Antimicrobial Culture and Susceptibility Testing Has Little Value for Routine Management of Secondary Bacterial Peritonitis

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The traditional surgical practice of routinely culturing specimens from patients with community-acquired intraabdominal infections, such as appendicitis, contributes little to the management of the individual patient, either initially or later when infectious complications have developed. Instead of performing routine cultures for peritonitis, a modified approach that still facilitates hospital surveillance for microbial resistance patterns should be used.

The traditional surgical practice of routinely culturing specimens from patients with community-acquired intraabdominal infections, such as appendicitis, has come under increasing scrutiny. It is argued that the results of such routine culturing seldom influence the management of the individual patient, either initially or later when infectious complications have developed. If such is the case, of course, routine culturing may not be cost-effective and should be abandoned. This review will explore these issues.

Broad-Spectrum Empirical Antibiotic Therapy for Peritonitis

Although some 400 species of bacteria may be isolated from the gut, especially the colon, apparently only a few species are actually involved in intraperitoneal infections, usually a combination of enteric aerobes and anaerobes [1]. *Escherichia coli* is the most common enteric aerobic isolated, while *Bacteroides fragilis* is the most frequently isolated anaerobe. Over the last two decades, the use of broad-spectrum empirical antibiotic therapy directed against these organisms has become commonplace in the treatment of secondary bacterial peritonitis.

The basis of this empirical approach to the drug management of peritonitis has largely been experimental. Animal studies performed since the mid-1970s have shown that peritonitis can be roughly divided into two stages: an early liquid or free-flowing stage followed in 7–14 days by an abscess stage [2, 3]. During the early stage, *E. coli* predominates numerically and is the organism most commonly recovered from the bloodstream. The natural mortality associated with this stage is ~40%, and virtually all surviving animals develop intraabdominal abscesses. The numerically dominant organism in the late or abscess stage, however, is *B. fragilis* (mean concentrations as high as 10⁹ organisms/mL of pus), although the presence of facultative organisms is apparently also necessary for abscess formation to occur [4]. Such results suggest that gram-negative aerobic organisms are responsible for early mortality due to acute peritonitis whereas anaerobic organisms are more important during abscess formation. Both types of bacteria, though, are present during each stage.

It is of interest that a similar pattern has been recognized clinically: the longer peritonitis has been present, the more likely the recovery of anaerobes from the septic focus. In one study, the number of aerobic strains from peritoneal cultures outnumbered anaerobes when the duration of illness was <3 days. When the illness had lasted >3 days, however, anaerobes outnumbered aerobes [5].

Working with the rat peritonitis model, Weinstein et al. [6] and Nichols et al. [7] showed that antibiotics effective against aerobes reduce early mortality but not late abscess formation. In contrast, antibiotics effective mainly against anaerobes do not reduce early mortality but do prevent abscesses in surviving animals. An antibiotic regimen (an aminoglycoside plus clindamycin) effective against both aerobes and anaerobes reduced both early mortality and late abscess formation. Indeed, comparable favorable results can be obtained with almost any drug or drug combination whose spectrum of antimicrobial coverage is similar [8]. Animal studies such as these suggest that intraabdominal sepsis of enteric origin is managed effectively with empirical antibiotics directed against the aerobic and anaerobic gut flora.

Though perhaps less definitive, the results of clinical trials on the antibiotic management of peritonitis have generally paralleled the findings of the animal studies. Thadepalli et al. [9] conducted a prospective, randomized study comparing the use of cefaloctin-kanamycin vs. clindamycin-kanamycin as presumptive therapy for penetrating bowel injuries. The drugs were administered parenterally before laparotomy. Anaerobic infections were almost twice as frequent in the cefaloctin-kanamycin group as they were among patients receiving anaerobic coverage with clindamycin-kanamycin. The overall septic complication rate was also significantly lower among the clindamycin-kanamycin group, the difference being due almost entirely to a reduction in infections involving anaerobic or mixed flora.
Berne et al. [10] conducted a comparative trial of gentami-
cin-clindamycin vs. two different cephalosporin regimens in the
management of perforated or gangrenous appendicitis. Patients
who received gentamicin-clindamycin therapy had far fewer
septic complications than those who received therapy with the
cephalosporin regimens. Primary therapy failed for 15% (7/47)
of patients treated with cefoperazone and for 23% (11/48) treated
with cefamandole but for only 2% (1/52) treated with
gentamicin-clindamycin. In a follow-up to this report, Heseltine
et al. [11] studied the causes of treatment failure and found
that most were associated with the recovery of resistant
*B. fragilis* from intraoperative cultures.

In a retrospective study of perforated appendicitis, David et
al. [12] found that children treated with ampicillin, gentamicin,
and clindamycin had markedly fewer wound infections (2%) and
abscesses (5%) than those receiving only ampicillin and/or
gentamicin (wound infections, 36%; abscesses, 18%).

Thus, broad-spectrum empirical drug therapy for peritonitis
appears to be effective. Indeed, it is the very success of this
approach, with its failure rate of only 10%–15%, that has led
surgeons to question the necessity of performing intraperitoneal
cultures when empirical therapy is being used [13–16]. Sur-
geons perceive that routine culturing does not affect antibiotic
selection or clinical outcome. By the time that culture and
susceptibility results become available, especially anaerobic
susceptibilities that may take up to 4 days and are seldom
routinely performed by hospitals anyway, clinical outcome has
already been determined.

**Retrospective Assessment of Routine Culturing for
Peritonitis**

To date, all studies of the performance of cultures in the
management of peritonitis have been retrospective [13–17].
Unfortunately, while such studies may demonstrate that routine
culture results are seldom used, it is doubtful that they can
establish whether routine culturing should be performed.

Jaffers and Pollock [13] were probably the first investigators
to suggest that routine culturing for peritonitis (appendectomy)
might not be cost-effective. In a review of 363 patients who had
undergone appendectomy and for whom intraoperative cultures
had been performed, the investigators found that in no case had
drug therapy been changed because of culture and susceptibility
results. However, Jaffers and Pollock [13] provided few details
of antibiotic therapy and did not indicate whether organisms
cultured intraoperatively were subsequently isolated from post-
operative infections. Nevertheless, they concluded that except
for high-risk patients, routine culturing during appendectomy
was costly and unnecessary.

My colleagues and I [14] reviewed 104 cases of perforated
or gangrenous appendicitis treated with aminoglycoside combi-
nation regimens, usually an aminoglycoside plus clindamycin
or metronidazole. The results of cultures appeared to influence
antibiotic therapy in only 7% of these cases, and the results of
routine cultures obtained at laparotomy appeared to influence
antibiotic therapy in only 2% of cases. Although discriminant
analysis identified postoperative infectious complications as the
principal determinant of the usefulness of culture, culture re-
sults were seldom used even in this connection. Only two
infectious complications resulted from organisms resistant to
all antibiotics that the patients had previously received.

Similarly, McNamara et al. [16] found that changes in antibi-
otic therapy that were based on culture results were made for
only 7% of 131 patients whose treatment for simple or compi-
lcated appendicitis included routine intraperitoneal cultures.
Moreover, the results of intraoperative cultures did not affect
therapy for any of the patients with infectious complications.

Mosdell et al. [17] reported that the antibiotic regimen was
changed on the basis of the results of routine intraoperative
cultures for only 10% of children with perforated appendicitis.
They concluded that routine culturing for patients with this
disease was of no clinical use.

In another study, Mosdell and colleagues [15] reviewed 480
cases of intraabdominal infection treated surgically at five dif-
ferent hospitals over a 2-year period. Antibiotic management
varied widely; up to 20% of patients did not receive empirical
coverage for anaerobes. Intraoperative cultures were obtained
in 68% of these cases; of these, only 7% of the cultures were
reported to have no growth—a surprisingly low figure. A com-
plicated algorithm requiring the literal application of culture
data (vs. clinical context) was used to classify patients ac-
cording to whether their empirical drug therapy was (A) exces-
sive, (B) adequate, or (C) inadequate. They were further classi-
cified into three groups: changes in the empirical drug regimen
were not made in Group 1, changes were made to bring therapy
into compliance with culture data in Group 2, and changes
were made inappropriately in Group 3.

The investigators concluded that changes in drug therapy
were appropriate from the standpoint of culture data in only
9% of cases. Moreover, from subset analysis of just 49 of the
patients (36 C1 and C3 patients vs. 13 C2 patients), they as-
serted that postoperative changes in the empirical drug regimen
based on culture results did not improve clinical outcome—a
rather sweeping generalization for so few patients.

In addition to illustrating the problems of retrospective anal-
ysis and the hazards of using too small a sample size (poten-
tially leading to type II statistical error), this study also raises
interesting questions about the interpretation of culture data
[15]. Should the results of intraperitoneal cultures be taken
literally or should they be interpreted in a clinical context? In
other words, should antibiotic therapy be a strict function of
culture results, or should appropriate use of antibiotics and
appropriate use of cultures be treated as separate, yet related
issues?

For example, if broad-spectrum empirical perioperative anti-
biotic coverage is instituted for a patient with peritonitis, fever,
and leukocytosis but no organisms are recovered from culture
(a frequent clinical occurrence [13, 14, 16, 18, 19]), should
antibiotic therapy be stopped simply because cultures are negative? Suppose resistant organisms are recovered from culture but the patient is doing well on postoperative day 4. Should antibiotic therapy be modified anyway based on the culture results? If culture yields only aerobes or only anaerobes, should anaerobic or aerobic drug coverage (respectively) be dropped?

Such questions could probably be answered only by a prospective, randomized investigation for which rapid—even intraoperative—culture and susceptibility data were available. In the meantime, rather than taking culture results literally, most surgeons will probably rely on broad-spectrum empirical drug coverage for patients with peritonitis and will interpret culture results within the context of the clinical circumstances.

Culture-Driven Changes in Empirical Antibiotic Therapy

It is perhaps not surprising that the results of intraoperative cultures are seldom used since, for various reasons, the postoperative modification of empirical antibiotic regimens in response to such results may be of little value. Although identification and susceptibility testing of anaerobic organisms may require up to 4 days, there is evidence that antimicrobials are most effective during the early “decisive period” (the first few hours) of antinfective therapy. Studies by Burke [20] showed that the likelihood of antibiotic cure of soft-tissue infection without the formation of an abscess diminishes rapidly after the first several hours.

In a study of gram-negative bacteremia of biliary or urinary origin, Anderson et al. [21] found that inadequate dosing of aminoglycosides quickly led to breakthrough blood-borne infection due to drug-susceptible organisms and resulted in high mortality, thus illustrating the importance of early adequate therapy with effective agents. For peritonitis in particular, bacterial clearance by the reticuloendothelial system is greatest during the early phase of the infection. Later on, bacterial sequestration within fibrin clot as well as microbial proliferation—and perhaps other factors—limit the effectiveness of antibiotics [22].

Thus, by the time that the results of routine intraoperative cultures become available, the outcome of therapy for peritonitis (resolution or persistent and/or recurrent infection) has probably already been determined. Indeed, failures of empirical antibiotic therapy for peritonitis are so often due to drug-susceptible organisms that factors other than antibiotics (e.g., status of the host defenses, and adequacy of surgical management) would seem to be of greater importance [14, 15].

Moreover, even when resistant organisms are recovered from culture, empirical drug therapy is typically continued if the patient is doing well [23]. For the individual patient with secondary bacterial peritonitis, therefore, culture and susceptibility results are probably most useful when collected later in the hospital course to handle postoperative infectious complications. Even for this purpose, however, culture results may seldom be used [14].

Despite the foregoing results, however, intraoperative culturing for most cases of peritonitis may still be warranted. Dramatic changes in the health care system with emphasis on managed care have led to early discharge from the hospital. As a result, nosocomial pathogens may be introduced into the community and resistant organisms may be recovered more frequently from patients with community-acquired infections. As bacterial resistance will likely vary from hospital to hospital, each institution will need to monitor its own resistance patterns. In turn, formulary drug selection and clinical decisions regarding empirical antibiotic therapy will be influenced by resistance patterns reflected in the hospital’s antibiogram [24]. Even so, these goals probably do not require routine culture of all cases of peritonitis.

References


