Multiple Antibiotic–Resistant *Klebsiella* and *Escherichia coli* in Nursing Homes

Janis Wiener, MD  
John P. Quinn, MD  
Patricia A. Bradford, PhD  
Richard V. Goering, PhD  
Catherine Nathan, MS  
Karen Bush, PhD  
Robert A. Weinstein, MD

**Antibiotic Resistance among Nosocomial Pathogens** is a cause of major concern. Three aspects of this problem have been particularly challenging: the frequent emergence of resistance to the newest antibiotics; the presence of antibiotic resistance genes on bacterial plasmids, which may be transferred among different bacterial species; and the spread of resistant bacteria among patients not only in the hospital but also in the community.

Since the late 1980s, there has been a proliferation of reports of nosocomial outbreaks caused by gram-negative bacilli that contain plasmid-mediated extended-spectrum β-lactamases (ESBLs) that confer resistance to many of the newest cephalosporins and other β-lactam antibiotics. This problem was reported first from Europe in 1983. Since then, there have been several reports of extensive nosocomial outbreaks from France and the United States, where there have been reports of limited hospital outbreaks and a large hospital outbreak that involved 155 patients. The most commonly reported problem has been nosocomial spread of ceftazidime sodium–resistant strains of *Klebsiella pneumoniae*, usually in the face of increased use of ceftazidime and inadequate hospital hygiene. The epidemic strain frequently has been resistant to multiple classes of antibiotics and has posed a major clinical dilemma. Most outbreaks have been

**Context** Infections caused by ceftazidime sodium–resistant gram-negative bacteria that harbor extended-spectrum β-lactamases (ESBLs) are increasing in frequency in hospitals in the United States.

**Objectives** To report a citywide nursing home–centered outbreak of infections caused by ESBL-producing gram-negative bacilli and to describe the clinical and molecular epidemiology of the outbreak.

**Design** Hospital-based case-control study and a nursing home point-prevalence survey. Molecular epidemiological techniques were applied to resistant strains.

**Settings** A 400-bed tertiary care hospital and a community nursing home.

**Patients** Patients who were infected and/or colonized with ceftazidime-resistant *Escherichia coli*, *Klebsiella pneumoniae*, or both and controls who were admitted from nursing homes between November 1990 and July 1992.

**Main Outcome Measures** Clinical and epidemiological factors associated with colonization or infection by ceftazidime-resistant *E coli* or *K pneumoniae*; molecular genetic characteristics of plasmid-mediated ceftazidime resistance.

**Results** Between November 1990 and October 1992, 55 hospital patients infected or colonized with ceftazidime-resistant *E coli*, *K pneumoniae*, or both were identified. Of the 35 admitted from 8 nursing homes, 31 harbored the resistant strain on admission. All strains were resistant to ceftazidime, gentamicin, and tobramycin; 96% were resistant to trimethoprim-sulfamethoxazole and 41% to ciprofloxacin hydrochloride. In a case-control study, 24 nursing home patients colonized with resistant strains on hospital admission were compared with 16 nursing home patients who were not colonized on hospital admission; independent risk factors for colonization included poor functional level, presence of a gastrostomy tube or decubitus ulcers, and prior receipt of ciprofloxacin and/or trimethoprim-sulfamethoxazole. In a nursing home point-prevalence survey, 18 of 39 patients were colonized with ceftazidime-resistant *E coli*; prior receipt of ciprofloxacin or trimethoprim-sulfamethoxazole and presence of a gastrostomy tube were independent predictors of resistance. Plasmid studies on isolates from 20 hospital and nursing home patients revealed that 17 had a common 54-kilobase plasmid, which conferred ceftazidime resistance via the ESBL TEM-10, and a 35-kilobase plasmid, which conferred resistance to trimethoprim-sulfamethoxazole and gentamicin and tobramycin; all 20 isolates harbored this ESBL. Molecular fingerprinting showed 7 different strain types of resistant *K pneumoniae* and *E coli* distributed among the nursing homes.

**Conclusions** Nursing home patients may be an important reservoir of ESBL-containing multiple antibiotic–resistant *E coli* and *K pneumoniae*. Widespread dissemination of a predominant antibiotic resistance plasmid has occurred. Use of broad-spectrum oral antibiotics and probably poor infection control practices may facilitate spread of this plasmid-mediated resistance. Nursing homes should monitor and control antibiotic use and regularly survey antibiotic resistance patterns among pathogens.

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limited to high-risk patient-care areas (e.g., intensive care or cancer units), although reports from the United States have described hospitalwide dissemination of ceftazidime-resistant strains and 2 reports from France describe spread of resistant strains in several hospitals.

In 1989, the occurrence in K pneumoniae of a unique β-lactamase, TEM-10, which mediated resistance to ceftazidime, was reported from a Chicago, Ill, hospital. In 1990, our hospital’s ongoing surveillance of antibiotic resistance detected the first case of ceftazidime-resistant Enterobacteriaceae in a patient admitted from a local nursing home with a bacteremic Escherichia coli urinary tract infection. After this case, we continued to note the recovery of ceftazidime-resistant Enterobacteriaceae from patients admitted from area nursing homes. In the present study, we report the clinical and molecular epidemiological investigation of ceftazidime-resistant K pneumoniae and E coli isolates from patients admitted to our hospital from several nursing homes throughout the Chicago area, and we describe the results of a culture survey in 1 of these nursing homes.

METHODS

Study Populations

Michael Reese Hospital is a 400-bed acute care facility in Chicago. Between 1990 and 1992, using prospective laboratory-based surveillance, we identified 55 hospital patients who were infected and/or colonized with ceftazidime-resistant E coli and/or K pneumoniae. Detailed demographic and epidemiological data were obtained for patients hospitalized between November 1990 and July 1992 (n = 24).

Because a majority of the resistant strains were recovered at the time of hospital admission from patients from 6 area nursing homes, 2 additional groups were studied. First, a control group was formed by selecting all nursing home patients who were admitted to our hospital on a Monday, Wednesday, or Friday during a 4-month period (October 1991 through January 1992) and who were neither infected nor colonized with ceftazidime-resistant Enterobacteriaceae; this group included 16 patients. Second, in July 1992, we performed a point-prevalence study at 1 of the involved nursing homes, which had contributed approximately a third of the infected patients. Cultures were obtained for all 39 patients on the skilled-care floor of that nursing home to determine the extent of and factors associated with colonization with ceftazidime-resistant Enterobacteriaceae.

Microbiology

Isolates identified in the hospital’s clinical microbiology laboratory by automated methods (Vitek Automated Microbiology System, bioMerieux Vitek Inc, Hazelwood, Mo) as ceftazidime-resistant E coli or K pneumoniae were verified in our laboratory by biochemical testing (API 20E, bioMerieux Vitek Inc) and by disk diffusion and agar dilution susceptibility testing to ceftazidime, gentamicin, tobramycin, imipenem, trimethoprim-sulfamethoxazole, and ciprofloxacin hydrochloride.

Cultures of the rectum, urine, and any gastrostomy tube site or decubitus ulcers were obtained from the 16 control patients from nursing homes within 24 hours of hospital admission and from the 39 patients in the nursing home point-prevalence study. These specimens were streaked on MacConkey agar (Difco Laboratories, Detroit, Mich) containing ceftazidime sodium, 10 µg/mL, and incubated for 18 to 24 hours at 35°C. The 3 most common morphologic types of bacterial colonies from each culture were identified and underwent disk diffusion susceptibility testing using the panel of antibiotics described herein.

Molecular Analysis

Plasmids conferring ceftazidime resistance were transferred from the clinical and survey isolates by filter mating to a ceftazidime-susceptible E coli host, selecting for ceftazidime resistance. Plasmid DNA was isolated from the resulting transconjugants by alkaline lysis. EcoRI restriction digests, recombinant DNA techniques, and transformations of plasmid DNA were performed as described by Sambrook et al. Resistance of transconjugants to non–β-lactam antibiotics was determined by disk diffusion testing. The presence of the TEM-10 β-lactamase gene was determined by nucleotide sequencing as previously described.

To determine relatedness of bacterial isolates, chromosomal DNA for pulsed-field gel electrophoresis (PFGE) was prepared as described by Murray et al. Restriction endonuclease digestion by Xbal was performed at 37°C for 18 hours. Pulsed-field gel electrophoresis was performed using a CHEF-DR III system (Bio-Rad Laboratories, Hercules, Calif) as described previously. Ethidium bromide–stained agar gels were examined visually and strain types were described as different if PFGE patterns differed in more than 3 chromosomal restriction fragment positions.

Demographic and Clinical Data

For the hospitalized nursing home case and control groups, we reviewed hospital records and made site visits to each patient’s nursing home to review nursing home charts. We recorded each patient’s age, sex, admitting diagnoses, level of care, underlying illnesses, instrumentation, prior hospitalizations within 4 months, prior antibiotic use in the nursing home and hospital within 4 months, and length of nursing home residence. For the 39 patients for whom cultures were obtained in the nursing home point-prevalence survey, similar data were obtained; information regarding antibiotic use was based solely on nursing home records for the prior 6 months in this patient group.

Definitions and Statistics

Sites of infection were defined by standard Centers for Disease Control and Prevention criteria. Infections that manifested more than 48 hours after hospitalization were considered nosocomial. Bivariate analyses were performed by χ², Fisher exact, or t tests as appropriate; P values are based on 2-tailed test results. Multivariate analyses were performed using logistic regression (SPSS for Windows, Version 5.0, SPSS Inc, Chicago, Ill), using stepwise in forced selection of variables based on statistical and clini-
RESULTS

Overview
From November 1990 to October 1992, we identified 55 patients with positive clinical cultures for ceftazidime-resistant E coli (n = 15), K pneumoniae (n = 35), or both (n = 5). Twenty patients were admitted from the community; 4 of the 20 were colonized and/or infected with resistant strains at the time of hospital admission and 16 acquired resistant strains in the hospital. Thirty-five patients were admitted from 8 different Chicago-area nursing homes; 31 of the 35 were colonized and/or infected with ceftazidime-resistant strains at the time of admission to our hospital and 4 manifested the resistant strain after admission to the hospital.

The majority of patients (37/55) had the resistant strains recovered from urine specimens. Seven patients had bacteraemia with resistant strains; 2 of these patients died within 24 hours of admission and 2 died at 6 and 18 days after onset of bacteraemia while receiving antibiotics active against the infecting strains. Nine patients had wound infections and 7 had resistant strains recovered from sputum specimens. Resistant E coli was more common in patients from nursing homes who were already colonized and/or infected at hospital admission (12 patients with E coli, 16 with K pneumoniae, and 3 with both) than in nursing home or community patients who subsequently had hospital-acquired infections or colonization (2 patients with E coli, 16 with K pneumoniae, and 2 with both) (15/31 vs 4/20; P = .04).

All strains were highly resistant to ceftazidime (mean minimum inhibitory concentration, 256 µg/mL; range, 32-512 µg/mL) and aztreonam; 87% were susceptible to ceftriaxone, 96% to cefoxitin sodium, and 23% to cefazolin. Among the β-lactamase inhibitor combination agents, piperacillin-tazobactam was most active, inhibiting 90% of the strains; 47% were inhibited by ticarcillin disodium–clavulanate. All strains were susceptible to imipenem and amikacin. Cross-resistance to other antibiotic classes was common: 100% of strains were resistant to gentamicin and tobramycin, 96% were resistant to trimethoprim-sulfamethoxazole, and 41% were resistant to ciprofloxacin.

Hospital-Based Case-Control Study
We focused our clinical-epidemiological study on the period November 1990 through July 1992. During this time, there were 27 patients transferred from nursing homes who had positive clinical cultures for resistant strains at the time of hospital admission. Medical records were available for 24 of these patients; they were colonized and/or infected with ceftazidime-resistant E coli (n = 10), K pneumoniae (n = 10),12 or both (n = 2).2 These 24 patients were compared with 16 control patients admitted from nursing homes during the same period. Case and control patients represented 8 nursing homes (A-H). In bivariate analysis, patient’s functional level, presence of a gastrostomy tube or decubitus ulcers, or prior receipt of ciprofloxacin and/or trimethoprim-sulfamethoxazole were significantly associated with presence of ceftazidime-resistant strains (TABLE 1). Of note, although ceftazidime use was associated with occurrence of resistant strains, only 5 case patients had received ceftazidime in the 4 months preceding positive culture. Multivariate analysis showed that presence of decubitus and/or gastrostomy tube, patient’s functional level, and receipt of trimethoprim-sulfamethoxazole and ciprofloxacin in the prior 4 months was each independently associated with presence of the ceftazidime-resistant strains.

Nursing Home Point-Prevalence Survey
Of 39 patients on the skilled-care floor of the surveyed nursing home (nursing home A), 18 had rectal colonization with ceftazidime-resistant E coli. No patient was colonized with ceftazidime-resistant K pneumoniae. In a bivariate analysis, risk factors for colonization with ceftazidime-resistant E coli included patient’s functional level, presence of a gastrostomy tube, and prior use of ciprofloxacin and/or trimethoprim-sulfamethoxazole (TABLE 2). Multivariate analysis showed that the prior use of ciprofloxacin and/or trimethoprim-sulfamethoxazole and the presence of a gastrostomy tube were independent predictors of resistance. None of the patients had received ceftazidime in the nursing home. Although data on antibiotic use during prior hospitalizations were not available, these patients had been in the nursing home without intercurrent hospitalization for a mean of more than 6 months.

Molecular Epidemiology
Resistance plasmids were analyzed from 12 E coli and 8 K pneumoniae isolates from 20 patients (12 nursing home patients who had positive cultures at hospital admission, 6 patients from the nursing home point-prevalence survey, and 2 patients with nosocomial infections). A common large (54-kilobase [kb]) conjugal plasmid was found in 17 of the 20 isolates (FIGURE 1); this plasmid conferred resistance to cefazidime, gentamicin, tobramycin, and trimethoprim-sulfamethoxazole and was detected in isolates from each of the nursing homes. The other 3 isolates (2 nursing home and 1 nosocomial) had ceftazidime-resistance plasmids with unique restriction digest patterns that encoded several different resistance markers. Nucleotide sequencing showed that the predominant plasmid, as well as the 3 unique plasmids, encoded a previously described TEM-10 β-lactamase.18 All ceftazidime-resistant E coli and K pneumoniae recovered from November 1990 through July 1992 produced a β-lactamase with an isoelectric point of 5.6, consistent with the TEM-10 enzyme (data not shown).

Pulsed-field gel electrophoresis showed 4 different strain types of resistant E coli and 3 of K pneumoniae (FIGURE 2). The strain types were distributed among the different nursing homes. Patients from 4 different rooms in the nursing home prevalence survey were colonized with 4 different strain types of E coli, each of which carried the predominant resistance plasmid. In addition, 3 different strain types were cultured from 3 patients within a single room.
Table 1. Comparison of Hospitalized Nursing Home Patients Based on Presence of Ceftazidime-Resistant *Escherichia coli* or *Klebsiella pneumoniae*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Yes (n = 24)</th>
<th>No (n = 16)</th>
<th>Bivariate OR (95% CI)</th>
<th>P Value</th>
<th>Multivariate OR (95% CI)</th>
<th>P Value</th>
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<td>Age, mean, y</td>
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<td>Female</td>
<td>14 (58.3)</td>
<td>11 (68.7)</td>
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<td>1.6 (1.1-2.3)</td>
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<td>Intermediate</td>
<td>0 (0)</td>
<td>6 (37.5)</td>
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<td>Total</td>
<td>24 (100)</td>
<td>10 (62.5)</td>
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<td>1.6 (1.1-2.3)</td>
<td>.01</td>
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<td>Presence of Decubitus ulcers</td>
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<tr>
<td>Foley catheters</td>
<td>17 (70.8)</td>
<td>6 (37.5)</td>
<td>4.1 (0.88-19)</td>
<td>.04</td>
<td>1.3 (1.0-1.7)</td>
<td>.03</td>
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<td>Gastrostomy tubes</td>
<td>16 (66.7)</td>
<td>6 (37.5)</td>
<td>3.3 (0.75-15)</td>
<td>.07</td>
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<td>Days in hospital during prior 4 mo, mean</td>
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<td>Days in nursing home before admission, mean</td>
<td>36.6</td>
<td>80.5</td>
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<td>Antibiotic use in prior 4 mo</td>
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<td>Ceftazidime sodium</td>
<td>5 (20.8)</td>
<td>8 (50)</td>
<td>0.26 (0.05-1.3)</td>
<td>.06</td>
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<td>Gentamicin or tobramycin</td>
<td>11 (45.8)</td>
<td>3 (18.8)</td>
<td>3.7 (0.71-24)</td>
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<td>Trimethoprism-sulfamethoxazole</td>
<td>13 (54.3)</td>
<td>5 (31.3)</td>
<td>2.6 (0.58-12)</td>
<td>.16</td>
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<td>Ciprofloxacin hydrochloride</td>
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<td>3 (18.8)</td>
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<td>Ciprofloxacin and/or trimethoprism-sulfamethoxazole</td>
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<td>6 (37.5)</td>
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<td>1.4 (1.1-1.7)</td>
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<td>Nursing home (before hospitalization)</td>
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<td>A</td>
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<td>10 (62.5)</td>
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<td>.23</td>
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<td>B</td>
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<td>1 (6.25)</td>
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<td>C</td>
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<td>2 (12.5)</td>
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<td>D</td>
<td>3 (12.5)</td>
<td>1 (6.25)</td>
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<td>E</td>
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<td>G</td>
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<td>2 (6.25)</td>
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<td>H</td>
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<td>0</td>
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*Data are number of patients (percentage) unless otherwise noted. OR indicates odds ratio; CI, confidence interval; and ellipses, data not applicable.

Table 2. Comparison of Patients in Nursing Home A Based on Colonization Status

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Yes (n = 18)</th>
<th>No (n = 21)</th>
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<th>P Value</th>
<th>Multivariate OR (95% CI)</th>
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<tr>
<td>Age, mean, y</td>
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<td>80</td>
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<tr>
<td>Female</td>
<td>14 (77.8)</td>
<td>17 (81.0)</td>
<td>0.9 (0.41-2.0)</td>
<td>&gt;.99</td>
<td>. . . . . . . . . . . .</td>
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<td>Level of care</td>
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<tr>
<td>Intermediate</td>
<td>5 (27.8)</td>
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<td>Total</td>
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<td>8 (38.1)</td>
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<tr>
<td>Presence of Decubitus ulcers</td>
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<tr>
<td>Foley catheters</td>
<td>2 (11.1)</td>
<td>1 (4.8)</td>
<td>1.5 (0.62-3.6)</td>
<td>.60</td>
<td>. . . . . . . . . . . .</td>
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<tr>
<td>Gastrostomy tubes</td>
<td>3 (16.7)</td>
<td>3 (14.3)</td>
<td>1.1 (0.45-2.7)</td>
<td>&gt;.99</td>
<td>. . . . . . . . . . . .</td>
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<tr>
<td>Days in hospital during prior 4 mo, mean</td>
<td>6.4</td>
<td>3.4</td>
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<td>. . . . . . . . . . . .</td>
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<tr>
<td>Days in nursing home before culture, mean</td>
<td>186</td>
<td>290</td>
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<td>Antibiotic use in prior 6 mo</td>
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<tr>
<td>Trimethoprism-sulfamethoxazole</td>
<td>4 (22)</td>
<td>1 (4.8)</td>
<td>1.9 (1.1-3.5)</td>
<td>.16</td>
<td>. . . . . . . . . . . .</td>
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<tr>
<td>Ciprofloxacin</td>
<td>6 (33)</td>
<td>1 (4.8)</td>
<td>2.3 (1.3-3.9)</td>
<td>.03</td>
<td>. . . . . . . . . . . .</td>
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<tr>
<td>Ciprofloxacin and/or trimethoprism-sulfamethoxazole</td>
<td>10 (56)</td>
<td>2 (9.5)</td>
<td>2.8 (1.5-5.3)</td>
<td>.002</td>
<td>21 (1.8-247)</td>
<td>.01</td>
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</table>

*Data are number of patients (percentage) unless otherwise noted. RR indicates relative risk; OR, odds ratio; CI, confidence interval; and ellipses, data not applicable.
COMMENT
We believe that this is the first report of a citywide outbreak of ceftazidime-resistant Enterobacteriaceae within the United States. The outbreak occurred within multiple nursing homes throughout the Chicago area during a period when no concurrent nosocomial outbreak could be identified in our hospital. Laboratory evaluation has shown that this outbreak was caused by an ESBL carried primarily on a single large plasmid that had spread widely among multiple strain types of *E coli* and *K pneumoniae* and within multiple nursing homes. Moreover, it appears that colonization and infection with these strains were most often not linked directly to ceftazidime use. This experience differs from most previous reports, in which outbreaks of ceftazidime resistance were centered largely in high-risk areas (eg, intensive care units) and attributed mostly to in-hospital person-to-person spread of the epidemic strains and/or to the pressure of increased ceftazidime use.4,6,8,13,17

There are several possible explanations for the dissemination of ceftazidime resistance in multiple nursing homes in Chicago. First, it is possible that frequent use of trimethoprim-sulfamethoxazole in nursing homes may select for ceftazidime-resistant strains because of plasmid linkage of the resistance determinants for these drugs. Although ciprofloxacin resistance in our strains and in almost all other strains studied is not plasmid-borne, 41% of our strains were resistant to this agent, and prior trimethoprim-sulfamethoxazole and/or ciprofloxacin use was associated with ceftazidime resistance in our survey of nursing home patients. Similar rates of chromosomally mediated ciprofloxacin resistance have been reported in other studies of ESBL-producing *K pneumoniae* and *E coli*,26,27 and recently transferable quinolone resistance has been identified in a strain of *K pneumoniae* with a plasmid-mediated ESBL.28 In any case, our experience differs from the 1 reported outbreak of ceftazidime-resistant Enterobacteriaceae in a long-term care facility, where the occurrence of resistant strains was attributed largely to selective pressure of ceftazidime, which 53% of infected patients in that study had received in the prior month.14

Second, because hand-washing rates during patient care often are low among nursing home personnel,29 risk of cross-infection may be great, especially for patients who are incontinent or have feeding gastrostomy tubes and require frequent contact with health care providers such as physicians, clinicians, and nurses. We found that occurrence of ceftazidime-resistant strains was associated significantly with such factors.

Third, even if nursing home residents have not been hospitalized recently (in our prevalence survey, the colonized nurs-
ing home patients had been in the nursing home for an average of 6 months), they are likely to be exposed to the flora of other residents who shuttle between nursing home and hospital. In fact, the problem of ceftazidime resistance in Chicago hospitals continues and appears to be related primarily to the extent to which hospitals receive admissions from nursing homes. A 1994-1996 survey of ceftazidime-resistant K pneumoniae and E coli in 6 Chicago-area hospitals showed that 55% of these strains were recovered from nursing home patients at the point of hospital admission; that a 54-kb plasmid, which encodes the TEM-10 β-lactamase, as well as resistance to gentamicin, tobramycin, and trimethoprim-sulfamethoxazole, is still responsible for ceftazidime resistance in almost all isolates; and that this plasmid was recovered from 15 different strain types of E coli and 9 of K pneumoniae. This recent experience from hospitals throughout Chicago and its suburbs and another report from 2 Chicago hospitals support the ongoing importance of the nursing home reservoir and our results, which may be particularly relevant for institutions that are just beginning to encounter similar problems. Future studies using the ceftazidime break point (2 µg/mL) recommended in 1998 for screening for ESBLs may disclose even more extensive resistance.

The relative importance of plasmid transmission in the overall epidemiology of antimicrobial resistance is not known. In Chicago, the occurrence of ceftazidime resistance in E coli and K pneumoniae appears to have resulted primarily from transmission of a single plasmid rather than from clonal expansion of a single strain. Such plasmid transmission as a cause of discrete epidemics of resistance has been documented relatively infrequently. There are a few reports of nosocomial plasmid outbreaks in intensive care units in which large numbers of ill patients were exposed to multiple antibiotics and 1 report of a plasmid outbreak in a long-term care facility. An experience more like ours—spread of a resistance plasmid in a broad geographic area—was reported from France, where a family of plasmids with a predominant prototype was detected sequentially in multiple different strains of cefotaxime-resistant Enterobacteriaceae in 4 hospitals. Our experience suggests that plasmid transfer may lead to widespread antimicrobial resistance and that, at least for β-lactamase resistance mediated by TEM-10, extensive intraspecies and even interspecies transfer of a single plasmid can underlie epidemic resistance.

The molecular mechanisms by which this plasmid outbreak has occurred are unknown. It is possible that genetic material was exchanged within the gut or in the environment of nursing home patients, particularly facilitated by the presence of foreign bodies, such as gastrostomy tubes and urinary catheters, and by fomites, such as urinary measuring devices. The predominant resistance plasmid involved in this outbreak may be very prone to transfer, as suggested by its occurrence in several strains of E coli, which has been a less-usual reservoir in the past for ESBLs. This plasmid may have entered strains that have a particular ability to persist in the gut of patients on the hands of health care workers, and/or in the health care environment. Escherichia coli may be an important gastrointestinal reservoir for survival of the plasmid, and transfer into K pneumoniae may increase the likelihood of clinical infection. The ongoing movement of patients between nursing homes and hospitals may allow further opportunity for the exchange of genetic material among nursing home and nosocomial bacteria. However, nosocomial emergence of ceftazidime resistance can be controlled by antimicrobial restrictions and hospital hygiene; less than 5% of E coli and K pneumoniae isolates were resistant in our hospital, where specific antibiotic resistance isolation precautions have been practiced for more than 20 years.

In conclusion, ceftazidime resistance appears to have spread outside of the hospital environment in Chicago because of intergenic and intraspecies transfer of a single resistance plasmid in the gastrointestinal flora of nursing home patients. Plasmid and bacterial spread may have been fostered by use of outpatient oral antimicrobials, in part because of plasmid linkage of several resistance determinants. This may hamper the ability to curb spread of resistance simply by controlling the use of newer parenteral antibiotics. Because nursing home patients may be a reservoir for resistant bacteria, nursing homes must now monitor the patterns of antibiotic use and resistance and proactively control antibiotic use in their patients just as suggested for acute care hospitals.

Author Affiliations: Michael Reese Hospital and Medical Center, Chicago, Ill (Dr Wiener, Quinn, and Weinstein and Ms Nathan); Wyeth-Ayerst Research, Pearl River, NY (Dr Bradford); Creighton University, Omaha, Neb (Dr Goering); and R. W. Johnson Pharmaceutical Research Institute, Raritan, NJ (Dr Bush). Dr Wiener is now in private practice in Oak Park, Ill; Dr Quinn is now with the Department of Medicine, University of Illinois at Chicago; and Ms Nathan and Dr Weinstein are now with the Division of Infectious Diseases, Cook County Hospital and Rush Medical College, Chicago.

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