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 Haematology Clinical Haematology Task Force

Overwhelming postsplenectomy infection should be preventable if simple precautions are taken. An ad hoc working party of the British Committee for Standards in Haematology has reviewed recommendations for patients without a spleen and drawn up a consensus. Members of the working party were selected for their personal expertise and to represent relevant professional bodies. The guidelines, which are set out below, include and extend the chief medical officer's 1994 update.

Fulminant, potentially life threatening infection is a major long term risk after splenectomy.[1,2] Splenic macrophages have an important filtering and phagocytic role in removing bacteria and parasitised red blood cells from the circulation.[3] Though the liver can perform this function in the absence of a spleen, higher levels of specific antibody[4] and an intact complement system are probably required. The ability of an asplenic patient to mount an adequate protective antibody response may relate more to the indication for or age at splenectomy and to the presence of underlying immune suppression than to the absence of the spleen.

This paper presents the conclusions of an ad hoc working party of the British Committee for Standards in Haematology on procedures for managing patients without a spleen. In accordance with guidance on best practice[5,6] the guidelines are based on an assessment of published evidence and the expert opinion of the working party.

Methods

Assessment of published evidence—The CD-ROM databases Silver Platter Medline (1966-95) and Excerpta Medica (1974-95) were searched by using the keywords infection, splenectomy, asplenia, and hyposplenism. Abstracts in English (of English and non-English articles) were reviewed. In addition, bibliographies of previous reviews and papers describing original research were cross checked.

Guideline development group—In view of the potential bias in guideline development by small groups[7] a national working group representative of key disciplines was convened under the auspices of the British Committee for Standards in Haematology. The working group members were from general practice, haematology, immunology, microbiology, paediatrics, surgery, and public health medicine. The formal consensus of the guideline development group was integrated with the findings of systematic review of published evidence to formulate the ensuing recommendations.

Background

INFECTING MICROORGANISMS

Most instances of serious infection are due to encapsulated bacteria such as *Streptococcus pneumoniae* (pneumococcus), *Haemophilus influenzae* type b, and *Neisseria meningitidis* (meningococcus).[8] Pneumococcal infection is most common and carries a mortality of up to 60%.[9,10] Infection with *H influenzae* type b is much less common but none the less significant, particularly in children.[11] The meningococcus may also be associated with serious infection.[12] Other infections include *Escherichia coli*,[13] malaria,[14] babesiosis,[15] and *Capnocytophaga canimorsus* (DF-2 bacillus), which is associated with dog bites.[16]

PATIENT CATEGORIES

Operative splenectomy

Surgical removal of the spleen is performed for severe splenic trauma, for splenic cysts, or as part of a resective procedure for tumours of the spleen or adjacent organs.[17] Partial splenectomy with retention of some splenic tissue is increasingly practised.[18] However, in view of the uncertainty of the level of splenic function achieved by partial splenectomy or autotransplantation of splenic tissue it is prudent to institute similar measures to prevent infection in these patients as for asplenic subjects.

Though there has been a reduction in the use of splenectomy for staging haematological malignancies such as Hodgkin's disease, the procedure may still be used in hereditary spherocytosis, immune thrombocytopenic purpura, and autoimmune haemolytic anaemia. Patients receiving immunosuppressive chemotherapy or radiotherapy or both are at greatest risk of serious infection after splenectomy.[19]

Functional hyposplenism

Functional hyposplenism may be detected on a blood film as red cells containing Heinz and Howell-Jolly bodies, thrombocytosis, and monocytosis.[20] Splenic dysfunction may occur secondary to sickle cell anaemia (HbSS, HbSC), thalassaemia major, essential thrombocythaemia, and lymphoproliferative diseases (Hodgkin's disease, non-Hodgkin's lymphoma, and chronic lymphocytic leukaemia). Functional hyposplenism may also occur in coeliac disease,[21] inflammatory bowel disease,[22] and dermatitis herpetiformis.[23]

Bone marrow transplantation is a further cause of functional hyposplenism, leading to an increased incidence of pneumococcal bacteraemia[24] and *H influenzae* type b pneumonia.[24] Though most studies have shown an association of infections with chronic graft versus host disease,[25] in some patients there is also impaired splenic function, with Howell-Jolly bodies.[25,26] Infections occur six months after bone marrow transplantation, after co-trimoxazole prophylaxis against pneumocystis pneumonia has been stopped.[26] More detailed recommendations for managing patients receiving bone marrow transplantation have been given by Fielding.[27] All patients having bone marrow transplantation should be immunised against pneumococcal infection 9-12 months after transplantation, and those with chronic graft versus host disease should receive appropriate long term prophylactic antibiotics, especially if the spleen has been removed or irradiated before transplantation.

Congenital asplenia

Congenital asplenia is associated with cardiac abnormalities and biliary atresia.[28]

Working Party of the British Committee for Standards in Haematology Clinical Haematology Task Force Members are listed at the end of this report.

Correspondence to: Dr I Cavill, Honorary Secretary, British Committee for Standards in Haematology, 2 Carlton House Terrace, London SW1Y 5AF.

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Effect of age

Asplenic children under 5—and especially infants splenectomised for trauma—have an infection rate of over 10%, much higher than in adults (<1%).[29] Children with sickle cell anaemia (HbSS, HbSC) are at especially high risk of overwhelming infection.[30]

Other groups of patients may for other reasons be considered at risk of infection with encapsulated organisms—for example, patients with chronic lymphocytic leukaemia or myeloma[31] and patients with HIV related disease or other immunodeficiency states. Local or national guidelines for the prevention of infection in these groups should be consulted.[32]

DURATION OF RISK

Though most infections occur within the first two years after 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.[33] The risk of dying of serious infection, though unquantifiable,[34] is clinically significant and almost certainly lifelong.

Patients falling into all the above categories, once identified, should receive appropriate vaccination and advice about lifelong antibiotic prophylaxis.

Guidelines

The chief medical officer has highlighted the importance of preventive measures for postsplenectomy sepsis.[35]

IMMUNISATIONS

Asplenia in itself is not a contraindication to routine immunisation. Normal inoculations, including live vaccines, can be given safely to children and adults with absent or dysfunctional spleens.

Pneumococcal immunisation

Current vaccine—The currently available polyvalent pneumococcal vaccine contains purified capsular polysaccharide from the 23 most prevalent serotypes.[36] The vaccine is more than 90% effective in healthy adults under the age of 55.[37] Once vaccinated, failure of protection may relate to waning specific antibody levels or be due to infection with serotypes not represented in the vaccine. Children under 2 years of age have inherently reduced ability to mount an antibody response to polysaccharide antigens. However, pneumococcal vaccine may have some (if reduced) efficacy for particular serotypes. The same considerations apply to other patients who have functional hyposplenism because of an underlying disorder.[38] The vaccine is best avoided in pregnancy.[39]

Timing—The vaccine should be given a minimum of two weeks before elective splenectomy in order to ensure an optimal antibody response. If this is not practicable the patient should be immunised as soon as possible after recovery from the operation and before discharge from hospital. The general practitioner should be notified of the splenectomy and vaccinations given in order to avoid potential reactions due to premature reimmunisation. Unimmunised patients splenectomised some time earlier should be immunised at the first opportunity. Immunisation, however, should be delayed at least six months after immunosuppressive chemotherapy or radiotherapy, during which time prophylactic antibiotics should be given. Hyposplenic patients should be immunised as soon as the diagnosis is made, though because of the reduced efficacy in young children[40] it may be better to rely initially on prophylactic antibiotics and immunise after the second birthday.

Reimmunisation of asplenic patients is currently recommended every 5-10 years.[40] It may be necessary to revaccinate more frequently, particularly if there is an underlying disease causing immunosuppression. Antibody levels may decline more rapidly than expected in asplenic patients[41] and reimmunisation may be required as early as three years after the first dose, especially in lymphoproliferative disorders or sickle cell anaemia.[42]

Adverse reactions—Side effects of immunisation are usually self limiting hypersensitivity, with pain and swelling at the site of the injection after 24 hours. Much less commonly fever, malaise, and generalised aches disappearing after 48-72 hours may occur. Occasional patients with chronic immune thrombocytopenic purpura may have a relapse of their thrombocytopenia after immunisation.[43]

H influenzae type b immunisation

Most children in Britain up to 4 years of age will have received *H influenzae* type b vaccine. Over 18 years most patients will have acquired some immunity through natural exposure but this may not provide adequate protection in the context of an absent or dysfunctional spleen. The vaccine has been shown to be immunogenic in patients with impaired splenic function associated with sickle cell anaemia.[44] The level of antibodies to *H influenzae* type b required for protection is known for people with an intact spleen. There is evidence that a higher specific antibody level is required in patients lacking a spleen.[44] The need for reimmunisation is unclear.

Meningococcal immunisation

In Britain meningococcal infection is most commonly due to a group B strain.[45] The present meningococcal vaccine covers groups A and C, which occur more commonly abroad. As the protection conferred with the current vaccine is of short duration, meningococcal immunisation is not routinely recommended for asplenic patients except when travelling to areas where there is an increased risk of group A infection. Otherwise the vaccine should be restricted to groups for whom it is already specifically recommended—that is, close contacts of cases due to group A or C disease and outbreaks in closed or semiclosed institutions.[39] Reimmunisation should be considered after two years in those remaining at risk, especially children. A forthcoming conjugated vaccine should provide longer lasting immunity.

Influenza immunisation

Influenza vaccine is recommended yearly for patients with "immunosuppression due to disease or treatment"[46] and may be of value to asplenic patients by reducing the risk of secondary bacterial infection.

ANTIBIOTIC PROPHYLAXIS

Prophylactic oral phenoxymethylpenicillin has been used effectively for years in children with sickle cell anaemia.[47] Though amoxycillin has been recommended more recently,[48] this drug may be less well tolerated in young children and is more expensive. The advantages of amoxycillin over penicillin in adults are that it is better absorbed as an oral preparation and it has a broader spectrum and a longer shelf life.[49] Patients who are allergic to penicillin should be offered erythromycin (see appendix).

Lifelong prophylactic antibiotics should be offered in all cases, especially in the first two years after splenectomy, for all children aged up to 16,[30] and when there is underlying impaired immune function.[50] In addition, for patients not allergic to penicillin a supply of amoxycillin should be kept at home (and taken on holiday) and used immediately should infective symptoms of raised temperature, malaise, or shivering develop. In such a situation the patient

should seek immediate medical help. In the event of a feverish illness patients taking erythromycin as prophylaxis should increase the dose to a therapeutic level or change to an alternative broader spectrum preparation and seek medical advice immediately.

Antibiotic prophylaxis may not prevent sepsis. Indeed, phenoxymethylpenicillin does not cover *H influenzae* and neither does amoxycillin reliably. The emergence of antibiotic resistant bacterial strains[51] must be considered if empirical treatment of sick patients is to be used. Local resistance patterns may dictate the need to use other antibiotics.

RECOMMENDATIONS FOR TRAVELLERS

Asplenic patients should be strongly advised of the increased risk of severe falciparum malaria. Scrupulous adherence to antimalarial prophylaxis cannot be overemphasised, and specialist advice from an infectious disease or tropical disease unit or the local consultant in communicable disease control should be sought. Meningococcal A plus C vaccine is recommended for all those travelling to sub-Saharan Africa, India, and Nepal.[27]

Patients who are not otherwise taking antibiotic prophylaxis should do so during periods of travel[52] and should keep a therapeutic course of antibiotics with them for the duration of the holiday, taking into account resistance patterns such as the high incidence of penicillin resistant pneumococci in Spain and some other European countries.

OTHER MEASURES

It is essential to educate patients regarding the risk and the importance of prompt recognition and treatment of infections. Asplenic patients should be encouraged to wear a Medic-Alert disc (Medic-Alert Foundation (a registered charity), 156 Caledonian Road, London N1 9UU) and carry a card with information about their lack of a spleen, other clinical details, and contact telephone numbers. In an emergency this information may be life saving. An information leaflet and patient card about splenectomy are available from the Department of Health (HMSO, Oldham Broadway Business Park, Broadgate, Chadderton, Oldham OL9 0JA).

Environmental—Protective clothing and washing after potential exposure in endemic areas for histoplasmosis, babesiosis, and malaria may be beneficial.

Animal bites—Ensure adequate antibiotic cover after dog (and other animal) bites, as asplenic patients are particularly susceptible to infection by *C canimorsus* (DF-2 bacillus) and should receive a five day course of co-amoxiclav (erythromycin in allergic patients).

Tick bites—Babesiosis is a rare tickborne infection, and patients (especially those in contact with animals) should be warned of the danger of tick bites transmitting the disease. Clinical presentation is with fever, fatigue, and haemolytic anaemia. Diagnosis is made by identifying parasites within red cells on blood films and by specific serology. Quinine (with or without clindamycin) is usually effective treatment.[53]

Mosquito bites—Travel to areas where malaria is endemic should be discouraged. Patients should be made aware of their increased risk and advised about chemoprophylaxis relevant to local patterns of resistance and measures to reduce exposure to malaria parasites.

Treatment of acute infection

In suspected pneumococcal, meningococcal, or other serious infection immediate medical attention is required. Primary care physicians attending a known asplenic patient with clinically significant infection should (provided there is no history of penicillin allergy) give an immediate dose of intramuscular or intravenous benzylpenicillin before transfer to hospital. The intravenous route is preferable. For adults and children over 10, 1200 mg (2 MU) benzylpenicillin should be dissolved in 10 ml water for injection and injected over three to four minutes. A blood sample can be taken for culture immediately before giving the penicillin but the injection should not be delayed if facilities are not immediately to hand.

Once the patient has been admitted to hospital blood samples should be taken and intravenous benzylpenicillin continued—but for patients who have been receiving antibiotic prophylaxis, patients allergic to penicillin, patients with possibly resistant organisms, and children under 5 cefotaxime or ceftriaxone should be given instead. Patients allergic to penicillin who are also allergic to cephalosporins may be given chloramphenicol after taking expert advice (appendix).

Key guidelines

- All splenectomised patients and those with functional hyposplenism should receive pneumococcal immunisation *(A, B)*
- Documentation, communication, and re-immunisation require attention *(A, B)*
- Patients not previously immunised should receive *Haemophilus influenzae* type b vaccine *(A, B)*
- Meningococcal immunisation is not routinely recommended *(B)*
- Influenza immunisation may be beneficial *(B)*
- Lifelong prophylactic antibiotics are recommended (oral phenoxymethylpenicillin or an alternative) *(A, B)*
- Asplenic patients are at risk of severe malaria *(A)*
- Animal and tick bites may be dangerous *(A)*
- Patients should be given a leaflet and a card to alert health professionals to their risk of overwhelming infection *(A, B)*
- Patients developing infection despite measures must be given a systemic antibiotic and urgently admitted to hospital *(A, B)*

A=Based on published evidence.

B=Expert opinion.

NB: There are no randomised controlled trials or case controlled studies on this issue.

Report redrafted by Dr J Sarangi (senior registrar in public health medicine, Avon Health) and Dr J G Smith (consultant haematologist, Royal United Hospital, Bath).

Working party members: P G Baddeley (general practitioner, Beacon Medical Practice, Stroud (representing the Royal College of General Practitioners)); R A Barnes (senior lecturer in microbiology, University of Wales College of Medicine); A H R Finn (senior lecturer in paediatrics, Sheffield Children's Hospital (representing the British Paediatric Association)); I M Hann (consultant haematologist, Hospital for Sick Children, Great Ormond Street, London); S J Kelly (consultant haematologist, Wycombe General Hospital); J Leese (senior medical officer, Department of Health, London (observer)); J E Lortan (senior lecturer in immunology, St Mary's Hospital Medical School, London); J Spencer (consultant surgeon, Hammersmith Hospital, London (representing the Royal College of Surgeons)); G P Summerfield (consultant haematologist, Middlesbrough General Hospital (secretary)); J A Whittaker (consultant haematologist, University Hospital of Wales, Cardiff (chairman)).

Appendix

Dosing regimens for antibiotic prophylaxis and treatment

Antibiotic	Oral prophylaxis	Treatment for suspected infection†
Penicillin		
Adult	250-500 mg 12 hourly‡§	1·2 g 4-6 hourly‖
Child aged 5-14 years	250 mg 12 hourly§	200-300 mg/kg per day in six
Child under 5 years¶	125 mg 12 hourly§	divided doses (maximum 6 g)‖
Erythromycin (base)		
Adult+child over 8 years	250-500 mg daily	0·5-1·0 g 6 hourly by mouth or intravenously by
Child aged 2-8 years	250 mg daily	250 mg 6 hourly by mouth 12·5 mg/kg/day intravenously by infusion in four divided doses
Child under 2 years	125 mg daily	12·5 mg/kg/day by mouth or intravenously by infusion in four divided doses
Amoxycillin/co-amoxiclav (doses according to amoxycillin content)		
Adult	250-500 mg daily	0·5-1·0 g 8 hourly by mouth or intravenously
Child aged 5-14 years	125 mg daily	250 mg 8 hourly by mouth 90 mg/kg/day intravenously in three divided doses
Child aged 1-5 years	10 mg/kg/day	125mg 8 hourly by mouth 90 mg/kg/day intravenously in three divided doses
Child under 1 year	10 mg/kg/day	62·5mg 8 hourly by mouth 90 mg/kg/day intravenously in three divided doses
Cefotaxime		
Adult	Not suitable	2 g 8 hourly intravenously
Child under 14 years	Not suitable	100 mg/kg/day intravenously in three divided doses (maximum 12 g)
Ceftriaxone		
Adult	Not suitable	1-2 g once daily intravenously
Child under 14 years	Not suitable	80 mg/kg/day intravenously in a single dose (maximum 4 g)
Chloramphenicol (only patients allergic to penicillins and cephalosporins)		
All patients	Not suitable	Expert advice

†Established infection may require much higher doses given in hospital.
‡If compliance is a problem 500 mg once daily is acceptable.
§Phenoxymethylpenicillin (oral).
‖Benzylpenicillin (intravenous).
¶Seek expert advice for neonatal doses.

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Lesson of the Week

Wernicke's encephalopathy after vertical banded gastroplasty for morbid obesity

H Seehra, N MacDermott, R G Lascelles, T V Taylor

Nutritional supplementation after surgery for morbid obesity is essential to prevent neurological sequelae

Thiamine deficiency is known to lead to certain neurological sequelae including Wernicke-Korsakoff encephalopathy. Signs attributable to this condition include ataxia, ophthalmoplegia, nystagmus, and mental confusion. Recognised predisposing conditions include alcoholism, gastric carcinoma, pyloric obstruction, hyperemesis gravidarum, and prolonged intravenous feeding.[1] We have recently encountered two cases of Wernicke's encephalopathy after vertical banded gastroplasty for morbid obesity. Other neurological sequelae are recognised after vertical banded gastroplasty, including Guillain-Barré syndrome, psychosis, and pseudoathetosis, but the causes of these are multifactorial.[2]

Case reports

CASE 1

A 55 year old women weighing 171·4 kg underwent a vertical banded gastroplasty on 16 March 1992. Her medical history included treated hypothyroidism, psoriasis, and mild, late onset asthma. After surgery she lost about 25 kg within six weeks and was tolerating a semiliquid diet. Two months after the procedure, however, she developed frequent vomiting of both solids and liquids. Gastroscopy showed a normal gastric outlet with no evidence of stasis; endoscopic dilatation of the pouch was performed. There was a little improvement, but she became clinically depressed. Four months after vertical banded gastroplasty she developed features of disorientation, ataxia of gait, and blurring of vision with diplopia. Detailed examination showed, in addition, severe vertical and horizontal nystagmus and depression of the deep tendon reflexes. These findings were consistent with a Wernicke's encephalopathy and responded rapidly to intravenous vitamin supplementation.

CASE 2

A 40 year old women weighing 97·4 kg underwent a vertical banded gastroplasty for morbid obesity in July 1986. She had an undue amount of postoperative vomiting, and at three month follow up the vomiting had persisted and she had lost 30 kg. Subsequent gastroscopy showed pouch outlet stenosis and a degree of oesophagitis. A further laparotomy was performed which showed ulceration in relation to the band, which was removed. About five months after surgery, after initially satisfactory postoperative progress, she became confused, disorientated, and developed incoordination. She was also found to have a complete horizontal conjugate gaze palsy and nystagmus, which in the context of the clinical setting suggested a diagnosis of Wernicke's encephalopathy. Computed tomography and examination of the cerebrospinal fluid showed nothing abnormal. The clinical signs responded to intravenous parenterovite.

Discussion

Gastric partitioning surgery can lead to a state of starvation: "starvation in the midst of plenty"[3] that can lead to serious protein-calorie and vitamin deficiency that may in turn cause serious neurological, as well as other, sequelae. Since increasing numbers of people are undergoing surgery for morbid obesity—typically, vertical banded gastroplasty—we are likely to see significantly more neurological complications, such as Wernicke's encephalopathy, which occurs as a result of thiamine deficiency and can be prevented by supplementation. Starvation is a complex process and we should not merely assume that replacing one vitamin is adequate. All patients should be given multivitamin and mineral supplements after gastroplasty. If repeated vomiting occurs nutritional assessment and a treatment regimen should be instigated. Treatment of vomiting necessitates intravenous glucose, which may increase the demand for thiamine.

Some authors have suggested that Wernicke's encephalopathy may be preventable by giving enteral[4] or parenteral nutrition[5] immediately after the gastroplasty, to ensure adequate thiamine supplementation. We would endorse this view and further emphasise the importance of all patients taking multivitamin supplements after vertical banded gastroplasty.

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Department of Surgery, Manchester Royal Infirmary, Manchester M13 9WL
H Seehra, *research registrar*
T V Taylor, *reader*

Department of Neurology, Manchester Royal Infirmary, Manchester M13 9WL
N MacDermott, *senior registrar*
R G Lascelles, *consultant*

Correspondence to:
Mr Seehra.

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