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Guideline up-date

UPDATE OF GUIDELINES FOR THE PREVENTION AND TREATMENT OF INFECTION IN PATIENTS WITH AN ABSENT OR DYSFUNCTIONAL SPLEEN

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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 the 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 certain infections. The recommendations for anti-infective prophylaxis remain unchanged. New recommendations for vaccination include the use of Meningococcal C vaccine in previously not 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.

KEY GUIDELINES

1. All splenectomised patients and those with functional hyposplenism should receive pneumococcal immunisation and 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). Life long 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 as to the potential risks of overseas travel, particularly with regards 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 re-vaccination status should be clearly and adequately documented (C).

GRADES OF RECOMMENDATIONS

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

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

INTRODUCTION

Overwhelming post splenectomy infection remains an area of concern. The previous BCSH guideline on the prevention and treatment of infection in patients with an absent or dysfunctional spleen was published in 1996¹ and 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, rather than re-format the original guideline in its entirety. With this remit the group identified two key areas for consideration, that is immunisation and antibiotic prophylaxis and treatment.

Methods

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

At Risk Groups

No major alteration in the patient categories at risk of infection were identified. The effect of age and duration of risk appeared similar to that previously reported, with a broad spectrum of infecting micro-organisms remaining responsible for serious infections. There may be an additional risk to splenectomised individuals, in terms of occupational exposure to certain pathogens.² This additional risk is at present not quantifiable. However, 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. Despite appropriate efforts some patients remain unvaccinated, while true vaccine failures may also contribute to pneumococcal infection post splenectomy.³

Education of both staff and patients as to the risks of post splenectomy sepsis should continue and the establishment of "At Risk Registries" may help in this regard. Patients and their relatives should be aware

that despite pneumococcal vaccine and prophylactic antibiotics, breakthrough pneumococcal infection may occur.^{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. Where splenectomy is unavoidable under the age of 2 years then a conjugate vaccine (see below) provides a more reliable serological response.

New Pneumococcal Vaccines

A seven valent conjugate vaccine has recently completed clinical studies (reviewed by Giebink)⁶. Early data suggests that the new conjugate vaccine is more immunogenic but has a more limited repertoire, in terms of sero-types.⁷ The seven valent vaccine may have a future role in primary immunisation of hypo or asplenic patients in tandem with the currently available vaccine, however, no data specifically related to asplenic or hyposplenic patients is currently available to support this approach.

Timing of 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 at 14 days post splenectomy. Functional antibody responses are, however, better with delayed (14 day) vaccination.⁸

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

Re-immunisation of asplenic patients is currently recommended every 5 years.⁹ 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 Influenza Type B Immunisation

There is no new data to support an alteration in the recommendations given in the original guideline. Patients not previously immunised should, therefore, receive Haemophilus Influenza type b vaccine. There is no data to support routine re-immunisation at the present time.

Meningococcal Immunisation

Background

In the United Kingdom there has been a shift in the strains responsible for meningococcal infection. Group A strains remain rare and account for less than 2% of clinical infections. However, Group A strains are epidemic in other areas of the world. Group B strains now account for 60% of all isolates, while there has been an increase in Group C strains, which now contribute 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 is 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 and by extra-polation should afford protection in hyposplenic or asplenic 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 Influenza B vaccine. It is, therefore, recommended that routine Meningococcal immunisation be given pre-splenectomy and for hyposplenic previously non-immunised individuals. Travellers abroad should, in addition, receive a Meningococcal vaccine which protects against Group A infections. There appears to be no contra-indication 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. The immunisation of hyposplenic individuals who have previously received the plain polysaccharide A and C vaccine with Meningococcal C conjugate vaccine is, therefore, recommended. Highly satisfactory serological responses are demonstrable if six months is allowed between administration of the plain polysaccharide A and C vaccine and subsequent re-immunisation with Meningococcal C conjugate vaccine.¹⁰

Influenza Vaccination

Influenza vaccine continues to be recommended yearly for hypo or asplenic patients.⁹

Antibiotic Prophylaxis and Treatment

There are no data to support or refute the previously published recommendations, as regards antibiotic prophylaxis and treatment of infection in asplenic individuals. It is accepted, however, that compliance may be a problem with life long oral antibiotic prophylaxis.¹¹ Overall pneumococcal resistance to penicillins remains low in the United Kingdom. However, 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 hyposplenic or asplenic 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. Preventative strategies continue to be based on education of staff and patients, appropriate immunisation schedules and chemoprophylaxis.

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Table 1.**KEY POINTS - IMMUNISATION IN HYPOSPLENIC INDIVIDUALS**

	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 Meningoccal C conjugate vaccine 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	