Peritonitis is a serious complication of peritoneal dialysis (PD) (1–3); it probably is the most important cause of technique failure in PD (2–5). In Hong Kong, >16% of the deaths in patients who are being treated with PD are secondary to peritonitis (6). Similarly, 18% of the infection-related mortality in PD patients is the result of peritonitis in the United States (7).

Gram-positive organisms remain the most common bacteriologic cause of PD-related peritonitis (1,5,8). Although coagulase-negative Staphylococcus species accounted for nearly half of all Gram-positive episodes (9,10), Staphylococcus aureus peritonitis generally is a more severe form of Gram-positive peritonitis (11,12). S. aureus peritonitis occurs predominantly in patients who have a history of S. aureus catheter infections. Patients who have S. aureus colonization in the nares (13–15), on the skin (16), or at the peritoneal catheter exit site (16–18) are at particular risk for developing S. aureus peritonitis. Even one positive nose culture increases the risk for S. aureus peritonitis (13,19). Patients with S. aureus peritonitis often have severe abdominal pain, require hospitalization, and may require catheter removal for resolution, especially when a concomitant tunnel infection is present (20,21). The outcome of peritonitis that is caused by S. aureus is worse than that of other staphylococci (11,12,22), and the risk for recurrent peritonitis is 60% within 6 mo (9).

Current guideline for the management of S. aureus peritonitis by the Ad Hoc Advisory Committee on Peritonitis Management recommends single effective antibiotics therapy, for example, cefazolin or vancomycin, for 3 wk (23). However, this recommendation was based largely on small clinical studies (11–13,21,22). The clinical course of PD-related S. aureus peritonitis remains unclear. In Hong Kong, PD is the first-line renal replacement therapy for all patients with ESRD (3). Patients are switched to long-term hemodialysis only when they have ultrafiltration failure or peritoneal sclerosis. This policy provides an excellent opportunity for us to examine the clinical feature and therapeutic outcome of S. aureus peritonitis in a large unselected group of PD patients.

Patients and Methods
All episodes of continuous ambulatory PD peritonitis in our unit from 1994 to 2005 were reviewed. The diagnosis of peritonitis was based on at least two of the following (24,25): (1) Abdominal pain or cloudy peritoneal dialysis effluent (PDE), (2) leukocytosis in PDE (white blood cell count >100/ml), and (3) positive Gram stain or culture from PDE. Episodes with peritoneal eosinophilia but negative
bacterial culture were excluded. Exit-site infection was diagnosed when there was purulent drainage, with or without erythema, from the exit site (26).

In the 12 yr of study period, 2065 episodes of peritonitis were recorded; 279 (13.5%) episodes were caused by \textit{S. aureus}. Thirty-four episodes were excluded from analysis because PDE culture showed mixed bacterial growth. The case records of the remaining 245 episodes in 152 patients were reviewed. The demographic characteristics, underlying medical conditions, previous peritonitis, recent antibiotic therapy, antibiotic regimen for the peritonitis episode, requirement of Tenckhoff catheter removal, and clinical outcome were examined.

**Microbiological Investigations**

Bacterial culture of PDE was performed by BacTAlert bottles (Organon Teknika Corp., Durham, NC). Species identification was performed by the API 20E identification system (BioMerieux, Marcy l’Etoile, France). Antibiotic sensitivity was determined by the disc-diffusion method according to the National Committee for Clinical Laboratory Standard (27).

**Clinical Management**

Peritonitis episodes were treated with standard antibiotic protocol of our center at that time, which was changed systemically over time. Initial antibiotics for peritonitis generally were intraperitoneal administration of a third- or fourth-generation cephalosporin, plus or minus intermittent vancomycin every 5 d, or cefazolin as continuous administration plus an aminoglycoside or ceftazidime (5). The dosages of intermittent vancomycin every 5 d, or cefazolin as continuous administration of a third- or fourth-generation cephalosporin, plus or minus antibacterial prophylaxis, eradication of a previous episode with the same organism (23). All bacteriological cause of exit-site infection is summarized in Table 2. Twelve (4.9%) episodes developed when the patient was hospitalized for other reasons. In another 39 (15.9%) episodes, the patient had had hospitalization within 30 d before the onset of \textit{S. aureus} peritonitis. There was a history of antibiotic therapy within 30 d before the onset of \textit{S. aureus} peritonitis in 133 (54.3%) episodes. Antibiotics were given in 36 (14.7%) cases for unrelated medical reasons. In 19 (7.8%) cases, the patient received two or more antibiotics within 30 d before the onset of \textit{S. aureus} peritonitis.

**Methicillin-Resistant \textit{S. aureus}**

Forty-five (18.4%) episodes were caused by methicillin-resistant \textit{S. aureus} (MRSA). In general, MRSA peritonitis was clinically severe and more likely to require hospital admission than were the episodes that were caused by methicillin-sensitive \textit{S. aureus} (MSSA; 17.8 versus 6.0%; \(P = 0.009\)).

We further analyzed the risk factors of isolating methicillin-resistant strains from the patient. Patients with a history of recent hospitalization had a higher risk for isolation of MRSA than did the others (30.6 versus 14.2%; \(P = 0.004\)), but a history of recent antibiotic therapy did not impose a higher risk (17.3 versus 19.6%; \(P = 0.6\)). Patients who developed \textit{S. aureus} peritonitis during hospitalization also had a higher risk for isolation of MRSA than did outpatients (50.0 versus 16.7%; \(P = 0.004\)), but the absolute number of inpatient MRSA peritonitis was small (six of the 45 episodes). Diabetes status, Charlson comor-
The overall primary response rate was 87.8%; the complete cure rate was 74.3%. Episodes that were caused by MRSA had a lower primary response rate (64.4 versus 93.0%; \( P < 0.001 \)) and complete cure rate (60.0 versus 77.5%; \( P = 0.023 \)) than did the others. The clinical outcome, according to the bacterial isolate’s sensitivity to methicillin, is summarized in Figure 1. Twelve (4.9%) patients died during the treatment of peritonitis (see Figure 1). The causes of death were peritonitis per se (five patients), nonperitonitis infection (three patients), myocardial infarction (three patients), and stroke (one patient). Another six patients died within 2 mo after completion of treatment; the causes of death were recurrent peritonitis by another organism (three patients), nonperitonitis infection (two patients), and intestinal obstruction (one patient). The overall 2-mo mortality was 7.3%. Tenckhoff catheter removal was needed in 14 (5.7%) episodes; resumption of PD was possible in eight patients after 3 to 4 wk of temporary hemodialysis.

We then analyzed the predicting factor of treatment response. Patients with primary response were significantly younger than those without response (51.6 ± 13.5 versus 57.3 ± 13.2 yr; \( P = 0.03 \)), but age had no effect on the complete cure rate. Episodes that were treated initially with vancomycin had a higher primary response rate than did those that were treated with cefazolin (94.0 versus 78.8%; \( P = 0.001 \)), but the complete cure rate was similar (76.9 versus 73.1%; \( P = 0.5 \)). Even after episodes that were caused by MRSA were excluded, initial treatment with vancomycin had a higher primary response rate than those with cefazolin (98.0 versus 85.2%; \( P = 0.001 \)). As compared with episodes that could be treated as outpatient, those that required hospital admission had a lower primary response rate (55.0 versus 90.7%; \( P < 0.001 \)) and complete cure rate (50.0 versus 76.4%; \( P = 0.01 \)). Patients who developed \( S. \) aureus peritonitis during hospitalization also had a lower primary response rate than did the others (66.7 versus 88.8%; \( P = 0.022 \)), but the complete cure rate was similar. Diabetes status, Charlson comorbidity score, concomitant exit-site infection, recent hospitalization, and recent antibiotic therapy did not affect significantly the primary response rate or complete cure rate (data not shown).

### Table 1. Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>152</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>81:71</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>52.3 ± 13.5</td>
</tr>
<tr>
<td>Duration of dialysis (mo)</td>
<td>39.3 ± 29.7</td>
</tr>
<tr>
<td>Body height (m)</td>
<td>1.60 ± 0.08</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>60.1 ± 11.2</td>
</tr>
<tr>
<td>Diagnosis (n [%])</td>
<td></td>
</tr>
<tr>
<td>glomerulonephritis</td>
<td>42 (27.6)</td>
</tr>
<tr>
<td>diabetes</td>
<td>38 (25.0)</td>
</tr>
<tr>
<td>hypertension</td>
<td>16 (10.5)</td>
</tr>
<tr>
<td>polycystic</td>
<td>6 (3.9)</td>
</tr>
<tr>
<td>obstruction</td>
<td>9 (5.9)</td>
</tr>
<tr>
<td>other/unknown</td>
<td>41 (27.3)</td>
</tr>
<tr>
<td>Major comorbidity (n [%])</td>
<td></td>
</tr>
<tr>
<td>coronary heart disease</td>
<td>32 (21.1)</td>
</tr>
<tr>
<td>congestive heart failure</td>
<td>43 (28.3)</td>
</tr>
<tr>
<td>peripheral vascular disease</td>
<td>9 (5.9)</td>
</tr>
<tr>
<td>cerebrovascular disease</td>
<td>20 (13.2)</td>
</tr>
<tr>
<td>dementia</td>
<td>10 (6.6)</td>
</tr>
<tr>
<td>chronic pulmonary disease</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>connective tissue disorder</td>
<td>9 (5.9)</td>
</tr>
<tr>
<td>peptic ulcer disease</td>
<td>12 (7.9)</td>
</tr>
<tr>
<td>mild liver disease</td>
<td>22 (14.5)</td>
</tr>
<tr>
<td>diabetes</td>
<td>9 (5.9)</td>
</tr>
<tr>
<td>hemiplegia</td>
<td>20 (13.2)</td>
</tr>
<tr>
<td>diabetes with end-organ damage</td>
<td>38 (25.0)</td>
</tr>
<tr>
<td>any tumor, leukemia, lymphoma</td>
<td>11 (7.2)</td>
</tr>
<tr>
<td>moderate or severe liver disease</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>metastatic solid tumour</td>
<td>0</td>
</tr>
<tr>
<td>AIDS</td>
<td>0</td>
</tr>
<tr>
<td>Charlson comorbidity score</td>
<td>4.7 ± 2.1</td>
</tr>
</tbody>
</table>

### Table 2. Summary of bacterial species that caused exit-site infection

<table>
<thead>
<tr>
<th>Organisms identified (n)</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>( S. ) aureus</td>
<td>35*</td>
</tr>
<tr>
<td>Coagulase-negative ( Staphylococcus ) species</td>
<td>3</td>
</tr>
<tr>
<td>( E. ) coli or other ( Enterobacteriaceae )</td>
<td>3</td>
</tr>
<tr>
<td>( Pseudomonas ) species</td>
<td>5</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>6</td>
</tr>
<tr>
<td>No growth</td>
<td>8</td>
</tr>
</tbody>
</table>

*Four of them were methicillin-resistant \( Staphylococcus \) \( aureus \).

Relapse and Repeat \( S. \) aureus Peritonitis

Of the 245 episodes, 21 (8.6%) developed relapse and 59 (24.1%) developed repeat \( S. \) aureus peritonitis. The time frame for development of repeat peritonitis is summarized in Figure 2. In four episodes, the initial bacterial isolate was methicillin sensitive, but the isolate became MRSA during the repeat episode. Contrary to general belief, peritonitis that was caused by MRSA had a slightly lower risk for relapse or repeat \( S. \) aureus peritonitis than did the episodes that were caused by methicillin-sensitive strains (20.7 versus 39.8%; \( P = 0.048 \)). The initial antibiotic regimen (cefazolin versus vancomycin) had no significant effect on the risk for relapse or repeat peritonitis (31.7 versus 40.9%; \( P = 0.15 \)). Age, diabetes status, Charlson comorbidity score, concomitant exit-site infection, recent hospitalization, and recent antibiotic therapy did not have any effect on the risk for relapse or repeat \( S. \) aureus peritonitis (data not shown).

The primary response rate was similar between patients with and without adjuvant rifampicin therapy (82.4 versus 89.8%;
and so was the complete cure rate (77.9 versus 72.9%; P = 0.4). However, adjuvant rifampicin treatment was associated with a significantly lower risk for relapse or repeat S. aureus peritonitis than was treatment without rifampicin (21.4 versus 42.8%; P = 0.004). Adjuvant rifampicin treatment resulted in 49.9% relative risk reduction in relapse or repeat S. aureus peritonitis (95% confidence interval 14.6 to 70.6%). In other words, one case of relapse or repeat peritonitis could be prevented by treating approximately five patients with rifampicin. The effect of rifampicin remained substantial even after exclusion of cases with early relapse (within 4 wk after completion of antibiotics): Adjuvant rifampicin significantly reduced the risk for repeat peritonitis (23.3 versus 38.0%; P = 0.012). In seven cases, we performed simultaneous Tenckhoff catheter.
the nasal cavity) is one of the most likely explanations. How-

ever, intraperitoneal sequestration of bacteria also is possible, at
least theoretically. A previous study showed that mesothelial
cells can ingest *S. aureus*, and the ingested staphylococcal prol-
erated abundantly within mesothelial cells, which may be
released subsequently (34). Recently, Haslinger-Loffler et al.
(35) showed that after host cell invasion, *S. aureus* resided
within phagocytotic vacuoles, and mesothelial cells seemed to be
able to degrade staphylococci. However, even after prolonged
infection, a high percentage of *S. aureus* remained alive within
mesothelial cells and might be released after host cell death
(35).

We found that adjuvant rifampicin is highly effective in
preventing relapse or repeat *S. aureus* peritonitis, presumably
by eradicating occult colonization in other body parts. It is
interesting that rifampicin also is particularly useful in target-
ing intracellular bacteria, as discussed. Our result is consistent
with previous reports (36–39). For example, Zimmerman et al.
(37) reported that periodic oral rifampin reduced the rate of
staphylococcal exit-site infection. Bernardini et al. (38) showed
that the use of either rifampin or mupirocin was associated
with low rates of staphylococcal catheter infections and catheter
loss. In another study with historical controls, the rate of staph-
ylococcal exit-site infection and peritonitis was lower after oral
rifampin prophylaxis (39). However, extensive use of rifampi-
cin for the eradication of *S. aureus* carriage is hindered by rapid
recolonization (39), and the risk for development of resistance is
considerable. Our data, however, provide support for the use of
rifampicin for the secondary prevention of *S. aureus* peritonitis
after an index episode, which probably can reduce the unnec-

Discussion

We found that the overall clinical outcome of *S. aureus* peri-
onitis is not encouraging. Only 51% of patients with MSSA peri-
onitis and 46% with MRSA peritonitis had complete cure
without need for catheter removal, relapse, or recurrent or
repeat peritonitis. Notably, repeat *S. aureus* peritonitis devel-
oped in almost one third of the patients with complete cure.
More important, we found that more than half of the repeat
peritonitis occurred within 3 mo after completion of antibiotics.
The result is distinctly different from that of our previous study
on *Enterobacteriaceae* peritonitis (28), which found that repeat
peritonitis occurred evenly in 1 yr after the index episode.
Traditionally, most cases of *S. aureus* peritonitis are associ-
ated with a catheter infection (29); catheter removal often is required
to resolve the peritonitis or to prevent repetitive episodes
(21,30,31) because concomitant colonization or infection of the
exit site with *S. aureus* is associated with a substantially in-
creased risk for relapse (32). In the present series, one fourth of
the patients had exit-site infection. Contrary to our previous
reports on *Pseudomonas* (33) and *Enterobacteriaceae* peritonitis
(28), exit-site infection was not associated with the treatment
response in the present study, and elective change of PD cath-
eter seemed ineffective in preventing repeat *S. aureus* periton-
itis. Our result suggests that there are important contributing
factors of relapse, and repeat episodes were caused by factors in
addition to an infected catheter. Persistent carrier state (e.g., in
the nasal cavity) is one of the most likely explanations. How-

Figure 2. Distribution histogram of the time of developing re-
peat peritonitis after antibiotic treatment was completed. *Re-
lapse S. aureus* peritonitis by definition.
the actual reason remains obscure, our result indicates that vancomycin is a valuable salvage agent of MSSA peritonitis when response to cefazolin is unsatisfactory.

In the present study, nearly 20% of the episodes were caused by MRSA. Published literature on MRSA peritonitis in PD patients is scarce; our series probably is the largest one to date. Conforming to the general belief, the major risk factor for MRSA was recent hospitalization but not recent antibiotic treatment. It could be argued that patients with recent hospitalization should receive vancomycin rather than cefazolin as first-line coverage of Gram-positive organisms. However, only 19 of the 51 patients with recent hospitalization before S. aureus peritonitis actually had MRSA isolated; a substantial proportion of patients would be treated with vancomycin unnecessarily if the antibiotic is used as the first-line agent.

**Conclusion**

S. aureus peritonitis is a serious complication of peritoneal dialysis. Recent hospitalization is a major risk factor for methicillin resistance in the bacterial isolate. However, in patients with inadequate response to cefazolin, vancomycin often is effective even when the bacterial isolate is sensitive to methicillin in *vivo*. Relapse and repeat peritonitis is common. Rifampicin is a valuable adjunct in preventing relapse and repeat S. aureus peritonitis after the index episode.

**Acknowledgments**

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**Disclosures**

None.

**References**


Khirsgar et al. (pages 239–244) and Szeto et al. focus on specific infections seen in patients undergoing renal replacement therapy. The devastating consequences of such infections on hospitalization rates and outcomes is summarized in data from the US ESRD population by Chavers et al. in this month’s issue of JASN (pages 952–959).