Preventing and treating infections in children with asplenia or hyposplenia

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Children with asplenia or hyposplenia are at risk of developing overwhelming sepsis. Health care providers caring for children with asplenia should ensure the best outcomes by using preventive strategies that focus on parent and patient education, immunization, antibiotic prophylaxis and aggressive management of suspected infection. The present position statement offers current guidance on each of these issues and replaces a previous CPS statement, 'Prevention and therapy of bacterial infections for children with asplenia or hyposplenia', published in 1999.

Key Words: *Antibiotic prophylaxis; Immunization; Sepsis; Splenectomy*

La prévention et le traitement des infections chez les enfants présentant une asplénie ou une hyposplénie

Les enfants présentant une asplénie ou une hyposplénie sont vulnérables à un sepsis fulgurant. Les dispensateurs de soins qui s'occupent d'enfants présentant une asplénie devraient s'assurer des meilleurs résultats cliniques possible grâce à des stratégies préventives axées sur l'éducation des parents et des patients, la vaccination, la prophylaxie antibiotique et la prise en charge vigoureuse de l'infection présumée. Le présent document de principes, qui propose des conseils à jour sur chacun de ces sujets, remplace le document de la SCP intitulé « La prévention et le traitement des infections bactériennes chez les enfants aspléniques ou hypospléniques », publié en 1999.

Children can have absent or defective splenic function as a result of congenital anatomical absence of a spleen, surgical removal of the spleen, or medical conditions that result in poor or absent splenic function. Sickle cell anemia is a common cause of this condition in Canada. Absent or defective splenic function is associated with a high risk of fulminant bacterial sepsis, especially with encapsulated bacteria. Splenectomized children younger than 15 years of age and congenitally asplenic infants are at greater risk of developing overwhelming postsplenectomy sepsis than adults.(1) Individuals with underlying blood disorders, such as hemoglobinopathies (eg, sickle cell disease, thalassemia major) or hereditary spherocytosis, are at greater risk than those who have undergone a splenectomy because of trauma.(1,2) Asplenic patients are at risk of overwhelming sepsis throughout their life span, with the highest frequency of sepsis reported in the first three years postsplenectomy or the first three years of life, if congenitally asplenic.(3) Asplenic patients with sepsis from encapsulated organisms have a 50% to 70% mortality rate, with the highest mortality rate reported in children younger than two years of age.(4)

Most fulminant sepsis in asplenic patients is due to bacteria encapsulated by a polysaccharide capsule. *Streptococcus pneumoniae* is the most common organism causing sepsis and is isolated in at least 50% of cases. *Haemophilus influenzae* type b (Hib), *Neisseria meningitidis*, *Salmonella* species and *Escherichia coli* are also common. Less commonly, *Pseudomonas*, *Klebsiella*, streptococci and staphylococci are found. Limited data suggest that in the first three months of life, coliform (*E coli* or *Klebsiella*) sepsis occurs more frequently.(5) Overwhelming sepsis associated with cat and dog bites has also been reported and is caused by *Capnocytophaga* species.(6) Asplenic patients are also more susceptible to severe or fatal malaria(7) and to infection by the protozoan *Babesia*,(8) which is transmitted by tick bites.

Health care providers caring for children with asplenia should ensure the best outcomes with preventive strategies: parent and patient education, immunization, antibiotic prophylaxis and aggressive management of suspected infection.

PARENT AND PATIENT EDUCATION

Although immunization and prophylactic antibiotics are effective, they do not provide complete protection. Children with asplenia and their families must be educated about the risk of sepsis and instructed to seek medical attention promptly when the child is ill or has a fever. Heightened infection risk continues into adulthood. Recognizing postsplenectomy sepsis can be difficult and death may occur in a matter of hours. The importance of using prophylactic antibiotics and vaccines should be emphasized repeatedly.

Vulnerable patients should wear a MedicAlert bracelet. When travelling, they should carry a note from their physician stating their diagnosis, associated risks and a suggested medical management plan should they become ill. They should be aware of their increased risk of infection after animal bites, especially with *Capnocytophaga canimorsus* from dog bites, and must be given appropriate antibiotics, such as amoxicillin-clavulanic acid, if they are bitten.

IMMUNIZATION

All patients should receive the standard childhood and adolescent immunizations at the recommended age. However, due to the risk of fulminant sepsis from encapsulated bacteria, immunizations against *S pneumoniae*, Hib and *N meningitidis* should be ensured, and may be administered on an earlier schedule than is routine. Conjugated vaccines activate a superior immune response compared with polysaccharide vaccines. Studies of group A and C meningococcal polysaccharide vaccine and repeated doses of PPV23 in adults and children have shown that a state of immune tolerance, or hyporesponsiveness, can develop in response to repeated polysaccharide vaccine antigen exposures.(9) Thus, conjugate vaccines are used preferentially whenever possible.

Pneumococcus

All asplenic patients should receive both the conjugated 13-valent pneumococcal vaccine and the 23-valent polysaccharide vaccine.

- The immunization schedule for pneumococcal conjugate vaccine (PCV13 [Prevnar-13, Pfizer, USA]) should be a

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TABLE 1
Antibiotic prophylaxis recommendations for children with asplenia or hyposplenia

Age	Oral prophylaxis*	Comments
Birth to three months	Amoxicillin/clavulanate 10 mg/kg/dose two times per day, with penicillin VK 125 mg two times per day OR amoxicillin 10 mg/kg/dose two times per day being an alternative if not tolerated	*Escherichia coli*, *Klebsiella* are of concern in this age group
>3 months to five years	Penicillin VK 125 mg per dose two times per day OR amoxicillin 10 mg/kg/dose two times per day	Liquid amoxicillin may be better tolerated than liquid penicillin because it tastes better
>5 years	Penicillin V 250 mg or 300 mg per dose two times per day OR amoxicillin 250 mg per dose two times per day	For penicillin, 250 mg is a convenient dose for suspension but tablets are only available as 300 mg

**For penicillin anaphylaxis, refer the patient for allergy testing and administer erythromycin pending results*

primary series of **four doses** at two, four, six and 12 to 15 months of age. Children between 12 and 24 months of age without previous doses of PCV13 should receive two doses *at least* eight weeks apart. Patients >24 months of age need only one dose. Even when children have received all the required doses of PCV7 or PCV10 in the past, they should be given one dose of PCV13 as soon as possible.

- The pneumococcal polysaccharide vaccine against 23 serotypes (PPV23 [Pneumovax, Merck, USA]) should be administered as soon as possible after 24 months of age for supplemental protection. The best method by which to immunize is not known but most experts suggest 'priming' with the conjugated protein vaccine, followed by the broader spectrum, although less immunogenic, polysaccharide vaccine *at least* eight weeks after all doses of the conjugated vaccine required for age have been administered. A booster dose of PPV23 should be given five years after the first dose. No more than two lifetime doses of PPV23 are currently recommended.
- If an asplenic patient has previously received only PPV23, the patient should receive one dose of PCV13 one year after receipt of the PPV23 vaccine.

Meningococcus

All asplenic patients should receive conjugate quadrivalent meningococcal vaccine (MCV4). There are currently three products available in Canada. Menveo (Novartis, Canada) can be used from two months of age and either Menveo, Menactra (Sanofi Pasteur, Canada) or Nimenrix (GlaxoSmithKline, Canada) can be used after 24 months of age.

- Infants with known asplenia should receive Menveo as a primary series of four doses at two, four, six and 12 to 15 months of age. Children identified as asplenic from 12 months to 23 months of age should receive two doses of Menveo, eight weeks apart. Patients identified after two years of age should receive two doses of any of the quadrivalent conjugate meningococcal vaccines, eight weeks apart.
- Patients vaccinated with MCV4 should be revaccinated every five years pending further information on duration of immunity.
- There is no role for meningococcal polysaccharide vaccine (Menomune).
- A new four-component meningococcal vaccine designed to protect against serotype B (4CMenB [Bexsero, Novartis, Canada]) became available in December 2013 and should be given to all asplenic patients including infants.

Haemophilus influenzae type b (Hib)

- The recommended vaccination schedule for Hib is a primary series of three doses given at two, four and six months of age, with a booster dose at 18 months of age.
- All patients ≥5 years of age who have never received Hib immunization or have missed one or more doses should receive one dose. Some experts recommend one additional dose of Hib vaccine for all asplenic patients older than five years of age even if fully immunized previously.
- Children with asplenia who present with a life-threatening Hib infection should receive Hib vaccine, because the infection itself does not confer lifelong protection.

Influenza

- Yearly seasonal influenza vaccine is recommended, starting at six months of age, to lower the risk of secondary bacterial infections.

Other

- All asplenic patients travelling to less developed areas of the world may be at risk of *Salmonella* infection and should be immunized for *S typhi*.

Household contacts

- Household contacts of asplenic patients should receive all age-appropriate vaccines and the yearly influenza vaccine.

Timing of immunizations in elective splenectomy

When a patient is undergoing an elective or semielective splenectomy, there is some evidence that the best responses occur when vaccines are administered at least two weeks before the surgery is performed. When this timing is not possible, it is optimal to start immunizations at least two weeks postsplenectomy.(10) However, in situations for which vaccines are not administered before splenectomy, the benefit of waiting two weeks postsplenectomy must be carefully weighed against the possibility that the patient may not be vaccinated at all; sometimes the best choice is to vaccinate the child before discharge from hospital.

ANTIBIOTIC PROPHYLAXIS FOR CHILDREN WITH ASPLENIA OR HYPOSPLENIA

Immunizations do not fully protect against infections with encapsulated bacteria, making antibiotic prophylaxis a second, vital aspect of care. Table 1 provides dosing information for antibiotic prophylaxis. Because *S pneumoniae* is the most common cause of severe infections in children with asplenia or hyposplenia, with significant associated mortality, patients younger than five years of age should all receive antibiotic prophylaxis.

Controversies exist with respect to optimal antibiotic prophylaxis. Topics include the degree of patient compliance, optimal duration and the effect of prophylaxis on the emergence of penicillin-resistant pneumococci. The single prospective controlled study that showed an 84% reduction in infection was conducted in a population of patients with sickle cell disease; these findings may not apply to all patients with poor splenic function. Also unclear is whether it is necessary to cover coliforms for the first three months of life; the studies that led to this

recommendation involved very small numbers of infants with bacteremia.(11)

The age at which antibiotic prophylaxis should be discontinued is the most controversial topic. The Red Book from the American Academy of Paediatrics recommends prophylaxis until the child is five years of age and a minimum of one year of prophylaxis for children older than five years of age postsplenectomy, provided the child has received all the appropriate pneumococcal vaccinations.(11) The British Committee for Standards in Haematology General Haematology Task Force recommends that lifelong prophylactic antibiotics should be offered in all cases and especially encouraged for children younger than 16 years of age and for all age groups in the first two years postsplenectomy or where there is an underlying immune function impairment.(12)

Because most postsplenectomy sepsis occurs within the first two to three years after surgery, the Canadian Paediatric Society's Infectious Diseases and Immunization Committee recommends antibiotic prophylaxis for a minimum of two years postsplenectomy and for all children <5 years of age. Furthermore, because fulminant septicemia has been reported in adults up to 65 years postsplenectomy, and invasive infection with penicillin-resistant pneumococci has not emerged as a problem for patients on long-term penicillin prophylaxis, lifelong prophylaxis in all cases is ideally recommended. However, the patient's or family's compliance and degree of access to medical care, current pneumococcal resistance rates and previous episodes of life-threatening sepsis must be considered when making or reviewing this decision.

Children who have had or are believed to have had an anaphylactic-type reaction to penicillin should be referred immediately to an allergist to verify the diagnosis and for challenge or desensitization as warranted. Erythromycin is a recommended alternative; however, this antibiotic is less successful at preventing invasive disease because of higher rates of pneumococcal resistance.

The optimal duration of antibiotic prophylaxis for children who undergo partial splenectomy or who have functional asplenia or polysplenia is unclear from the literature. Until there are recommendations to the contrary, following the guidelines described for children undergoing total splenectomy appears to be the most prudent course.

Malaria prophylaxis

Asplenic and hyposplenic children must be advised of their increased risk of severe malaria and should always seek travel advice. They should also take malaria prophylaxis as appropriate for their age and the type of malaria found in the area to which they are travelling. Preventive measures should be taken, including sleeping under an insecticide-treated bed net or in air-conditioned accommodations, and using insect repellent. Within the first month of returning from a malarious area, and for up to a year afterward, the patient with fever should inform their health care provider and malaria should be included in the differential diagnosis.(13)

Initial treatment of suspected sepsis: A medical emergency

Children with asplenia must be seen by a physician immediately for every febrile illness. Sepsis in individuals with asplenia or hyposplenia is a medical emergency because they can die within several hours of fever onset despite appearing well initially. Unless there is an obvious nonbacterial source, a blood culture should be performed but should not delay the administration of antibiotic therapy. All patients should receive ceftriaxone (100 mg/kg/dose, maximum 2 g/dose). Where intermediate or high penicillin-resistant pneumococci are prevalent, administer both ceftriaxone and vancomycin (60 mg/kg/day in divided doses every 6 h). If the patient is being treated in a clinic or office setting, refer immediately to the nearest emergency department. Clinical deterioration can be rapid even after antibiotic administration. Antibiotics should be modified once blood culture results become available.

If the patient has a serious penicillin or cephalosporin allergy, vancomycin and ciprofloxacin can be used. Antibiotics should be modified once blood culture results become available.

RECOMMENDATIONS

To prevent and treat infections in children with asplenia or hyposplenia, the Canadian Paediatric Society recommends that:

- Physicians educate patients and families about the risks associated with asplenia and hyposplenia, preventive measures that can be taken and interventions that are necessary when a child develops a febrile illness. Because parents often encounter a clinician who underestimates the risk of fever in this setting, providing them with a copy of this statement to show emergency department staff may be helpful.
- Children with asplenia and hyposplenia should receive all routine childhood immunizations, and some routine vaccinations should be administered on an accelerated schedule with extra doses. All children with these conditions, regardless of age, should receive vaccines to protect against *S pneumoniae*, *N meningitidis*, Hib and seasonal influenza.
- Prophylactic antibiotics should be administered until patients are at least 60 months of age, and longer for children who experience an episode of invasive pneumococcal disease. Consideration should be given to lifelong prophylaxis, although adherence issues and the development of resistant bacteria may favour eventual discontinuation.
- Patients with asplenia or hyposplenia must be considered at high risk of serious bacterial infection (ie, as presenting with a medical emergency). They should wear a MedicAlert bracelet, be promptly assessed whenever fever occurs and started on antimicrobial therapy immediately unless a nonbacterial source is apparent.

Note: Information for parents, 'Reducing the danger of infection for children with spleen problems', can be accessed at www.caringforkids.cps.ca.

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