The Microbiology of Postoperative Peritonitis

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Postoperative peritonitis carries a higher risk of complications and mortality than does community-acquired disease. Little, however, is known about the specific microbiology of this condition. To gain insight into this problem, the microbiological findings of 67 patients with postoperative peritonitis were compared with those of 68 patients with community-acquired peritonitis. In a comparison of postoperative peritonitis with community-acquired disease, the number of isolates of enterococci (23 versus 6) and Enterobacter species (13 versus 4) were increased and the number of isolates of Escherichia coli (21 versus 42) were reduced. Antibiotic therapy before reintervention increased the number of resistant organisms at relaparotomy (33% versus 8%). The in vitro efficacy of the primary antibiotic or combination of drugs did not affect mortality rates (40% versus 38% after effective and ineffective treatment, respectively). Thus, the microbiology of postoperative peritonitis differs significantly from that of community-acquired disease, and specific antibiotic therapy is required, despite the doubtful impact on survival.

The microbiology of secondary peritonitis is well characterized. Because it is mainly a community-acquired disease, advanced antimicrobial resistance does not usually occur, and effective antibiotic strategies have been derived from the knowledge of the bacteria involved [1–5]. Postoperative peritonitis is considered a particularly threatening form of intra-abdominal infection. With regard to the bacteria involved, however, little information is available thus far about whether antibiotic schemes of secondary peritonitis in general can be applied indiscriminately to the postoperative disease or whether other bacteria have to be expected [6]. In cases of postoperative peritonitis, the situation may be far more complex than in community-acquired cases. The patient has usually been hospitalized for >1 week, with ample opportunity to acquire resistant bacteria. Prior use of antibiotics can also increase resistance, but it may also change the bacterial spectrum because of selection [7–9]. The fact is that a patient might have a postoperative complication caused by an underlying disease, such as a systemic malignancy, chronic alcohol abuse disease, or autoimmune disease, which has not yet been diagnosed but which still has an impact on, for example, anastomotic healing or the ability to overcome an infectious challenge. Finally, postoperative peritonitis is far less common than is community-acquired disease, which makes it more difficult to collect a significant number of bacterial findings within a single institution [10]. Thus, information in the literature about the microbiology involved in postoperative peritonitis is scarce [6, 11].

Therefore, we collected the microbiological findings of 67 cases of postoperative peritonitis to characterize specific microbiological problems associated with this condition. The data should provide insight into the bacterial spectrum of postoperative peritonitis, identify microbiological prognostic factors, and lead to a rational antibiotic therapy.
METHODS

From September 1994 through June 2000, patients with postoperative peritonitis were prospectively documented at our institution. Cases of anastomotic leakage after pancreatic surgery were included when purulent peritonitis was present, and postoperative abscesses were included if prior interventional treatment was considered impossible or had failed. Postoperative peritonitis as a sequela of nonresolved community-acquired peritonitis was excluded. Along with other patient and disease data, all microbiological findings that had originated from the relaparotomy were entered into a database.

Microbiological workup was based on routine procedures. Swabs were taken at relaparotomy from the abdominal cavity and stored for transport in standard media (BBL swabs and Port-a-cul tubes; Becton Dickinson).

Smears of all specimens were Gram stained. The mean number of inflammatory WBCs and organisms seen in 10–20 high-power fields was recorded for each specimen. Samples were then inoculated on blood agar, heated blood agar, Endo agar, and Columbia-cysteine–yeast extract agar. The number of bacteria in the specimen was assessed semiquantitatively by use of the 4-quadrant streak plate method and was considered high when bacteria were present up to quadrants 3 or 4. Enterobacteriaceae were identified using the API 20E system (BioMérieux).

The microbiological findings were compared with those from cases of community-acquired peritonitis from a multicenter trial on antibiotic treatment of this condition, which was organized at our institution [12]. Both studies were conducted simultaneously, and the microbiological workup did not differ.

Relative frequencies were used for descriptive statistics. Comparisons between groups were made by means of the χ² test or, for small sample sizes, Fisher’s exact test. A P value of .05 was considered significant. The α error was not corrected for repeated significance testing.

RESULTS

During the time period of the study, 93 patients underwent operations for postoperative peritonitis. Cultures yielded bacteria from 67 of these patients, who are the study population of this report. The colon (27 cases) was, in most cases, the site of the primary procedure. The stomach (14 cases), pancreas (10 cases), small intestine (9 cases), and others were less frequently the site (figure 1). At relaparotomy, the source of the infection was most often a suture dehiscence (44 cases; figure 2). Sixty-eight of 114 patients with community-acquired peritonitis yielded bacteria in the peritoneal exudate. The cause of the infection was equally often the stomach, the colon, and the appendix (figure 3). The median Acute Physiology and Chronic Health Evaluation (APACHE) II score was 14 for patients with postoperative peritonitis and 10 for those with community-acquired disease. Forty-one (61%) of 67 patients with postoperative peritonitis survived, and 26 (39%) died of the complication. Six (9%) of 68 patients with community-acquired peritonitis died.

The overall number of bacteria cultured from abdominal swabs at relaparotomy for postoperative peritonitis was 111. In cases of community-acquired peritonitis, 118 strains were cultured. Enterococci found in the postoperative cases (23 isolates) by far outnumbered those in patients with community-acquired disease (6 isolates; P = .001). The number of Escherichia coli, in contrast, which was the strain most typical for community-acquired peritonitis (42 isolates), was reduced to only 21 isolates in the postoperative cases (P = .005). Enterobacter species, the third most common bacterium in patients with postoperative peritonitis (13 isolates), was found only 4 times in patients with community-acquired peritonitis (P < .05). Among the gram-positive isolates, 21 isolates of various streptococci were cul-
tured from cases of community-acquired peritonitis, but only 4 isolates were found in the patients with postoperative cases (P < .005; table 1). *Staphylococcus aureus* and coagulase-negative staphylococci (7 and 6 isolates in patients with postoperative peritonitis, respectively) were each found only once in patients with community-acquired disease (P < .05). Although *Pseudomonas* species were more common in postoperative cases, the difference did not reach significance (table 1).

The differences in microbiological findings between postoperative and community-acquired peritonitis are mainly based on the bacteriology of those patients who did not survive. The low overall incidence of *E. coli* in postoperative cases can be split into only 5 isolates from nonsurvivors (9% of all isolates from this group) compared with 16 from survivors (28% of the respective group; P < .05; table 2). Conversely, *Enterobacter* species were recovered only 3 times (5%) in survivors but 10 times (19%) in nonsurvivors (P < .05). This pattern applied to enterococci as well (17% in survivors and 25% in nonsurvivors), but the difference was not significant. With regard to community-acquired peritonitis, the analysis of survivors versus nonsurvivors did not show marked differences because of the low mortality rates.

In 3 patients, antimicrobial treatment was not initiated at relaparotomy but only after cultures had yielded organisms. The remaining 64 patients received a wide spectrum of different antibiotics and combinations from the time point of relaparotomy onward. The most-frequently used drugs or combinations were cefotaxime–metronidazole (19 cases), piperacillin–tazobactam (13 cases), imipenem–cilastatin (12 cases), and mezlocillin with or without metronidazole (7 cases).

Forty-three patients received antibiotics for at least 3 days before relaparotomy. When these patients were compared with the 24 patients who were not treated with antibiotics before relaparotomy, the observed shift of the intraabdominal microbial spectrum in postoperative peritonitis compared with community-acquired disease was found to be associated with antibiotic treatment before relaparotomy. Patients who did not receive interval antibiotics had a spectrum more typical of community-acquired peritonitis, with *E. coli* representing ~36% of the bacteria detected, whereas, after interval antibiotics, *E. coli* was reduced to 11% (P < .005). Enterococci, in contrast, accounted for 24% of isolates after interval antibiotics and for 14% of isolates in patients who did not receive this treatment (not significant). *Enterobacter* species were equally distributed (table 3). Coagulase-negative staphylococci were found only after antibiotic treatment, but the number was too small for us to draw conclusions.

Antibiotic treatment before relaparotomy had a major impact on the efficacy of the subsequent treatment. After interval treatment, the bacteria found at relaparotomy were completely resistant to the antibiotic chosen in 14 of 43 patients, whereas there were only 2 such cases among 24 patients not treated between the operations (P < .05). This resistance problem, however, did not have an impact on survival. Sixteen (62%) of 26 nonsurvivors and 25 (61%) of 41 survivors had received interval antibiotics.

The use of substances without activity against enterococci was not followed by an increased frequency of this bacterium at relaparotomy. Twenty-one patients who received such treatment had 7 isolates of enterococci, whereas the other 46 patients had 16.

When disease data of patients with or without interval antibiotics were compared, there were no differences between groups in terms of age, interoperative interval, duration of symptoms, organs involved, preoperative organ failure, or source control. The median APACHE II score calculated before relaparotomy, however, was 17 for patients who received interval antibiotics and 12 for patients who did not, which indicates a more severe disease in the first group.

In the group of nonsurvivors, 14 of 45 bacteria were not covered by the antibiotic treatment, whereas there were 17 such cases out of 61 strains in the group of survivors. Similarly, when looking at overall efficacy of antibiotics or combinations given to individual patients against all of the bacteria obtained by culture from the respective patients, we failed to see a relation between efficacy of antibiotic treatment and outcome (table 4).

**DISCUSSION**

Postoperative peritonitis is one of the most serious complications in abdominal surgery. This stands in contrast to the small number of publications referring to this condition as an entity of its own [6, 10, 11, 13]. Under the assumption that
Table 1. Bacteriology of postoperative versus community-acquired peritonitis.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Postoperative peritonitis (n = 111)</th>
<th>Community-acquired peritonitis (n = 118)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococci</td>
<td>23 (21)</td>
<td>6 (5)</td>
<td>.001</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>21 (19)</td>
<td>42 (36)</td>
<td>.005</td>
</tr>
<tr>
<td><em>Enterobacter</em> species</td>
<td>13 (12)</td>
<td>4 (3)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td><em>Bacteroides</em> species</td>
<td>8 (7)</td>
<td>12 (10)</td>
<td>.05</td>
</tr>
<tr>
<td><em>Klebsiella</em> species</td>
<td>8 (7)</td>
<td>8 (7)</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>7 (6)</td>
<td>1 (1)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>6 (5)</td>
<td>1 (1)</td>
<td>.05</td>
</tr>
<tr>
<td><em>Candida</em> species</td>
<td>4 (4)</td>
<td>8 (7)</td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas</em> species</td>
<td>7 (6)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>Streptococci</td>
<td>4 (4)</td>
<td>17 (14)</td>
<td>.005</td>
</tr>
<tr>
<td>Hemolyzing streptococci</td>
<td>4 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10 (9)</td>
<td>13 (11)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>111</td>
<td>118</td>
<td></td>
</tr>
</tbody>
</table>

The bacterial spectrum observed in the control group of patients with community-acquired peritonitis matches the reports by other authors well [15, 16, 18, 19], but the data from the postoperative cases stand out. Montravers et al. [6] reported similar findings with regard to enterococci (42 isolates), but in his group of patients with postoperative peritonitis, *E. coli* (56 isolates) was detected more frequently. The data are reconfirmed to some extent by Carlet et al. [11]; although they reported findings from only 10 patients, they still found enterococci to be the most common strain. The emergence of enterococci in patients with postoperative peritonitis can be expected from data in the literature, in which severely sick and immunocompromised patients are characterized to be at risk for enterococcal infections [7, 18, 20, 21]. A similar pattern applies to *Enterobacter* species, which are also known to be promoted by prior antibiotic therapy and deteriorated patient condition [22]. A significant increase in enterococci after therapy with third-generation cephalosporins when compared with other antibiotics, however, as found by Dahms et al. [7] and Magnussen and Cave [9], was not observed in our study.

The reduction in *E. coli* can be attributed to various factors, of which the impact of antibiotic therapy between the laparotomies is probably more important than the effect of perioperative prophylaxis, as discussed below. The reduction in streptococci, in contrast, may be a selection phenomenon of perioperative prophylaxis effective against these organisms.

*Candida* species were found more frequently in patients with community-acquired peritonitis than they were in patients with postoperative cases. Commonly recommended treatment schemes for community-acquired peritonitis do not call for treatment, because, in these cases, *Candida* species can be readily overcome by the physiological defense [5, 23, 24]. In cases of postoperative peritonitis, the source and importance of these organisms initially might be the same, whereas in later stages after treatment schemes with broad-spectrum antibiotics, they can represent a severe threat to the patient; however, only 4 isolates were found, which does not allow for speculation regarding their background.

To a large extent, the bacteriologic pattern observed resembles that of persistent [25] or tertiary peritonitis [26, 27], but the fact must be stressed that our patient cohort exclusively contained cases of new-onset postoperative peritonitis, whereas all patients with persistent disease were excluded. Sawyer et al.
Table 2. Bacteriologic findings at relaparotomy in survivors and nonsurvivors of postoperative peritonitis.

<table>
<thead>
<tr>
<th>Strain</th>
<th>No. (%) of isolates recovered from Survivors (n = 58 isolates)</th>
<th>Nonsurvivors (n = 53 isolates)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococci</td>
<td>10 (17)</td>
<td>13 (25)</td>
<td>.05</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>16 (28)</td>
<td>5 (9)</td>
<td></td>
</tr>
<tr>
<td><em>Enterobacter</em> species</td>
<td>3 (5)</td>
<td>10 (19)</td>
<td>.05</td>
</tr>
<tr>
<td><em>Bacteroides</em> species</td>
<td>4 (7)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella</em> species</td>
<td>4 (7)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>3 (5)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>4 (7)</td>
<td>2 (4)</td>
<td></td>
</tr>
<tr>
<td><em>Candida</em> species</td>
<td>1 (2)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas</em> species</td>
<td>6 (10)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Streptococci</td>
<td>1 (2)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (10)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>58</strong></td>
<td><strong>53</strong></td>
<td></td>
</tr>
</tbody>
</table>

[22] described a cohort of patients with peritonitis who had APACHE II scores of >15 and, consequently, high mortality rates. Of interest, in this group, the bacteria found were similar to those obtained by culture from patients with postoperative peritonitis in our study. This seems to indicate a correlation between the severity of the disease and the bacteria involved.

Our observation of a different bacteriologic pattern of survivors compared with nonsurvivors has not been reported before. Although the microbiology found in nonsurvivors does not seem to represent a more serious threat, it can be assumed that the condition of those patients, who eventually die, triggers the infection with such bacteria. However, it is not clearly understood why the incidence of *E. coli* in fatal cases is decreased. Because a correlation between the antibiotic treatment and the outcome of the patient could not be shown, it does not seem likely that antibiotics are responsible for the different microbial spectrum between survivors and nonsurvivors. It is possible that the condition of the patients allows or even favors overgrowth of other bacteria that then reduce the load of *E. coli*. The study by Sawyer et al. [22] lends support to this assumption that patient factors are involved in the development of the bacterial inoculum that can finally be yielded from the abdominal cavity.

The fair prognosis of patients who harbored *Pseudomonas* organisms in their abdominal cavities might be caused by the fact that all isolated strains of this bacterium were sensitive to commonly used anti-*Pseudomonas* antibiotics and were covered by the treatment in 5 of the 6 surviving patients from the beginning.

The number of patients who received interval antibiotics before relaparotomy seems to have been fairly high (62%), but Montravers et al. [6] reported a rate as high as 80% for these cases, which reflects the fact that most surgeons do not dare to leave these patients without antibiotics before the decision to reoperate. The difference between the bacteriologic findings of patients with or without interval antibiotics shows that those patients who had antibiotics prior to relaparotomy account for, to some extent, the different findings of postoperative versus community-acquired peritonitis. Although the explanation seems obvious—that the use of broad-spectrum antibiotics has reduced the number of common and susceptible gram-negative organisms—other mechanisms should be involved as well. Although the patient groups do not differ with regard to other data, the patients with interval antibiotics have a significantly higher APACHE II score than do the others. Delay of the relaparotomy in this group, which might be caused by the antibiotic treatment, cannot be shown by comparing the intervals before and after relaparotomy.
between laparotomies (antibiotic vs. no antibiotic: median, 9 vs. 8 days; mean, 10.5 vs. 9.2 days; not significant) or by comparing the duration of symptoms prior to the relaparotomy. Therefore, the differences in bacteriology could be related to the underlying patient condition as well. The higher APACHE II scores of the patients who received antibiotics preoperatively is indicative of a more threatening disease, which may in turn call for antibiotics to be administered earlier, with the result of the changes in bacteriologic flora described above.

Although several factors ranging from patient condition to the bacterial findings were related to survival, the choice of the antibiotic both prior to and after relaparotomy was not. In our study, the selection of the antibiotic was made by the surgeon according to his impression of the severity of the disease. This implies a very strong selection bias when the efficacy of different antibiotics is compared. In some cases, a patient might have even recovered after eradication of an intraabdominal focus without the use of antibiotics at all, whereas highly effective broad-spectrum antibiotics did not salvage a patient whose condition was otherwise desperate. It is therefore impossible to compare the efficacy of different antibiotic regimens in this setting. Similarly, in a study of the Surgical Infection Society, Christou et al. [28] found that, in an observational multicenter trial on different types of secondary peritonitis, no correlation was seen between outcome and type of antibiotic used.

It is surprising that we even failed to see a difference in outcome between patients treated initially with antibiotics that are effective against the bacteria cultured and those treated with antibiotics that are ineffective against the bacteria. Even a complete lack of bacteriologic efficacy was not associated with higher mortality rates. This finding stands in sharp contrast to the result of Montravers et al. [6], which was that the adequacy of the primary antibiotic treatment is decisive for the final outcome, no matter which secondary adjustments are being made.

Montravers et al. [6] excluded from analysis all patients among whom source control was not achieved. With the exception of gallbladder perforation, we consider source control impossible in almost all cases of upper-abdominal postoperative peritonitis. These patients account for approximately one-half of the cohort, and they have a particularly high mortality rate, which does not seem to depend much on the antibiotics used. Thus, a selection bias might cause the different conclusions drawn from our study and that of Montravers et al. [6].

The importance of the primary choice of antibiotic in abdominal sepsis is challenged as well by the findings of Christou et al. [2], who compared the effect of antibiotic treatment of abdominal sepsis with cefoxitin with that with imipenem-cilastatin. Although the microbiological effectiveness was 72% versus 98% for cefoxitin and imipenem-cilastatin, respectively, there was no significant difference in the clinical failure rate.

When comparing these findings with those of an infection in which the adequacy of the primary antibiotic has a significant impact on survival, such as nosocomial pneumonia or bloodstream infection [29, 30], the more complex character of peritonitis has to be considered. Although the antibiotic is more or less the only therapeutic means in pneumonia, in peritonitis the surgical treatment, the organ support, and other factors contribute to the result, which may obscure antibiotic failures. Therefore, we consider the lack of correlation between outcome and antibiotic effectiveness not to affect future choices of antibiotics under these severely threatening conditions. It can be concluded from the bacteriologic spectrum found in this study that the common treatment of community-acquired peritonitis by third-generation cephalosporins and metronidazole is not adequate for postoperative cases, because gram-positive bacteria, which are not covered by this regimen, outnumber gram-negative bacteria, among which the most threatening, Enterobacter species, are not sufficiently covered either.

Although the decision on a pending relaparotomy must be made as soon as possible with all available diagnostic means, the antibiotic therapy should address the specific bacteriologic characteristics of postoperative peritonitis. As for other conditions, it seems appropriate to set up a standard of antibiotic therapy within an institution, which should provide broad gram-negative and gram-positive coverage for these cases and can be modified after results of individual bacteriologic treatment are available.

### References

7. Dahms RA, Johnson EM, Statz CL, et al. Third generation cephalo-