

Update of guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen

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Clin Med JRCPL
2002;2:440-3

These guidelines were prepared on behalf of the British Committee for Standards in Haematology (BCSH) by a Working Party of the Haematology/Oncology Task Force.

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ABSTRACT – Guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen were first published by the British Committee for Standards in Haematology in 1996. Key aspects of these guidelines related to anti-infective prophylaxis, immunisation schedules and treatment of proven or suspected infection. A recent review of the guidelines was undertaken, with a view to updating the recommendations where necessary.

The guideline review process did not reveal any major change in patient groups considered at risk. Occupational exposure to certain pathogens may, however, be a new risk factor for some infections. The recommendations for anti-infective prophylaxis remain unchanged. New recommendations

for vaccination include the use of meningococcal group C vaccine in previously non-immunised hyposplenic patients and a need to consider the use of seven-valent pneumococcal vaccine. Recommendations for treatment of suspected or proven infection have not been significantly amended, but a local protocol should take into account relevant resistance patterns. There is an identified urgent need for further research into the effectiveness of varying vaccination strategies in the hyposplenic patient, and audit of infective episodes in this patient group should continue long term. Key guidelines are summarised below, together with grades of recommendation.

Key guidelines

- 1 All splenectomised patients and those with functional hyposplenism should receive pneumococcal immunisation. Patients not previously immunised should receive haemophilus influenza type B vaccine (B,C). Patients not previously immunised should receive meningococcal group C conjugate vaccine (C). Influenza immunisation should be given (C). Lifelong prophylactic antibiotics are still recommended (oral phenoxymethylpenicillin or erythromycin) (B,C).
- 2 Patients developing infection despite measures must be given systemic antibiotics and admitted urgently to hospital (B,C).
- 3 Patients should be given written information and carry a card to alert health professionals to the risk of overwhelming infection. Patients may wish to invest in an alert bracelet or pendant (C).
- 4 Patients should be educated about the potential risks of overseas travel, particularly with regard to malaria and unusual infections, for example those resulting from animal bites (B,C).
- 5 Patient records should be clearly labelled to indicate the underlying risk of infection. Vaccination and revaccination status should be clearly and adequately documented (C).

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Grades of recommendations

- A Requires at least one randomised controlled trial (RCT) as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
- B Requires the availability of well conducted clinical studies, but no RCTs on the topic of recommendation.
- C Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality.

These grades of recommendations, which have now been widely adopted, originate from the US Agency for Health Care Policy and Research.

Background

Overwhelming post-splenectomy infection remains an area of concern. The previous British Committee for Standards in Haematology guidelines on the prevention and treatment of infection in patients with an absent or dysfunctional spleen were published in 1996¹. Since then, significant changes, particularly in vaccine technology, have prompted a review of the recommendations. A reconvened guideline group chose to focus on areas of actual or potential change in clinical management.

Methods

The databases, Medline (1996–2001), BIDS Embase (1996–2001) and the current Cochrane Library CD-ROM, were searched using the original key words: infection, splenectomy, asplenia and hyposplenism. Relevant identified abstracts were reviewed and cross-checked.

At risk groups

No major change was identified in the patient categories at risk of infection. The effect of age and duration of risk appeared similar to that previously reported. There may be an additional risk, at present not quantifiable, to splenectomised individuals in terms of occupational exposure to certain pathogens². In the absence of firm data on which to base recommendations, it would seem reasonable to ask both employer and employees to consider carefully the implications of exposure to potentially infective biological material.

Immunisation

There is no new evidence to suggest that normal inoculations, including live vaccines, cannot be given safely to children or adults with an absent or dysfunctional spleen. Key recommendations for vaccination schedules in hyposplenic individuals are summarised in Table 1.

Pneumococcal immunisation

The currently available polyvalent pneumococcal vaccine provides a high degree of immunity in normal subjects. There are well documented failures of protection in hyposplenic individuals, although the mechanism underlying this failure is not entirely clear. Some patients remain unvaccinated despite appropriate efforts, while true vaccine failures may also contribute to pneumococcal infection after splenectomy³.

Education of both staff and patients about the risks of post-splenectomy sepsis should continue; the establishment of 'at risk registries' may help in this regard. Patients and their relatives should be aware that breakthrough pneumococcal

Table 1. Key recommendations for immunisation in hyposplenic individuals.

Vaccine	Timing	Revaccination schedule	Comments
Pneumococcal vaccine polyvalent	Administer at least 2 weeks pre-splenectomy if possible or 2 weeks post-splenectomy	5 years	Immunity may decline rapidly in certain patient groups Monitoring of antibody levels may be useful
Pneumococcal vaccine conjugate	Not known	Not known	May complement polyvalent vaccine in the near future
Haemophilus influenza B conjugate	Administer at least 2 weeks pre-splenectomy if possible or 2 weeks post-splenectomy	Not currently recommended	Use in previously unvaccinated individuals
Meningococcal C vaccine conjugate	Administer at least 2 weeks pre-splenectomy if possible or 2 weeks post-splenectomy	See text	Use only in unimmunised individuals
Meningococcal A & C polyvalent	Administer at least 2 weeks pre-splenectomy if possible or 2 weeks post-splenectomy	See text	Recommended only for short-term protection for at risk individuals undertaking overseas travel
Influenza vaccine	Administer as soon as practicable pre- or post-splenectomy to afford seasonal protection	Yearly	

infection may occur, despite pneumococcal vaccine and prophylactic antibiotics^{4,5}.

Children under two years of age have an inherently reduced ability to mount an antibody response to polysaccharide antigens, and are therefore at particular risk of vaccine failure. If splenectomy is unavoidable in this age group, a conjugate vaccine (see below) provides a more reliable serological response.

New pneumococcal vaccines. A seven-valent conjugate pneumococcal vaccine has recently completed clinical studies (reviewed by Giebink⁶). Early data suggest that this new vaccine is more immunogenic but has a more limited repertoire in terms of serotypes⁷. The seven-valent vaccine may have a future role in primary immunisation of asplenic or hyposplenic patients in tandem with the currently available vaccine. However, no data specifically related to either of these groups of patients are currently available to support this approach.

Timing of pneumococcal vaccination. The current pneumococcal vaccine should be given at least two weeks before splenectomy. Following splenectomy, post-vaccination immunoglobulin G serum antibody concentrations to pneumococcal antigens do not differ significantly from normal control subjects, whether vaccination is undertaken immediately or 14 days after splenectomy. Functional antibody responses are, however, better with delayed (14 day) vaccination⁸.

All other non-immunised patients at risk should be immunised at the first opportunity. In general, immunisation should be delayed for at least three months after immunosuppressive chemotherapy or radiotherapy.

Re-immunisation of asplenic patients is currently recommended every five years⁹. However, it is known that antibody levels may decline more rapidly, particularly in patients with sickle-cell anaemia and lymphoproliferative disorders. Decisions on re-immunisation in these particular circumstances may be made on the basis of antibody levels.

Haemophilus influenzae type B immunisation

There are no new data to support a change in the recommendations given in the original guideline for haemophilus influenzae type B immunisation. Patients not previously immunised should therefore receive haemophilus influenzae type B vaccine. There are currently no data to support routine re-immunisation.

Meningococcal immunisation

Background. In the UK there has been a shift in the strains responsible for meningococcal infection. Group A strains remain rare in the UK, accounting for less than 2% of clinical infections, but they are epidemic in other areas of the world. Group B strains now account for about 60% of all isolates, while there has been an increase in Group C strains, which now contribute about 40% of the total. Overall mortality from meningococcal infection remains significant, at around 10%.

Meningococcal C conjugate vaccine. Immunisation with meningococcal C conjugate vaccine is now part of the routine childhood immunisation programme in the UK. The conjugate vaccine is immunogenic, even in children under two years of age, and is likely to provide long-term immunological memory. There are no data specific to hyposplenic individuals. However, the administration of three doses to infants and two doses to previously non-immunised children between four months and twelve months of age would seem appropriate.

In previously non-immunised older children and adults a single dose of conjugate vaccine is recommended in normal individuals. By extrapolation, this should afford protection in asplenic or hyposplenic patients. This recommendation is the subject of current review and booster doses may be introduced in the future.

The conjugate vaccine is likely to support long-standing protection against Group C meningococcal disease, in a similar way to the conjugate haemophilus influenzae B vaccine. It is therefore recommended that routine meningococcal immunisation be given before splenectomy and for previously non-immunised hyposplenic individuals. Travellers abroad should, in addition, receive a meningococcal vaccine which protects against Group A infections. There appears to be no contraindication to the administration of meningococcal plain polysaccharide A and C vaccine to subjects who have previously received meningococcal C conjugate vaccine.

Conversely, protection afforded by plain polysaccharide A and C vaccine is short-lived. Immunisation with meningococcal C conjugate vaccine is therefore recommended for hyposplenic individuals who have previously received the plain polysaccharide A and C vaccine. Highly satisfactory serological responses are demonstrable if there is a six-month interval between administration of the plain polysaccharide A and C vaccine and subsequent re-immunisation with meningococcal C conjugate vaccine¹⁰.

Influenza vaccination

Influenza vaccine continues to be recommended yearly for asplenic or hyposplenic patients⁹.

Antibiotic prophylaxis and treatment

There are no data to support or refute the previously published recommendations for antibiotic prophylaxis and treatment of infection in asplenic individuals. It is accepted, however, that compliance may be a problem with lifelong oral antibiotic prophylaxis¹¹. Overall, pneumococcal resistance to penicillins remains low in the UK. Knowledge of local resistance patterns may be used to guide the choice of chemoprophylactic agents.

Research and audit

There is an unmet need for a prospective assessment of serological response to vaccination in asplenic or hyposplenic patients, particularly those immunised with the more recently available

vaccines. Such information, if available, would be invaluable in guiding future vaccination strategies.

Regular audit, quite properly, continues to be undertaken in this area¹². Readily auditable areas include vaccination rates, adherence to antibiotic prophylaxis and the current outcome of severe infection in asplenic or hyposplenic patients.

Conclusion

Infection in patients with an absent or dysfunctional spleen remains largely preventable. Preventive strategies continue to be based on education of staff and patients, appropriate immunisation schedules and chemoprophylaxis.

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