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MINIREVIEW

Role of Aminoglycoside Antibiotics in the Treatment of Intra-abdominal Infection

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INTRODUCTION

Aminoglycosides are widely used in the treatment of gram-negative bacillary infections, including intra-abdominal infections. However, these drugs may produce side effects of nephrotoxicity and ototoxicity, particularly when there is volume depletion, shock, advanced age, or renal impairment (23), risk factors which are common in patients with intra-abdominal infection. The impact of treatment with aminoglycosides on the incidence of nephrotoxicity, as evidenced by an elevation in the serum creatinine concentration, in patients with intra-abdominal infection is shown in Table 1. There was an appreciably higher incidence of nephrotoxicity with the aminoglycoside-containing regimen in four randomized trials; the effect was statistically significant in at least two studies. Aminoglycoside-induced ototoxicity is potentially more important than nephrotoxicity because it is often not reversible. Cochlear toxicity, as defined by audiometric changes, has been reported in 8 to 10% of patients and was clinically evident in as many as 4% of patients treated with aminoglycosides for various infections (10). Vestibular toxicity, as detected by electronystagmographic changes, has been found in 5 to 10% of patients and was clinically significant in 1 to 5% of patients (10, 19).

The development of new beta-lactam antibiotics with potent activity against *Bacteroides fragilis* and facultative gram-negative bacilli has made it possible to design regimens without aminoglycosides for the treatment of mixed intra-abdominal infection. However, these new drugs are costly, and their efficacy as single agents may be questioned by physicians accustomed to using combinations of drugs that include an aminoglycoside.

The purpose of this review is to assess the role of the aminoglycosides in the treatment of intra-abdominal infection. We consider the pathogenesis of this infection, the outcome of comparative studies with and without an aminoglycoside, and the potential utility of aminoglycosides for selected subgroups of patients to ascertain whether these drugs offer an identifiable therapeutic advantage.

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PATHOGENESIS OF INTRA-ABDOMINAL INFECTION

The microbial species which are commonly present in intra-abdominal infection include anaerobic, facultative, and aerobic bacteria, as well as *Candida* species (Table 2; 11, 25). The predominant facultative species is *Escherichia coli*; however, *Pseudomonas aeruginosa* has been reported in peritoneal cultures of 3 to 15% of patients with peritonitis. The major anaerobic isolates are *Bacteroides* species, particularly *B. fragilis*.

Studies in animals have shown that the facultative aerobes are important in producing bacteremia and early mortality in intra-abdominal infection, whereas the anaerobic organisms, especially encapsulated strains of *B. fragilis*, are instrumental in leading to the formation of abscesses (20, 36). Implantation of gelatin capsules containing viable *E. coli* into the abdominal cavity of rats produced an acute bacteremic illness with a mortality rate of 30 to 40% but without abscess formation. In contrast, implantation of capsules containing *B. fragilis* resulted in abscess formation without death (35, 37). The implantation of capsules containing both species reproduced the sequence of events seen in clinical intra-abdominal infection. Studies in animals suggest that the facultative and anaerobic species operate synergistically to produce tissue destruction in mixed infections (9).

Further evidence of the role of facultative and anaerobic species emerges from studies of the treatment of experimental infections. Treatment with clindamycin, an agent active against *B. fragilis* but not *E. coli*, strikingly reduced the rate of abscess formation but did not influence the lethality of peritonitis, whereas treatment with gentamicin protected against lethality but not against abscess formation (26; Table 3). The combination of drugs was effective in reducing both acute mortality and late abscess formation. A number of studies have corroborated these findings in humans (3, 4, 7, 21, 52). These investigations underline the need to address both the anaerobic component, primarily *B. fragilis*, and the facultative components, primarily members of the family *Enterobacteriaceae*, for the optimal treatment of intra-abdominal infections.

THEORETICAL CONSIDERATIONS REGARDING EFFICACY

A variety of antibiotics, either singly or in combination, are active in vitro against the predominant species of bacteria found in intra-abdominal infections and might be expected to be effective in treatment. However, there are theoretical reasons why they might not work well clinically. For example, aminoglycosides function poorly in acidic or hypoxic environments (12), such as would be encountered in abscesses and ischemic tissues. Beta-lactam antibiotics are

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TABLE 1. Incidence of nephrotoxicity in patients receiving aminoglycosides or other drugs for the treatment of intra-abdominal infection

Reference	Regimen	Incidence of nephrotoxicity (%)[a]	
		Nonaminoglycoside regimen	Aminoglycoside regimen
Nichols et al. (32)	Cefoxitin vs clindamycin + gentamicin	1/70 (1.5)	3/75 (4)
Drusano et al. (8)	Cefoxitin vs clindamycin + aminoglycoside	1/26 (4)	7/21 (30)[b]
Schentag et al. (44)	Moxalactam vs clindamycin + tobramycin	12/49 (24)	29/49 (60)
Tally et al. (50)	Moxalactam vs cefoxitin + tobramycin	2/36 (6)	3/44 (7)
Scandinavian Study Group (43)[c]	Imipenem vs clindamycin + gentamicin	4/56 (7)	22/62 (35)[b]
Solomkin et al. (48)	Imipenem vs clindamycin + gentamicin	1/37 (3)	10/37 (30)

[a] Nephrotoxicity was defined in the study by Nichols et al. (32) as an increase in the serum creatinine concentration of ≥2 mg/dl; in all the other studies, it was defined as an increase in the serum creatinine concentration of >0.5 mg/dl above the baseline measurement.
[b] $P < 0.01$, Fisher's exact two-tailed test.
[c] Includes patients with intra-abdominal and other infections.

not highly effective when bacterial inocula are great and the rate of bacterial multiplication is low, as occurs in intra-abdominal abscesses. The concentration of beta-lactamases is likely to be high in the same circumstances, further impairing the efficacy of beta-lactam antibiotics. Gram-negative bacteria in nutrient-depleted environments, such as abscesses, may shut down some of their outer membrane porins, thereby limiting access of antibiotics to their sites of antibacterial action (33); moreover, reduced access augments the effect of beta-lactamases. These changes may explain the propensity of certain bacterial species, notably *P. aeruginosa* and *Enterobacter* spp., to become resistant to beta-lactam antibiotics during treatment of infections (28, 29, 45, 46, 54). It is difficult to predict which, if any, of these factors may be important clinically. Therefore, it is crucial to rely on carefully conducted clinical trials in judging the relative efficacy of these regimens. These considerations regarding antibiotic efficacy also underline the necessity for thorough surgical drainage and debridement, without which antibiotic treatment frequently fails in patients with intra-abdominal infection.

TABLE 2. Bacteriology of peritonitis and intra-abdominal abscess

Organism(s)	% Patients[a]	
	Mean	Range
Facultative and aerobic		
Escherichia coli	61	56–65
Proteus species	19	11–26
Klebsiella or *Enterobacter* spp.	20	8–26
Pseudomonas aeruginosa	9	3–15
Enterococcus	14	12–15
Other streptococci	31	15–47
Anaerobic		
Bacteroides fragilis group	86	80–93
Other *Bacteroides* spp.	42	25–59
Peptococcus spp.	22	16–28
Peptostreptococcus spp.	28	27–29
Clostridium spp.	36	9–64
Eubacteriales	24	11–36
Fusobacterium spp.	20	20–21

[a] Data from Finegold et al. (11) and Lorber and Swenson (25). Values are the percentage of patients with these isolates identified on culture.

REGIMENS EFFECTIVE FOR INTRA-ABDOMINAL INFECTIONS

Regimens which have been shown in well-designed, prospective, randomized comparative clinical trials to be of equivalent efficacy in the treatment of intra-abdominal infection are shown in Table 4. For a detailed analysis of these studies, we refer the reader to a recent review (F. P. Tally and J. L. Ho, *in* J. S. Remington and M. N. Swartz, ed., *Current Clinical Topics in Infectious Diseases*, vol. 8, in press). The regimens listed in the upper part of Table 4 include an aminoglycoside. However, in one investigation, carbenicillin was given alone to patients with penetrating abdominal trauma with apparent success (34). Studies with the penicillins were done mainly with ticarcillin; the other congeners are considered acceptable on the basis of their in vitro activity against *B. fragilis* and limited studies in animals and humans. The regimens shown in the lower part of Table 4 do not contain an aminoglycoside. However, if cefoxitin is used, there are certain circumstances, which are discussed below, in which it is desirable to administer an aminoglycoside concurrently. Two potential regimens for the treatment of intra-abdominal infection are metronidazole plus cefuroxime (39) and clindamycin plus aztreonam. Although present information is limited, future clinical studies may demonstrate the efficacy of these regimens.

COMPARISON OF TRIALS WITH AND WITHOUT AN AMINOGLYCOSIDE

We reviewed publications in peer-reviewed journals of the results of prospective, randomized trials comparing regimens with and without an aminoglycoside in which the dosages of drugs used appeared appropriate to us. We restricted our analysis to studies which had at least 20

TABLE 3. Antimicrobial therapy of experimental peritonitis[a]

Treatment	Acute mortality (%)	Abscess formation in survivors (%)
Untreated	37	100
Gentamicin alone	4	98
Clindamycin alone	35	5
Gentamicin + clindamycin	7	6

[a] From Louie et al. (26).

TABLE 4. Regimens proven effective for treatment of intra-abdominal infection

Regimen	References
Clindamycin + aminoglycoside	5, 6, 15–17, 24, 52, 53
Chloramphenicol + aminoglycoside	15, 16, 24
Metronidazole + aminoglycoside	5, 6, 47, 53
Carbenicillin, ticarcillin, piperacillin, or mezlocillin + aminoglycoside[a]	15, 16, 31
Cefoxitin ± aminoglycoside	8, 16, 31, 32, 51
Moxalactam	22, 44, 50
Imipenem	13, 43, 48

[a] Limited data, except for ticarcillin.

assessable patients in each therapeutic arm, except in one instance (43) in which patients with intra-abdominal infection formed part of a larger study. In most studies, the aminoglycoside was given with clindamycin. The results for cefoxitin, moxalactam, and imipenem are shown in Table 5. The criteria for failure of treatment are summarized in the footnotes to Table 5.

Cefoxitin has good activity against *B. fragilis* and many species of the family *Enterobacteriaceae* but not against *P. aeruginosa* or most strains of *Enterobacter* spp. In two comparative trials, the results with cefoxitin alone were as good as those with the combination of clindamycin and an aminoglycoside. In the study by Drusano et al. (8), the patients were seriously ill at the start of treatment because of severe underlying diseases and failure of multiple organs. Five of the twenty-six patients given cefoxitin were also given an aminoglycoside because of the fear that they might harbor cefoxitin-resistant bacteria. Although the outcome with cefoxitin appeared to be better than with the clindamycin-aminoglycoside combination, the differences were not statistically significant in terms of either the cure rate or the failure rate. Nichols and colleagues (32) studied young, previously healthy people who had sustained penetrating intestinal trauma: only 50% of these patients had colonic injuries. As would be expected, the overall outcomes were better than in the study by Drusano and colleagues (8).

Moxalactam is as active as cefoxitin against *B. fragilis* but more active than cefoxitin against members of the *Enterobacteriaceae*, *P. aeruginosa*, and *Enterobacter* species. Schentag and colleagues (44) compared moxalactam with the combination of clindamycin and tobramycin for the treatment of intra-abdominal infections in elderly, debilitated patients. The rates of cure, failure, and superinfection were

TABLE 5. Randomized, comparative trials of antibiotic regimens for intra-abdominal infection

Reference	Population	Regimen	*n*	Cure or improvement (%)	Failure (%)	Superinfection (%)
Drusano et al. (8)[a]	Many seriously ill patients with multiple organ failure, underlying diseases	Cefoxitin (five patients also received aminoglycoside)	26	62	38	
		Clindamycin + aminoglycoside	21	48	52	
Nichols et al. (32)[b]	Young, healthy patients with penetrating intestinal trauma; 50% with colonic injuries	Cefoxitin	70	80	20	
		Clindamycin + gentamicin	75	77	23	23
Schentag et al. (44)[c]	Debilitated older patients with multiple underlying diseases; 25% had failed previous treatment	Moxalactam	49	76	24	23
		Clindamycin + tobramycin	49	74	26	21
Tally et al. (50)[d]	Varied group of patients; 46 of 66 had intra-abdominal infection, mainly of colonic orgin	Moxalactam	33	79	12	9
		Cefoxitin + (in 13 patients) tobramycin	33	88	12	0
Scandinavian Study Group (43)[e]	Part of larger study; characteristics of the subgroup not stated	Imipenem	11	91	9	9
		Clindamycin + gentamicin	16	69	31	12.5
Solomkin et al. (48)[f]	Two-thirds of patients had intra-abdominal infections; many were elderly with serious underlying diseases	Imipenem	37	92	8	13.5
		Clindamycin + gentamicin	37	81	19	11

[a] Failure was defined as (i) persistence of signs or symptoms of infection requiring addition of another antibiotic(s), (ii) recurrence of infection requiring second drainage procedure, or (iii) bacteremia with one of initial infectious organisms and no other source.

[b] Failure was defined as any infection occurring during or up to 2 months after protocol treatment.

[c] Failure was defined by us as responses deemed unsatisfactory by Schentag et al. (sum of patients who failed to improve, required changes in therapy, or died of infection) plus recurrent symptoms. Late abscesses and mortality were listed as additional categories (44), but we could not discern whether these were already included in the categories termed unsatisfactory or recurrence.

[d] Failure was defined by us as the persistence of signs or symptoms related to the original infection. Tally et al. also included superinfections as failures, which increased the failure rate with moxalactam to 7 of 33 (21%). This was not significantly different from the failure rate with cefoxitin ± tobramycin.

[e] Failure was defined as lack of response to treatment. Overall study showed significant benefit for imipenem in terms of efficacy.

[f] Failure was defined as need to change antibiotic treatment because of lack of response or adverse reaction or need for additional surgical procedure. Imipenem appeared superior in seriously ill patients, but results were skewed by high incidence of gentamicin-resistant, gram-negative bacteria in the institution.

TABLE 6. Correlation between isolation of *P. aeruginosa* from initial peritoneal cultures and outcome of treatment[a]

Pseudomonas aeruginosa	No. of patients by indicated outcome after treatment with:					
	Cefamandole		Cefoperazone		Clindamycin + gentamicin	
	Cure	Failure	Cure	Failure	Cure	Failure
Resistant	4	6	0	0	1	0
Susceptible	0	0	7	5	7	0

[a] Source: Heseltine et al. (18).

almost identical between the two regimens. The incidence of superinfection was substantial (21 to 33%). The study by Tally and colleagues (50) compared the efficacy of moxalactam with that of cefoxitin, the latter sometimes given with an aminoglycoside, in a varied group of patients, not all of whom had intra-abdominal infections. Because only 13 patients in the cefoxitin-treated group were given the aminoglycoside, this trial does not fully meet our purposes. Nevertheless, the outcome of the two regimens was again similar in the two study trials.

Imipenem has potent activity against most bacterial species likely to be encountered in intra-abdominal infection, including *B. fragilis*, most members of the *Enterobacteriaceae* (including *Enterobacter* spp.), *P. aeruginosa*, and *Streptococcus faecalis* (2). The efficacy of imipenem has been compared with that of the combination of clindamycin and gentamicin in two trials. The first was part of a larger study of various kinds of infections; the overall results showed a statistically significant benefit for imipenem over the combination of clindamycin and gentamicin (43). The subset of patients with intra-abdominal infection shown in Table 5 was small. Although the results suggested better efficacy of imipenem than of the combination, the differences were not significant. In the second trial, the differences between the regimens were modest and, again, not statistically significant (48). The failure rate with clindamycin and gentamicin in the second study may have been skewed upward by an unusually high incidence of gentamicin-resistant, gram-negative bacilli in the institution during the study period. In both trials with imipenem, about 10% of patients in each treatment group developed superinfections. A third study, by Guerra and colleagues (13), also yielded a somewhat better outcome with imipenem than with the combination of clindamycin and gentamicin, but it involved few patients with intra-abdominal infection. The suggestion of a better outcome with imipenem than with the aminoglycoside-containing regimen in these studies is interesting but needs to be confirmed in larger trials. Although imipenem has excellent activity against *P. aeruginosa*, some strains have become resistant to the drug during clinical trials involving other kinds of infections (27, 40).

Cefoperazone has good activity and cefamandole has moderate activity against facultative gram-negative bacilli, but these agents have relatively poor activity against *B. fragilis* in vitro (49). Therefore, these drugs would not be expected to produce optimal results as single agents for the treatment of intra-abdominal infection. In a study of patients with perforated appendix or periappendiceal abscess, Berne et al. (3) found the failure rate to be significantly higher after treatment with cefamandole (28%) or cefoperazone (16%) than after treatment with the combination of clindamycin and gentamicin (0%; $P < 0.05$). Lau et al. (22) also showed a failure rate with cefoperazone (20%) significantly higher than that with moxalactam (8%) in patients with perforated or gangrenous appendicitis. In a further analysis of data from the first study, the likelihood of failure was found to be greatest in patients from whom *B. fragilis* isolated from the abdominal cavity at surgery was resistant to the antibiotics used (18). A previous report likewise suggested that failures of treatment of intra-abdominal infection with moxalactam were predicted by the finding of moxalactam-resistant anaerobic bacteria in the initial cultures (30). These studies again underline the importance of using a regimen with good activity against *B. fragilis* in the treatment of intra-abdominal infection.

Many of the newer cephalosporins have potent activity against members of the *Enterobacteriaceae* but not against *B. fragilis*; this deficiency could be corrected by giving the cephalosporin in combination with a drug such as metroni-

TABLE 7. Incidence of *P. aeruginosa* and *Enterobacter* sp. in initial cultures

Reference	Regimen	No. of patients with positive cultures	No. of patients (%) with:	
			P. aeruginosa	*Enterobacter* sp.
Drusano et al. (8)	Cefoxitin vs clindamycin + aminoglycoside	45	7 (15.5)	4 (9)
Nichols et al. (32)	Cefoxitin vs clindamycin + aminoglycoside	145	Not stated	Not stated
Schentag et al. (44)	Moxalactam vs clindamycin + tobramycin	85	13 (15)	15 (18)
Tally et al. (50)	Moxalactam vs cefoxitin + tobramycin	53	12 (18)	Not stated
Scandinavian Study Group (43)	Imipenem vs clindamycin + gentamicin	163	15[a] (25)	10 (6[a])
Solomkin et al. (48)	Imipenem vs clindamycin + gentamicin	74	12[b] (9)	4 (5[b])

[a] Based on number of isolates rather than patients with these isolates. Calculation was made as if each isolate were from a different patient. Only 27 of 163 patients had intra-abdominal infection.

[b] Based on number of isolates rather than patients with these isolates. Calculation was made as if each isolate were from a different patient. Fifty of seventy-four patients had intra-abdominal infection.

dazole. In one study, the combination of metronidazole and cefuroxime was compared with the combination of metronidazole and gentamicin in 42 patients with perforated appendicitis (39). The outcome of the two regimens was similar in terms of length of hospital stay and the percentage of patients with postoperative fever.

It can be concluded on the basis of these trials that there are no demonstrable differences in efficacy or in the incidence of superinfections between regimens containing or lacking an aminoglycoside when used for the treatment of intra-abdominal infection. However, differences in efficacy rates of as much as 10% might easily be missed because of the sizes of the groups studied. For example, if we assume an 80% response rate in the control group and a 90% response rate in the group receiving putatively better treatment, there would have to be 120 patients in each limb of the study to achieve significance at the 95% level (55).

OUTCOME OF INFECTIONS WITH *P. AERUGINOSA* OR *ENTEROBACTER* SPP.

The patients most likely to benefit from the inclusion of an aminoglycoside in the treatment regimen for intra-abdominal infections presumably are the subset from whom *P. aeruginosa* or an *Enterobacter* spp. was isolated from the initial culture. In a study of patients with a perforated or gangrenous appendix, Heseltine et al. (18) examined the correlation between the susceptibility or resistance of *P. aeruginosa* strains isolated from the initial culture and the outcome of treatment with various regimens (Table 6). In that study, 30% of patients had peritoneal cultures which were positive for *P. aeruginosa*. Treatment with cefamandole, to which all initial isolates of *P. aeruginosa* were resistant, or with cefoperazone, to which all initial isolates were susceptible, resulted in cure of about half of the patients. In contrast, treatment with gentamicin, to which most strains were susceptible, was almost uniformly successful. This suggests that patients from whom *P. aeruginosa* is cultured from the initial infection may benefit from treatment with an aminoglycoside. Of course, other beta-lactam antibiotics are more potent than cefoperazone against *P. aeruginosa* and *Enterobacter* species, and the results with such agents might be more impressive. However, there continues to be concern because of the recognized tendency of *P. aeruginosa* and *Enterobacter* spp. to become resistant to beta-lactam antibiotics during treatment (14, 41).

To determine the frequency of isolation of these relatively resistant species, we reviewed the studies summarized in Table 7. *P. aeruginosa* was obtained in the initial cultures of 12 to 18% of patients, and *Enterobacter* spp. were obtained in cultures of 5 to 18% of patients (Table 7). Unfortunately, the studies were not large enough to permit us to compare the therapeutic outcome of treatment with or without an aminoglycoside in these subgroups of patients. The study of Nichols et al. (32) showed a significant correlation between the isolation of any bacteria from the initial peritoneal culture and subsequent infection but found no correlation between the isolation of antibiotic-resistant, gram-negative aerobic bacteria initially and the outcome of treatment. However, the trial involved relatively healthy patients who were operated on shortly after the occurrence of penetrating abdominal injury, and the results may not apply to patients with serious underlying diseases or more advanced infections. Thus, the question of whether patients with infection caused by *P. aeruginosa* and *Enterobacter* spp. might benefit from treatment with an aminoglycoside remains unanswered by these studies.

COMPOSITION OF FLORA FROM INFECTIOUS COMPLICATIONS

The final question we asked was whether the inclusion of an aminoglycoside in the regimen determined the species and susceptibility patterns of the bacteria recovered from the site of infectious complications after treatment of intra-abdominal infection.

In the study by Nichols and colleagues (32), the rate of isolation of *Kebsiella*, *Enterobacter*, and *Serratia* species from sites of infectious complications in patients treated with an aminoglycoside was lower than that in patients treated with cefoxitin (Table 8). In contrast, Schentag and colleagues (44) found no difference in the composition of the microbial flora at sites of infectious complications between patients treated with moxalactam or with the combination of clindamycin and tobramycin. The discrepancy in results between the two studies may reflect the spectrum of activity of moxalactam, which is broader than that of cefoxitin.

Drusano et al. (8) analyzed the outcome of treatment of 16 patients who had cefoxitin-resistant, gram-negative species in their initial operative cultures. The presence of these organisms could be correlated with recent exposure of the patient to antibiotics. Among the patients with cefoxitin-resistant organisms, treatment failed in 2 of 6 patients treated with cefoxitin alone as opposed to 6 of 10 patients treated

TABLE 8. Microorganisms isolated from patients with infectious complications

Organism(s)	No. of patients on indicated regimen in:			
	Nichols et al. (32)[a]		Shentag et al. (44)	
	Cefoxitin	Clindamycin + gentamicin	Moxalactam	Clindamycin + tobramycin
Coliforms	11	15		
Escherichia coli	3	8		
Klebsiella, *Enterobacter*, or *Serratia* species	10	3 ($P = 0.008$)		
Noncoliform gram-negative bacteria (*Pseudomonas* spp.)	4	2	4	5
Gram-positive cocci	9	10		
Enterococci	6	5	8	8
Staphylococcus epidermidis			5	5
Anaerobes			1	4
Candida spp.	2	3	1	1

[a] Nine of sixteen (56%) isolates were resistant to cefoxitin versus four of seventeen (24%) resistant to clindamycin-gentamicin.

with an aminoglycoside-containing regimen. Thus, the inclusion of an aminoglycoside did not enhance the efficacy of treatment in these patients. However, all patients in whom there was failure of treatment with cefoxitin alone harbored cefoxitin-resistant organisms at the site of infectious complications, whereas none of the patients in whom there was failure of treatment with an aminoglycoside harbored such organisms. This suggests that the use of an aminoglycoside in patients with infection containing beta-lactam-resistant organisms does not affect the clinical outcome but may influence the composition of the flora at the site of infectious complications.

CONCLUSIONS

On the basis of our review of the literature, we find no evidence of a difference in efficacy for the treatment of intra-abdominal infection between regimens which contain and do not contain an aminoglycoside. This holds true even for studies of seriously ill patients and patients whose initial cultures contain beta-lactam-resistant bacteria. There was also no evidence of a difference in the incidence of superinfections between regimens with and without an aminoglycoside. However, the studies were not large enough to determine whether the subgroup of patients (5 to 18%) whose initial cultures yielded *P. aeruginosa* or *Enterobacter* spp. might have had a particular benefit from the aminoglycoside-containing regimen. Such a benefit was suggested by one study (18).

The inclusion of an aminoglycoside in the regimen appeared in certain studies to influence the composition (32) and susceptibility patterns (8) of the flora isolated from infectious complications after treatment for intra-abdominal infection. Thus, patients from whom the initial cultures yielded beta-lactam-resistant bacteria tended to have these organisms present in the infectious complications after treatment with a beta-lactam drug but not after treatment with an aminoglycoside-containing regimen (8). However, even in these patients, there was no apparent difference in clinical outcome whether or not an aminoglycoside was given.

Leaving aside considerations of cost and of the potential toxicities of the nonaminoglycoside drugs which may be of particular importance in certain patients (1, 42), the decision to include an aminoglycoside in the antibiotic regimen for the initial empiric treatment of intra-abdominal infection remains a difficult one. It may be particularly justifiable to include an aminoglycoside when there is substantial risk that *P. aeruginosa* or *Enterobacter* spp. are present at the site of infection as, for example, in patients who sustain their infections in hospitals or nursing homes and in patients who have recently received broad-spectrum antibiotics (38) or immunosuppressive treatments. In any event, if the cultures fail to yield beta-lactam-resistant bacteria, there appears to be no benefit to continuing the administration of an aminoglycoside antibiotic.

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