Prevention and management of infections in patients without a spleen

R. N. Davidson and R. A. Wall

Departments of Infectious Diseases and Microbiology, Northwick Park Hospital, Harrow, London, UK

Patients who lack a functioning spleen become vulnerable to sepsis caused by bacteria and, occasionally, protozoa. The risk is higher in children and in those who have had immunosuppressive treatment, and the risk remains lifelong. Overwhelming post-splenectomy infection (OPSI) occurs at an estimated incidence of 0.23–0.42% per year, with a lifetime risk of 5%. Episodes of OPSI are emergencies, requiring immediate parental antibiotics and intensive care; intravenous immunoglobulins may be useful. OPSI carries a mortality of 38–69%. Streptococcus pneumoniae is the commonest infecting organism, accounting for 50–90% of isolates from blood cultures in reported series; it is particularly common in children with sickle cell disease. Less commonly, the infecting organisms are other bacteria, Babesia or Ehrlichia. OPSI may be, to some extent, preventable by several interventions. These are surgical conservation of the spleen; immunization against S. pneumoniae, Haemophilus influenzae type b, and Neisseria meningitidis; prophylactic antibiotics; stand-by antibiotics; patient information sheets; and a medical alert bracelet. Asplenic patients living in malaria-endemic areas require optimal prophylaxis. The initial step in prevention of OPSI is the creation of an asplenia register, as many patients are not covered by these simple measures.

Keywords Splenectomy, antibiotic prophylaxis, OPSI, immunization

Clin Microbiol Infect 2001; 7: 657–660

INTRODUCTION

Surgical removal of the spleen results in: reduced clearance of particulate antigens, be they extracellular (e.g. bacteria) or intracellular (e.g. malaria); diminished response to new antigens, particularly polysaccharides; impaired phagocytosis of unopsonized and opsonized bacteria and cells; and decreased levels of tuftsin and properdin [1]. Asplenic individuals are thus particularly vulnerable to sepsis caused by bacteria and, occasionally, protozoa. Such infections are often fulminant, with high mortality. Similar risks of infection exist where the spleen is non-functional, e.g. due to atrophy in sickle cell disease [2].

The commonest infecting organism in most series is Streptococcus pneumoniae, which accounts for 50–90% of isolates from blood cultures in many cohorts of patients [1,3]. It is particularly common in children with sickle cell disease [2]. Haemophilus influenzae type b was the second most frequent organism in the era before the Hib conjugate vaccine. Other bacteria include Streptococcus group B, Staphylococcus aureus, Salmonella species, Escherichia coli and other coliforms, Capnocytophaga canimorsus, and, rarely, Pseudomonas aegyptiaca. Whether splenectomy increases susceptibility to Neisseria meningitidis is unclear [4].

Babesiosis (transmitted by ticks in temperate and tropical countries) is almost completely confined to asplenic patients, and may be confused microscopically with Plasmodium falciparum infection [5]. Compared to normal individuals, asplenic patients living in malaria-endemic areas are more commonly parasitemic, and have delayed clearance of parasites after treatment [6,7]; in addition, the disease may be severe or even fatal [8]. Ehrlichiosis is more severe in asplenic individuals [9].

The risk of infection appears highest in the first 2 years post-surgery [10]. In one series, 3.3% developed bacteremia during the first month after surgery, but, notably, most of these patients had gastrointestinal malignancies [11]. Thereafter, the risk of sepsis is lower. Whereas some series indicate that the risk of overwhelming post-splenectomy infection (OPSI) declines with the time elapsed since splenectomy [1], other series do not show a significant reduction [3]. Reasonable estimates of the annual incidence of serious bacterial infections after splenectomy derived from cohort studies are 0.42% per year [12] and 0.23% per year [13], with a lifetime risk of OPSI of 5% [1]. The risk is higher in children, in those splenectomized for hematologic conditions (especially malignancy), and in those who have another cause for immunosuppression, such as corticosteroids or cytotoxics. OPSI carries a mortality of 38–69% [3].

Although the risk of infection in the splenectomized has been recognized for nearly 50 years [13], most splenectomized patients have not received adequate advice or interventions to reduce their risk of OPSI [3,11,14].

Theoretically, the risk of OPSI should be reduced by the measures discussed below: but it should be recognized that no trials of any of these interventions have been carried out.
**Autotransplantation and Splenic Conservation**

Embedding sections of splenic tissue in the greater omentum can preserve a degree of splenic function. In one series, no patients who underwent autotransplantation had episodes of bacteremia, versus 4.8% of splenectomized patients who did not [11]. However, other series do not show the same success. Splenic repair may also be successfully used to conserve a damaged spleen: in a study from Papua New Guinea, the prevalence of malaria was 88% among patients who had a splenectomy for trauma, versus 18% among those who had splenic conservation and 16% of controls [6].

**Immunization**

**Pneumococcal vaccine**

Because of the pre-eminent role of pneumococcal infection in OPSI, all patients undergoing splenectomy should receive immunization against *S. pneumoniae* using the 23-valent pneumococcal polysaccharide vaccine (Pneumovax; Pnu-Immune), which covers ~73% of strains causing OPSI. If possible, vaccines should be given ~2 weeks prior to surgery, as the immune response to the vaccines is thought to be better when the spleen is intact. Although there are no data on the optimum timing of vaccine given post-operatively, it is logical to give it at time of discharge, thus minimizing the immunosuppressive effect of surgery. Pneumococcal vaccine failures should be anticipated, either because of strains not included in the vaccine, or because of poor vaccine-induced antibody response as a consequence of the splenectomy or underlying disease.

A booster dose is recommended at 3–5 years [14] or 5–10 years [15]. Pneumococcal vaccination may have other protective effects. In a cohort of Danish patients, 60% of whom were immunized against pneumococcus, the vaccination was significantly protective against all bacteremia [11], possibly because of cross-protective antibodies against Enterobacteriaceae [16].

A 7-valent pneumococcal protein conjugate vaccine has recently become available (Prenevar). It is probably more immunogenic, and does not require a booster dose. The value of measuring antipneumococcal antibodies post-immunization is unclear.

**Hib vaccine**

Although the role of *H. influenzae* type b in OPSI in the new millennium is unclear, a single dose of *H. influenzae* type b protein conjugate vaccine is thought to be immunogenic in asplenic patients, and is recommended [15].

**Meningococcal vaccine**

Meningococcal vaccine is available in three forms, a monovalent protein–polysaccharide conjugate vaccine against C strains, a polysaccharide vaccine against serogroups A and C, or a quadrivalent vaccine containing A, C, Y and W135 polysaccharides. Although the role of meningococci in OPSI is not clearly established, the increased severity of disease suggests that the vaccine should be used. With the current prevalence of serogroup C and the advantages of protein conjugate vaccines, patients in Europe should receive this vaccine. Travel to areas where other serogroups of meningococci are prevalent is an indication for revaccination with the A, C, Y, W135 vaccine.

**Influenza vaccine**

Annual influenza vaccination is also recommended for asplenic individuals [15]. All of the vaccines listed above can be given together, if necessary.

**Prophylactic Antibiotics**

In children with sickle cell disease, prophylactic penicillin conferred great protection against pneumococcal infections. Similar studies have not been carried out in splenectomized adults, and are unlikely ever to be conducted. Some guidelines advise prophylactic antibiotics for the first 3–5 years after splenectomy, but many data indicate that the risk of OPSI does not decline with time. However, long-term antibiotic therapy may be a risk factor for selection of resistant strains, and efficacy may be reduced by non-compliance. Thus the decision of whether to use prophylactic antibiotics or not depends largely on patient and physician preference. Penicillin would provide prophylaxis only against sensitive pneumococci, meningococci, and streptococci, but is suitable for adults at 500 mg daily or twice daily. Amoxicillin would be a preferred choice in children. Macrolides do not represent a suitable alternative of antibiotic resistance—for example, currently ~12% of pneumococci in UK are resistant to macrolides. In penicillin-allergic individuals, alternatives are either co-trimoxazole or a fluoroquinolone with Gram-positive activity such as moxifloxacin.

**Stand-by Antibiotics**

Whether asplenic patients receive daily prophylaxis or not, they should be given a 5-day supply of stand-by antibiotics. Logical choices for an adult would be co-amoxiclav 625 mg 8-hourly or, for those with a history of a penicillin rash, cefuroxime 250 mg 12-hourly. For patients with serious penicillin allergy, a fluoroquinolone with Gram-positive activity such as moxifloxacin could be used. Where there is a high prevalence of...
penicillin-resistant pneumococci (MIC > 1 mg/L), linezolid 600 mg 12-hourly would be suitable. Stand-by antibiotics will need to be replaced if their shelf-life expires, and patients can greatly extend the shelf-life by storing them in the household refrigerator at ~4 °C.

To ensure that they are used correctly, the antibiotics should be accompanied by clear written instructions.

‘If you become suddenly unwell with a high temperature, shivering or shaking, and feel dizzy or faint, you should immediately take a dose of your stand-by antibiotic’.

‘Contact your own doctor at once’.

‘If your own doctor is not available or there is any delay, go at once to the nearest hospital. Show this card and your antibiotics to the hospital doctors’.

(Adapted from Spickett et al. [14])

**TREATMENT OF OPSI**

OPSI is a medical emergency requiring early recognition and aggressive management. When patients present to general practitioners, the latter should, if possible, take a blood culture, immediately give parental penicillin, ceftiraxone, or similar antibiotic, and transport the patient immediately to hospital. In hospital, the patient should be resuscitated and managed in the intensive therapy unit. A combination of antibiotics should be given to cover the wide spectrum of bacteria implicated. Where moderately or highly penicillin-resistant pneumococci are prevalent, ceftiraxone plus vancomycin or teicoplanin (plus rifampicin if highly resistant pneumococci are prevalent) provide suitable initial cover. A peripheral blood or buffy coat film should be examined immediately for the presence of circulating or intraleukocytic bacteria. If Gram-negative rods are seen, cover for *Pseudomonas* should be added. The presence of intracellular bacteria or morulae within leukocytes (suggestive of chlamydiosis), and intraerythrocytic parasites (malaria or babesiosis) should be sought. Blood cultures are positive in ~95% of cases of OPSI [1,3], and antibiotics can be modified once the cultures are available. As well as intravenous antibiotics, we advise intravenous immunoglobulin 0.4 g/kg daily for 3 days: although there are no studies to show it is beneficial, there is good theoretical evidence for its use [17,18] and it is a practice endorsed by others [19].

**PATIENT INFORMATION AND AWARENESS**

As well as written advice on immunizations and stand-by antibiotics, patients should wear a medical bracelet (MedicAlert; http://www.medicalert.co.uk) or carry a laminated medical alert card [14]. This is intended to increase the awareness of patients and their doctors, to increase compliance with prophylactic and stand-by antibiotics, and to improve the speed and appropriateness of treatment for OPSI. Patients should be encouraged to obtain further information on splenectomy, e.g. http://dspace.dial.pipex.com/lrf-/diseases/index.htm.

**BITES AND WOUNDS**

Patients should be aware of the danger of OPSI following animal or human bites, or any other contaminated wound, and should take prophylactic antibiotics—co-amoxiclav is an ideal first choice.

**MALARIA**

When travelling to a malaria-endemic area, asplenic patients should take particular care to avoid mosquito bites and should take antimalarial prophylaxis with high efficacy. In this situation, doxycycline 100 mg daily would double as antibiotic and antimalarial prophylaxis. Other antimalarial regimens with high efficacy (but lacking antibiotic effect) are mefloquine 250 mg weekly and atovaquone-proguanil one tablet daily. Asplenic patients resident in malaria-endemic areas should consider taking lifelong prophylaxis against malaria.

**CONCLUSION**

The simple interventions of immunization, prophylaxis and stand-by antibiotics can be expected to reduce the frequency of OPSI and its mortality. Unfortunately, splenectomy registers are not commonly kept, and most asplenic patients do not receive appropriate advice.

**REFERENCES**


