

INFECTION IN PATIENTS WITH AN ABSENT OR DYSFUNCTIONAL SPLEEN

Fulminant, potentially life-threatening infection, especially caused by encapsulated bacteria, is a major long-term risk after splenectomy. Most instances of serious infection are due to *Streptococcus pneumoniae* (pneumococcus, 59% of deaths, 90% of blood-stream infections); other bacteria commonly responsible for severe infections in these patients include *Haemophilus influenzae* type B, *Neisseria meningitidis*, *E. coli*, *Pseudomonas* spp., other streptococci, other gram-negative bacilli and staphylococci. Malaria and *Capnocytophaga canimorus* (see dog bites – below) may also have serious consequences in hyposplenic patients.

Asplenic children under 5 years have an incidence of septicaemia of over 10%, much higher than in adults (<1%). Though most infections occur within the first two years of splenectomy, up to a third may be manifested at least five years later. Cases of fulminating infection have been reported more than 20 years after splenectomy.

To whom do these guidelines apply?

Hypo- or asplenia may be congenital or caused by surgical removal or certain medical illnesses (e.g., Coeliac disease, sickle-cell disease, inflammatory bowel disease, severe liver disease). The presence of Howell-Jolly bodies in red cells on a peripheral blood film is an important clue to a degree of functional hyposplenism that represents a risk of overwhelming post-splenectomy infection.

Recommendations – General

1. Refer all patients to Richard Everts, Infectious Diseases Specialist at Nelson Hospital, for entry onto the NMDHB splenectomy/hyposplenism database, assessment and education
2. Educate the patient about the risk of infection and the importance of prompt treatment. Reinforce understanding and advice annually as retention has been found to be very poor in more than half of patients and poor knowledge is associated with a 10-fold increased risk of overwhelming post-splenectomy infection compared with those with good knowledge
3. Patients should wear a Medic-Alert bracelet or necklace
4. Patients should carry a card with information about their asplenia and contact numbers – to order these see Appendix 1 of this guideline

Recommendations – Immunisations

Ideally, immunisations should be given two weeks before elective splenectomy or before severe hyposplenism has developed. If this is not possible or did not happen, give immunisations as soon as possible (after recovery from surgery) except in those

receiving immunosuppressive chemotherapy or radiotherapy – in which cases immunisation should be delayed for at least six months.

All vaccines for hyposplenic patients are funded for administration in General Practice. Refer to the Medsafe website www.medsafe.govt.nz for the manufacturers' datasheets for each vaccine.

Pneumococcal vaccine

Polysaccharide Pneumococcal Vaccine (23PPV, Pneumovax[®] 23) contains the 23 most prevalent or invasive pneumococcal serotypes, including those isolated most often in New Zealand. Most healthy adults develop a good antibody response to a single dose of the vaccine by the third week following immunisation; overall vaccine efficacy in preventing severe pneumococcal infection in adults is probably 60-70%. The vaccine is not recommended for children under two years of age as it is poorly immunogenic in this group. Instead, a conjugate 7-valent vaccine (PCV7, Prevenar[®]) has been licensed for use in at-risk children aged under two years of age. It has immunogenicity, even in infancy and is active against approximately 70% of isolates causing invasive disease.

Response to pneumococcal vaccine is unpredictable. Poor responders to 23PPV generally do not respond to revaccination with 23PPV but there are reports of individual 23PPV non-responders subsequently responding to PCV7. Patients who have inadequate serological responses are at higher risk of pneumococcal infection. Measure pneumococcal antibody levels before and approximately 1 month after vaccination. Protective pneumococcal antibody levels are not well defined – opinions range from 0.15 µg/mL to 1.9 µg/mL for total pneumococcal IgG. Alternatively, an adequate response to vaccine is considered as a greater than 2-fold increase in antibody levels. If there is an adequate level or response, follow the schedules below; if inadequate level or response after repeated vaccination, long-term prophylactic antibiotics should be considered.

Schedule for pneumococcal vaccines for adults and children pre- and post-splenectomy or with functional asplenia – no previous pneumococcal vaccine

Age at start of course	Conjugate pneumococcal vaccine (PCV7, Prevenar [®])	Polysaccharide pneumococcal vaccine (23PPV, Pneumovax 23 [®])
6 weeks to 6 months	3 doses PCV7 at least 6 to 8 weeks apart or at same time as the usual schedule; <u>plus</u> a 4 th dose at age 15 months	One dose of 23PPV at age 2 years and a second dose at age 4 to 5 years Booster dose of 23PPV every 5 years
7 to 11 months	2 doses of PCV7 at least 6 to 8 weeks apart <u>plus</u> a 3 rd dose at age 15 months	One dose of 23PPV at age 2 years and a second dose at age 4 to 5 years Booster dose of 23PPV every 5 years
1 to 4 years	2 doses of PCV7 given at 6 to 8 weeks apart	One dose of 23PPV at age 2 years and a second dose at age 4 to 5 years Booster dose of 23PPV every 5 years
5 to 9 years	One dose of PCV7	One dose of 23PPV 6 to 8 weeks after PCV7, then Booster dose of 23PPV every 5 years
10 to 16 years	(A dose of PCV7 may be recommended for some children)	One dose of 23PPV, then Booster dose of 23PPV every 5 years

Adults > 16 years	-	One dose of 23PPV Booster dose of 23PPV every 5 years
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Catch-up schedules for children under five years of age (high-risk or pre/post splenectomy) with prior history of pneumococcal vaccine

Age of child	Previous dose(s) of conjugate (PCV7) or polysaccharide (23PPV) vaccines	Recommendations
23 months or under	Any	Complete the course as in table above
24 to 59 months	4 doses of PCV7	One dose of 23PPV at age 2 years, 6 to 8 weeks after the last dose of PCV7, and 1 dose of 23PPV 3 to 5 years after the first dose
24 to 59 months	1 to 3 doses of PCV7	1 dose PCV7 1 dose of 23PPV vaccine 6 to 8 weeks after the last dose of PCV7, and 1 dose of 23PPV 3 to 5 years after the first dose
24 to 59 months	1 dose of 23PPV	2 doses of PCV7, 6 to 8 weeks apart, beginning at 6 to 8 weeks after the dose of 23PPV, and 1 dose of 23PPV 3 to 5 years after the first dose of 23PPV.

PCV7 (Prevenar[®]) is given intramuscularly, preferably into the antero-lateral muscles of the thigh of infants and young children or the deltoid muscle of the upper arm of older children. Pneumovax[®]23 can be administered intramuscularly or subcutaneously.

Meningococcal group A, C, Y, W135 vaccine

The quadrivalent polysaccharide meningococcal vaccine (Menomune[™] ACYW-135, Sanofi Pasteur) is recommended for adults and children aged two years and over. It is administered as a single dose and a booster is only recommended (and funded) for individuals considered at special risk. Individuals scheduled for elective splenectomy should be immunised at least 14 days before the operation. It is given subcutaneously.

***Haemophilus influenzae* type B (Hib) vaccine**

The data to support administration of Hib vaccine for older children and adults is not strong but most authorities recommend Hib for hyposplenic and asplenic individuals. The Hib PRP-T vaccine is immunogenic in adults. Give the Hib PRP-T vaccine (Hiberix[™], GSK) vaccine as a single dose, intramuscularly. No boosters are recommended.

Influenza vaccine

Overseas guidelines strongly recommend annual influenza vaccination for adults and children with asplenia or splenic dysfunction.

Recommendations - Antibiotic prophylaxis and self-treatment

Studies on antibiotic prophylaxis have shown a benefit in children and adults. The 2002 British Committee for Standards in Haematology recommended maintaining patients on prophylaxis for life. The American Academy of Paediatrics in 2003 (Red Book, 23rd edition) recommended stopping antibiotics at 5 years of age provided there is no history of invasive pneumococcal disease and the child is receiving regular medical attention. Since most cases of overwhelming sepsis occur within 2-3 years of splenectomy, several sources recommend that chemoprophylaxis be given for at least that period. Animal studies show that antibiotic prophylaxis is not needed as long as prompt antibiotic treatment is given for acute infection. Disadvantages of life-long prophylaxis include resistance and lack of compliance.

NMDHB recommendation for prophylactic antibiotics:

- Continue until 2 years after splenectomy and until at least 5 years of age
- Thereafter, antibiotics prophylaxis can stop in most cases provided the patient is fully vaccinated and has antibiotics and instructions on-hand for prompt self-treatment
- Consider continuing antibiotics in the following exceptional circumstances:
 - Recurrent infections (give prophylaxis for at least 6 months after the last infection)
 - Failure to respond to pneumococcal vaccine
 - High risk (e.g., co-existent Hodgkins disease or other haematological malignancy, immunoglobulin deficiency, chemotherapy, sickle-cell disease, thalassaemia).

Antibiotics recommended for prophylaxis:

- Penicillin
 - Adult 250-500 mg 12 hourly
 - Child aged 5-14 years 250 mg 12 hourly
 - Child under 5 years 125 mg 12 hourly
- Amoxicillin
 - Child 20 mg/kg/day
 - Adult 250-500 mg daily
- Roxithromycin (in case of penicillin allergy)
 - Adult 150mg daily
- Erythromycin (base, in case of penicillin allergy)
 - Adult and child over 8 years 250-500 mg daily
 - Child aged 2-8 years 250 mg daily
 - Child under 2 years 125 mg daily

Penicillin is the antibiotic of choice in children as amoxicillin may be less well tolerated. The advantages of amoxicillin over penicillin in adults are that it is better absorbed, has a broader spectrum and a longer shelf life and is only once daily administration.

Antibiotics for self-treatment should be kept at home and carried with the patient on holidays. If rigors or fever ($> 38^{\circ}\text{C}$) develop, take a STAT dose of antibiotic (see options below, whether prophylaxis is being taken or not) and seek go to the nearest

hospital for medical attention. In addition, seek medical attention that day if any of the following symptoms develop:

- Cough with purulent sputum
- Moderate to severe sore throat, or
- Flu-like illness with malaise, myalgia, headache, vomiting, diarrhoea and/or abdominal pain.

The recommended antibiotic for urgent outpatient treatment is Augmentin 1.2g orally STAT (if mild penicillin allergy take cefaclor 1g orally STAT; if severe penicillin allergy or any degree of cephalosporin allergy take moxifloxacin 400mg STAT). Adult patients admitted with severe infection should be given IV ceftriaxone.

Recommendations for Travellers

Asplenic patients should be strongly advised of the increased risk of severe falciparum malaria. Travel to areas where malaria is endemic should be discouraged. If patients do travel to such areas scrupulous adherence to antimalarial prophylaxis and anti-mosquito measures is essential.

Give a booster of meningococcal A,C,Y+W135 vaccine before travelling to areas and seasons where there is an increased risk of meningococcal infection (e.g., sub-Saharan Africa.)

Other Measures

Animal bites. After dog, cat, human or other animal bite, give five days of Augmentin, doxycycline, erythromycin or roxithromycin prophylaxis. Irrigate, debride, explore, x-ray, close, elevate, administer tetanus or rabies vaccine as appropriate and follow up as per usual bite management.

References

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Australasian Society for Infectious Diseases 2006. Recommendations for the prevention of post-splenectomy sepsis (Draft)

Appendix 1

Patient information card. Laminated cards are available from Richard Everts, Infectious Diseases Specialist, Nelson Hospital (email: richard.everts@nmhs.govt.nz or via my secretary 546-1089)



KEEPING SAFE WITHOUT A SPLEEN

Severe infections may occur up to many years after splenectomy or loss of spleen function.

- Get a Medic-alert bracelet, especially if you travel alone
- Show this card to any doctor treating you
- From your GP get free vaccines against pneumococcus, meningococcus (A/C/Y/W-135), Hib and influenza. Repeat the pneumococcal vaccine every 5 years and the influenza vaccine annually
- Take regular preventative antibiotics (e.g., penicillin, amoxycillin, roxythromycin) for at least 2 years after splenectomy or splenic failure – longer if advised by your doctor.

Side one



- Carry extra antibiotics with you wherever you go – if you develop chills or fever > 38 °C then take Augmentin 1.2g (first choice) or cefaclor 1g or moxifloxacin 400mg immediately and seek urgent medical help
- If you cough brown phlegm, get a very sore throat or feel very sick (like you have the flu), see your doctor that day
- If travelling to a country with malaria, take all anti-mosquito precautions and anti-malaria medications
- Get immediate medical help for an animal or human bite, including thorough wound cleaning and antibiotics.

This card and further information available from:
Richard Everts, Infectious Diseases Specialist and Microbiologist, Nelson Hospital, Private Bag 18, Nelson.
Email richard.everts@nmdhb.govt.nz

Side two