POST-SPLENECTOMY VACCINE PROPHYLAXIS

SUMMARY
The splenectomized patient should be vaccinated to decrease the risk of overwhelming postsplenectomy sepsis (OPSS) due to organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and *Neisseria meningitidis*. Patients should be educated prior to discharge on the risk of OPSS and their immunocompromised state. An understanding of the need for prompt medical attention should be instilled in such patients to reduce the morbidity and mortality of postsplenectomy infection.

RECOMMENDATIONS

- **Level 1**
  - None

- **Level 2**
  - Non-elective splenectomy patients should be vaccinated on or after postoperative day 14.
  - Asplenic patients should be revaccinated at the appropriate time interval for each vaccine.

- **Level 3**
  - Elective splenectomy patients should be vaccinated at least 14 days prior to the operation.
  - Asplenic or immunocompromised patients (with an intact, but nonfunctional spleen) should be vaccinated as soon as the diagnosis is made.
  - Pediatric vaccination should be performed according to the recommended pediatric dosage and vaccine types with special consideration made for children less than 2 years of age.
  - When adult vaccination is indicated, the following vaccinations should be administered:
    - *Streptococcus pneumoniae*
      - Polyvalent pneumococcal vaccine (Pneumovax 23)
    - *Haemophilus influenzae* type B
      - *Haemophilus influenzae* b vaccine (HibTITER)
    - *Neisseria meningitidis*
      - Age 16-55: Meningococcal (groups A, C, Y, W-135) polysaccharide diphtheria toxoid conjugate vaccine (Menactra)
      - Age >55: Meningococcal polysaccharide vaccine (Menomune-A/C/Y/W-135)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose</th>
<th>Route</th>
<th>Revaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyvalent pneumococcal</td>
<td>0.5 mL</td>
<td>SC*</td>
<td>Every 6 years</td>
</tr>
<tr>
<td>Quadravalent meningococcal/diphtheria conjugate</td>
<td>0.5 mL</td>
<td>IM upper deltoid</td>
<td>Every 3-5 years†</td>
</tr>
<tr>
<td>Quadravalent meningococcal polysaccharide</td>
<td>0.5 mL</td>
<td>SC*</td>
<td>Every 3-5 years</td>
</tr>
<tr>
<td>Haemophilus b conjugate</td>
<td>0.5 mL</td>
<td>IM*</td>
<td>None</td>
</tr>
</tbody>
</table>

*Administered in the deltoid or lateral thigh region.
†Contact the manufacturer for the latest recommendations prior to revaccination.

EVIDENCE DEFINITIONS
- **Class I**: Prospective randomized controlled trial.
- **Class II**: Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III**: Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment**: A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS
- **Level 1**: Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2**: Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3**: Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.
INTRODUCTION
Blunt abdominal trauma commonly injures the spleen resulting in either irreparable parenchymal disruption (necessitating removal of the injured organ) or devascularization of varying degrees. Non-operative management may avoid splenectomy, but can also result in functional asplenia if the devascularization is extensive or therapeutic embolization of a portion or all of the spleen is required. Elective splenectomy may be indicated for specific primary disease of the spleen. Loss of functional splenic tissue places such individuals at high risk for infection by encapsulated organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and *Neisseria meningitidis*. Although the risk of fulminant septicemia or meningitis as a result of infection by such organisms appears to be less in the adult population (by virtue of prior exposure to these bacteria), overwhelming postsplenectomy sepsis (OPSS) remains a significant concern in the asplenic patient (1).

The incidence of OPSS is estimated to occur in 0.05% to 2% of splenectomized patients (2). It may develop immediately or as late as 65 years postsplenectomy (2-4). Mortality is significant and reported to be as high as 50% (4,5). OPSS incidence reduction is dependent upon (2,5-7):

1) Prophylactic education of the patient and physician as to its risk and prevention
2) Rapid recognition of the asplenic individual when infection is suspected

Reduced post-splenectomy levels of opsonins, splenic tuftsin, and immunoglobulin (IgM) (which promote phagocytosis of particulate matter and bacteria), hamper the body’s ability to clear encapsulated organisms (4,6,7). Vaccination, to impart immunity against such infections, is commonly performed despite the absence of Class I or Class II data to support its efficacy. As 50 to 90% of OPSS infections are secondary to *Streptococcus pneumoniae* infection, the polyvalent pneumococcal vaccine has been the most commonly administered postsplenectomy vaccine. In recent years, the meningococcal and *Haemophilus influenzae* type b vaccines have also been advocated (2-17).

Timing of vaccine administration following splenectomy has been the topic of a longstanding debate. Two major concerns include the patients’ immunogenicity in the perioperative period and the impaired immune function of the critically ill (2,13,16,17). The patient’s present state of health should be considered prior to the administration of postsplenectomy vaccines. In patients with moderate to severe acute illness, vaccination should be delayed until the illness has resolved. This minimizes adverse effects of the vaccine which could be more severe in the presence of illness or could confuse the patient’s clinical picture (such as a post-vaccine fever) (16).

All of the vaccines cause adverse reactions which are generally self-limiting and resolve 24-72 hours after vaccine administration. The polyvalent pneumococcal vaccine causes a transient and self-limited fever (in 5% of vaccinated patients), as well as pain and redness at the site for 1-2 days. A hypersensitivity reaction can occur at the injection site of the *Haemophilus influenzae* type b vaccine along with occasional fever, aches, and malaise. Both meningococcal vaccines can cause headaches, fatigue, malaise and injection site reactions.

There are two meningococcal vaccines currently on the market: the meningococcal polysaccharide vaccine (Menomune A/C/Y/W-135) and the meningococcal (groups A, C, Y, W-135) polysaccharide diphtheria toxoid conjugate (Menactra). Both products provide the same level of immunity against *Neisseria meningitidis*. Differences between the two products are as follows (29-32):

1) Menactra is for intramuscular injection only, Menomune is administered subcutaneously.
2) Menactra is a conjugated vaccine (adding the diphtheria toxoid).
3) Menomune requires revaccination every 3-5 years. Long-term data with Menactra is not yet available. The manufacturer, Sanofi Pasteur, has data demonstrating adequate levels for up to 3-5 years (similar to Menomune). Due to on-going duration studies, it is recommended by the manufacturer that healthcare providers contact Sanofi-Pasteur prior to revaccination in order to obtain the most current information.
4) Menactra is approved only for use in adolescents and adults between the ages of 11 and 55 (14-16,25-27) Menactra has applied for a license for use in children ages 2-10 years of age. There is currently no data on adults > 55 years of age.
LITERATURE REVIEW

Two Class I studies have demonstrated that the polyvalent pneumococcal vaccine results in the highest antibody titers, for the most common serotypes, when administered 14 days post-splenectomy (16,17). These prospective, randomized trials evaluated the efficacy of the vaccine when administered at 1, 7, 14, and 28 days post-splenectomy. As these trials were designed to demonstrate the immunogenicity of the vaccines and not the prevention of OPSS, they can only be used to advocate timing of vaccination.

In 2004, Landgren et al. published a prospective study on antibody response to repeated vaccination. This study included 28 (out of 311) post-trauma splenectomized patients. Their results showed that time between splenectomy and first pneumococcal vaccine was not associated with pre-vaccination, peak or follow-up antibody levels. 25 of the 28 trauma patients received their 1st vaccine post-splenectomy. A major limitation of this study is that the time from splenectomy to first vaccine was only documented in 24% of the cases, yet they claimed that timing had no effect (18). Similarly, Grimfors et al. conducted a longitudinal study of 173 patients (33 trauma) for three years. Pneumococcal antibody responses declined to pre-treatment values at three years in all groups. They also found no correlation between the interval from splenectomy to vaccination and response to vaccination. The data to support this conclusion was not published (19).

Schreiber et al., published a study in rats in 1998 looking at timing of vaccination and subsequent ability to survive pneumococcal challenge. There was no difference in ability to survive a pneumococcal challenge between rats vaccinated on post-operative day 1, 7, or 42 (20). In another study, Werner et al. looked at the effect of perioperative hypovolemic shock and response to vaccination and found no difference if splenectomized rats were vaccinated on post-operative day 1, 7, or 28. Both of these studies raise the question of whether delaying vaccination for 14 days as suggested in the Shatz et al. studies is necessary (21). Further human studies are needed to address the timing of post-splenectomy vaccines.

Class II data supports the vaccination of asplenic patients based on studies of the spleen’s role in immune function and its ability to provide defense against encapsulated organisms (5). Current Center for Disease Control (CDC) recommendations for post-splenectomy vaccinations include the polyvalent pneumococcal (Pneumovax 23), the meningococcal (groups A, C, Y, W-135) polysaccharide diphtheria toxoid conjugate (Menactra, for patients ages 11-55) or the meningococcal polysaccharide (Menomune A/C/Y/W-135, ages <11 or >55), and the Haemophilus influenzae type b vaccines (Hib TITER) (12-14, 25-28). All three of these vaccines may be administered simultaneously (15).

Revaccination needs have been established by Class II studies of immune antibody levels and efficacy after initial vaccination (3). Patients receiving the pneumococcal vaccine should be revaccinated 5 years later (28). Patients who receive the meningococcal polysaccharide vaccine (Menomune A/C/Y/W-135) should be revaccinated every 3-5 years (12-14, 26, 27). Patients who receive the meningococcal (groups A, C, Y, W-135) polysaccharide diphtheria toxoid conjugate vaccine (Menactra) probably should be revaccinated every 3-5 years. However, long-term studies are currently on-going and the manufacturer, Sanofi-Pasteur, suggests contacting them (1-570-839-7187) for the latest recommendations prior to revaccination. The Haemophilus influenzae type b vaccine does not require revaccination (12-14).

There is no Class I data identifying the appropriate timing for pre-splenectomy Haemophilus, Pneumococcal or Meningococcal vaccination for patients with nonfunctional or diseased spleens. Vaccination two weeks prior to surgery is commonly practiced, but this is supported only by Class III data (16, 17). Pre-splenectomy vaccination has been demonstrated to induce antibody formation in both adults and children (18). The types of antibody produced and time to antibody formation (generally 1 to 4 weeks) does vary from patient to patient (18-20). The antibody titer required to prevent either pneumococcal carriage or disease is unknown and has been extrapolated from data obtained from the literature on Haemophilus influenzae titers (21). In the elective splenectomy patient, therefore, vaccination as soon as splenic disease is diagnosed appears prudent to allow time for antibody production (13). The CDC has outlined recommendations for both initial vaccination in the pediatric population as well as booster (revaccination) requirements in patients with an anatomically present, but non-functional spleen (23).
The CDC recommends that asplenic travelers contact an international health clinic or the CDC (www.cdc.gov) to obtain information on disease risks within the intended country of travel. Asplenic travelers should be advised of the increased risk for Meningococcal meningitis and recommendation of the A and C vaccine for all asplenic individuals traveling to sub-Saharan Africa, India, and Nepal.

REFERENCES


POSTSPLENECTOMY PATIENT INFORMATION SHEET

Name: __________________________________________

Splenectomy (splee-nec-tuh-mee) is the name of the operation that was done to remove your spleen. The spleen is a fist-sized organ located in the upper left side of your abdomen (belly). The spleen helps you fight infections, get rid of old or damaged red blood cells, and store blood for your body. Because of either disease or damage to your spleen, it had been removed. You can live without a spleen, but you may be at a higher risk for certain types of blood infection. To help you fight these infections in the future, you have been given the following immunizations (shots):

- **Pneumococcal vaccine, polyvalent (Pneumovax 23)**
  - **Revaccinate every 6 years**
  - Date: ________

- **Age > 55: Meningococcal polysaccharide vaccine**
  - (Menomune A/C/Y/W-135)
  - **Revaccinate every 3-5 years**
  - Date: ________

- **Age 16-55: Meningococcal polysaccharide/diphtheria toxoid conjugate vaccine**
  - (Menactra A/C/Y/W-135)
  - **May need revaccination every 3-5 years**
  - Date: ________

- **Haemophilus influenzae type b conjugate vaccine**
  - **No revaccination needed**
  - Date: ________

It is important that you go and see a doctor IMMEDIATELY if you have any of the following symptoms:

- Fever
- Chills
- Abdominal pain
- Skin rash, swelling, redness, or infection
- Diarrhea
- Achy or weak feeling
- Cough
- Vomiting

These are signs that you may have an infection. Without your spleen, a small or minor infection may become very serious and your doctor needs to examine you and possibly start antibiotics to help your body fight the infection. Always check with your doctor before any dental or invasive procedures, as you may need to take antibiotics before the procedure.

The effect of the vaccines in preventing infection varies from patient to patient and depends on the strength of your immune system when the vaccines were given. You will need to be re-immunized (have the shots again) approximately every 5 years for the rest of your life. You should make sure that your doctor has a copy of this information sheet so that they can help remind you when it is time to be re-immunized.

**If you or your doctor have any questions about the above information, you should contact your surgeon:**

Surgeon’s Name: ________________________________

Surgeon’s Phone Number: ________________________