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Clinical and Microbiological Features of Necrotizing Fasciitis

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The microbiological and clinical characteristics of 83 patients with necrotizing fasciitis (NF) treated over a period of 17 years are presented. Bacterial growth was noted in 81 of 83 (98%) of specimens from patients with NF. Aerobic or facultative bacteria only were recovered in 8 (10%) specimens, anaerobic bacteria only were recovered in 18 (22%) specimens, and mixed aerobic-anaerobic floras were recovered in 55 (68%) specimens. In total, there were 375 isolates, 105 aerobic or facultative bacteria and 270 anaerobic bacteria, for an average of 4.6 isolates per specimen. The recovery of certain bacteria from different anatomical locations correlated with their distribution in the normal flora adjacent to the infected site. Anaerobic bacteria outnumbered aerobic bacteria at all body sites, but the highest recovery rate of anaerobes was in the buttocks, trunk, neck, external genitalia, and inguinal areas. The predominant aerobes were *Staphylococcus aureus* ($n = 14$ isolates), *Escherichia coli* ($n = 12$), and group A streptococci ($n = 8$). The predominant anaerobes were *Peptostreptococcus* spp. ($n = 101$), *Prevotella* and *Porphyromonas* spp. ($n = 40$), *Bacteroides fragilis* group ($n = 36$), and *Clostridium* spp. ($n = 23$). Certain clinical findings correlated with some bacteria: edema with *B. fragilis* group, *Clostridium* spp., *S. aureus*, *Prevotella* spp. and group A streptococci; gas and crepitation in tissues with members of the family *Enterobacteriaceae* and *Clostridium* spp.; and foul odor with *Bacteroides* spp. Certain predisposing conditions correlated with some organisms: trauma with *Clostridium* spp.; diabetes with *Bacteroides* spp., members of the family *Enterobacteriaceae*, and *S. aureus*; and immunosuppression and malignancy with *Pseudomonas* spp. and members of the family *Enterobacteriaceae*. These data highlight the polymicrobial nature of NF.

Necrotizing fasciitis (NF) is an uncommon subcutaneous tissue and superficial fascia infection that is associated with systemic toxicity, a fulminant course, and a mortality rate of 30 to 60% (12, 22). The prognosis of NF depends on early recognition and treatment (26). Knowledge of the common bacterial causes of NF can assist in the selection of empiric antimicrobial therapy before the results of bacterial cultures are available.

The importance of group A beta-hemolytic streptococci (GABHS) and *Staphylococcus aureus* in NF is well established (12, 22, 24, 25, 29). Although anaerobic bacteria were recovered from many patients with NF, not all previous reports attempted to elucidate the roles of these bacteria by using methods adequate for their recovery (12, 22, 24, 25, 29). Furthermore, a correlation between the site of infection or the predisposing conditions with the microbiology of NF was not established.

This report of a retrospective study describes the 17-year experience of a military hospital in the diagnosis of the bacterial etiology of NF by using specific methods for the recovery of aerobic as well as anaerobic bacteria. Correlations between the site of the infection, the clinical findings, the predisposing conditions, and the microbial isolates were explored.

MATERIALS AND METHODS

Between June 1973 and June 1990, 83 specimens obtained from patients with NF were submitted to the clinical microbiology laboratory at the Naval Hospital in Bethesda, Md., for the isolation of aerobic and anaerobic bacteria. Excluded were 15 additional specimens from subjects for whom no clinical data were available and 24 specimens that were submitted in an improper transport medium for anaerobes. The diagnosis of NF was based on intraoperative findings of macroscopic observation of extensive edema and necrosis of fascia and subcutaneous tissues. Clinical and microbiological data were compiled. Of the 83 patients, 61 were males, and the patients' ages ranged between 14 months and 81 years (mean age, 46 years).

Antimicrobial therapy was given to 59 patients prior to sample collection. Specimens were obtained during surgery either by swabbing from deep areas of primary lesions or by needle aspiration. The swab was placed into anaerobic transport medium (Port-A-Cul; BBL Microbiological Systems, Cockeysville, Md.) and was generally inoculated within 2 h after collection. Needle aspiration was performed with an 18- or 20-gauge needle attached to a 5- or 10-ml syringe. The syringe was immediately sealed and was generally transported to the laboratory within 30 min of specimen collection.

Sheep blood, chocolate, and MacConkey agar plates were inoculated for the isolation of aerobic organisms. The plates were incubated at 37°C aerobically (MacConkey agar) and under 5% carbon dioxide (blood and chocolate agars) and were examined at 24 and 48 h. For the isolation of anaerobes, specimens were plated onto prereduced vitamin K_1-enriched brucella blood agar, anaerobic blood agar plates containing kanamycin and vancomycin, and anaerobic blood plates containing colistin and nalidixic acid and were then inoculated into enriched thioglycolate broth. The plated media were incubated in GasPak jars (BBL Microbiology Systems) and were examined at 48, 96, and 120 h. The thioglycolate broth was incubated for 14 days. Aerobes and anaerobes were identified by previously described techniques (15, 21, 27). The data were organized according to anatomic location: head, neck, trunk, extremities, inguinal and perirectal areas, buttocks, and external genitalia.

Blood for culture was drawn, most often from an antecubital vein, following preparation of the area with povidone-iodine, and the blood was inoculated at the bedside into one bottle each of BACTEC (Johnston Laboratories, Cockeysville, Md.) aerobic and anaerobic media.

Statistical analysis was conducted by the χ^2 and t tests.

RESULTS

Microbiology. Of the 81 culture-positive specimens, 9 were from the head, 11 were from the neck, 7 were from the trunk, 5 were from an arm, 14 were from a leg, 4 were from the inguinal area, 7 were from the buttocks, 15 were from the perirectal area, and 9 were from the external genitalia (Tables 1 and 2).

Aerobic or facultative bacteria alone were present in 8 (10%) culture-positive specimens, anaerobic bacteria only were present in 18 (22%) culture-positive specimens, and

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TABLE 1. Aerobic and facultative organisms isolated from 81 NF lesions

Organism	No. of isolates									
	Head (9)[a]	Neck (11)	Trunk (7)	Arm (5)	Leg (14)	Inguinal area (4)	Buttocks (7)	Perirectal area (15)	External genitalia (9)	Total (81)
Streptococci										
Alpha-hemolytic	1	2	3	1	3			2	1	13
Gamma-hemolytic	1	2				1	2	2	1	9
Group A	1	2	2	1	2					8
Group B		1							1	2
Group D					2	1	1	2		6
Staphylococcus aureus	3	2	3	2	2			1	1	14
Staphylococcus epidermidis	1	1			1		1		1	5
Proteus species							1	2	1	4
Pseudomonas aeruginosa	1	1		1	1					4
Other *Pseudomonas* species			1		1		1	1	1	5
Escherichia coli			2		3	1	2	3	1	12
Klebsiella pneumoniae	1		1		1				1	4
Enterobacter species					2	1	1	1		5
Other *Enterobacteriaceae*[b]			1		4	1	2	1	2	11
Haemophilus influenzae	1	1								2
Eikenella corrodens				1						1
Total	10	12	13	6	22	5	11	15	11	105

[a] Values in parentheses are numbers of specimens.
[b] Other *Enterobacteriaceae* include *Klebsiella* species other than *Klebsiella pneumoniae*, *Serratia* spp., *Providencia* spp., *Morganella* spp., and *Acinetobacter* spp.

mixed aerobic-anaerobic floras were present in 55 (68%) culture-positive specimens. In total, there were 375 bacterial isolates, 105 aerobic or facultative isolates and 270 anaerobic isolates, for an average of 4.6 isolates per specimen (3.3 anaerobic bacteria and 1.3 aerobic or facultative bacteria per specimen) (Tables 1 to 3).

The number of isolates per infected site varied between one and nine. The average number of isolates per infected site is reported in Table 3. The rate of recovery of anaerobic bacteria was always higher than the rate of recovery of aerobic or facultative organisms. The highest rate of recovery of anaerobes was in the buttock, trunk, external genitalia, neck, and inguinal areas. The highest rate of recovery of aerobic bacteria was in the trunk.

Six (7%) specimens yielded only one organism. These were GABHS in four cases and *S. aureus* in two cases. In the 85 specimens in which polymicrobial aerobic-anaerobic infection was observed, several bacterial combinations were noted. Members of the *Bacteroides fragilis* group were recovered with *Escherichia coli* eight times, with *S. aureus* six times, and with group D streptococci four times. Pigmented *Prevotella* and *Porphyromonas* spp. were isolated with *Fusobacterium* spp. in nine instances and with *Peptostreptococcus* spp. in eight instances. Anaerobic cocci were recovered with *E. coli* in nine instances.

The predominant aerobic organisms were *S. aureus* ($n = 14$ isolates), *E. coli* ($n = 12$), and GABHS ($n = 8$) (Table 1). The predominant anaerobic organisms were *Peptostreptococcus* spp. ($n = 101$, 24 of which were *Peptostreptococcus magnus*), *Prevotella* and *Porphyromonas* spp. ($n = 40$), members of the *B. fragilis* group ($n = 36$), *Clostridium* species ($n = 23$), and *Fusobacterium* species ($n = 15$) (Table 2).

The distribution of aerobic and facultative organisms showed the following trends. *S. aureus* was recovered from all body sites but predominated in infections of the head, neck, and extremities. The highest recovery rates for members of the family *Enterobacteriaceae* were in the trunk, leg, buttocks, the perirectal area, and external genitalia.

The following trends were noted regarding the distributions of anaerobic organisms. *Peptostreptococcus* spp. were isolated from all sites; members of the *B. fragilis* group and *Clostridium* spp. were isolated from sites below the diaphragm; *Fusobacterium* spp. were isolated from the hand and neck; pigmented *Prevotella* and *Porphyromonas* spp. were isolated from the head and neck; and *Prevotella bivia* and *Prevotella disiens* were isolated from the external genitalia, the perirectal area, and the buttocks.

Bacteremia caused by organisms identical to those found in NF lesions occurred in 20 instances (24% of all cases). Single-organism bacteremia was detected in 11 instances, and polymicrobial bacteremia was found in 9 instances. The organisms recovered were GABHS in five instances (all single isolates), *Peptostreptococcus* spp. in seven instances, *B. fragilis* group in five instances, *Clostridium* spp. in four instances, *Fusobacterium nucleatum* in four instances, *E. coli* in three instances, members of the family *Enterobacteriaceae* in three instances, *Veillonella parvula* in two instances, and a *Eubacterium* sp. in one instance.

Clinical presentation. The presenting signs were necrosis in 83 (100%) patients, cellulitis in 74 (89%) patients, fever in 71 (86%) patients, tachycardia in 66 (80%) patients, leukocytosis (more than 12,000 leukocytes per mm^3) in 65 (78%) patients, edema in 64 (77%) patients, foul odor in 58 (70%) patients, gas and crepitation in tissue in 32 (39%) patients, hypotension (systolic blood pressure, <90 mm/Hg) in 28 (33%) patients, hyperglycemia in 22 (27%) patients, local anesthesia in 20 (24%) patients, disorientation in 19 (23%) patients and anemia (hemoglobin concentration, <9 g/dl) in 8 (10%) patients.

The clinical presentation of NF correlates with certain organisms. Since a comprehensive description of each infection site was not always documented in the patients' records, the data analysis may not be complete. General trends, however, were observed. No correlation between previous antimicrobial therapy and microbial isolates was found. Edema was noted mostly in patients with infections associated with members of the *B. fragilis* group (recovered from 30 of the 64 patients [47%] with edema), *Prevotella* spp. (25 [40%]), *Clostridium* spp. (18 [28%]), *S. aureus* (11 [17%]), and GABHS (6 [9%]). Gas and crepitation in tissues were seen mainly in patients with infections with *Clostridium* spp. (17 of 32 [53%]), *E. coli* (10

TABLE 2. Anaerobic organisms isolated from 81 NF lesions

Organism	No. of isolates									
	Head (9)[a]	Neck (11)	Trunk (7)	Arm (5)	Leg (14)	Inguinal area (4)	Buttocks (7)	Perirectal area (15)	External genitalia (9)	Total (81)
Peptostreptococcus magnus	2	2	4	1	5	2	3	2	3	24
Peptostreptococcus micros		1	2		2		1	1		7
Peptostreptococcus asaccharolyticus		1			2	2	2	3	2	12
Peptostreptococcus morbilorum	1	2	1	2	1	1	2	1	2	13
Peptostreptococcus prevotii	2	1	3		3	1	1		1	12
Peptostreptococcus saccharolyticus	1	2	2		1					6
Peptostreptococcus anaerobius	1	1	1		2	1	1	3	2	12
Peptostreptococcus spp.	2	3		1	3		1	2	3	15
Streptococcus intermedius		2			1			1	2	6
Streptococcus constellatus	1		1		1		1		1	5
Veillonella parvula	2	1	1		1		1		2	8
Veillonella alcalescens	1				1		1	1		4
Bifidobacterium spp.		2					1	2	1	6
Eubacterium lentum		1						2		3
Eubacterium spp.		1						1	1	3
Propionibacterium acnes	1			1	1	1	2	2	1	9
Clostridium septicum					2			1	1	4
Clostridium perfringens		1	2		1	2	2	3	1	12
Clostridium spp.	1				2		1	2	1	7
Fusobacterium nucleatum	3	5		1					1	10
Fusobacterium spp.	2	1			1			1		5
Bacteroides fragilis[b]		1	2		4		2	4	3	16
Bacteroides distasonis[b]	1		1			1	1	1		5
Bacteroides ovatus[b]			1						1	2
Bacteroides vulgatus[b]					1		1	1		3
Bacteroides thetaiotaomicron[b]		1	2		2	1	1	2	1	10
Bacteroides sp.	1	2	2	1	2	1	1		1	11
Prevotella melaninogenica	2	1		1						4
Prevotella intermedia	1	4	1				1	1		8
Porphyromonas asaccharolytica	1	3			1					5
Prevotella ureolytica					1	1				2
Prevotella oralis	2	1		1						4
Prevotella bivia			1			1	1	2	3	8
Prevotella disiens							1	1	4	6
Prevotella oris-buccae	2	1								3
Total	30	41	27	9	41	15	29	40	38	270

[a] Values in parentheses are numbers of specimens.
[b] These species all belong to the *B. fragilis* group.

[31%]), and other members of the family *Enterobacteriaceae* (16 [50%]). Foul odor was mostly observed in patients with infections with *Bacteroides* spp. (41 of 58 [71%]). Classical hemolytic streptococcal gangrene was observed in 4 patients, whose specimens grew a pure culture of GABHS. These patients presented with systemic toxicity, rapid progression, no gas in tissue, and painful edematous lesions with extensive necrosis (12). Fifteen specimens from the perirectal area and nine specimens from the external genitalia presented in a general fashion that resembled Fournier gangrene (9). The flora was polymicrobial (in 22 of 24 [92%] instances), gas in the tissue was noticed in 16 (67%) instances, foul exudate was noticed in 18 (75%) instances, and systemic toxicity and rapid progression were noticed in 20 (83%) and 19 (79%) instances, respectively.

Predisposing and associated conditions. Seventy-six of the patients (92%) had a predisposing or associated condition(s). A single condition was present in 47 (57%) patients, two conditions were found in 20 (34%) patients, and three conditions were found in 9 (11%) patients. These conditions were trauma in 28 (34%) patients, prior surgery in 17 (20%) patients, diabetes mellitus in 15 (18%) patients, immunosuppression in 14 (17%) patients, arteriosclerosis in 13 (16%) patients, odontogenic infection in 9 (11%) patients, renal failure in 7 (8%) patients, malignancy in 6 (7%) patients, and alcoholism in 5 (6%) patients.

Some predisposing conditions were found to be associated with the recovery of certain organisms. Prior surgery was associated with *Bacteroides* spp. (isolated from 12 of 17 patients [71%] who had prior surgery), *Clostridium* spp. ($n = 8$ [47%]), a group D streptococcus ($n = 5$ [29%]), and *S. aureus* ($n = 5$ [29%]); trauma was associated with *Clostridium* spp. ($n = 13$ of 28 [46%]); diabetes was associated with *B. fragilis* group ($n = 7$ of 15 [47%]), other gram-negative anaerobic bacilli ($n = 12$ [80%]), members of the family *Enterobacteriaceae* ($n = 10$ [67%]), and *S. aureus* ($n = 4$ [27%]); immunosuppression and malignancy were associated with *Pseudomonas aeruginosa* ($n = 6$ of 14 [43%] with immunosuppression and $n = 3$ of 6 [50%] with malignancy) and members of the family *Enterobacteriaceae* ($n = 8$ of 14 [57%] with immunosuppression and $n = 3$ of 6 [50%] with malignancy); arteriosclerosis was associated with *Streptococcus* spp. ($n = 11$ of 13 [85%]) and *Clostridium* spp. ($n = 4$ [31%]); and odontogenic infection was associated with pigmented *Prevotella* and *Porphyromonas* spp. ($n = 9$ [all in head and neck sites]) and *Fusobacterium* spp. ($n = 8$ [89%]).

Clinical outcome. Patients were treated by prompt surgical

debridement and with broad-spectrum antimicrobial agents. The antimicrobial agents used were an aminoglycoside ($n = 68$ patients), clindamycin ($n = 35$), metronidazole ($n = 20$), methicillin ($n = 26$), cefoxitin ($n = 16$), ceftazidime ($n = 15$), vancomycin ($n = 6$), ticarcillin-clavulanate ($n = 5$), and imipenem ($n = 3$). Surgical treatment included debridement of all necrotic fascia, subcutaneous tissue, and muscle. Multiple debridement was required in 27 patients. Amputation of extremities was done in six instances, and hyperbaric oxygen treatment after debridement was delivered to 10 patients (12%). Twenty-three (28%) of the patients died. Ten of these patients had diabetes (mortality rate, 67% of all patients with diabetes). No correlation was found between the organisms isolated and age, predisposing or underlying condition, and mortality. No change in the rate of isolation of different bacterial species occurred over the 17 years of study.

DISCUSSION

The present study demonstrated the recovery rate of aerobic and anaerobic bacteria from patients with NF. In contrast to previous reports (12, 22, 24, 25, 29), this one demonstrates a higher frequency of isolation of anaerobes in general and *Prevotella*, *Porphyromonas*, and *Fusobacterium* species in particular from patients with NF. This finding may be due to the specific methods for specimen collection, transportation, and cultivation for anaerobes used in our study and for the inclusion in our study of only specimens submitted for the recovery of both aerobic and anaerobic bacteria. We were also able to detect a higher number of anaerobic isolates per specimen (average, 4.6) compared with the number found in any previous study (12, 22, 24, 25, 29). Anaerobes were frequently isolated and outnumbered aerobic and facultative bacteria at all sites. Their rates of recovery from the external genitalia, buttocks, trunk, inguinal area, and neck and head areas were especially high. The rate of isolation of anaerobes from these sites as reported in this study of NF was similar to the rate of recovery of anaerobes in other studies that have investigated the microbiology of wounds and subcutaneous abscesses in adults (5, 18) and children (4). In those studies the numbers of anaerobes were similar to or greater than the numbers of aerobes in infections proximal to the oral, rectal, and vulvovaginal areas. These findings are explained by the predominance of anaerobes in the normal mucous membrane flora in these sites, reaching concentrations of 10^{11} organisms per g in the rectum and 10^9 organisms per g in the oral cavity, outnumbering aerobes 1,000 to 1 in the rectum and between 10 to 1 and 100 to 1 in the oral cavity (11, 13).

We found an association between the location of the NF lesion and the recovery of certain types of the organisms. Infections in and around the oral, rectal, and vulvovaginal regions are prone to yield mixed aerobic and anaerobic floras similar to those that are part of the normal microbial flora at the adjacent mucous membrane. The infections were mostly associated with the introduction of these organisms into the tissues after trauma and surgery and the presence of vascular disease. Mixed aerobic and anaerobic infections are also common in the breast area, fingers, and nail beds (4, 5). This may be due to the direct inoculation of mouth flora (which are predominantly anaerobic) by sucking or biting. Conversely, specimens obtained from areas remote from mucous membranes primarily contained constituents of the microflora indigenous to the skin.

The data presented here illustrate the relative frequencies of isolation of *Peptostreptococcus*, *Bacteroides*, *Prevotella*, *Porphyromonas*, *Clostridium*, and *Fusobacterium* species from patients

TABLE 3. Bacteriological characterization of organisms from 81 NF lesions

Type of bacterial growth	No. of specimens										No. of bacterial isolates per specimen									
	Head (9)[a]	Neck (11)	Trunk (7)	Arm (5)	Leg (14)	Inguinal area (4)	Buttocks (7)	Perirectal area (15)	External genitalia (9)	Total (81)	Head (9)	Neck (11)	Trunk (7)	Arm (5)	Leg (14)	Inguinal area (4)	Buttocks (7)	Perirectal area (15)	External genitalia (9)	Total (81)
Aerobic only	0	1	1	1	2	0	0	2	1	8	1.1	1.1	1.9	1.2	1.6	1.2	1.6	1.0	1.2	1.3
Anaerobic only	3	2	3	0	3	1	0	4	2	18	3.3	3.7	3.9	1.8	2.9	3.7	4.1	2.7	4.2	3.3
Aerobic and anaerobic	6	8	3	4	9	3	7	9	6	55	4.4	4.8	5.7[b]	3.0	4.5	5.0[b]	5.7	3.7	5.4	4.6

[a] Values in parentheses are numbers of specimens.
[b] Values do not add to total because of rounding error.

with NF. The rates of recovery of these organisms from infected sites are similar to their distributions in the normal flora (11, 13). As was described in previous reports, we also recovered more often *B. fragilis* group and *Clostridium* spp. from sites proximal to or inoculated by gastrointestinal tract floras, oral *Prevotella* and *Porphyromonas* spp., and *Fusobacterium* spp. from infections close to or inoculated by the oral cavity (14, 17, 23) and *P. disiens* and *P. bivia* from infections proximal to the vulvovaginal area (1, 9).

Anaerobic cocci were isolated from all body sites. The predominance of *Peptostreptococcus* spp. in general and especially *Peptostreptococcus magnus* in skin infections was demonstrated previously (1, 8, 9, 14, 17, 23). Anaerobic cocci exhibit virulence in animals infected with those organisms alone and also have synergistic interactions with other aerobic and anaerobic bacteria (7).

The rate of recovery of aerobic and facultative organisms also correlated with the infection site. The organisms that originate from the gastrointestinal flora, members of the family *Enterobacteriaceae* and group D streptococci, predominated in leg, rectal, external genitalia, and trunk infections. *S. aureus* and GABHS, which can be a part of the skin flora, were distributed throughout the whole body, although they predominated in the extremities and head and neck areas. Knowledge of this general pattern of distribution can assist the clinician in making a logical empiric choice of antimicrobial agents adequate for the therapy of infections at these sites.

We recovered GABHS alone from only four patients, who presented with typical streptococcal gangrene. The ability of hemolytic streptococci by themselves to induce NF was described by Meleney (19) in his original report of NF and was confirmed by other investigators (12, 22, 24, 25, 29). However, GABHS can also participate in an infection mixed with other bacteria, as occurred in four of our other patients.

Certain clinical presentations were associated more often with certain organisms. Swelling and tenderness were associated with gram-negative anaerobic bacilli, GABHS, and *S. aureus* infections; foul odor was associated with anaerobic gram-negative bacilli; and gas and bullous lesions were associated with members of the family *Enterobacteriaceae* and *Clostridium* spp. However, since many of these clinical features were also seen in patients with infections caused by other organisms, they can only serve as a general guideline in the clinical assessment.

The virulence of *Bacteroides*, *Clostridium*, *Peptostreptococcus*, and *Fusobacterium* species is well documented in animal studies (6) and in clinical infections (3, 10). The infection is often polymicrobial, in which the number of isolates may range from two to six per specimen. Although the exact pathogenic role of all bacterial isolates is not always certain, the synergistic interactions in polymicrobial infections have been extensively studied (2, 16, 20, 28). Several hypotheses have been proposed to explain such microbial synergy. It may be due to mutual protection from phagocytosis and intracellular killing (28), production of essential growth factors (16), and lowering of oxidation-reduction potentials in host tissues (20).

The present study underscores the importance of obtaining specimens adequate for the recovery of both aerobic and anaerobic bacteria from patients with NF. The observed isolation trends in different body sites and the clinical presentation and predisposing conditions could guide the selection of empiric antimicrobial therapy. However, the final choice of antimicrobial agents should be based, when possible, on the isolation of specific organisms, aerobes as well as anaerobes.

The gram-negative anaerobic bacilli, *Prevotella* species, and *Fusobacterium* species previously susceptible to penicillins have been shown in the last decade to have increased rates of resistance to these and other antimicrobial agents (3). The production of the enzyme β-lactamase is one of the main mechanisms of resistance to penicillins by many gram-negative anaerobic bacilli, including members of the *B. fragilis* group. Complete identification and testing for antimicrobial susceptibility and β-lactamase production are therefore essential for the management of infections caused by these bacteria.

Intensive surgical and medical therapy that includes the administration of intravenous fluids and management of septic shock are the hallmarks of treatment for NF. Antimicrobial therapy for mixed aerobic and anaerobic bacterial infections is required (3, 10). Antimicrobial agents that generally provide coverage for *S. aureus* as well as anaerobic bacteria include cefoxitin, clindamycin, imipenem, and the combinations of a β-lactamase inhibitor (i.e., clavulanic acid) and a penicillin (i.e., ticarcillin) and the combination of metronidazole plus a β-lactamase-resistant penicillin. Cefoxitin, imipenem, and a penicillin plus a β-lactamase inhibitor also provide coverage against members of the family *Enterobacteriaceae*. However, agents effective against these organisms (i.e., aminoglycosides and quinolones) should be added to the other agents when treating infections that include these bacteria.

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