

# Overwhelming Postsplenectomy Infection: A Critical Review of Etiologic Pathogens and Management

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Literature sources cite pneumococcus as a cause of overwhelming postsplenectomy infection (OPSI) in only about 50% of cases, but the impression based on clinical experience was that the incidence of pneumococcus was considerably higher. A literature review of cases from 1978-1994 without distinct risk factors for other bacteria showed that the proportion of *Streptococcus pneumoniae* infection in OPSI was at least 80%. Given this high frequency, including penicillin as an integral part of initial empiric therapy for OPSI is recommended. [Infect Med 13(9):779-783, 1996]

Key words: *Streptococcus pneumoniae* • Splenectomy • Penicillin • Ceftriaxone

**F**ulminant infection has been recognized as a remote complication of splenectomy since 1952, when 5 cases of sepsis were reported in infants who had undergone splenectomy for hereditary spherocytosis.<sup>1</sup> Overwhelming postsplenectomy infection (OPSI) was once thought to be a complication in patients with underlying hematologic or malignant disease; however, cases of OPSI also have been reported in previously healthy patients who had undergone splenectomy for trauma.<sup>2</sup>

We present a case of OPSI in a previously healthy 30-year-old woman who had undergone splenectomy for idiopathic thrombocytopenic purpura 12 years previously. The causative organism was *Streptococcus pneumoniae* (pneumococcus). This case was of interest to us because textbook discussions of postsplenectomy infection typically give pneumococcus a causative role in only about 50% of cases. Our impression, based on clinical experience, was that 50% was an underestimate. We

therefore conducted a literature review to address this issue.

## Case Report

A 30-year-old white woman had undergone splenectomy 12 years previously for treatment of idiopathic thrombocytopenic purpura. She had not received corticosteroid therapy. Pneumococcal vaccine had not been administered.

She presented to another hospital with a 4-day history of nausea, vomiting, abdominal pain, and diarrhea. She also complained of severe headache and fever. She was alert. Her temperature was 38.5°C (101.3°F), pulse 147/minute, respiration 28/minute, and blood pressure 50/palpable mm Hg. Her neck was supple, and her lungs were clear. She was cyanotic and had cold extremities as well as large ecchymotic areas over her legs and torso. Hemoglobin was 12g/dL and a white blood cell count was 17,100 cells/mm<sup>3</sup> with 53% neutrophils, 27% bands, and 8% lymphocytes. Toxic granulation was noted. Her platelet count was 87,000/μL, prothrombin time was 26.6 seconds, activated partial thromboplastin

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Figure 1. Gangrenous digits with mottled ecchymoses. Fingers were later amputated.

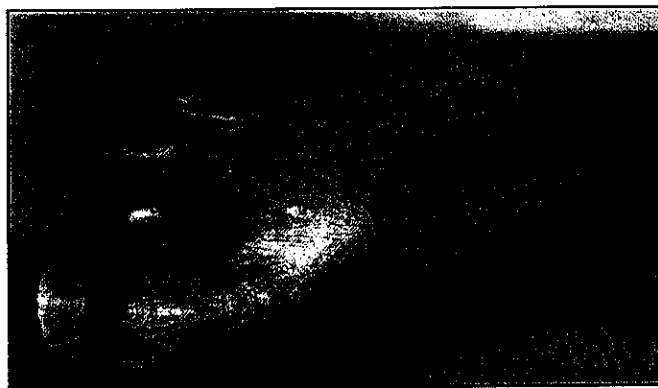


Figure 2. Foot of patient with digital infarctions caused by purpura fulminans. Erythematous areas of skin necrosis are also visible.

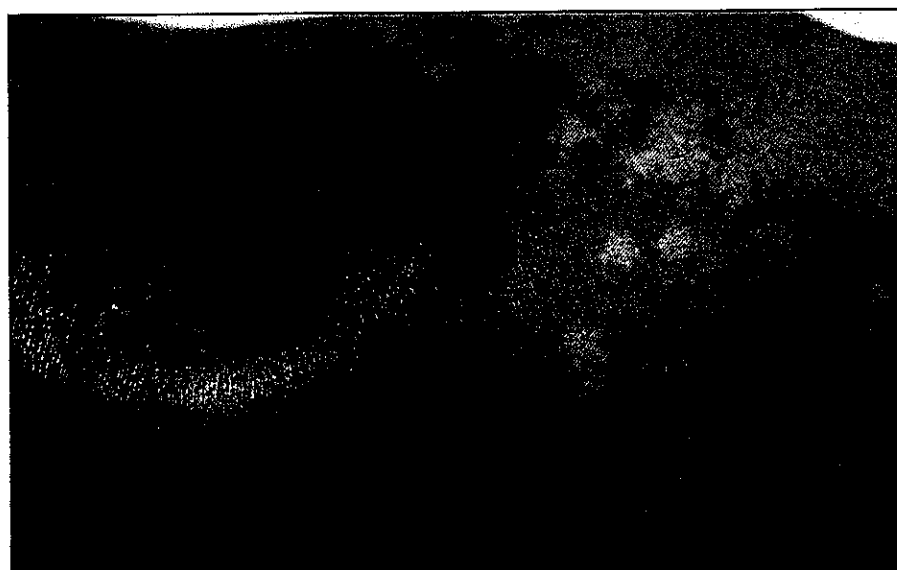


Figure 3. Thigh with extensive areas of geographic cutaneous infarctions with necrosis.

time was greater than 100 seconds, and fibrinogen level was 77mg/dL. Blood urea nitrogen was 33mg/dL, serum carbon dioxide was 16mmol/L, and creatinine was 5.1mg/dL. Chest radiograph showed no infiltrates. Intravenous fluids and dopamine were infused. Ceftriaxone 2g IV was administered after 2 sets of blood cultures were drawn.

The patient was then transferred to our institution for further management. On arrival, her systolic blood pressure was 124mm Hg, pulse was 150/minute, temperature was 36.6°C (97.8°F), and respiration rate was 18/minute. Extensive areas of mottled purpuric lesions over the face,

abdomen, chest, and extremities were seen (Figs. 1-5). Petechial hemorrhages were present over the face. Livedo reticularis on the thighs and legs was present. The digits on her hands and feet were cyanotic. Administration of vancomycin and ceftriaxone was begun, as well as metronidazole because of concern of an intraabdominal process. Blood cultures subsequently revealed *S pneumoniae*. The patient received 14 days of intravenous ceftriaxone. Packed red blood cells, cryoprecipitate, fresh frozen plasma, and platelets were administered.

Plastic surgical repair of necrotic skin over the torso and thighs was

performed with grafts and repeated debridements. Transmetatarsal amputation of both feet and amputation of her fingers were performed on day 25. Bilateral below-the-knee amputations were performed on day 37. She was discharged home after 84 days and is stable 9 months after discharge.

#### Literature Review

**Methods.** We conducted a Medline search of all cases of OPSI reported from 1978-1994. The year 1978 was chosen as a cutoff because pneumococcal vaccine became available after that year, which should have decreased the incidence of invasive pneumococcal infections and led to a correspondingly larger proportion of other bacteria causing OPSI. Key words for the literature search included splenectomy plus sepsis, septicemia, or bacteremia.

To focus on previously healthy adults who acquired their infections in the community, we excluded:

- patients who had undergone splenectomy as part of therapy or staging for hematologic malignancy such as Hodgkin's disease;
- immunosuppressed patients as defined by receipt of corticosteroids or cytotoxic drugs for hematologic malignancy or organ transplantation;
- children younger than 15 years,



Figure 4. Early hemorrhagic bullae formation with extensive areas of mottling.

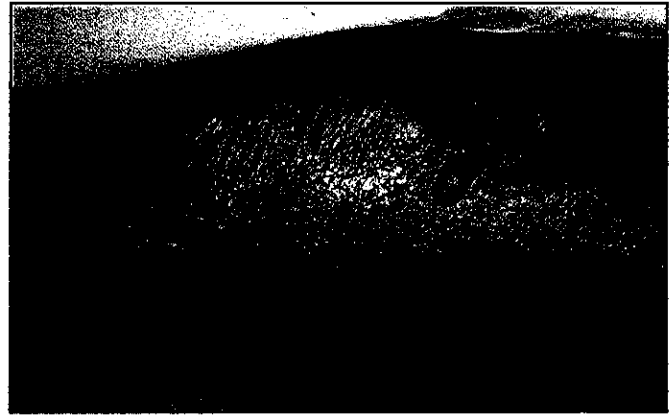


Figure 5. Large flaccid bullous lesion on lower leg.

because other streptococci and aerobic gram-negative bacilli have been implicated in seemingly immunocompetent children;

- patients with nosocomial infections associated with invasive procedures; and
- patients with immediate history of dog bite because of the possibility of *Capnocytophaga canimorsus* (formerly, CDC group DF-2) infection.

**Results.** We reviewed 81 reports; 25 reports were excluded on the basis of the 5 exclusion criteria listed in Methods. Cases from 2 series in which clinical information was lacking were excluded.<sup>3,4</sup> The bacteria in these 2 series included 2 *Streptococcus*, 1 *Klebsiella*, 1 *Salmonella*, and 1 *Staphylococcus*. Six *S pneumoniae* from these 2 series were also excluded. Once those distinct settings that predispose to organisms other than *S pneumoniae* were excluded, we found only 11 cases of community-acquired OPSI in the literature that were caused by pathogens other than pneumococci (Table I).

### Discussion

OPSI follows a characteristic course of fulminant infection preceded by a prodrome of nonspecific symptoms. The prodrome can occur from a few hours to days before medical atten-

tion is sought, with a typical duration of 1-2 days. Symptoms include fever, headache, nausea, vomiting, diarrhea, abdominal pains, myalgias, malaise, lethargy, and occasionally sore throat and cough. Fever was invariably present in our review of the literature.

Most patients develop disseminated intravascular coagulation with purpura fulminans as well as signs of acidosis and renal failure. The mortality ranges from 50% to 70%.<sup>5</sup> Death is often within a few hours of admission despite administration of antibiotics and other supportive therapy; a few patients expire before they can receive medical care. For patients who survive their initial episode, a complicated hospital stay with sequelae such as limb amputation is commonplace.

Our patient had a splenectomy as elective therapy for idiopathic thrombocytopenic purpura 12 years earlier and was in good health. Her illness followed a classic course, with development of disseminated intravascular coagulation and renal complications. Gangrene in her extremities necessitated amputation below the knee bilaterally and at the fingers. *S pneumoniae* was isolated from blood.

Of cases reported in the literature, numerous authors cite *S pneumoniae* as the causative agent in about 50% of cases<sup>5,9</sup>; other organisms cited in-

clude the encapsulated organisms *Haemophilus influenzae* and *Neisseria meningitidis*. However, group B streptococcus (GBS), *Staphylococcus*, *Salmonella*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Listeria monocytogenes* have also been mentioned in selected reports.<sup>7</sup> The implications for therapy given the diversity of these pathogens is that broad-spectrum therapy (eg, a third-generation cephalosporin) is often administered empirically rather than as narrow-spectrum therapy such as penicillin.

Although bacteria other than the pneumococcus have indeed been reported, in our review of the literature we found these bacteria to be isolated in patients with immunosuppression or in the context of nosocomial infection, including postoperative complications in patients undergoing surgery other than their splenectomy, burn patients, and 1 patient with chronic myeloid leukemia undergoing bronchoscopy.<sup>10,11</sup> *H influenzae* infection occurred primarily in children. In one review of splenectomized children following trauma, *S pneumoniae* was the most commonly occurring organism in those with known bacterial etiologies (4/8), followed by *H influenzae* (3/8) and *N meningitidis* (1/8).<sup>12</sup> *C canimorsus* was also reported in 8 patients in the literature

**Table I**  
**Nonpneumococcal Cases of Community-Acquired OPSI in Adults Without Underlying Disease**

Organism	No. of Cases	Comment	Reference
<i>Streptococcus milleri</i>	1	Odontogenic abscess and dental extraction	14
<i>Escherichia coli</i>	1	Appendicitis	13
<i>Haemophilus influenzae</i>	2		22, 23
Group B streptococcus	4		24, 25, 26, 27
<i>Neisseria meningitidis</i>	2	Both cases from same hospital on consecutive days	8
<i>Streptococcus sanguis</i>	1		28

published between 1978 and 1994. Seven of these 8 had a history of dog bite, and the eighth, although having no history of a dog bite, was a dog owner. *C canimorsus* is part of the normal oral flora of dogs, and human infection is intimately associated with exposure to dogs.

Specifically, in our review of cases of adults with community-acquired infection, with the 5 exclusion criteria listed in Methods, we found the incidence of pneumococcus as the causative organism to be 80% (45/56). Other organisms reported included GBS in 4 patients, *Haemophilus* in 2, *N meningitidis* in 2, *E coli* in 1, *Streptococcus milleri* in 1, and *Streptococcus sanguis* in 1 (Table I). It is interesting to note that while *H influenzae* and *N meningitidis* were frequently mentioned as causes of OPSI, GBS occurred more often than these 2 pathogens in the literature reports from 1978 to 1994. We would also like to point out that the 2 meningococcal infections cited in the literature were unusual in that they emanated from 1 report describing 2 cases in the same hospital on consecutive days.<sup>8</sup> The infection from *E coli* was in a 26-year-old woman with appendicitis,<sup>13</sup> while the *S milleri* infection occurred in a patient with an odontogenic abscess and a dental extraction 10 days prior to illness.<sup>14</sup>

Thus, the incidence of pneumococcal infection in OPSI appears to be significantly higher than the 50% figure commonly quoted in the literature, and most of the nonpneumococcal cases occurred in specific

settings such as nosocomial acquisition and immunosuppression. While the literature reviewed for this report may not have been entirely representative of the patient population at large, it is not clear that bias existed for identifying pneumococci in OPSI. In fact, the reverse was more likely true, because pneumococcal infections in splenectomized individuals are recognized as common and no longer warrant reporting in the peer-reviewed medical literature. Furthermore, the period of literature review was confined to the period when the pneumococcal vaccine was available, which should have decreased rather than increased the number of pneumococcal cases. For example, Kingston and colleagues<sup>15</sup> reported in a review of cases prior to 1979 that 100% (26/26) of cases of fulminant septicemia in asplenic adults were caused by pneumococcus; patients receiving steroids or other immunosuppressive agents were excluded. Thus, we conclude that pneumococcus remains the predominant cause of OPSI in previously healthy adults and should be considered the most likely organism in the absence of other significant history from the patient.

Given the high morbidity and mortality associated with such infection, we suggest that penicillin be considered as an integral part of the initial regimen. An advantage of penicillin is its extremely high serum:MIC ratio for pneumococci, even in penicillin-resistant strains. For example, steady-state serum concentrations of penicillin range from 12-20µg/mL

(3g or 5 million units IV after 2 hours),<sup>16</sup> while the MIC for a sensitive pneumococcus is about 0.01µg/mL. The serum:MIC ratio may be as high as 2000:1, which is much higher than similar ratios for pneumococcus and third-generation cephalosporins. We caution that while a higher serum:MIC ratio may be theoretically superior, such a correlation has not yet been shown in controlled studies. Nevertheless, given the fulminating nature of OPSI, administration of the most potent antibiotic available seems reasonable. Furthermore, penicillin is highly active against many of the other, less common organisms implicated in OPSI, including *C canimorsus*, *N meningitidis*, and GBS.

Although penicillin has been the antibiotic of choice for pneumococcal infections and continues to be so for susceptible strains, an increasing prevalence of penicillin-resistant pneumococci has been documented worldwide. High-dose penicillin still appears to be effective against penicillin-resistant strains in bacteremic pneumonias,<sup>17</sup> since the serum and tissue concentrations of penicillin exceed the MIC of resistant strains. Ceftriaxone, which is active against penicillin-resistant pneumococci, can be added as part of the initial empiric regimen to cover the meningeal complications of pneumococcal sepsis, given the lesser concentrations of penicillin in the cerebrospinal fluid. Ceftriaxone could be discontinued if the organism has been documented to be a penicillin-susceptible pneumococcus. Ceftriaxone would

also provide coverage against the possibility of gram-negative bacilli, which we have shown are exceptionally rare causes of community-acquired OPSI in immunocompetent adults.

If the patient survives the initial septic episode, complications from disseminated intravascular coagulation often dictate amputation of distal extremities because of ischemic necrosis. Surgery is indicated when gangrene of the limbs develops and foci of secondary infection ensue.<sup>9,18</sup> Areas of skin necrosis are approached in the same manner as with burn patients, with debridement and grafting of the wounds; fasciotomy also may be necessary.<sup>18</sup> Surgical intervention is rarely indicated in the initial management, and limb amputation, if necessary, might await the recovery of the patient from the resuscitative phase of treatment.

Although the risk for the splenectomized patient of contracting an overwhelming infection is low, it is elevated in relation to the population at large. The risk is lifelong and exists even in those splenectomized for trauma. Thus, pneumococcal vaccine should be administered to all patients undergoing elective splenectomy, and preferably this should be done 2 weeks before the splenectomy. This is not always possible, particularly in the case of a traumatic rupture of the spleen. In these cases, pneumococcal vaccine should still be administered postoperatively. Rise in antibody levels in splenectomized patients given the vaccine has been documented, although it is lower than in normal individuals, and there is little risk to administering the pneumococcal vaccine, even to immunocompromised patients.<sup>19</sup> Daily penicillin prophylaxis has also been suggested as a possible preventive measure, but this is extremely controversial,<sup>20</sup> and we would not recommend its routine use for adults with splenectomy, especially given

the association of prior  $\beta$ -lactam antibiotic use and emergence of penicillin-resistant pneumococci.<sup>17</sup>

Several authors have suggested that self-administration of oral penicillin be considered in any splenectomized individual at the first sign of febrile illness.<sup>5,21</sup> Studies supporting a preemptive course of oral penicillin have not been performed. However, we believe this may be a rational consideration for selected patients with

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splenectomy, since hypotension and disseminated intravascular coagulation with overwhelming sepsis have occurred by the time many patients seek medical attention. Regardless, splenectomized patients should be educated about their increased risk for infection (our patient was not) and encouraged to seek prompt medical attention at the onset of any febrile illness. □

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## Drugs Mentioned in This Article

Ceftriaxone	<i>Rocephin</i>
Dopamine	Generic
Metronidazole	<i>Flagyl, Protostat,</i> generic
Penicillin	Generic
Vancomycin	<i>Vancocin</i>

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