In Defense of Routine Antimicrobial Susceptibility Testing of Operative Site Flora in Patients with Peritonitis

Samuel Eric Wilson and Joseph Huh

From the Department of Surgery, University of California, Irvine, Irvine, California

The species and number of bacteria present at a surgical site correlate with postoperative wound infection. When organisms cultured from intraabdominal infections are resistant to the presumptive antimicrobial therapy, the incidence of postoperative wound and intraabdominal infections is significantly increased. Knowledge of operative site culture data allows identification of resistant organisms, leads to an early change in therapy, and guides selection of antimicrobials for treatment of postoperative complications. Anaerobic susceptibility data vary geographically, even differing within hospitals in the same city. Surveillance of resistance patterns of bacteria causing intraabdominal infections facilitates accurate initial therapy. Failure of treatment in the absence of bacteriologic results confirming appropriate antimicrobial therapy may be difficult to rationalize on a medicolegal basis. In summary, it is advisable for surgeons to perform cultures and susceptibility tests for both aerobic and anaerobic organisms present in intraabdominal infections.

Clinicians and microbiologists have engaged in a vigorous debate on whether testing the antibiotic susceptibilities of bacterial isolates obtained from purulent fluid within the peritoneal cavity or abdominal incision (operative sites) during an operation for peritonitis is indicated routinely [1]. Some infectious disease specialists have argued that since the susceptibilities of anaerobes are reasonably predictable, periodic reference testing should be adequate for selecting antibiotics for the treatment of anaerobic infections [2].

Even among surgeons, there are differing opinions regarding routine antibiotic susceptibility testing. One of us attended a scientific meeting in 1996 at which an informal survey of 60 surgeons experienced in the treatment of intraabdominal infections revealed that only 36% routinely performed cultures and susceptibility testing for patients with peritonitis. Up to 18% indicated that they never obtained specimens for culture. A retrospective survey of 480 patients with secondary bacterial peritonitis treated in Albuquerque, New Mexico, showed that surgeons typically ignored culture data [3]. In a 1989 study on complicated appendicitis, Dougherty et al. [4] discovered that culture reports influenced antimicrobial therapy for only 7% of patients.

Even if the surgeon decides to obtain a specimen for culture, anaerobic microbiology may not be available to the clinician in many medical centers. According to a 1995 survey of United States hospital laboratories, 77% of these laboratories did not routinely test anaerobic susceptibilities, and 59% would not offer the susceptibility testing even if an individual physician requested it [5]. These figures show a decline from those in a 1993 survey showing that only 30% of hospital laboratories did not perform anaerobic susceptibility testing [6].

Internists as much as surgeons have come to rely on “the primacy of drainage procedures” or debridement in determining the outcome of anaerobic infections, which deemphasizes the importance of knowledge of individual pathogens [2]. Antimicrobial therapy is considered adjunctive to the intervention and thus is not directed at specific virulent organisms. In this article, we will address the causes of this drift toward incomplete culture and susceptibility testing for mixed infections, and we will present the case for more general use of these procedures.

Methods of Susceptibility Testing

Lack of physician confidence in the ability of the clinical microbiological laboratory to accurately identify pathogens in surgical specimens and variations in antimicrobial susceptibility data have been cited as reasons why surgeons ignore culture data [3]. Indeed, before 1980, 15%−20% of cultures of surgical infections yielded no microbial growth, but with improvements in methods of collection, transport, and culture, anaerobic organisms have been recovered in circumstances where routine cultures previously did not yield any identifiable bacteria [7]. The reasons for selecting certain techniques, as well as the differing results in susceptibility testing according to the laboratory method that was chosen, are poorly understood by the surgical community and deserve explanation. For example, of the three generally accepted methods of testing bacterial susceptibilities, the agar dilution method preferred by many microbiologists is labor intensive. The broth microdilution method reduces the workload, although it limits susceptibility testing to the antibiotics and the concentrations available in commercially prepared tray panels [8]. The disk diffusion method, with the longer incubation period for anaerobes and the unsteady levels of antibiotic gradients over time, has not been endorsed by the...
National Committee for Clinical Laboratory Standards (NCCLS). Several authors, however, have shown reproducible results [8], and many smaller clinical laboratories use the disk diffusion method because it is simple and inexpensive [5, 6].

The Etest (Epsilometer test, AB BIODISK, Solna, Sweden), a modification of the disk method that establishes stable antibiotic levels surrounding an antibiotic-coated plastic strip, is largely unknown to surgeons [9]. The strip is placed on an agar plate streaked with an organism and is incubated for 24–48 hours. An inhibition zone is established around the strip, and the MICs can be read directly from the strip. Correlation of the results with those of the agar dilution technique has generally been good; however, before clinical use of the Etest in anaerobic susceptibility testing is accepted, more experience with the optimal inoculum size, medium, and duration of incubation needs to be determined [10, 11].

Surgeons should know that method-dependent factors also affect susceptibility data. The type of medium used may not support all organisms present in a clinical specimen. Wilkins-Chalgren agar has been recommended as a medium for anaerobes by the NCCLS; however, not all anaerobic organisms are recovered from Wilkins-Chalgren agar [12]. MICs may vary depending on the test method. Aldridge and Schiro [13] have shown that MICs of ceftriaxone, cefoxitin, and clindamycin are distinctly higher for Bacteroides species than for clostridia, which may be transferred by plasmid-mediated mechanisms. Data from Johannesburg, South Africa, show yet another pattern of susceptibilities [14]. The reasons for these variations in susceptibility results and their clinical implications, while well understood by anaerobic microbiologists, have not been communicated effectively to the nonspecialist practitioner.

Regional Variations in Susceptibility

The concept of a “predictable susceptibility pattern” is advancing as a reason not to perform cultures of intraabdominal infections, but regional resistance patterns have been identified for clinical anaerobic isolates. The mechanisms of antibiotic resistance in anaerobes are similar to those in aerobes, and many of the genetic loci of these resistance genes and the mechanisms of gene transfer have been described. These determinants of resistance may be transferred by plasmids as well as by chromosomal conjugations. The resistance determinants can be highly specific for a single anaerobe or a group of anaerobes. The resistance to penicillin, cefoxitin, amoxicillin/clavulanate, clindamycin, erythromycin, and tetracycline [15]. Tunér and Nord [17] compared Bacteroides group susceptibility data collected in Europe on the basis of geographic region. Overall, they found high rates of resistance to ampicillin (93%), ciprofloxacin (56%), and tetracycline (64%). Resistance to imipenem (0.3%), amoxicillin/clavulanate (1%), cefoxitin (3%), and clindamycin (9%) was uncommon. Several differences in the regions were apparent. Clindamycin resistance was more common in Europe than in the United States, and within Europe, resistance rates ranged from none in Austria and Sweden to 19% in Belgium and 25% in Spain. The mean MICs were lower for isolates from western Europe than they were for isolates from the northern region. Although the MICs were not high enough to confer resistance, there were significant variations in susceptibility to imipenem [17].

Results of susceptibility testing of isolates obtained in Japan showed that resistance of Bacteroides fragilis to imipenem increased from 2% in 1987 to 5.4% in 1991. A corresponding increase in the average MICs for the nonresistant strains was noted over the same period of time [18]. The resistant strains have been shown to produce a metallo-β-lactamase, the gene for which may be transferred by plasmid-mediated mechanisms. Data from Johannesburg, South Africa, show yet another pattern of susceptibilities [19]. β-lactamase production occurred in 99% of the Bacteroides group isolates obtained in South Africa, a rate higher than that documented in the United States and Europe. Consequently, 57% of B. fragilis isolates are resistant to cefoxitin, an agent commonly used peripherally for gastrointestinal surgery; the rate of B. fragilis resistance to imipenem is 5%, and resistance to clindamycin is 9%. This variation in antimicrobial susceptibility of anaerobes suggests that investigators who perform ongoing testing of clinical isolates should continue to track regional differences.

Local Variations in Susceptibility

In the United States, several studies have shown hospital-to-hospital variations in anaerobic susceptibilities, even within the same city. With these patterns in emergence of resistance, individual institutions need to document their susceptibility profiles. Since anaerobic cultures provide specific susceptibilities within several days on average, initiation of empirical antibiotic therapy depends on accurate, contemporaneous, local susceptibility data.

Comparisons for four local hospitals in Southern California (San Bernardino and Riverside Counties) have shown that the rates of susceptibility of Bacteroides and Fusobacterium to cefoxitin varied from 64% to 89% [20]. Susceptibility to cefotetan varied from 38% to 65%, and susceptibility to clindamycin varied from 74% to 94%. Metronidazole, chloramphenicol, imipenem, and ticarcillin/clavulanate all demonstrated satisfactory activity against Bacteroides and Fusobacterium, with only 0–1% resistance. Similar local hospital-to-hospital variability was seen in six Chicago-area hospitals [21]. In met-
ropolitan Chicago, *B. fragilis* group organisms displayed susceptibility to cefotetan that varied from 67% to 95%, while clindamycin susceptibility varied from 61% to 100%. With these wide variations in local susceptibility patterns, the antimicrobial profiles at each hospital are needed to allow clinicians to make reliable and accurate decisions regarding antibiotic therapy.

**Impact on Patient Care**

The key issue is whether anaerobic cultures and susceptibility testing alter treatment plans and ultimately the outcome for the patient. Evidence is mounting that they do. Analysis of anaerobic blood cultures in a mid-size community hospital during 1991 showed that 6.2% of 569 true-positive cultures yielded anaerobic organisms [22]. In the culture-positive group, 16 patients had significant anaerobic bacteremia; antibiotic therapy for nine of these patients was changed on the basis of the culture results, which resulted in better outcomes. In another study, the MIC of cefotetan and the dose and duration of therapy were independent predictors of outcome in a retrospective analysis of 19 patients with *B. fragilis*–group infections [23].

Common anaerobes recovered from operative site cultures during colorectal surgery include *B. fragilis* group organisms, *Eubacterium* species, and *Peptostreptococcus* species. Grant et al. [27] have shown a positive correlation between operative site bacteriology (intraoperative cultures from irrigation of the peritoneal cavity and the subcutaneous wound at completion of the operation) and the bacteriology of subsequent infectious complications. The results of operative site cultures can be used as a predictor of the pathogens likely to be found in postoperative wound and intraabdominal infections. Further, isolation of three or more species from incisional wounds cultured at the time of closure correlated with development of postoperative infectious complications. Susceptibility data from intraoperative cultures can greatly facilitate the treatment of these complications by allowing specific and accurate antibiotic therapy. Culture of bowel contents or the appendiceal stump is unlikely to yield worthwhile information with regard to potential pathogens.

Christou et al. [25], representing the Canadian Intra-abdominal Infection Study Group, reported a comparison of a comprehensive broad-spectrum agent (imipenem/cilastatin) versus a limited-spectrum empirical antibiotic (cefotetan) in the setting of intraabdominal infections. The study group found higher rates of treatment failures as well as a higher mortality rate related to inadequate antibiotic coverage in the group receiving cefotetan only. Operative cultures verified the presence of cefotetan-resistant pathogens (*Clostridium perfringens, Enterobacter cloacae,* and *Pseudomonas aeruginosa*) at the site of infection. The authors concluded that “treatment failure in intra-abdominal infections may be due to the presence of resistant pathogens . . . therefore, routine culture of these sites appears worthwhile.”

The role of drainage is undeniably paramount in the treatment of surgical infections, but antimicrobials are also essential for combating bacteremia induced by operative manipulation, for limiting the spread of peritonitis, and resolving the inflammatory process. The use of antibiotics is even more important in patients who are undergoing percutaneous drainage via a small drain, such as an 8F or 10F pigtail catheter, resulting in a slow evacuation and collapse of the abscess cavity. Operative site bacteriology is a highly accurate predictor of postoperative complications as well as an early indicator of the infecting pathogens. Knowledge of the operative site culture data allows identification of resistant organisms, which may lead to an early change in therapy, and guides selection of antimicrobials for treatment of postoperative complications.

**Medicolegal Issues**

The NCCLS currently recommends anaerobic susceptibility testing of specimens of blood, bones and joints, brain abscesses, empyema fluid, and other body fluids that are normally sterile. This policy has been viewed by some infectious disease specialists as too restrictive [1]. With increasing variance in anaerobic susceptibility, testing should be considered for all clinical specimens when the presence of anaerobes is suspected. Further, in cases of treatment failure, if no cultures have been performed, it may be difficult to defend the poor clinical outcome on the grounds that culture and susceptibility testing are not done routinely.

**Conclusion**

Anaerobic susceptibility testing remains controversial, although recent data indicate that it does improve clinical outcome for patients with serious anaerobic infections [23–25]. Hospitals should maintain infection-control data on anaerobic infectious complications and local resistance patterns. Culture and susceptibility testing provide the data clinicians must have to make informed decisions on antimicrobial treatment for their patients and are indispensable tools for the surgeon in treatment of postoperative complications. Published antibiograms may be inaccurate because of increasing regional and hospital variations in anaerobic resistance. Surgeons should be informed by microbiologists of the correct methods for obtaining and transporting culture specimens [26, 27]. Although testing of anaerobes remains labor intensive, as technology improves, routine anaerobic culture and susceptibility testing data will become an integral part of therapeutic decision-making in the treatment of intraabdominal infection.

**References**