

# Overwhelming postsplenectomy infection: Managing patients at risk

Decreased or absent splenic function can result in life-threatening sepsis. Prompt diagnosis and treatment of infection, along with prevention through immunization, are essential.

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Patients who are asplenic, either because of physical absence of a spleen or functional splenic compromise, are at an increased risk of contracting a life-threatening condition known as overwhelming postsplenectomy infection (OPSI). This infection is commonly described as a fulminant bacteremia that develops very quickly and carries a high mortality rate. The incidence of OPSI has been difficult to establish, partially because of the wide variation in occurrence rates among particular groups of patients. In one population-based study, the incidence of OPSI in splenectomy patients was found to be 0.23%.<sup>1</sup> However, other studies have demonstrated rates of serious bacterial infection as high as 21% to 22% in patients with specific medical conditions, such as thalassemia major or hematologic malignancy.<sup>2,3</sup> The risk of contracting OPSI can vary depending on how long the patient has been asplenic. For most patients, the risk of sepsis is substantially increased in the first 2 to 3 years following splenectomy. However, patients have developed life-threatening infection as many as 10 years after their surgery.<sup>4</sup> The lifetime risk of OPSI has been estimated at 5%.<sup>5</sup>

While the risk of contracting OPSI may be low in some populations, once an infection occurs, the mortality rates are high, ranging from 38% to 69%, and fulminant infections frequently develop in patients who are relatively young and have few other health problems.<sup>6</sup> Early diagnosis and intervention are the keys to a good outcome. The purpose of this article is to encourage PAs to identify patients who are at risk of developing sepsis and establish care plans designed to prevent or limit overwhelming infection, thereby reducing the morbidity and mortality associated with OPSI.

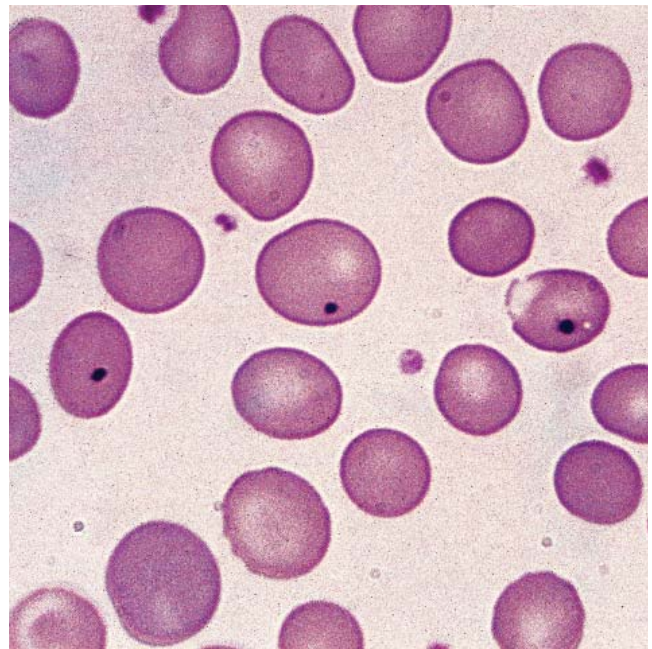
## SPLENIC FUNCTION AND ASPLENIA

The spleen's primary function is to filter the blood. Through a process known as *culling*, abnormal or senescent erythrocytes are removed from the bloodstream and phagocytosed during their slowed circulation through the spleen. The spleen is also responsible for eliminating intra-erythrocyte inclusions, such as Heinz bodies, Howell-Jolly bodies (see Figure 1), and Pappenheimer bodies, through a similar process termed *pitting*.

Bacteria are cleared from the bloodstream in a process that is expedited by *opsonization*—the coating of microorganisms with complement fragments. These coated bacteria join with circulating antibodies to form immune complexes, which are then trapped and destroyed by both the liver and the spleen. Encapsulated bacteria are more difficult for the body to eradicate because of their resistance to complement binding. Clearance of these bacteria is facilitated by opsonins, such as antigen-specific IgM, an immunoglobulin manufactured and secreted by the B cells present in lymph tissue, such as lymph nodes and the spleen. Patients lacking a functioning spleen have fewer of these opsonins, resulting in a limited ability to filter circulating encapsulated bacteria.<sup>7</sup> The bacteria multiply rapidly, culminating in the development of overwhelming sepsis and shock.

## CAUSES OF ASPLENIA

Asplenia is most commonly caused by surgical removal of the spleen. Splenectomy is undertaken on an elective basis



**FIGURE 1.** Howell-Jolly bodies (small dark spots) are fragments of RBC nuclei that are removed by the spleen.

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for a variety of hematologic conditions, such as hereditary spherocytosis, autoimmune thrombocytopenia, primary hypersplenism, and  $\beta$ -thalassemia; or for neoplastic diseases, such as Hodgkin's lymphoma.<sup>8</sup> Splenectomy is performed emergently for severe bleeding caused by blunt or penetrating injuries. Splenic function may also decline over a period of time because of a specific medical condition. Termed *functional hyposplenism* or *functional asplenia*, this phenomenon is associated with sickle cell disease, celiac disease, inflammatory bowel disease, alcoholic liver disease, and systemic lupus erythematosus.<sup>9</sup> Significantly reduced splenic function can be diagnosed by the presence of Howell-Jolly bodies, fragments of RBC nuclei remaining after hematopoiesis and seen as pits or craters on the surface of erythrocytes on a peripheral blood smear.<sup>10</sup> These bodies increase in number as splenic function declines, and their presence is a strong indicator of risk for bacterial infection.

#### IMPLICATED BACTERIA

Asplenic patients are susceptible to a host of pathogenic microorganisms. *Streptococcus pneumoniae* is the most common pathogen implicated in OPSI and may be responsible for up to 90% of these overwhelming infections.<sup>6</sup> Other encapsulated bacteria, such as *Haemophilus influenzae* type b and *Neisseria meningitidis*, are also known to be causative agents. *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* are less commonly involved.<sup>1</sup> Occasionally, asplenic patients may develop fulminant sepsis from *Capnocytophaga canimorsus* (a type of bacteria associated with dog bites). In addition, asplenic patients have an increased risk of developing debilitating infections from the parasites *Babesia microti* and *Plasmodium falciparum*.<sup>11-13</sup> Coexisting medical conditions, such as malignancy or immunosuppressive disorders, may predispose asplenic patients to infection, further increasing their risk for OPSI.

#### DIAGNOSING AND TREATING INFECTION

The clinical presentation of OPSI often begins with mild, non-specific symptoms. Patients usually have a fever and may complain of headache, chills, malaise, and various GI symptoms. However, this prodrome is usually very brief and progresses rapidly to symptoms of septic shock, including hypotension, oliguria, hypoglycemia, and disseminated intravascular coagulopathy. Patients may develop concomitant meningitis or pneu-

monia, or they may experience convulsions or cardiovascular collapse. Death can occur within 24 to 48 hours of illness onset.<sup>14</sup> Mortality is high despite aggressive antibiotic therapy and intensive medical care, and patients who survive often have prolonged and complicated recovery periods with serious long-term sequelae, such as deafness; osteomyelitis; or extensive tissue necrosis, which may potentially require amputation when extremities are involved.<sup>15</sup>

Diagnosis of a bacterial infection and subsequent identification of the involved pathogen are accomplished through laboratory testing. Blood, urine, and sputum should be cultured on hospital admission. Blood cultures often display positive results within 24 hours and are helpful in directing antibiotic therapy. However, initiation of treatment should never be postponed until the results of these tests are avail-

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able because bacterial proliferation occurs at an accelerated pace. The number of bacteria observed on the peripheral smear of some asplenic patients has suggested bacterial counts greater than 1 million/mL.<sup>14</sup> A CBC and serum chemistries are usually ordered as well. Lumbar puncture is an important tool in diagnosing possible meningitis, especially in small children, and chest radiographs are indicated anytime pneumonia is suspected. The decision on what other studies to order should be based on the patient's presenting symptoms.

Empiric oral antibiotics may be started by the patient at home, or antibiotics can be given IM or IV at the primary care provider's office.<sup>16</sup> The antibiotic of choice for treating OPSI has traditionally been IV penicillin. However, with the increasing prevalence of resistant bacterial infections, many providers are choosing broader-spectrum antibiotics.<sup>17</sup> One source suggests that patients be given an initial dose of ceftriaxone 100 mg/kg IV or IM, maximum 2 g per dose, before

#### KEY POINTS

- Patients who have undergone splenectomy or whose splenic function is decreased are susceptible to overwhelming postsplenectomy infection (OPSI). Though rare, OPSI is fatal in 38% to 69% of cases. OPSI frequently develops in patients who are young and in otherwise good health.
- The most likely pathogen in OPSI is *Streptococcus pneumoniae*. Other pathogens include *Haemophilus influenzae*, *Neisseria meningitidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.
- Diagnosis is by blood, urine, and sputum culture, but in suspected cases of OPSI, treatment should not wait for culture results. Antibiotics used empirically include penicillin, ceftriaxone, and vancomycin.
- The primary approach to OPSI is prevention through partial splenectomy, rather than total splenectomy, when possible. In splenectomized patients, preventive strategies involve vaccination against pneumococcus, *H influenzae*, meningitis; daily use of prophylactic antibiotics; and education.

being transported to the nearest emergency department.<sup>18</sup> IV vancomycin 60 mg/kg/d in divided doses every 6 hours, maximum 4 g per day, should be added to a ceftriaxone regimen after hospital admission in regions with high levels of penicillin-resistant pneumococci.<sup>14</sup> Regimens may be adjusted as the results of sensitivity testing become available.

## PREVENTION OF OPSI

While mortality rates may be modestly reduced with prompt identification and treatment of a developing infection, the key to reducing the mortality associated with OPSI lies in preventing asplenia. Emergency care of patients with blunt abdominal trauma currently involves the use of selective criteria that discourage immediate removal of the spleen in favor of careful assessment and nonoperative management of splenic injuries.<sup>19</sup> If the spleen must be removed because of excessive

bleeding, surgeons frequently employ techniques for partial splenectomy, depending on the extent of the injury.<sup>20</sup> Procedures involving autotransplantation of resected splenic tissue have also allowed the patient to preserve some immunologic function.<sup>21</sup>

When a total splenectomy becomes necessary, prevention of infection is the optimal goal. This is accomplished through the use of three effective strategies.

**Immunization, the first of these strategies,** is essential to prevent disease caused by the encapsulated bacteria *S pneumoniae*. The 23 serotypes of pneumococci covered by the polysaccharide vaccine are responsible for about 90% of pneumococcal infections in the United States.<sup>22</sup> Updated guidelines put forth by the Working Party of the Haematology/Oncology Task Force of the British Committee for Standards in Haematology suggest that the vaccine should be given at least 2

Your spleen is an organ that works to help your body fight infection. If you do not have a spleen or your spleen is not working well, you may be at risk for a serious infection—one that could be life-threatening. Here are some steps you can take to lower this risk:

- When you are not sick, visit your health care provider at least once each year to make sure you remain in good health. Check to be sure you are up-to-date on all your shots, including a booster shot for pneumonia and a yearly flu shot.
- Try to stay away from people who are sick.
- Watch for signs that you may be coming down with an infection, like a high fever and chills, a headache, dizziness, a fast heartbeat, a bad cough or sore throat, or vomiting and diarrhea.
- If you have any of the signs listed, call your primary health care provider right away. If your provider has given you an antibiotic to take at home when you get sick, take one dose before you call. Tell the person you talk to at the doctor's office that you may be getting a serious infection and need to be seen right away.
- If your provider gives you medicine, make sure that you take all of the doses and that you take them at the right times. If there is a reason why you are not able to take all of the medicine, tell your provider about it.
- If you go to see any other doctors or health care providers, make sure to tell them that you don't have a working spleen.
- Ask your provider about a bracelet you can wear to let others know about your condition in an emergency.
- If you plan to travel to another country, ask your provider about other types of infections you may get and ways to stay safe.

FIGURE 2. Patient information on asplenia

Patient diagnosis: \_\_\_\_\_

\_\_\_\_ Patient chart flagged

### EDUCATION:

\_\_\_\_ Patient information sheet provided, discussed, and understood

\_\_\_\_ Information given concerning identification tags/wallet cards

### IMMUNIZATIONS:

\_\_\_\_ Polyvalent pneumococcal vaccine:

Date \_\_\_\_\_ Booster \_\_\_\_\_

\_\_\_\_ *Haemophilus influenzae* type b vaccine.

Date \_\_\_\_\_

\_\_\_\_ Meningococcal vaccine

Date \_\_\_\_\_

\_\_\_\_ Influenza vaccine (yearly)

Dates \_\_\_\_\_

\_\_\_\_ Other (specify) \_\_\_\_\_

Dates \_\_\_\_\_

\_\_\_\_ Other (specify) \_\_\_\_\_

Dates \_\_\_\_\_

### ANTIBIOTICS:

\_\_\_\_ Long-term prophylaxis (children younger than 5 years or splenectomy less than 2 years ago)

\_\_\_\_ Barriers to compliance with dosing schedule discussed

\_\_\_\_ Standby antibiotics to keep at home (adults)

Type \_\_\_\_\_

Dose \_\_\_\_\_

Expiration date \_\_\_\_\_

FIGURE 3. Patient chart checklist for asplenia

weeks before an elective splenectomy, if possible. In situations involving emergent splenectomy, unimmunized patients should receive the vaccine shortly after surgery. Reimmunization is recommended every 5 to 10 years but may be required more frequently in patients with lymphoproliferative disorders or sickle cell anemia, as identified by declining antibody levels. Children younger than 2 years should receive vaccination with the conjugate heptavalent pneumococcal vaccine because of their reduced ability to mount an antibody response to the polysaccharide vaccine. Patients should also be immunized against disease caused by the two other encapsulated bacteria, *H influenzae* and *N meningitidis*, and a yearly influenza vaccine is recommended.<sup>23</sup> The 2009 Recommended Adult Immunization Schedule put forth by the CDC's Advisory Committee on Immunization Practices suggests very similar guidelines.<sup>24</sup> Patients who travel frequently may need additional immunizations.

**The second strategy for prevention of infection** is the use of daily prophylactic antibiotics. Prophylaxis is widely advocated for asplenic children younger than 5 years and is usually prescribed for a period of at least 2 years following splenectomy. The American Academy of Pediatrics Committee on Infectious Diseases recommends penicillin V potassium 125 mg twice a day for children younger than 3 years and 250 mg twice a day for children older than 3 years, with discontinuation at age 5 years in healthy immunized children.<sup>25</sup> In asplenic adults, however, there is much controversy surrounding the use of prophylactic antibiotics. This is partly because the life-long risk of sepsis in this group requires long-term use of maintenance doses. Continuous antibiotic use over an extended period can lead to poor compliance, which may increase the risk of developing antibiotic-resistant strains of bacteria. Chemoprophylaxis can also provide a false sense of security, which may be dangerous should symptoms of infection occur.<sup>26</sup> A better alternative is to provide the adult patient with a 5-day supply of standby antibiotics, such as amoxicillin/clavulanate 500 mg/125 mg every 8 hours or cefuroxime axetil 250 mg every 12 hours, either of which can be self-administered at the first sign of infection. A fluoroquinolone with gram-positive activity, such as moxifloxacin 400 mg/d, is a viable alternative, especially for patients with a penicillin allergy.<sup>16</sup> Patients who start standby antibiotics should be advised to seek professional medical care as soon as possible.

**Education is the third component** necessary for successful prevention of postsplenectomy infection. Patients should be made aware of their increased risk of developing life-threatening sepsis through discussion and the provision of reading material appropriate to their educational level. Degree of patient understanding should be carefully assessed. The sample patient information sheet offers suggestions for educational material designed to enhance patients' knowledge and increase their confidence in their ability to manage any illnesses (see Figure 2). Asplenic patients should be urged to seek medical attention at the first sign of infection and to communicate their asplenic status to the person scheduling their appointment so they can be seen promptly. Patients

should also be encouraged to wear an identification bracelet or carry a wallet card notifying others of their condition in emergency situations. Asplenic persons traveling to areas with a high incidence of *B microti* infection, such as Cape Cod and Nantucket Island in Massachusetts, or to areas where malaria is endemic should be counseled about their increased susceptibility to such infections.<sup>17</sup>

The life-threatening nature of OPSI has been recognized for many years. However, despite generalized knowledge of prophylactic measures, studies have shown that recommended guidelines are not being followed by a large percentage of providers and their patients.<sup>6,27</sup> This may, in part, result from lack of a systematic approach to identifying and following at-risk patients.<sup>28</sup> When treating patients with routine illnesses, primary care providers need to be aware of any past surgical procedures that may have included splenectomy. They also need to be aware of declining splenic function in their patients with hematologic diseases and to consider the possibility of asplenia in patients with other predisposing conditions. The charts of these individuals should be flagged, and checklists

**“Patients should communicate their asplenic status to the person scheduling their appointment so they can be seen promptly.”**

should be utilized to ensure that prophylactic recommendations are being followed (see Figure 3). This is especially important in patient populations whose poor access to health care is likely to result in low immunization rates. At future appointments, a flagged chart will serve as a visible reminder to assess the patient's presenting complaints for any similarities to the symptoms of OPSI, increasing the chances that an infection will be caught early and treated before fulminant sepsis develops.

#### CONCLUSION

While the risk of contracting OPSI is relatively low for many asplenic individuals, it is a lifetime risk. The mortality rate associated with this rapidly progressing infection is alarmingly high. Identification of those at risk and routine systematic administration of prophylactic measures for these patients can further reduce their incidence of infection and improve outcomes. Patients who are educated about their condition can learn to recognize warning symptoms and take the necessary steps to protect themselves from serious illness. For those who do develop sepsis, immediate empiric antibiotic treatment offers the best opportunity for survival and limits the associated complications. A committed partnership between patient and provider will assure the best outlook for the patient's continued good health. **JAAPA**

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**Sandra Moffett** is a PA with Lancaster Neuroscience and Spine Associates in Lancaster, Pennsylvania. She has indicated no relationships to disclose relating to the content of this article.

## DRUGS MENTIONED

Amoxicillin/clavulanate (Augmentin)  
Ceftriaxone (Rocephin, generics)  
Cefuroxime axetil (Ceftin, Zinacef)  
Moxifloxacin (Avelox)  
Penicillin  
Penicillin V potassium  
Vancomycin (Vancocin, generics)

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