutes of presentation).
- Stop prophylactic penicillin.
- Close observation for 6-12 hours even if a viral etiology is suspected.

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**Appropriate cultures, including a blood culture before antibiotics if possible.**

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**Early administration of parenteral antibiotics (within 30 minutes of presentation).**

**Stop prophylactic penicillin.**

**Close observation for 6-12 hours even if a viral etiology is suspected.**

*Where intermediate of high penicillin-resistant pneumococci are prevalent, use a combination Cefotaxime + Vancomycin.*

If treated with vancomycin, adjust dosage if abnormal renal function and with levels.

Local infections ex. tonsillitis and impetigo can be treated with penicillin; otitis media with amoxicillin.

Antibiotic treatment should be modified depending on culture results.

**Antibiotic dosing:**

- **2 month old - vancomycin 50 mg/kg/day IV q6h (maximum 1 g/dose; 4 g/day), cefuroxime 75-150 mg/kg/day IV q8h (maximum 6 g/day).** Penicillin 250,000 units/kg/day IV q6h (maximum 24 million units/day). Clarithromycin 15 mg/kg/day PO q12h (maximum 500 mg/dose). Erythromycin 40 mg/kg/day IV q6h (maximum 4 g/day). Azithromycin 5 mg/kg/day PO once daily (maximum 250 mg/day). Clindamycin 40 mg/kg/day IV q8h (maximum 4.8 g/day).

If patient has a confirmed anaphylactic penicillin reaction consult ID for possible alternatives include meropenem.

**NEVER delay treatment due to an allergy BUT be prepared to treat reaction.**

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Asplenia and Hyposplenia Guidelines – July 2009  
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### Table 1.
**Recommendations for immunization in children with asplenia:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-23 months</td>
<td>• <strong>Hib</strong>, DTaP, IPV at 2, 4, 6 months of age; booster at 18 months</td>
</tr>
<tr>
<td></td>
<td>• <strong>Hepatitis B</strong> at 2, 4, 12 months of age</td>
</tr>
<tr>
<td></td>
<td>• <strong>Hepatitis A</strong> (dosing and schedule depends on product)</td>
</tr>
<tr>
<td></td>
<td>• <strong>PCV7</strong> at 2, 4, 6 months of age; booster at 18 months of age (if &gt;6 months old and previously unvaccinated see Table 2 for modified schedule)</td>
</tr>
<tr>
<td></td>
<td>• <strong>MenC</strong> at 2, 4, 6 months of age (if 4-11 months old and previously unvaccinated, give 2 doses at least 4 weeks apart if ≥ 12 months old &amp; previously unvaccinated, give 1 dose).</td>
</tr>
<tr>
<td></td>
<td>• <strong>Varicella</strong> at 12 months</td>
</tr>
<tr>
<td></td>
<td>• Annual influenza vaccine if over the age of 6 months</td>
</tr>
<tr>
<td></td>
<td>• MMR at 12 months; booster at 18 months or 4-6 years</td>
</tr>
<tr>
<td>2-5 years</td>
<td>• <strong>Hib</strong> (if not previously immunized)</td>
</tr>
<tr>
<td></td>
<td>• DTaP, IPV booster 4-6 years</td>
</tr>
<tr>
<td></td>
<td>• <strong>Pneumococcal</strong> vaccine - see Table 3</td>
</tr>
<tr>
<td></td>
<td>• <strong>Men C</strong> (if not given earlier).</td>
</tr>
<tr>
<td></td>
<td>• <strong>Meningococcal</strong> conjugate ACYW (Menactra®) (Give at least 1 month after MenC).</td>
</tr>
<tr>
<td></td>
<td>• Annual influenza vaccine</td>
</tr>
<tr>
<td>5 years - adolescence</td>
<td>• <strong>Hib</strong> (if not given earlier; booster not required)</td>
</tr>
<tr>
<td></td>
<td>• dTap 14-16 years</td>
</tr>
<tr>
<td></td>
<td>• <strong>Hepatitis B</strong> (0, 1 and 6 months) in grade 4 if not received at birth</td>
</tr>
<tr>
<td></td>
<td>• <strong>Pneumococcal</strong> vaccine - see Table 3. If given before 5 years, then give 1st booster dose 3 years after the initial vaccination; otherwise, repeat vaccination once, 5 years after the initial vaccination.</td>
</tr>
<tr>
<td></td>
<td>• <strong>Men C</strong> (if not given earlier).</td>
</tr>
<tr>
<td></td>
<td>• <strong>Meningococcal</strong> conjugate ACYW (Menactra®) (Give at least 1 month after MenC).</td>
</tr>
<tr>
<td></td>
<td>• Annual influenza vaccine</td>
</tr>
</tbody>
</table>

**Abbreviations:** DTaP = diphtheria, tetanus, pertussis (acellular) vaccine; Hib = *Haemophilus influenzae* type b conjugate vaccine; IPV = inactivated polio vaccine; Menactra = quadrivalent meningococcal conjugate vaccine; MenC = meningococcal C conjugate vaccine; MMR = measles, mumps, rubella vaccine; PCV7 = heptavalent pneumococcal conjugate vaccine; Td = tetanus and diphtheria toxoid (adult); dTap = tetanus and diphtheria toxoid, acellular pertussis (adolescent/adult).

1. Adapted from the Canadian Pediatric Society Infectious Diseases and Immunization Committee position statements reference numbers: ID99-04 Prevention and therapy of bacterial infections for children with asplenia or hyposplenia (Pediatr Child Health 1999; 4(6):417-21) [reaffirmed April 2002], ID02-01 Pneumococcal vaccine for children, ID02-02 Meningococcal vaccine for children; the 2006 Red Book: Report of the Committee on Infectious Diseases, American Association of Pediatrics; Canadian Immunization Guide 7th edition 2006. All provinces do not provide all vaccines universally as part of a publicly funded vaccine program.
2. Consult the Canadian Immunization Guide 7th edition 2006 (or most recent edition) for routine immunization schedules for children not immunized in infancy.
3. When elective splenectomy is planned, vaccines should be given at least 2 weeks **prior** to surgery; vaccines can be given concurrently at separate injection sites.
4. The immune response gained for meningococcal serogroup C by Menactra® may not be as good as that seen with MenC® and it is therefore recommended at this time for asplenia or high risk patients to receive both the Menactra® and the MenC® vaccines (they should be spaced by at least 1 month- preferably the MenC® given first).
5. Annual influenza vaccine may decrease the risk of secondary bacterial infection (Price, 2005).
Table 2
Recommendations for Vaccine Presplenectomy in addition to routine immunizations

<table>
<thead>
<tr>
<th>AGE</th>
<th>Vaccines received</th>
<th>Vaccines to be given</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 9 yrs</td>
<td>Conjugate (Prevnar®) &amp; polysaccharide (Pneumovax®) pneumococcal</td>
<td>Conjugate H. influenzae type b&lt;sup&gt;1&lt;/sup&gt;. If greater than 3 yrs since 1&lt;sup&gt;st&lt;/sup&gt; dose, give Pneumovax® if both Prevnar® and Pneumovax® were given. If only Pneumovax® was given, give Prevnar® followed by Pneumovax®. If only Prevnar® was given, given Pneumovax®.</td>
</tr>
<tr>
<td></td>
<td>Conjugate C (Men C®) &amp; conjugate ACYW (Menactra®)&lt;sup&gt;2&lt;/sup&gt; and/or polysaccharide meningococcal</td>
<td>In only MenC® was given, give Menactra®. If only Menactra® was given, give MenC®. Give Men C® and Menactra® 1 month apart.</td>
</tr>
<tr>
<td>None of the above</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 9 yrs</td>
<td>Conjugate (Prevnar®) &amp; polysaccharide (Pneumovax®) pneumococcal</td>
<td>Conjugate H. influenzae type b. Prevnar® (see schedule above for ≤ 9 yrs).</td>
</tr>
<tr>
<td></td>
<td>Conjugate C (MenC®) &amp; conjugate ACYW (Menactra®) and/or polysaccharide meningococcal</td>
<td>If greater than 5 years since 1&lt;sup&gt;st&lt;/sup&gt; dose: (see schedule above for ≤ 9 yrs).</td>
</tr>
<tr>
<td>None of the above</td>
<td></td>
<td>Conjugate H. influenzae type B. Prevnar® (1 dose) Pneumovax® (2 months after Prevnar®) MenC® first, 1 month apart from Menactra®</td>
</tr>
</tbody>
</table>

1. Infants should be immunized with H. influenzae type b according to regional schedule. Those > 15 months who have not previously received H. influenzae type b, should receive 1 dose. Vaccines should be completed 14 days prior to splenectomy. If this is not possible vaccines should be given 14 days after splenectomy. If compliance after discharge is not assured then vaccines should be given before discharge from the hospital even if < 14 days has elapsed since splenectomy. (Davies, 2001), (Price, 2005)

2. Menactra® (conjugate ACYW) may replace MenC® (conjugate C) for the serogroup C coverage, when more information about immune response to the C component of Menactra® becomes available. Until that time we recommend both vaccines.
### Table 3
**Recommended heptavalent pneumococcal conjugate vaccine (PCV7) schedule in previously unvaccinated children aged 2 to 23 months**

<table>
<thead>
<tr>
<th>Age at first dose</th>
<th>Primary series</th>
<th>Booster dose&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 6 months</td>
<td>3 doses given each separated by 8 weeks</td>
<td>12 to 15 months of age</td>
</tr>
<tr>
<td>7 to 11 months</td>
<td>2 doses given each separated by 8 weeks</td>
<td>12 to 15 months of age</td>
</tr>
<tr>
<td>12 to 23 months</td>
<td>2 doses given each separated by 8 weeks</td>
<td>none</td>
</tr>
</tbody>
</table>

<sup>1</sup> Booster dose is given at least 6 to 8 weeks after the final dose in the primary series.

### Table 4
**Recommended pneumococcal immunization with heptavalent pneumococcal conjugate vaccine (PCV7) or 23-valent pneumococcal polysaccharide vaccine (PPV23) for children with asplenia aged 23 months**

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Previous doses</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>none</td>
<td>•PCV7 as per Table 2</td>
</tr>
<tr>
<td>24-59</td>
<td>4 doses of PCV7</td>
<td>•PPV23 x 1 dose at 24 months (give at least 6-8 weeks after last dose of PCV7)</td>
</tr>
<tr>
<td></td>
<td>1 dose of PPV23</td>
<td>•PPV23 booster x 1 dose given 3 to 5 years after the first dose of PPV23</td>
</tr>
<tr>
<td>24-59</td>
<td>1 to 3 doses of PCV7</td>
<td>•PCV7 x 1 dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>•PPV23 x 1 dose given 6 to 8 weeks after the last dose of PCV7</td>
</tr>
<tr>
<td>24-59</td>
<td>1 dose of PPV23</td>
<td>•PPV23 x 1 dose given 3 to 5 years after the first dose of PPV23</td>
</tr>
<tr>
<td>24-59</td>
<td>none</td>
<td>•PCV7 x 2 doses given 6 to 8 weeks apart beginning at least 6 to 8 weeks after last dose of PPV23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>•PPV23 x 1 dose given 3 to 5 years after the first dose of PPV23</td>
</tr>
<tr>
<td>24-59</td>
<td>none</td>
<td>•PCV7 x 2 doses given 6 to 8 weeks apart</td>
</tr>
<tr>
<td></td>
<td></td>
<td>•PPV23 x 1 dose given 6 to 8 weeks after the last dose of PCV7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>•PPV23 x 1 dose given 3 to 5 years after the first dose of PPV23</td>
</tr>
<tr>
<td>60</td>
<td>none</td>
<td>•PPV23 x 1 dose (PCV7 may be given as an initial dose followed by PV23 given at least 8 weeks later)&lt;sup&gt;1&lt;/sup&gt;:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>•PPV23 x 1 dose given after 3 years if aged 10 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>•PPV23 x 1 dose given after 5 years if aged &gt;10 years</td>
</tr>
</tbody>
</table>

<sup>1</sup> Further data are required regarding efficacy of PCV7 in children aged 5 years and adults; however, limited studies indicate PCV7 is safe and immunogenic among persons aged 4 to 30 years with sickle-cell disease. If families have difficulty getting PCV7 funded then the local medical officer of health (MOH) should be contacted and the specific risk factor of the patient explained as the use of this vaccine in this population is recommended by the IWK infectious disease service.

The antibody responses in children with asplenia may not be comparable with that of normal children. As a result, repeated immunization may be necessary (Infectious Diseases and Immunization Committee, Canadian Pediatric Society, 1999 & 2002) Polysaccharide vaccine (Pneumovax®) should be used for booster doses (American Academy of Pediatrics 2000) A single booster after 5 years in those aged > 10 years at the time of initial immunization. A single booster after 3 years in those aged 10 years and younger at the time of initial immunization.
Table 5  
Recommendations for prophylactic antibiotics in children with asplenia\(^1\).  

<table>
<thead>
<tr>
<th>Age</th>
<th>Prophylactic Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 2 months</td>
<td>Cefixime 8 mg/kg/day orally once to twice daily (<em>E.Coli</em> concern at this age)</td>
</tr>
<tr>
<td>2 months - 3 years</td>
<td>Penicillin 25 mg/kg/day up to a maximum of Penicillin 150 mg(^2) orally bid</td>
</tr>
<tr>
<td>&gt; 3 years - adolescence</td>
<td>Penicillin 300mg(^2,3) orally bid</td>
</tr>
</tbody>
</table>

APPHON recommends that all children continue prophylaxis at least until adulthood \(^4\)

Children allergic to penicillin should be referred to an allergist. If true allergy recommend erythromycin.

Abbreviations: APPHON = Atlantic Provinces Pediatric Hematology Oncology Network; bid = twice a day;


2. Children with a penicillin allergy should be referred to a pediatric allergist to verify the allergy and to select an appropriate alternative.

3. Although current guidelines from the Canadian Paediatric Society, American Association of Pediatrics and others recommend penicillin 250mg orally bid, commercially available penicillin tablets are available only in 300mg strength.

4. The duration of prophylaxis is controversial; however, some recommend life-long prophylaxis. Compliance and emergence of penicillin resistance are important issues to consider in this decision (Working Party of the British Committee for Standards in Hematology 1996 and Update 2002).

5. Consider erythromycin estolate 125mg orally daily (child < 2 years); 250 mg orally daily (child 2-8 years); 250-500 mg orally daily (> 8 years) for patients with beta-lactam allergies (Guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen - Working party of the British Committee for Standards in Hematology Clinical Hematology Task Force, 1996).
The following orders will be carried out by a nurse ONLY ON THE AUTHORITY OF A PHYSICIAN.
Where choice occurs, check as appropriate.
Refer to APPHON Guidelines for Management of Sickle Cell Disease.

**ASSESSMENT AND MONITORING:**
- Immediate vital signs (temperature, heart rate, respiratory rate, blood pressure)
- Vital signs q2h until stable, and then q4h and/or q as indicated
- Daily weight and intake/output
- Quiet activities x 24 h and normal diet (avoid very cold drinks and caffeine)
- P/E: Evidence of infection, degree of pallor, cardiopulmonary status, neurologic exam, spleen size.
- If O₂ saturation < 94%, notify doctor and give O₂ by mask to maintain O₂ saturation > 96%

**INVESTIGATIONS:**
- CBC, diff, platelets; NA, K, CL, ALT, AST, BILITD, CREAT; venous/cap blood gas; then daily CBC, diff, platelets, NA, K, CL, plus: as indicated
- Reticulocyte count once daily until improving
- Chest X-Ray (even if asymptomatic and normal P/E)
- Test for ABO and screen if Hgb < 85 g/L or > 10 g/L below normal baseline and/or decreased reticulocytes
- LP if suspicion of meningitis if and patient is hemodynamically stable
- Consider evaluation for osteomyelitis
- Obtain Blood cultures: bacterial and fungal, repeat both in 24 hours
- Repeat blood cultures once daily if temperature ≥ 38.3°C and/or if appears ill.
- Urinalysis; and Urine culture (mid-stream or clean catch sterile bag) x 2
- Culture any clinically indicated site as follows:
  - Stool culture: bacterial; viral
  - Nasopharyngeal swab for C&S and viral culture PCR and Mycoplasma PCR from throat swab

**TREATMENT:** Date started:
- Total Hydration: IV/PO and tube feeds if applicable, at a total of 100 mL/m²/hour (avoid over-hydration) = mL/hour (up to 150 mL/hour). If IV required, use DSW + 0.45% NaCl.
- Acetaminophen mg PO/PR q4h pm, if temperature > 38.3°C orally.
  (15 mg/kg/dose, maximum 5 doses/day or 4 grams/day)
- Give initial doses of antibiotics within 30 minutes of presentation, before test results are available.
  - Child less than 2 months:
    - Ampicillin mg IV q6h (100-200 mg/kg/day, maximum 12 g/day, refer to neonate dosing) and
    - CefotAXime mg IV q8h (100-200 mg/kg/day, maximum 8 g/day, refer to neonate dosing)
  - Child greater than 2 months:
    - CefUROXime mg IV q8h (75-150 mg/kg/day, maximum 6 g/day)
Patient:
Age  Wt:  kg  Date of Wt (dd/mm/yyyy)  
Allergies:

The following orders will be carried out by a nurse ONLY ON THE AUTHORITY OF A PHYSICIAN.

Where choice occurs, check as appropriate.

☐ Child < 2 months with suspicion of meningitis:
  • Ampicillin mg IV q6h (200-400 mg/kg/day, maximum 12 g/day, refer to neonate dosing)  
  and  
  • CefoTAXime mg IV q8h (200-300 mg/kg/day, maximum 8 g/day, refer to neonate dosing)  
  If CSF shows positive gram cocci:
    Add vancomycin mg IV q6h (50 mg/kg/day, maximum 1 g/dose and maximum 4 g/day)

☐ Child > or equal to 2 months old with suspicion of meningitis:
  • CefoTAXime mg IV q8h (200-300 mg/kg/day, maximum 8 g/day)  
  • Vancomycin mg IV q6h (50 mg/kg/day, maximum 1 g/dose and maximum 4 g/day)

If patient has had a confirmed anaphylactic reaction to beta-lactam antibiotics consult the Infectious Diseases. NEVER delay treatment due to an allergy but be prepared to treat a reaction.

☐ If patient ≥ 5 years with respiratory symptoms or patients < 5 years, with evidence of Mycoplasma or any suspicion that patient non-compliant with prophylactic penicillin ADD
  • Clarithromycin mg PO q12h (15 mg/kg/day, maximum 500 mg/dose)  or  
  • Erythromycin mg IV q6h (40 mg/kg/day, maximum 4 g/day)

☐ When culture and sensitivity results indicate the organism is penicillin-susceptible change to:
  • Penicillin units IV q6h (250,000 units/kg/day, maximum 24 million units/day)  
  If allergic to beta-lactam antibiotics:
    • Clindamycin mg IV q8h (40 mg/kg/day, maximum 4.8 g/day)

  • If patient appears seriously ill, call doctor:
    Add vancomycin mg IV q8h (50 mg/kg/day, maximum 1 g/dose and maximum 4 g/day)
    If vancomycin levels are required aim for pre level of 5-10 micrograms/mL. Determine levels after 3rd or 4th dose (post levels are not routinely needed).

  • Stop prophylactic penicillin while on therapeutic antibiotics.

PAIN:
  • If no contraindication: Ibuprofen mg PO q8h prn (> 6 months 10 mg/kg/dose, maximum 40 mg/kg/day or 2.4 g/day).
  • If uncontrolled pain refer to Sickle Cell Anemia Pain Orders.

OTHER:
  • Encourage activity and ambulation.
  • Continue supplementation with folic acid 1 mg PO once daily.
  • Prior to discharge: Verify if patient is up-to-date on pneumococcal and other immunizations and restart prophylactic penicillin.

DATE (dd/mm/yyyy)  
Time (24hr/hh:mm)  
Physician Signature  
Printed Surname/Registration#  

DATE (dd/mm/yyyy)  
Time (24hr/hh:mm)  
Verified By (Nurse Signature)  
Printed Surname  
Sickle Cell/Asplenia – Fever
Asplenic patients are known to be at risk of infection, and are particularly susceptible to encapsulated organisms. Vaccinations are recommended to reduce the risk of infection in this patient population.

Your patient needs to receive these vaccinations at least 14 days prior to splenectomy or 14 days postsplenectomy. Please update your records, and note the patient’s need for future vaccinations.

- □ Meningococcal C conjugate (Menjugate<sup>®</sup>)
  - (See APPHON asplenia guidelines for # doses needed)
  - #1 Date Due: ________ Date given: ________
  - #2 Date Due: ________ Date given: ________
  - #3 Date Due: ________ Date given: ________

- □ Meningococcal ACYW-135 conjugate (Menactra<sup>®</sup>)
  - Date Due: ________ Date given: ________

- □ Haemophilus influenzae type b (Act-Hib<sup>®</sup>)
  - Date Due: ________ Date given: ________

- □ Pneumococcal conjugate (Prevnar<sup>®</sup>)
  - (See APPHON asplenia guidelines for # doses needed)
  - #1 Date Due: ________ Date given: ________
  - #2 Date Due: ________ Date given: ________
  - #3 Date Due: ________ Date given: ________
  - #4 Date Due: ________ Date given: ________

- □ Pneumococcal polysaccharide (Pneumovax<sup>®</sup>)
  - Date due: ________ Date given: ________
  - (2 years and older). **A booster is recommended after 3 years if child < 10 years of age at time of splenectomy and after 5 years if ≥ 10 years at time of splenectomy.**

- **Yearly influenza vaccine is also recommended.**
- **All routine immunizations should be up to date.**

If you have any questions regarding these vaccinations please call the numbers above.

Thank you.
References:


Brigden ML. Detection, Education and Management of the Asplenic or Hyposplenic Patient. American Family Physician 2001; 63(1).


Shatz DV, Schinsky MF, Pais LB, et al. Immune responses of splenectomized trauma patients to the 23-valent pneumococcal polysaccharide vaccine at 1


ASPLENIA/HYPOSPLENIA
Parent/Patient Information

The spleen is a large organ close to the stomach on the left side of the body. The spleen’s most important job is to help protect the body from infection. It does this by filtering bacteria (germs that cause infection) out of the blood. The spleen usually destroys these germs before they can cause serious infection. Asplenia means that the spleen is not there (has been taken out because of an accident or some other medical problem), or hyposplenia where the spleen is still there but does not work properly, for example in a disease called sickle-cell anemia.

Children with asplenia and hyposplenia have a higher chance of getting infections caused by certain kinds of bacteria than children who have a healthy spleen. One of the most important bacteria the spleen removes is called Streptococcus. If the spleen is not able to get rid of these bacteria then they can multiply in the blood stream and very quickly cause severe infection.

It is important that children with asplenia and hyposplenia (or their families) know the following information:

- all recommended vaccinations must be received to decrease the risk of serious infection;
- an antibiotic should be taken every day to help prevent infection;
- danger signs to look for that might mean an infection is starting and what action to take;
- they should see a doctor quickly if the child develops a fever;
- if the child cannot be quickly seen by a doctor, he/she should immediately take a dose of penicillin (or other antibiotic if allergic to penicillin);
- the child should wear a medical alert bracelet or carry a wallet card.

Other important information for children with asplenia and their families:

- the risk of serious infection lasts for a lifetime;
- serious infections may start from a scratch or wound which breaks the skin, or from animal bites, even by dogs or cats, because of the kind of bacteria they have in their mouths;
- serious infections may also be caused by tick bites;
- bites from mosquitoes that carry malaria can cause serious infections;
- the risk of serious infection is related to the cause of asplenia/hyposplenia. The risk is low (less than 1%) if the spleen was removed because of an accident or because the spleen was destroying blood cells. The risk of infection is higher (about 10%) if the spleen was taken out because of leukemia or lymphoma, or if the spleen works poorly because of sickle cell anemia;
- what may seem like minor signs of infection could mean a very serious infection has started;
- an infection can get much worse, and may even cause death, in a very short time (within hours);
• daily treatment with antibiotics (called prophylaxis) is extremely important and decreases the risk of infections;
• parents/patients should always carry a supply of penicillin with them when traveling;
• parents/patients should keep an updated supply of penicillin in the home or at school if access to a hospital or clinic is not available within an hour;
• see the Question & Answer section for other ways to decrease infection.

### Vaccines and prophylaxis recommended

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunization</th>
<th>Prophylactic antibiotic</th>
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</table>
| 0-2 years            | • Hemophilus influenzae [Hib], tetanus/diphtheria/pertussis (DTaP) and polio (IPV) vaccine at 2, 4, 6 months of age; booster at 18 months  
                        • Hepatitis B at 2, 4, 12 months of age  
                        • Hepatitis A  
                        • Pneumococcal conjugate (Prevnar®) at 2, 4, 6 months of age; booster at 18 months of age  
                        • Meningococcal conjugate (MenC) at 2, 4, 6 months of age  
                        • Varicella at 12 months  
                        • Annual influenza vaccine if over the age of 6 months  
                        • MMR at 12 months; booster at 18 months or 4-6 years | 0-2 months: Cefixime 8 mg/kg/day orally once to twice daily  
                                                                                     2 months to 3 years: Penicillin 25 mg/kg/day up to a maximum of Penicillin 150 mg orally bid |
| 2-5 years            | • Hib (if not previously immunized)  
                        • DTaP, IPV booster 4-6 years  
                        • Pneumococcal polysaccharide (Pneumovax®) vaccine with one booster in 3-5 years.  
                        • Men C (if not given earlier).  
                        • Meningococcal conjugate ACYW (Menactra®)  
                        • Annual influenza vaccine | 2-3 years: Penicillin 25 mg/kg/day up to a maximum of Penicillin 150 mg orally bid  
                                                                                     greater than 3 years: Penicillin 300mg orally twice daily |
| 5 years to adolescence| • Hib (if not given earlier; booster not required)  
                        • Tetanus/diphtheria/pertussis (Td or dTap) 14-16 years  
                        • Hepatitis B (0, 1 and 6 months) in grade 4 if not received at birth  
                        • Pneumovax® - If given before 5 years, then give 1st booster dose 3 years after the initial vaccination; otherwise, repeat vaccination once, 5 years after the initial vaccination.  
                        • Men C (if not given earlier)  
                        • Meningococcal conjugate ACYW (Menactra®)  
                        • Annual influenza vaccine | Penicillin 300mg orally twice daily |

When a splenectomy [surgical removal of the spleen] is planned, these vaccines should be given 2 or more weeks prior to surgery.

For children with penicillin allergy, a referral should be made to verify the allergy and to select an appropriate antibiotic.

Influenza vaccine may decrease the risk of secondary bacterial infection.
Questions and Answers:

If my child develops a fever, what should I do?
- call your family doctor or pediatrician immediately - phone number
- if your child’s doctor is not available right away, give your child a dose of penicillin then take him/her to the nearest hospital emergency room.
- in the hospital, if an infection is suspected or seems likely, the doctor will probably take a blood sample to see if bacteria is present and causing infection and start treatment immediately with antibiotics given intravenously (into a vein).

If my child does not look well, even if she or he does not have a fever, what should I do?
- call your family doctor or pediatrician;
- if your family doctor is not immediately available, give your child a dose of penicillin then take your child to the nearest hospital emergency department.

What are the chances that my child will develop a serious infection?
- the chance that your child will develop a serious infection is small. It is less than 1% if your child has had her/his spleen removed because of an accident or increased destruction of blood cells. It is less than 10% if your child had her/his spleen removed because of leukemia or lymphoma or if your child has sickle cell anemia. However, the chances are still much higher than those of a child with a normal spleen;
- we cannot tell which child will get a serious infection; therefore, all children with asplenia and hyposplenia need to be seen by a doctor if a fever develops.

What can I do to decrease the risk of my child getting a serious infection?
- make sure that your child takes her/his penicillin daily;
- make sure that your child receives the recommended vaccinations;
- whenever possible, avoid close contact with others who have an infection;
- practice good hand washing habits;
- wash any cuts and scrapes promptly;
- help your child to understand why he or she needs to be extra careful about infections.

Who should know that my child is at increased risk of infection?
- your family doctor or pediatrician;
- your dentist;
- your child’s teacher;
- anyone who might look after your child, for example grandparents, day-care workers, babysitters, etc;
- a medical alert bracelet or wallet card is important to make sure the needed information is available if your child becomes ill or is in an accident.
Medical Alert
Asplenic Patient

Patient Name: ____________________________________

Physician Name: ____________________________________

Physician Phone: ____________________________________

Patient is at risk of potentially fatal, overwhelming infections. Medical attention required for:
- Signs of infection- fever > 38°C, sore throat, chills, unexplained cough.
- Animal and tick bites.

Vaccination Record
Patient has received the following vaccinations:
- **Meningococcal C conjugate**
  Date given: _________________________________
- **Meningococcal ACYW-135 conjugate**
  Date given: _________________________________
- **Pneumococcal conjugate**
  Date given: _________________________________
- **Pneumococcal polysaccharide**
  Date given: _________________________________
- **Pneumoccal booster**
  Date due: □ 3 years or □ 5 years after initial vaccine
  Date given: _________________________________
- **Hib conjugate vaccine**
  Date given: _________________________________
Guideline Development

Potential organizational barriers/cost implications to applying the recommendations found in this guideline include:

- inability to obtain vaccines

Patient/family preferences:

- not considered applicable
- appropriate information and support will be provided

Key review criteria for monitoring/audit include:

- Vaccine administration records
- Prophylactic antibiotic compliance
- Number of children requiring admission for fever and infection

The Guideline development group included:

- Tamara MacDonald, PharmD, pharmacist
- Dorothy Barnard, pediatric hematologist/oncologist
- Vicky Price, pediatric hematologist/oncologist
- Joanne Langley, pediatric infectious disease specialist

The individuals involved in the development of this guideline had no conflicts of interest with respect to the development of the guideline. The guideline was developed independently from any funding body.

The guideline was piloted at the IWK Health Centre in Halifax, Nova Scotia.

The guideline was externally reviewed by pediatricians, hematologists, oncologists, nurses and a psychologist.

The guideline will be updated in July 2011 by the APPHON Guidelines Committee, and resubmitted to the APPHON Board and Cancer Care Nova Scotia Clinical Practice Guidelines Committee for ratification. If significant changes to the prevention and treatment of asplenia, changes based on new evidence or best practice developed prior to July 2011, the guideline will be updated to reflect those changes. As per the standard practice for APPHON guidelines, individuals will be assigned to regularly review applicable literature to monitor for significant changes. If literature documenting evidence-based or best practice based indications for changes to this guideline, the guideline will be updated with the applicable information as soon as feasible.