Epidemiology of Infection

Serratia Infection in the Surgical Patient

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Serratia marcescens is a major cause of nosocomial infection in the surgical patient. Infection by this organism generally occurs during the postoperative course of a patient with complications. Risk factors include prior broad-spectrum antimicrobial therapy and prolonged intensive care. Manipulative procedures of the urinary and respiratory tract are important predisposing factors for spread of the organism. The aminoglycosides (gentamicin, netilmicin, amikacin) and/or the cephalosporins (moxalactam, cefotaxime, cefoxitin, ceftriaxone) are the antibiotics of choice.

Key words: Serratia marcescens • Nosocomial infections • Surgical infections

Serratia marcescens infection has emerged as a major cause of morbidity in postoperative patients, especially those hospitalized in intensive care units. In the largest series of Serratia infections reported, 90% occurred in patients who had previously undergone surgery. In the surgical intensive care unit at the Pittsburgh VA Medical Center, S. marcescens now accounts for 26% of gram-negative bacteremias.

Serratia infections pose special problems to the surgical patient. The first issue confronting the surgeon is the difficulty in establishing the significance of isolation of Serratia from a nonsterile site such as sputum. Patients (especially those receiving broad-spectrum antibiotics) may be colonized rather than infected with the organism.

Assuming the organism is pathogenic, the second issue is selection of appropriate antibiotic therapy. The organism is not only resistant to many of the commonly used antibiotics, notably cephalosporins, but it has a predilection for ready acquisition of resistance. For example, 60% of the Serratia isolated from blood in the Pittsburgh VA surgical intensive-care unit are now resistant to gentamicin, for many years the mainstay of antibiotic therapy against this organism. This article addresses both these issues and reviews the historical background and clinical presentation of this fascinating bacterium.

Historical Review
S. marcescens is an aerobic gram-negative rod. Because of a red pigment produced by some strains, it has accumulated folklore as a masquerader of blood. The first account by classical historians of the appearance of blood on foodstuffs occurred at the siege of Tyre in Phoenicia (Lebanon) in 322 B.C. There, the stalemated army of Alexander the Great took inspiration from an omen: drops of blood appearing on the soldiers' bread. This was interpreted by Macedonian seers as prophesying the destruction of Tyre. Tyre was eventually stormed and left in ruins, and its inhabitants were sold into slavery. Historians of religion have reported numerous episodes of

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blood appearing on communion bread symbolizing the body of Christ. (Fig. 1)³

The distinctiveness of the pigment also led to its experimental use as a biologic indicator. It was used in experiments demonstrating aerosolization of respiratory flora after speaking and coughing, hand carriage of respiratory flora, appearance of bacteremia after dental extraction, and entry of perirethral bacterial flora into bladders via indwelling Foley catheters.⁴

The most controversial use as an indicator organism involved covert aerosolization experiments conducted by the U.S. Army to study the vulnerability of the population to germ warfare techniques (Table I, Fig. 2). Pigmented Serratia was released over cities, in bus terminals, and in subways.⁴ (Another “nonpathogenic” organism used in these experiments was Aspergillus fumigatus.) One of the first documented outbreaks of nosocomial Serratia infection occurred in a San Francisco hospital within the time period that Navy ships released massive numbers of Serratia near San Francisco to study wind and water currents.⁵ One of the patients infected during this outbreak developed and succumbed to endocarditis—the first case of endocarditis caused by S. marcescens. This revelation was publicized on the television program 60 Minutes in 1980. Relatives of the deceased failed in their legal attempt to recover damages from the U.S. government because they were unable to make a definitive link to the Army’s aerosolization experiments.

Importance as a Surgical Pathogen

Altemeier noted the growing importance of S. marcescens as a postoperative pathogen as early as 1969.⁶ Since that time, the organism has been found to be a common pathogen affecting postoperative patients in neurosurgery,⁶,⁷ cardiothoracic surgery,⁸⁻¹₂ abdominal surgery,¹³ and obstetric/gynecology, where it generally occurs in the context of nosocomial infection, especially in the intensive care unit. Serratia also may present as a nosocomial urologic infection with urinary manipulative procedures playing the major role for initiating and disseminating the infection.¹⁴,¹⁵

Serratia seems to be a relatively unusual cause of ocular infections, although cases have occurred in the context of nosocomial infection with local inoculation of the organism into the conjunctiva or traumatic inoculation into the cornea.¹⁶,¹⁷ Similarly, the organism is a rare cause of otolaryngologic infections, although cases of otitis⁰,¹⁰ and sinusitis⁰,¹¹ have been reported.

Orthopedic infections involving Serratia osteomyelitis and septic arthritis have also occurred as nosocomial infections in the postoperative patient.²² Manifestations unique to orthopedics include endocarditis in drug addicts²³ and point-source outbreaks involving iatrogenic inoculation of the organism into a joint space.²⁴ Patients with nosocomial infections or endocarditis develop their bone or joint infection as a result of seeding via bacteremia.

Of particular concern to the surgeon is contamination of disinfectedants, especially benzalkonium chloride¹² and skin cleansers. Aortic mycotic aneurysms have occurred after arterio-

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**Table 1**

<table>
<thead>
<tr>
<th>Location</th>
<th>Date of Test</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Washington, DC</td>
<td>Aug 1949, Dec 1949, March 1980</td>
<td></td>
</tr>
<tr>
<td>Hampton Roads, VA</td>
<td>April 1959</td>
<td></td>
</tr>
<tr>
<td>San Francisco, CA</td>
<td>Sept 1950</td>
<td></td>
</tr>
<tr>
<td>Key West, FL</td>
<td>1952</td>
<td></td>
</tr>
<tr>
<td>Panama City, FL</td>
<td>March to May 1952</td>
<td></td>
</tr>
<tr>
<td>Hawaii, HI</td>
<td>Jan to March 1968</td>
<td></td>
</tr>
</tbody>
</table>

* Serratia released from ships at sea or at anchor.
graphy in which contaminated benzalkonium chloride had been applied to syringe barrels used to inject contrast media. Septic arthritis has resulted from intraarticular steroid injection when cotton balls soaked with contaminated benzalkonium chloride were used as a skin disinfectant, which subsequently contaminated sterile vials of steroid medication.

Contamination of skin cleansers by *Serratia* has been documented, including chlorhexidine, OR/Scrub, and pHisoDerm.

**Clinical Setting for Serratia Infection**

The usual situation encountered by the surgeon is the isolation of *S. marcescens* in the high-risk patient with an already complicated postoperative course. Interestingly, organisms encountered in this setting are usually nonpigmented. Risk factors for the acquisition of *Serratia* include prolonged hospitalization, intensive-care unit stay, and prior antimicrobial-agent therapy.

The gastrointestinal tract is a primary reservoir in outbreaks involving children and may be important in adults as well. The predominant mode of spread is hand-to-hand transmission. Point-source outbreaks have been traced to contaminated water from nebulizers and respiratory machines, intravenous solutions, heparin vials, and even hand lotions.

Medical equipment implicated in hospital epidemics include respirators, vascular catheters, arterial pressure monitors, and fiber-optic bronchoscopes.

The urinary tract has received special emphasis as a primary reservoir. The indwelling Foley catheter is the major risk factor. The risk of a catheterized patient becoming infected with *Serratia* is directly related to the proximity of other catheterized patients colonized or infected with *Serratia*. Urinometers (specific-gravity-measuring devices), urine containers, and diabetic-urine-testing equipment have been implicated as inanimate reservoirs for *Serratia*.

The respiratory tract is now being found to constitute the major portal of entry into the surgical patient. Eighty percent of postoperative patients developing *Serratia* bacteremia in the author's hospital previously had *Serratia* isolated from the respiratory tract. A common source is a patient with an indwelling bladder catheter who becomes colonized or infected with *Serratia*. This patient then serves as a disseminating point for health workers, who transmit the organism to other patients. Since so much of intensive-care unit monitoring involves respiratory tract manipulation, respiratory colonization occurs as a result of contamination of the hands of hospital personnel. Respiratory colonization then leads to skin and total body colonization with multiple portals of possible entry, including intravascular access.

*Serratia* may also cause postoperative wound infections. These may present as pus at the incision site or without accompanying systemic signs. The infection usually has its onset 5 to 7 days following the procedure.
and is more common in those colonized with *Serratia* at the time of surgery. Although postoperative wound infections rarely result in bacteremia or death, they do cause significant morbidity and result in a prolonged hospitalization.

**Approach to Therapy**

If *Serratia* is isolated from the blood, the clinical decision-making is relatively easy. The organism is obviously pathogenic, and appropriate antimicrobial therapy must be selected. The thoughtful physician will go one step further and will attempt to determine the portal of entry of the organism. Given the epidemiologic profile of the organism as discussed above, it is obvious that indwelling bladder catheters and intravenous catheters must be scrutinized with particular care. Urine culture should be performed. Indwelling vascular lines should be removed and quantitatively cultured.

If *Serratia* is isolated from a sputum culture (or from an endotracheal or tracheostomy site), then interpretation of the significance of this isolation is difficult, because colonization of the respiratory tract occurs readily. The Gram stain of the sputum should show abundant neutrophils with predominantly gram-negative flora. Cultures should be taken immediately of blood and pleural fluid, if present. Should cultures of these normally sterile sites be unrevealing, then the surgeon must make a decision based on clinical presentation, Gram stain of the specimen, and x-ray findings as to the significance of the isolation from sputum. The author's approach to this situation is straightforward, although not necessarily academic or intellectual. If the patient is clinically unstable with recent pulmonary infiltrates visualized on x-ray, the author administers empiric antimicrobial therapy on the assumption that the isolation of *Serratia* from the respiratory tract is pathogenic.

Undoubtedly, on some occasions the isolation actually constitutes colonization; if the infection is indeed present, however, early administration of appropriate antibiotic therapy will be critical in salvaging the patient. One must continually consider the possibility of other diseases and pathogens during the administration of empiric therapy. "Shotgun" therapy should not be a replacement for attempts at definitive diagnosis.

Since a major precipitating factor in the emergence of *S. marcescens* is the use of broad-spectrum antibiotics, antibiotic prophylaxis should be used with restraint. Narrow-spectrum therapy should be favored whenever possible, and the duration of prophylaxis should be limited. Antibiotics should not be given prophylactically for colonization with *Serratia*, since this would predispose to the emergence of highly resistant *S. marcescens*.

If a subjective increase in the incidence of *Serratia* infections in postop-

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**Editorial Comment**

Dr. Yu's comments on the management of *Serratia marcescens* infections in surgical patients are very important. At The New York Hospital-Cornell Medical Center, we have had 3 outbreaks of hospital-acquired *S. marcescens* infections. In the neonatal intensive care unit, 22 infants were colonized with a multi-resistant, nonaugmented strain, and 8 other neonates had clinical infections. The primary reservoir for this outbreak was gastrointestinal colonization. Other contributing factors included inadequate hand washing by personnel and overuse of broad-spectrum antibiotics. In the burn intensive care unit, 7 multi-resistant *S. marcescens* colonized most patients over a 2-year period and contributed to increased morbidity and mortality in many of them. Contaminated equipment such as the air-fluidized bed and mattresses as well as inadequate hand washing by staff were significant factors in spreading this infection. On the urology service, inadequate cleaning of cystoscopy equipment and cross-contamination among patients due to inadequate hand washing by personnel were responsible for urinary tract infections in 105 patients.

An infection-control team consisting of an infectious disease physician, a nurse epidemiologist, a pharmacist, and a hospital sanitarian must work closely with the surgeon both to prevent and to control outbreaks. The nurse epidemiologist must maintain effective prospective surveillance. This might also include random sample culturing of high-risk patients to identify colonization with resistant organisms before clinical infection is apparent. The pharmacist must monitor patterns of antibiotic usage. The sanitarian should design appropriate protocols for adequate cleaning of equipment and environmental surfaces.

When an outbreak occurs, the team conducts an investigation to identify a common source, if possible, and makes an intervention appropriate for control. Infected patients are usually isolated. Isolation procedures vary depending on the mode of transmission for a particular pathogen, e.g., enteric, respiratory, direct contact, blood, or secretion. Exposed patients might be cohorted, which means they are segregated to prevent the potential spread of a pathogen to nonexposed patients. The same personnel should preferably not take care of both exposed and nonexposed patients at the same time. Finally, the infection-control team must supervise a program of continuing education for patient-care personnel to prevent hospital-acquired infections in the future.

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**References**

erative patients is noted by the surgeon, it should be called to the attention of the infection-control practitioner. The infection-control practitioner must consider the possibility of a point-source outbreak from a contaminated reservoir and should decide how to handle individual patients with Serratia infections to prevent widespread colonization within the hospital.

The advent of the third-generation cephalosporins has produced antimicrobial agents—such as ceftazidime, moxalactam, cefotizoxime, and cefotaxime—with extraordinary activity against Serratia.

Hand washing should always be the standard of care, but when S. marcescens is encountered, the practice should be reemphasized to health care personnel, especially physicians. Cohorting patients (i.e., placing colonized and infected patients in specified rooms or units to minimize contact between personnel and noninfected patients) with consideration of isolation measures and use of gowns is indicated with the appearance of Serratia that is newly resistant to the commonly used antimicrobial agents.1-3,7

Although chloramphenicol and cefoxitin possess reasonable in vitro activity against Serratia, gentamicin has emerged as the mainstay of therapy.1 Cephalosporins might be added for broader coverage and synergistic interaction. Within the past several years, however, the emergence of gentamicin-resistant Serratia has posed special problems to university health centers and hospitals with an intensive-care unit population.1-3,9,10 In these instances amikacin is generally effective, although the emergence of amikacin-resistant organisms has been reported.1,9

Fortunately, the advent of the third-generation cephalosporins has produced antimicrobial agents with extraordinary activity against this organism. Specifically, ceftazidime, moxalactam, cefotizoxime, and cefotaxime have superb activity.4,4,5 Considerations for other antibiotics are given in Table II. Administration of therapy should range from 2 to 3 weeks. Longer duration is discouraged because of the increasing risk of superinfection.

Conclusions
The emergence of S. marcescens as a major pathogen has special relevance for the surgeon. Infection with this organism represents a tangible cost of widespread antibiotic usage. The lessons to be derived for the surgeon are worth reiterating: strict attention to sterile technique, continuing emphasis on compulsory postoperative management, judicious use of antibiotics, and minimizing the use of intravascular and indwelling catheters.

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References

Table II
Antimicrobial Therapy for Serratia marcescens

<table>
<thead>
<tr>
<th>Aminoglycosides</th>
<th>amikacin reserve for gentamicin-resistant organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin: current treatment of choice</td>
<td>netilmicin tobramycin, kanamycin: good activity, but gentamicin/amikacin generally preferred</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>moxalactam: may be new treatment of choice</td>
</tr>
<tr>
<td>Ceftaxime</td>
<td>Cefotaxime</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Cefotin</td>
</tr>
<tr>
<td>Ceferone</td>
<td>Cefoperazone, cefamandole: good activity, but generally not preferred therapy</td>
</tr>
<tr>
<td>Cephalothin, cefazolin, cephalaprin: generally inactive</td>
<td></td>
</tr>
<tr>
<td>Penicillins</td>
<td>Phenoxymethylpenicillin, mezlocillin: use only if in vitro confirmation of sensitivity</td>
</tr>
<tr>
<td>Carbencillin, ticarcillin: generally inactive</td>
<td></td>
</tr>
<tr>
<td>Nafcillin, oxacillin, methicillin, ampicillin, penicillin: always inactive</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>chloramphenicol: use only if disc sensitivity is confirmed by MIC determinations</td>
</tr>
<tr>
<td>Nalidixic acid: for urinary tract infections only; use only if sensitivity is confirmed</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole: usually active but little experience with use as sole agent, not preferred therapy</td>
<td></td>
</tr>
<tr>
<td>Rifampin: must be used in combination with another agent</td>
<td></td>
</tr>
</tbody>
</table>

Combination therapy
cephalosporin plus amnoglycoside: most potent combination
moxalactam amikacin
or cephalosporin gentamicin or cefoxitin netilmicin
trimethoprim/sulfamethoxazole:
plus amnoglycoside plus rifampin
clinical experience is limited

continued
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reduced the incidence of gas gangrene and made delayed primary closure of war wounds a safer procedure. In British military surgical experience since World War II, gas gangrene and tetanus have been extremely rare, and soft tissue infection in limb wounds has been minor and easily controlled by appropriate antibiotics. In the few thousand limb wounds seen from the conflicts of recent years, infections of the long bones and joints have not been a serious problem and have responded to appropriate antibiotics including cephalosporins.

The surgical treatment of penetrating brain injuries has been totally dominated by prophylactic antibiotics; infection, the principal cause of death in World War I, has been practically eliminated. Similarly, infection in penetrating chest wounds has not been a problem when the correct surgical principles of drainage of hematomata have been observed.

Peritonitis following surgery for penetrating abdominal wounds is still an important cause of hospital mortality. Improper management of wounds of the large bowel is the principal cause; but, especially when there has been delay in reaching surgery or there is gross contamination of the peritoneal cavity, the choice of antibiotic for prophylaxis or treatment becomes very important. Penicillin and metronidazole are a useful combination, and some military surgeons still favor chloramphenicol. The use of cephalosporins in a large series has not yet been reported, but they have proved to be of value in some cases.4

Burns are an important injury in modern war. Silver sulfadiazene cream has proved its value as a first-aid treatment and also as a definitive treatment for the superficial burns of hands and face that make up the majority of cases.7

Serious infection in war wounds will always occur when there is a delay in treatment and when surgery is inadequate. Prophylactic antibiotics are no substitute for surgery, but they minimize complications. The newer antibiotics have been especially useful in eliminating chronic bone and joint sepsis. As a result, modern orthopedic and plastic surgical reconstructive procedures can be employed in the long-term treatment of the more severe disabling wounds of the limbs.

References

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