

Enterobacter Bacteremia in the Community Hospital

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Background. The purpose of this study was to examine the epidemiological and clinical characteristics of *Enterobacter* bacteremia in the community hospital, where nosocomial infections are not commonly studied.

Methods. The blood culture records of five community hospitals in the Dayton, Ohio, area were reviewed to find cases of *Enterobacter* bacteremia. The respective hospital charts were then reviewed.

Results. Seventy-five episodes of *Enterobacter* bacteremia were reviewed. Eighty percent (60) of the organisms were nosocomially acquired, and 20% (15) were community acquired. The median age of the patients was 64 years. In 39% (29) of the episodes, fever was not the primary manifestation. The mortality rate was 29% (22). In 30% of the cases, the portal of entry for the bacteremia was unknown. The most common known portals of entry were genitourinary, gastrointes-

tinal or biliary, and peritoneal. The most common underlying disorders were malignancy, postoperative states, and diabetes mellitus. In 9% of the cases, no underlying disorder was detected. The organisms showed high sensitivity to chloramphenicol, aminoglycosides, piperacillin sodium, and cefotaxime sodium. High degrees of resistance were shown to ampicillin, first-generation cephalosporins, and cefoxitin. Eighty-four percent (46) of the patients treated appropriately survived, and 55% (11) of the patients treated inappropriately died.

Conclusions. *Enterobacter* bacteremia is most commonly nosocomially acquired and appears to be a problem in the community hospital. Appropriate therapy improves rates of patient survival.

Key words. Septicemia, cross infection, Enterobacteriaceae infections. *J Fam Pract* 1991; 32:601-606.

Gram-negative bacteria of the genus *Enterobacter* are members of the family Enterobacteriaceae, which also includes the genus *Klebsiella* and the genus *Serratia*. There are nine species in the genus *Enterobacter*; not all cause infection in humans. Pathogenic bacteria of the genus *Enterobacter* are believed to cause largely nosocomial infections.¹ Bacteremia due to this genus has been reported only in the past three decades.

It is important for physicians who treat hospitalized patients to have some knowledge of nosocomial infections, which are common and often cause unanticipated complications. While not the most common cause of hospital-acquired infection, *Enterobacter* species cause typical infections of this type.¹ Family physicians occasionally inadvertently treat *Enterobacter* infections when treating urinary tract infections, salpingo-oophoritis, and occasionally intra-abdominal abscesses.

The study was limited to actual cases of bacteremia to allow study of the organisms that were definitely pathogens. When the organism is cultured from other body sites it may be either a pathogen or merely represent colonization. Based on previous studies, it was expected that *Enterobacter* bacteremia would be primarily nosocomial, would be found in community hospitals, and would have a fairly high mortality rate.

There has not been a large number of clinical reviews of *Enterobacter* bacteremia. Watanakunakorn and Weber² recently reviewed 58 episodes of *Enterobacter* bacteremia in a community teaching hospital. Fung et al³ described 41 cases seen in a veterans hospital in Taipei, China. Bouza et al⁴ reported a review of 50 episodes from a referral hospital in Madrid, Spain. The findings of the current study are of interest because the research was done in community hospitals rather than in tertiary care settings.^{5,6}

Methods

Seventy-five episodes of *Enterobacter* bacteremia from five community hospitals in the Dayton, Ohio, area that

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occurred between February 11, 1985, and September 29, 1987, were collected and analyzed in detail under the direction of the Department of Family Practice at the Wright State University School of Medicine. A patient was said to have had an episode of bacteremia if a culture of the patient's blood was positive for an *Enterobacter* species. Blood cultures positive for *Enterobacter* species were not considered contaminants unless there was some clinical reason to treat them as such.

Cases were found by reviewing records in the microbiology laboratory of each hospital. The charts of patients who had blood cultures positive for *Enterobacter* species were then reviewed in the respective hospital's medical records department after permission to access the patients' records was received from the Research and Human Subjects Committee of each hospital. Because some of the hospital laboratories kept more complete microbiology records than others, and because for various reasons not all charts were available in the medical records departments during the period of the study, the study sample had to be limited to those charts that could be retrieved. All five hospitals used standard laboratory techniques for identifying organisms.⁷ An organism was defined as a *community-acquired organism* if it was isolated in a blood culture taken less than 48 hours after admission, and as a *nosocomial-acquired organism* if it was isolated from a culture taken 48 hours or more after admission.⁸

Demographic data (sex, race, and marital status) were taken from the face sheet of each chart. Fever at the onset of the bacteremic episode was defined as an oral temperature of 100.5°F or greater at any time during the 24 hours before drawing the blood for which a culture was positive. Normal values for leukocyte counts differed slightly for each hospital and were therefore defined for each patient using the laboratory criteria of the hospital at which the subject was a patient. Usually this definition was 5000 to 10,000 leukocytes per mm³. The portal of entry of the organism was defined as the site at which the organism entered the bloodstream. In many of the cases this could be documented by a positive culture from the site of infection. For example, the portal of entry was considered to be the urinary tract if 100,000 colonies of the same *Enterobacter* species that was cultured from the patient's blood was cultured from the patient's urinary tract. In many cases, however, the portal of entry was decided upon clinically, based on the judgments of the chart reviewer and the patient's attending physician. If, for example, the patient had a bacteremic episode concurrent with a severe burn, the portal of entry was listed as skin or subcutaneous.

In all cases, the underlying disorder was defined as the underlying illness that the patient had that would

have predisposed him or her to the bacteremia. If the patient had multiple disorders that could be considered predisposing to bacteremia, the disorder considered by the reviewer to be most predisposing was listed as the underlying disorder. For example, if the patient had both a malignancy and diabetes mellitus as underlying disorders, malignancy was listed for the episode. The patient was considered to have died from the bacteremia if death occurred within 7 days after the blood from which a positive culture resulted was drawn. Shock with bacteremia was defined in an adult as a systolic blood pressure of less than 90 mm Hg at some point during the bacteremic episode.⁴

Antibiotic sensitivities were performed at all five hospitals by the method of Bauer et al.⁹ Appropriate treatment for *Enterobacter* bacteremia was defined as the use of at least one bactericidal antibiotic, to which the organism was later proven to be susceptible, administered intravenously within 12 hours after drawing the blood from which the positive culture resulted, and given continuously for at least 3 days. Underlying disorders were classified according to the method of McCabe and Jackson.¹⁰ A rapidly fatal illness was defined as an illness from which the patient was likely to die within 6 months (eg, advanced intracranial hemorrhage). An ultimately fatal illness was defined as an illness from which the patient was likely to die within 5 years (eg, carcinoma with metastases). A nonfatal illness was defined as an illness from which the patient was not likely to die (eg, ileal conduit with frequent urinary tract infections).

Chi-square analyses were used to test for statistical significance.

Results

Seventy-six episodes of *Enterobacter* bacteremia documented by the aforementioned criteria were found among the five hospitals surveyed. An estimated 262,119 patients (including live births) were admitted to the five hospitals during the study period, resulting in a minimum rate of occurrence of *Enterobacter* bacteremia of 0.029% among all admissions at all five hospitals. One case was omitted from the investigation because part of the patient's chart was unavailable for review. Thus, 75 episodes were included in the study. Twenty-nine episodes were from Miami Valley Hospital, 26 from Kettering Medical Center, 11 from Good Samaritan Hospital, 6 from St Elizabeth Medical Center, and 3 from Greene Memorial Hospital (located in Xenia, Ohio, a satellite city of Dayton). Forty-three (57.3%) of the organisms were *Enterobacter cloacae*; 27 (36.0%) were *Enterobacter aerogenes*; 4 (5.3%) were *Enterobacter ag-*

Table 1. Portals of Entry for *Enterobacter* Bacteremia Among Patients in a Community Hospital (N = 75)

	No.	(%)
Unknown	22	(30)
Genitourinary	14	(19)
Gastrointestinal or biliary	14	(19)
Peritoneal*	9	(12)
Lung	6	(8)
Skin or subcutaneous tissue	6	(8)
Infected aorto-iliac graft	2	(3)
Female genital tract	1	(1)
Mediastinum	1	(1)

*Intra-abdominal abscess, intra-abdominal drainage catheter, or open wound.

glomerans; and one (1.3%) was *Enterobacter amnigenus*. Eighty percent (60) of the infections were nosocomial by the aforementioned definition, and 20% (15) were community acquired. No clustering of cases was seen in a single medical unit over a short period. Thirty-seven (50%) of the organisms were isolated from patients in intensive care units (cardiac, surgical, or other); 34 (45%) were isolated on medical and surgical wards; 3 (4%) were isolated from cultures drawn in emergency rooms; and 1 (1%) was isolated on an obstetrics floor.

The median patient age was 64 years, with patients' ages ranging from 10 days to 98 years. Forty-four (59%) of the patients were male and 31 (41%) were female. Sixty-five (87%) of the patients were white, and 10 (13%) were black. Forty-eight of the patients were married, 26 were single, and one patient had no marital status listed. Forty-six (61%) of the patients had fever and 29 (39%) did not. Forty-eight (64%) had high leukocyte counts at the onset of bacteremia by the aforementioned hospital criteria, 14 (19%) had normal counts, and 7 (9%) had low counts. Leukocyte counts were not done in 6 (8%).

In Table 1 the sources of the organisms are listed. In 30% of the cases the portal of entry of the organism was unknown. The most common portals of entry were, in descending order: gastrointestinal or biliary, 19%; genitourinary, 19%; peritoneal, 12%; lungs, 8%; and skin or subcutaneous tissue, 8%. The underlying disorders of the bacteremias are listed in Table 2. The most common underlying disorders or conditions were malignancy, 23%; postoperative states, 20%; diabetes mellitus, 8%; and burn, 4%. In 9% of the cases there were no underlying disorders. Twenty-two (29%) of the patients died from their episodes of bacteremia, and 53 (71%) survived. Five cases of shock with bacteremia (9% of the episodes) and one case of disseminated intravascular coagulation were noted.

Table 3 shows the antibiotics to which the organisms were tested. More than 80% of the isolated organ-

Table 2. Underlying Disorders of Patients in Five Community Hospitals Who Were Diagnosed as Having *Enterobacter* Bacteremia (N = 75)

Disorders	No.	(%)
Malignancy	17	(23)
Postoperative states		
Intestinal resection	7	(9)
Craniotomies for severe head injury	2	(3)
Abdominal aortic aneurysm repair	1	(1)
Cardiac catheterization	1	(1)
Coronary artery bypass graft	1	(1)
Hysterectomy	1	(1)
Orthopedic procedures, multiple, legs	1	(1)
Spinal fusion	1	(1)
None	7	(9)
Diabetes mellitus	6	(8)
Burn	3	(4)
Renal failure	3	(4)
Ascending cholangitis and abscess after cholecystoduodenostomy	2	(3)
Arteriosclerotic cardiovascular disease, severe	2	(3)
Obstructive pulmonary disease, chronic	2	(3)
Abortion, septic	1	(1)
Anemia, severe	1	(1)
Aortoduodenal fistula	1	(1)
Bladder rupture, traumatic	1	(1)
Cerebrovascular accident, major	1	(1)
Cholecystitis	1	(1)
Colitis, ulcerative	1	(1)
Guillain-Barré syndrome	1	(1)
Heart disease, valvular	1	(1)
Immunosuppressive medication	1	(1)
Intestinal perforation secondary to vascular insufficiency	1	(1)
Ischemia, lower extremity	1	(1)
Laennec's cirrhosis	1	(1)
Pancreatitis, hemorrhagic	1	(1)
Prematurity	1	(1)
Splenectomy, previous	1	(1)
Stomach perforation, traumatic	1	(1)
Urethral transection, traumatic	1	(1)

isms were susceptible to chloramphenicol, tobramycin, gentamicin, amikacin sulfate, piperacillin sodium, cotrimoxazole, cefotaxime sodium, and mezlocillin. More than 80% of the organisms showed resistance to cephalothin, ampicillin, cefazolin, and cefoxitin. Of the patients treated appropriately as defined by study criteria, 46 (84%) survived and 9 (16%) died (Table 4). Of the 20 patients judged to be treated inappropriately, 9 (45%) survived and 11 (55%) died ($P = .0008$). Table 5 displays a comparison of the classification of principal underlying illnesses and patient survival by the method of McCabe and Jackson.¹⁰

Discussion

Three clinical reviews pertaining to *Enterobacter* bacteremia were found through a MEDLINE search of the literature from 1969 to the present. One was conducted

Table 3. Antibiotic Sensitivities of Blood Isolates of *Enterobacter* Bacteremia in Bacteremic patients in Five Community Hospitals by the Method of Bauer et al⁹

Drug	Sensitive No. (%)	Intermediate No. (%)	Resistant No. (%)	No. Tested
Carbenicillin	13 (65)	—	7 (35)	20
Cephalothin	6 (13)	—	41 (87)	47
Chloramphenicol	57 (88)	1 (1)	7 (11)	65
Tetracycline	26 (72)	1 (3)	9 (25)	36
Kanamycin	4 (80)	—	1 (20)	5
Tobramycin	62 (93)	—	5 (7)	67
Gentamicin	63 (93)	—	5 (7)	68
Amikacin	51 (100)	—	—	51
Ampicillin	13 (19)	—	56 (81)	69
Cefazolin	6 (17)	1 (3)	28 (80)	35
Cefoperazone	19 (76)	1 (4)	5 (20)	25
Cefoxitin	4 (8)	—	46 (92)	50
Piperacillin	44 (81)	—	10 (19)	54
Ticarcillin	16 (64)	—	9 (36)	25
Cefamandole	14 (54)	—	12 (46)	26
Co-trimoxazole	30 (94)	—	2 (6)	32
Cefotaxime	21 (84)	1 (4)	3 (12)	25
Ceftazidime	7 (88)	—	1 (12)	8
Cefuroxime	11 (52)	2 (10)	8 (38)	21
Mezlocillin	13 (81)	3 (19)	—	16
Ampicillin/clavulinate potassium	—	—	4 (100)	4
Ceftriaxone	4 (80)	1 (20)	—	5
Cefotaxime	1 (100)	—	—	1
Clindamycin	—	—	1 (100)	1
Ceftizoxime	1 (100)	—	—	1
Azlocillin	1 (100)	—	—	1
Aztreonam	1 (100)	—	—	1
Cefotetan	1 (100)	—	—	1
Netilmicin	1 (100)	—	—	1

in a Veterans Administration hospital in Taipei, Republic of China,³ and another in a referral hospital in Madrid, Spain.⁴ The third study was done in the United States at a community teaching hospital in Ohio and had the largest number of case episodes (58).² A fourth study of 63 cases of *Enterobacter* bacteremia involving surgical patients was also found.¹¹ The authors believe the present study, which involved 75 episodes of *Enterobacter* bacteremia, to be the largest reported case series of bacteremia due to this organism. The study is also unique in that the data for it were collected from multiple hospitals in a single community during the same period.

Previously, most information on *Enterobacter* bacteremia was included in general studies of gram-negative

bacteremia or was considered together with *Klebsiella* and *Serratia* species as members of the Klebsiellaceae tribe.¹²⁻¹⁴ Recent studies suggest, however, that the *Enterobacter* species as pathogens are, in themselves, worthy of review.^{2,4}

The calculated rate of 0.029% of hospital admissions acquiring *Enterobacter* bacteremia is a minimum calculation because the study was limited only to cases that could be retrieved. Many additional cases may have been present during the study period that were not diagnosed. While it can be concluded from this study that *Enterobacter* bacteremia exists in the community, an accurate estimate of its prevalence cannot be made. The

Table 4. Relationship Between the Appropriateness of Antibiotic Therapy for Patients with *Enterobacter* Bacteremia and Patient Survival

Patient Outcome	Antibiotic Therapy		Total
	Appropriate No. (%)	Inappropriate No. (%)	
Survived	46 (84)	9 (45)	55
Died	9 (16)	11 (55)	20

$P = .0008.$

Table 5. Classification of Principal Underlying Illnesses by the Method of McCabe and Jackson¹⁰ and Survival of Patients with *Enterobacter* Bacteremia

Patient Outcome	Illness Classification		
	Not Fatal No. (%)	Ultimately Fatal No. (%)	Rapidly Fatal No. (%)
Survived	32 (82)*	12 (44)†	3 (33)‡
Died	7 (18)	15 (56)	6 (66)

* $P = .0014$; † $P = .0108$; ‡ $P = .8433.$

extent of the prevalence of *Enterobacter* bacteremia in the community is probably understated by this study.

The most common *Enterobacter* species that caused bacteremia in this study was *Enterobacter cloacae*. This finding agrees with previous work showing that this organism is the most pathogenic of the *Enterobacter* genus.^{3,4} Eighty percent of the bacteremic episodes were nosocomially acquired, an observation that is congruous with the other studies (72%,² 76%,⁴ and 68%³). The large percentage of episodes (50%) occurring in intensive care units is consistent with the nosocomial nature of the organism but greater than the figure of 30% reported by Bouza et al.⁴ Intensive care units are characterized by many seriously ill patients, use of many intravenous lines, and much hands-on nursing care. In general, however, *Enterobacter* bacteremia cases did not occur in clusters or "outbreaks." This concurs with the findings of the other three studies reviewed.²⁻⁴ While hospital clusters of *Enterobacter* bacteremia have been reported,^{15,16} outbreaks do not appear to be the rule with this illness.¹ The high male-to-female ratio in this study (3:2) correlates with earlier data (3:1,³ 4:3,⁴ and 4:3¹¹). Thirty-nine percent of the patients did not have fever at the onset of bacteremia, suggesting that *Enterobacter* bacteremia may often not have fever as a presenting sign. This is consistent with the notion that not all cases of bacteremia (especially in the elderly) have fever as a presenting sign.^{5,6} Considering that 28% of the patients studied showed either normal or low leukocyte counts at the onset of bacteremia, we can conclude that leukocytosis at the onset of *Enterobacter* bacteremia is not an inevitability. This finding is consistent with data on other forms of bacteremia.^{5,6} The median age of 64 years in this study compares well with a median age of 65 years given by Watanakunakorn and Weber² and is similar to the mean age of 56 years given by both Bouza et al⁴ and Fung et al.³

It was not possible to prove with absolute certainty what the portals of entry were for *Enterobacter* in all cases in this study. Other authors doing comparable research have encountered similar difficulties. It is reasonable that a large portion of this uncertainty could have been erased if *Enterobacter* species could have been consistently cultured from other sites (eg, wound, intravenous line catheter tip, or urinary tract). Unfortunately, this was not attempted or was attempted in some cases but was unsuccessful. The most common portals of entry for *Enterobacter* in this study (Table 1), however, compare with the genitourinary, hepatobiliary, and skin and surgical wound portals of entry reported by Fung et al,³ and contrasts with the lungs, peritonitis, urinary tract, meningitis, and cholangitis portals of entry reported by Watanakunakorn and Weber²; the unknown, surgical wounds, respiratory tract, and urinary tract portals of

entry reported by Bouza et al⁴; and the sputum, open skin wounds, and central venous lines portals of entry reported by Burchard et al¹¹ in surgical patients. While there is no way to prove this, many of the organisms in this study for which portals of entry were unknown could have entered the patients' bloodstreams through intravenous lines.

Since malignancy is often listed as the most common underlying disorder in many studies of bacteremia,^{5,6} it is not surprising that it should be the most common underlying disorder associated with *Enterobacter* bacteremia in this study. Malignancy usually leaves the host immunosuppressed and susceptible to severe infection.

The overall mortality rate of patients in this study (29%) is low in contrast to the mortality rates of 69%,² 46%,³ and 42%⁴ reported in the three other studies on *Enterobacter* bacteremia; however, in none of the other studies was death due to bacteremia defined as rigorously as it was in this study. Five of the 75 bacteremia cases in this study had concurrent shock, whereas only two of 50 cases in the study by Bouza et al⁴ had shock.

The antibiotic susceptibility studies for this study indicate that ampicillin, first-generation cephalosporins, and cefoxitin should not be used as first-line drugs in *Enterobacter* bacteremia. Favorable bacterial susceptibilities were noted for amikacin sulfate, gentamicin, tobramycin, chloramphenicol, piperacillin sodium, and cefotaxime sodium. These susceptibility patterns are similar to those reported by Watanakunakorn and Weber² and Bouza et al.⁴ It is interesting, however, that Fung et al³ in China showed surprisingly low susceptibility rates in *Enterobacter* strains for piperacillin sodium (46%), gentamicin (49%), amikacin sulfate (66%), and chloramphenicol (37%). These rates indicate that the genus *Enterobacter* may have different antibiotic susceptibility patterns in different parts of the world and warrants further study.

The survival figures shown in Table 4 (84% surviving with appropriate therapy and 55% dying with inappropriate therapy, $P = .0008$) suggest that appropriate therapy for *Enterobacter* bacteremia significantly improves survival. In interpreting these data, however, one should be cautioned that ethical and moral considerations may have been taken into consideration in treating bacteremia in some of the patients. For example, a terminally ill cancer patient may have been treated less vigorously with antibiotics than an otherwise healthy patient would have been; this may have been appropriate "management," though inappropriate "treatment." That ethical considerations may have been taken into consideration in the treatment of some of these patients should not, however, interfere with the conclusion that appropriate treatment appears to positively affect survival. As

can be seen in Table 5, the more severe the patient's underlying illness is, the more likely the patient is to die as a result of bacteremia.

In summary, *Enterobacter* bacteremia appears to exist as a problem in community hospitals. Diagnosis may be delayed because fever and leukocytosis do not necessarily accompany the disease onset; therefore, the condition is often inadequately treated (26.6% of cases).

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