cases have been reported, as follows: pleural metastases with invasion of the thoracic wall;\textsuperscript{4} invasion of the pleural cavities, possibly due to a spread through a diaphragmatic defect;\textsuperscript{10} pulmonary metastases;\textsuperscript{11} invasion of an axillary lymph node;\textsuperscript{1} subcutaneous localization in the thoracic wall;\textsuperscript{1} metastasis in periortic lymph nodes;\textsuperscript{2} and metastasis in the liver, pancreas, urinary bladder, periaortic lymph nodes, pleura, and pericardium.\textsuperscript{8} In the patient described herein, the extraperitoneal localizations can be explained in two ways. The invasion of the spleen (to our knowledge, not previously noted in cases of pseudomyxoma peritonei) suggests a highly malignant primary tumor, which makes hematogenous dissemination possible; however, since the pleural and pericardial metastases were superficial, a spread through a diaphragmatic defect seems likely. We were not able to prove its existence.

Pseudomyxoma peritonei has to be treated surgically by removal of as many of the lesions as possible, appendectomy, and bilateral oophorectomy. It has to be noted that a combined involvement of the two ovaries and the appendix is possible.\textsuperscript{1} Relapse is very common, but by systematic reintervention a prolonged survival can be obtained. Intraperitoneal or systemic administration of alkylating agents could improve the prognosis.\textsuperscript{8} The use of trypsin during surgery could facilitate the removal of the lesions.\textsuperscript{12} Radiotherapy and intraperitoneal administration of hyaluronidase are ineffective.\textsuperscript{1,6}

\textbf{REFERENCES}


\textbf{Endocarditis due to Pseudomonas aeruginosa in a Heroin Addict\textsuperscript{*}}

\textbf{Successful Treatment with Trimethoprim-Sulfamethoxazole Mixture plus Colistin}

Thomas T. Yoshikawa, M.D.; Arnold S. Bayer, M.D.; and Lucien B. Guze, M.D.

Endocarditis of the tricuspid valve due to \textit{Pseudomonas aeruginosa} in a heroin addict failed to respond to therapy with gentamicin, carbencillin, and amikacin. Clinical and bacteriologic cure was achieved with oral administration of a trimethoprim-sulfamethoxazole mixture plus parenteral therapy with colistin. \textit{In vitro} synergy was demonstrated for the three drugs at concentrations achievable in the serum. Therapy for endocarditis due to \textit{Pseudomonas} continues to be a major problem; however, the successful treatment of this patient warrants consideration for instituting therapy with a trimethoprim-sulfamethoxazole mixture plus colistin in individuals with this infection who fail to respond to standard therapeutic regimens for severe infections with \textit{Pseudomonas}.

Infective endocarditis has been well established as a complication of drug addiction.\textsuperscript{1-3} Although \textit{Staphylococcus aureus} has been the most prevalent pathogen isolated from these patients, \textit{Pseudomonas aeruginosa} is not uncommonly recovered.\textsuperscript{1,2} The results of antimicrobial therapy for endocarditis due to \textit{Pseudomonas} has been disappointing, and therefore, newer chemotherapeutic approaches must be constantly investigated. In this report, we describe a heroin addict with infective endocarditis due to both \textit{S aureus} and \textit{P aeruginosa}. The former pathogen was easily eradicated by therapy with methicillin; however, the latter gram-negative organism persisted in the blood, despite therapy with carbencillin, gentamicin, and amikacin. Institution of treatment with a trimethoprim-sulfamethoxazole mixture plus colistin resulted in clinical and bacteriologic cure.

\textbf{CASE REPORT}

A 26-year-old male heroin addict came to Harbor General Hospital, Torrance, Calif., on May 10, 1975, with a four-week history of fever, loss of weight, pleuritic pain in the left side of the chest, and hemoptysis. There was no prior history of heart disease.

Physical examination on admission revealed an oral temperature of 38.9°C (102°F), blood pressure of 140/80 mm Hg, pulse rate of 120 beats per minute, and respiration rate of 25/min. Abnormal findings included bibasilar moist rales and a grade 2/6 systolic ejection murmur at the left sternal border. Findings from the remainder of the examination were normal.

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unremarkable.

Pertinent laboratory data on admission were a hematocrit reading of 37 percent and normal renal function. Multiple cultures of blood yielded S. aureus and P. aeruginosa. A chest x-ray film demonstrated an infiltrate in the left lower pulmonary field, a transtracheal aspirate grew P. aeruginosa, and an electrocardiogram showed sinus tachycardia.

The patient's therapy and course of hospitalization is depicted in Figure 1. Various antimicrobial agents administered during the first six weeks of hospitalization included methicillin, gentamicin, amikacin, and carbenicillin. Staphylococci were eradicated from the blood, but bacteremia with Pseudomonas persisted. Bone, gallium, and liver-lung scans were normal, as were an intravenous pyelogram and an echocardiogram. The patient refused surgery, and therefore, on the 39th day, he received oral therapy with a trimethoprim-sulfamethoxazole mixture (tablets containing 80 mg of trimethoprim and 400 mg of sulfamethoxazole; three tablets every six hours) and intramuscular injection of colistin (100 mg every eight hours). The patient responded clinically and bacteriologically. Therapy was briefly discontinued because of advancing renal failure, and the patient suffered a relapse. The results of cardiac catherization were unremarkable. Reinstitution of therapy with the trimethoprim-sulfamethoxazole mixture plus colistin again resulted in a salutary response.

With the tenuous nature of the patient's renal function and the uncertainty of his eventual clinical response, cardiac surgery was again advised. The patient consented, and an exploratory cardiotomy revealed normal valves, except for a thickened fibrotic tricuspid valve. Histologic examination of the biopsy of the valve showed healed endocarditis, and a culture was negative. Replacement or ablation of the valve was not performed.

After surgery, after oral alimentation was begun, therapy with the trimethoprim-sulfamethoxazole mixture plus colistin was resumed, and the patient had an uneventful recovery. He remained clinically and bacteriologically cured 3½ months after completion of therapy.

### Methods and Results

*Pseudomonas aeruginosa* was identified from cultures of blood using standard laboratory procedure. The minimal inhibitory concentrations and minimal bactericidal concentrations of gentamicin, carbenicillin, amikacin, and colistin, and the trimethoprim-sulfamethoxazole mixture against this pathogen are listed in Table 1. The organism was resistant in studies with a trimethoprim-sulfamethoxazole mixture and colistin; and, therefore, synergistic studies for these drugs were performed employing the checkerboard technique. Bactericidal synergy was demonstrated with the three-drug combination, as evidenced by at least a fourfold reduction in the minimal bactericidal concentration of each drug when tested alone; i.e., when each drug was tested alone, the minimal bactericidal concentration for *P. aeruginosa* was 40 µg/ml for trimethoprim, 760 µg/ml for sulfamethoxazole, and 25 µg/ml for colistin; vs values of 1.25 µg/ml, 24 µg/ml, and 3.25 µg/ml, respectively, when the drugs were tested in combination.

Serum bactericidal titers (determined one hour after completion of infusion of aminoglycoside or injection of colistin) never exceeded 1:4 while the patient was receiving therapy with the aminoglycoside and carbenicillin; however, during treatment with the trimethoprim-sulfamethoxazole mixture, the titer rose to 1:32.

### Table 1—Antibiotic Sensitivity of *P. aeruginosa* Isolated from Our Patient

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Minimal Inhibitory Concentration, µg/ml</th>
<th>Minimal Bactericidal Concentration, µg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>3.25</td>
<td>3.25</td>
</tr>
<tr>
<td>Carbenicillin</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Amikacin</td>
<td>2.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Trimethoprim*</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Sulfamethoxazole*</td>
<td>380</td>
<td>760</td>
</tr>
<tr>
<td>Colistin</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

As trimethoprim-sulfamethoxazole mixture at ratio of 1:19.
azole mixture plus colistin, titers were consistently greater than 1:4. The serum concentration of amikacin one hour after infusion was 12.0 μg/ml; however, levels of gentamicin and carbenicillin were not determined.

**Discussion**

Endocarditis due to Pseudomonas is now a well-recognized complication of intravenous drug abuse, primarily heroin addiction. The tricuspid valve is most commonly involved. The case reported herein was not dissimilar from the usual case of heroin-associated endocarditis due to Pseudomonas.

Medical therapy for endocarditis due to this pathogen has been disappointing, as noted by Carruthers and Kanokvechayant and by Saroff et al. Most recently, despite the availability of chemotherapeutic agents effective against Pseudomonas, the two largest series of cases of heroin-associated endocarditis due to Pseudomonas reported by Reyes et al and Archer et al had medical cures in 23 and 33 percent of their patients, respectively. Our patient failed to respond to the agents usually effective against Pseudomonas, ie, gentamicin, carbenicillin, and amikacin. Continued bacteremia and refusal of surgery by our patient necessitated a search for an alternative therapeutic regimen.

A recent report suggested that the combination of sulfonamides, trimethoprim and a polymyxin drug demonstrated enhanced activity to gram-negative bacilli, including some strains of *P aeruginosa*. Therefore, it was elected to initiate therapy with a trimethoprim-sulfamethoxazole mixture plus colistin. The patient's fever rapidly abated, and cultures of blood became sterile. Because progressive azotemia ensued, therapy was discontinued, and the patient relapsed with fever and bacteremia. In vitro studies of susceptibility performed in our laboratory demonstrated synergism when all three agents were tested in combination against the pathogen. Therefore, following improvement of renal function, therapy with the trimethoprim-sulfamethoxazole mixture and colistin was reinstituted. An open cardiotomy was subsequently performed, which confirmed the diagnosis of endocarditis but showed that the active infection had resolved. Subsequently, the patient was treated with the trimethoprim-sulfamethoxazole mixture plus colistin for 11 weeks.

To the best of our knowledge, there have been no previous reports of endocarditis due to *P aeruginosa* that was successfully treated with the combination of a trimethoprim-sulfamethoxazole mixture and a polymyxin drug. Rosenblatt et al described two patients treated with a trimethoprim-sulfamethoxazole mixture and polymyxin B, one of whom had endocarditis due to *P aeruginosa*. That patient initially responded and remained without bacteremia for 19 days but subsequently relapsed while receiving therapy. The in vitro testing for susceptibility suggested that the three-drug combination was effectively bactericidal against the Pseudomonas.

In conclusion, endocarditis due to *P aeruginosa* continues to be a major therapeutic problem. Medical cures have been disappointing, even with the availability of several chemotherapeutic agents effective against Pseudomonas. Consideration of administering a trimethoprim-sulfamethoxazole mixture with a polymyxin drug may be warranted when clinical and bacteriologic cure is not achieved with standard chemotherapeutic agents known to be effective against *P aeruginosa*. Moreover, a trimethoprim-sulfamethoxazole mixture is given orally, whereas colistin is generally administered intramuscularly, which may be advantageous in heroin addicts who lack accessible venous sites for intravenous medication.

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**References**


**Putrid Pulmonary Abscess and Empyema with Inappropriate Secretion of Antidiuretic Hormone**

**Joel C. Seidman, M.D.**

The syndrome of inappropriate secretion of antidiuretic hormone has been associated with many pulmonary inflammatory diseases. The origin of the hormone in these cases is the neurohypophysis, although the afferent stimulus has not been adequately characterized. A previously unreported association of this syndrome with putrid pulmonary abscess and empyema is documented.

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796 JOEL C. SEIDMAN

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