

## ***Multi-Resistant Gram-Negative Bacteria***

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Increase in Fluoroquinolone-Resistant Gram-Negative Clinical Cultures among Hospitalized Older Adults Over an Eight-year Period

**Ram R. Miller, MD, MSc<sup>1</sup>**, Eli N. Perencevich, MD, MS<sup>2</sup>, Anthony D. Harris, MD, MPH<sup>1</sup>, Jessina C. McGregor, PhD<sup>3</sup>, Ebbing Lautenbach, MD, MPH, MSCE<sup>4</sup>, Jon P. Furuno, PhD<sup>1</sup>.

<sup>1</sup>University of Maryland School of Medicine, Baltimore, MD, USA, <sup>2</sup>VA Maryland Health Care System, Baltimore, MD, USA, <sup>3</sup>Oregon State University College of Pharmacy, Portland, OR, USA, <sup>4</sup>University of Pennsylvania School of Medicine, Philadelphia, PA, USA.

### Background:

Fluoroquinolones (FQ) are commonly used antimicrobial agents in older adults. Despite this, few studies have assessed the prevalence of FQ resistance among hospitalized elders.

### Objective:

To examine the prevalence of FQ resistance among Gram-negative clinical cultures in older adults in an acute-care hospital over an eight-year period.

### Methods:

This study was completed at the University of Maryland Medical Center, a 650-bed tertiary-care hospital located in Baltimore. We collected microbiology data on all positive clinical cultures for *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Enterobacter cloacae*, *Klebsiella* species (*K. pneumoniae* and *K. oxytoca*) among adult patients age 65 years or older admitted between January 1, 1998 and December 31, 2005. Consistent with Clinical and Laboratory Standards Institute guidelines, only the first organism-specific clinical culture per patient, per year was included. We defined isolates as being FQ resistant if the organism was resistant or intermediately resistant to any of the FQ antibiotics against which it was tested. We calculated the cumulative and species-specific proportions of FQ resistance at each year using descriptive statistics. Chi-square tests for trends were used to assess whether increasing resistance was statistically significant over time.

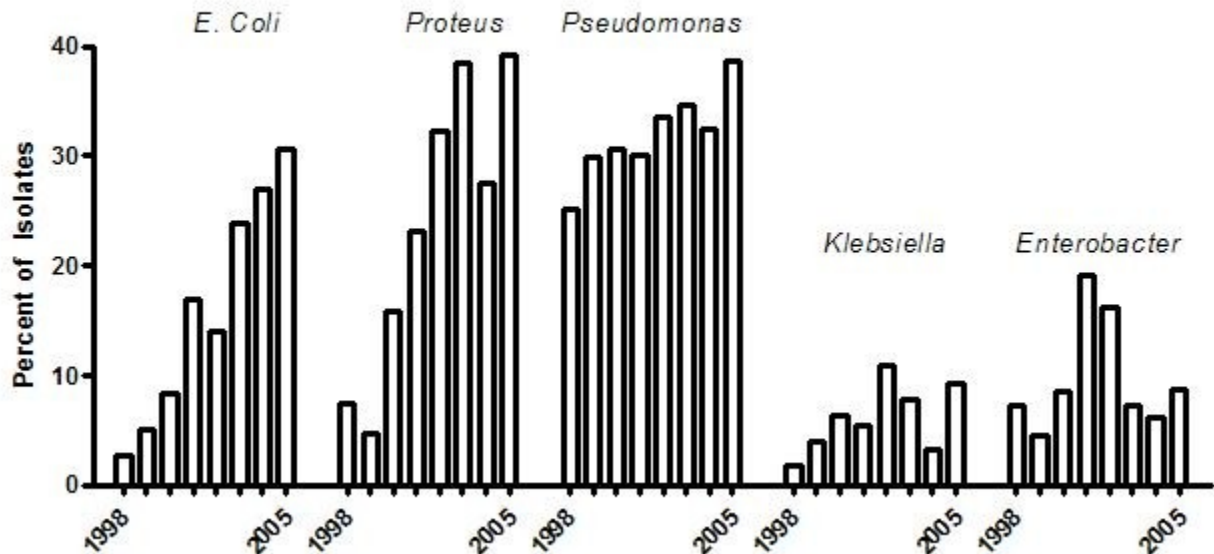
### Results:

Over the eight years of study, 4985 Gram-negative cultures obtained from 4089 patients were included in the analyses: 1839 *E. coli*, 554 *P. mirabilis*, 1044 *P. aeruginosa*, 1068 *Klebsiella* sp., and 480 *E. cloacae*. Across all species, the prevalence of FQ resistance rose from 8.4% in 1998 to 26.9% in 2005 ( $p < 0.01$ ). Species-specific prevalence estimates are displayed in the Figure. Although the prevalence of resistance varied by species, the highest and lowest prevalence of FQ resistance were observed in *Pseudomonas* (32.6%) and *Klebsiella* sp. (5.7%) cultures respectively. Over the eight years of study, statistically significant increases in the prevalence of FQ resistance of *E. coli* (1998: 2.8%, 2005: 30.6%), *P. mirabilis* (1998: 7.4%, 2005: 39.3%), and *Klebsiella* sp. (1998: 1.7%, 2005: 9.3%) were observed ( $p < 0.05$  for all).

### Conclusions:

Among hospitalized older adults, the prevalence of FQ-resistant, Gram-negative clinical cultures increased significantly from 1998 to 2005. The increasing prevalence of FQ resistance should be considered when choosing empiric antimicrobial therapy in this age group.

### Prevalence of Fluoroquinolone Resistance by Year



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### Tigecycline Use in Multi-drug Resistant Gram-negative Infections

**Kara B. Anthony, MD**, Neil O. Fishman, MD, Darren R. Linkin, MD, MSCE, Leanne B. Gasink, MD, MSCE, Paul H. Edelstein, MD, Ebbing Lautenbach, MD, MPH, MSCE. Hospital of the University of Pennsylvania, Philadelphia, PA, USA.

#### Background:

Tigecycline (TG) is a broad-spectrum glycylicycline with *in vitro* activity against multi-drug resistant (MDR) gram-negative rods (GNR) including *Acinetobacter baumannii* (AC) and most enterobacteriaceae. Few clinical data exist regarding the role of TG in treating MDR GNR infections.

#### Objective:

To describe the use of TG in treating infections caused by MDR AC and MDR enterobacteriaceae.

#### Methods:

Medical records of patients who received  $\geq 7$ d of TG between 3/1/04 and 8/30/06 for infections due to MDR AC or MDR enterobacteriaceae were reviewed. MDR was defined as resistance to  $\geq 3$  classes of antibiotics. Primary outcomes were clinical response (CR) and microbiological response (MR) at end of therapy, and in-hospital mortality. Antimicrobial susceptibility to TG was performed by E-test and, for purposes of this study, interpretive MIC criteria for enterobacteriaceae were used (sensitive,  $S \leq 2$ ;

intermediate, I=4; resistant, R<sub>≥</sub>8).

#### Results:

18 patients were included. Median age was 60 and 10 (56%) were male. 7 (39%) were solid-organ transplant recipients and 11 (61%) were in an ICU. Anatomic sites of infection for which TG was used were: lung (n=11), urinary tract (n=2), skin/soft tissue (n=2), mediastinum (n=1), abdomen (n=1), and blood (n=1). Causative organisms were: *AC* (n=10), *Klebsiella pneumoniae* (n=5), *Enterobacter cloacae* (n=2), and *Escherichia coli* (n=1). 10 patients had pre-therapy isolates susceptible to ampicillin/sulbactam or a carbapenem, but had a  $\beta$ -lactam allergy which prompted TG therapy. Of the 15 patients with pre-therapy isolates tested against TG, 9 were S and 6 were I (5 *AC*, 1 *E. cloacae*). All patients received TG as first-line therapy, 14 as monotherapy. Median duration of therapy was 15d (range 7-133). CR was positive in 7 patients, negative in 7, and could not be determined in 4. MR was positive in 3 patients, negative in 3, and not documented in 9. Despite limited renal excretion of TG, one patient with *AC* urinary tract infection achieved CR and MR after 14d of therapy. One patient with *AC* pneumonia developed TG resistance on therapy (MIC from 2 to 12 after 14d of therapy) but ultimately survived. Overall in-hospital mortality was 50%. 6 patients died on therapy, 5 due to infection. Of the 6 patients with pre-therapy isolates I to TG, 5 (83%) died compared to only 2 of 9 (22%) patients with isolates S to TG (p=0.02).

#### Conclusions:

Despite lack of clinical data, TG is being used to treat MDR GNR infections. In >50% of cases, TG was used because of a  $\beta$ -lactam allergy. Until comparative studies with TG are done,  $\beta$ -lactams or carbapenems should be used preferentially (with desensitization if needed) in infections caused by MDR GNRs that are susceptible. Poorer outcomes in patients with pre-therapy isolates I to TG suggest susceptibility testing may predict outcome and should be used to guide therapy. Evolution of resistance in one *AC* strain on therapy suggests TG be used with caution in such organisms with a propensity to acquire resistance.

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Utility of Multidrug-Resistant Gram Negative Bacilli (MDR-GNB) Surveillance as part of an Admission Surveillance Culture (ASC) Protocol

Zakir Hussain A. Shaikh, MD, MPH, CPE, FIDSA, Elizabeth R. Wallace, MPH, Kimberly S. Strelczyk, MSN, APRN, CCRN, CIC.  
Methodist Health System, Dallas, TX, USA.

#### Background:

Review of antimicrobial susceptibility over the past decade indicates an overall trend of emergence of MDR-GNB. Selective antimicrobial pressure from indiscriminate use of broad-spectrum antibiotics has led to a significant increase in hospital-acquired infections (HAI) with MDR-GNB, especially *Acinetobacter* species, *P. aeruginosa*, and extended-spectrum  $\beta$ -lactamase-producing (ESBL) *K. pneumoniae*. While hospital-wide and focused ICU surveillance activities reported in antibiograms provide a retrospective measure of the increasing resistance trends, they are not beneficial in the infection control endeavors to initiate empiric contact precautions (CP) for patients at high risk for MDR-GNB colonization. Lack of treatment options for MDR-GNB associated HAI make it imperative to employ strategies aimed at early detection to minimize the nosocomial transmission.

**Objective:**

To determine the utility of MDR-GNB surveillance as part of a comprehensive admission surveillance culture (ASC) protocol.

**Methods:**

A hospital-wide ASC protocol was implemented at our 478-bed community hospital aimed at identifying multi-drug resistant organism (MDRO) colonization in high-risk patients (details of protocol described elsewhere). Empiric CP was initiated among patients meeting the criteria, and appropriate cultures were obtained per protocol. In response to an increasing prevalence of MDR-GNB among patients from surrounding long-term care facilities (LTCF), the decision was made to evaluate respiratory specimens, rectal swabs, urine samples (from catheterized patients) and wound cultures (if available) for the presence of MDR-GNB, in addition to evaluating specimens for MRSA and VRE. MDR-GNB were defined by the identification of ESBL or by resistance to  $\geq 3$  classes of antibiotics to which a GNB organism is usually susceptible.

**Results:**

Of the 300 patients who met criteria for ASC during the first 2 months of implementation, 35 patients (11%) cultured positive for MDR-GNB. Of the 695 culture specimens, 424 specimens (excluding 271 nasal swabs) were evaluated for MDR-GNB; 41 (9.7%) were found to be positive for MDR-GNB (two different MDR-GNB being isolated in 6 patients). Of the 41 MDR-GNB isolates, the 4 most common organisms included *E. coli* (16), *K. pneumoniae* (8), *P. aeruginosa* (6), and *Acinetobacter* species (5). Additional isolates included: *E. aerogenes* (2), *K. ascorbata* (1), *S. marcescens* (1), *S. odorifera* (1), and *S. maltophilia* (1).

**Conclusions:**

A significant proportion of our patients meeting criteria for ASC were found to have colonization with MDR-GNB. Implementing an ASC protocol incorporating MDR-GNB surveillance can be an effective preventive strategy for hospitals faced with the challenge of reducing nosocomial transmission from an increasing proportion of colonized patients being admitted from LTCF and other healthcare facilities.

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**Aztreonam-Resistant *Pseudomonas aeruginosa*: Risk Factors and Impact on Mortality**  
Leanne B. Gasink, MD, MSCE, Warren B. Bilker, PhD, Irving Nachamkin, PhD, Ebbing Lautenbach, MD, MPH, MSCE.

University of Pennsylvania, Philadelphia, PA, USA.

**Background:**

*Pseudomonas aeruginosa* (PA) is a common nosocomial pathogen that causes significant morbidity and mortality. The increasing prevalence of resistance to anti-pseudomonal drugs is of great concern. Risk factors and outcomes of drug resistant PA have been examined for a variety of antibiotic resistance patterns. However, the risk factors and impact of aztreonam resistant PA (ARPA) has not been well studied.

**Objective:**

To investigate risk factors for ARPA and to examine the impact of ARPA on economic and clinical outcomes

**Methods:**

An ecologic study was conducted to examine ARPA trends from 1989 to 2000. Subsequently, a case control study was performed to identify risk factors for ARPA among inpatients with a clinical culture positive for PA between 1/1/99 and 12/31/00. A cohort study was then performed to determine the impact of ARPA infection on clinical and economic outcomes. For the case control and cohort studies, a given subject could only be included once (i.e., if more than one isolate was identified only the first PA isolate was included).

**Results:**

From 1989 through 2000, annual prevalence of ARPA increased from 27% to 36% (p=0.04, trend). Between 1999 and 2000, 940 PA isolates were identified in 720 inpatients with complete data available. 183 (25.4%) isolates were aztreonam resistant and 537 (74.6%) were aztreonam susceptible. On multivariable analysis, prior fluoroquinolone use, prior use of antibiotics with anaerobic coverage and renal disease were associated with ARPA (see table). Compared to subjects with aztreonam susceptible PA, subjects with ARPA had higher median hospital charges (\$68,688 vs \$47,350) (p=0.01) and higher mortality (25.7% vs 16.8%) (p=0.009). However, when controlling for other patterns of resistance of the PA isolate in a multivariate model, ARPA was no longer significantly associated with mortality.

**Conclusions:**

ARPA has increased significantly and is associated with prior FQ use, prior use of antibiotics with anti-anaerobic coverage and renal disease. ARPA is associated with increased hospital charges, but does not have an independent impact on mortality. Given the continued emergence of multi-drug resistant PA, efforts should be made to preserve this agent as useful therapy for PA infections.

**Risk factors for arpa**

	OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Fluoroquinolone use	2.45 (1.64, 3.64)	<0.001	1.79 (1.16, 2.77)	0.008
Anti-anaerobic use	2.04 (1.43, 2.92)	<0.001	1.61 (1.10, 2.37)	0.02
Renal disease	1.74 (1.21, 2.48)	0.002	1.52 (1.06, 2.18)	0.02
Age (per year)	0.99 (0.98, 1.00)	0.005	0.98* (0.97, 0.99)	0.001

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**Patient-to-Patient Transmission is Important in Extended Spectrum beta-Lactamase-Producing *Klebsiella pneumoniae* Acquisition**

**Anthony D. Harris, MD, MPH<sup>1</sup>, Eli N. Perencevich<sup>1</sup>, Kristie Johnson<sup>1</sup>, David Paterson<sup>2</sup>, J. Glenn Morris<sup>1</sup>, Sandra Strauss<sup>1</sup>, Judith A. Johnson<sup>1</sup>.**

<sup>1</sup>University of Maryland, Baltimore, MD, USA, <sup>2</sup>University of Pittsburgh, Pittsburgh, PA, USA.

**Background:**

Extended spectrum β-lactamase (ESBL)-producing *Klebsiella* are of increasing public health importance. Some studies suggest that antimicrobial control is the preferred method to limit the emergence of antibiotic-resistant gram negative bacteria. However, the causal role of antibiotic selective pressure in driving this emergence has not been assessed.

**Objective:**

To quantify the amount of patient-to-patient transmission of extended spectrum  $\beta$ -lactamase-producing *Klebsiella* based on peri-anal surveillance cultures in an intensive care unit population.

**Methods:**

We performed a prospective cohort study of all patients admitted to the medical and surgical intensive care units at the University of Maryland Medical Center between September 1, 2001 and September 1, 2004. Patients had peri-anal cultures obtained on admission, weekly and upon discharge. Pulsed-field gel electrophoresis and epidemiological criteria were used to quantify the amount of patient-to-patient transmission of *Klebsiella pneumoniae* and *K. oxytoca*. To verify that the PFGE had good discriminatory ability, i.e. the test is able to determine that epidemiologically unrelated strains are unrelated, we obtained 8 isolates of *K. pneumoniae* taken from eight distinct countries that were part of a *K. pneumoniae* bacteremia study and analyzed them using identical PFGE methodology.

**Results:**

1806 patients were admitted to the ICUs and had negative admission cultures for extended spectrum  $\beta$ -lactamase-producing bacteria and thus were at risk for acquisition. Among 27 patients who acquired a *K. pneumoniae*, 14 (52%) met our definition of patient-to-patient transmission. Of the 27 acquisitions, 6 (22%) had a subsequent positive extended-spectrum-  $\beta$ -lactamase clinical culture. Among 8 patients who acquired a *K. oxytoca*, 1 (13%) met the definition of patient-to-patient transmission. The PFGE analysis of the eight isolates from eight distinct countries had eight unique PFGE types demonstrating that our PFGE methodology had a high discriminatory ability.

**Conclusions:**

Patient-to-patient transmission is an important contributor to the spread of extended spectrum  $\beta$ -lactamase-producing *Klebsiella pneumoniae* colonization acquisition in the intensive care unit setting.

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Outcomes in Patients Infected During an Outbreak of Carbapenemase producing *Klebsiella pneumoniae* (KP): Efficacy of Treatment with Carbapenem

**Nimisha Mishra, MD,MS**, Judith A. O'Donnell, M.D, Barbara Fry-Arrighy, B.S., CIC, Patricia Daly, B.S, Christopher Emery, MD.  
Hahnemann University Hospital, Philadelphia, PA, USA.

**Background:**

Infections caused by multi-drug resistant (MDR) KP are a problem in many institutions. Outbreaks with carbapenemase-producing KP strains are unusual. Treating MDR KP infections is challenging as the organisms are resistant to most antibiotic classes.

**Objective:**

To identify the clinical outcome in patients infected with carbapenemase producing KP, treated with various antibiotic regimens.

**Methods:**

Between April and September of 2005 our institution had an outbreak of infections due to MDR KP. We conducted a retrospective analysis on the treatment and outcomes of inpatients with MDR KP infections. Charts were reviewed and MDR KP isolates were sent out for isoelectric focusing and other tests to identify resistance mechanisms.

**Results:**

31 patients with MDR KP infection were identified during the study period. Four were excluded; 2/4 were diagnosed as outpatients, and 2/4 had positive cultures reported after discharge, and were lost to follow-up. Of the remaining 27 patients, 24 (88%) were treated with a carbapenem (20 with imipenem, 4 with meropenem); 3/27 received levofloxacin alone. Eleven patients (40%) received 2 or more days of an aminoglycoside along with the carbapenem. Four patients were switched to, or received adjunctive therapy with, colistin. Thirteen/27 (48.1%) were cured. Ten of 13 received a carbapenem with or without an aminoglycoside. Nine of these 13 cured patients had isolates producing carbapenemase; 7 patients (25.9%) had treatment failure with clinical relapse. All 7 had received a carbapenem (6 imipenem and 1 meropenem), and had a carbapenemase-producing organism. Seven had indeterminate outcomes, with 6 expiring before a course of therapy was completed, and the 7<sup>th</sup> being discharged to home hospice. 96.3% of the isolates were ESBL producing; 74.1% had an identified KPC-like carbapenemase. Seven of the 27 patients were renal transplant recipients; 5/7 relapsed with urinary tract infection and/or urosepsis.

**Conclusions:**

Forty-eight percent of MDR KP-infected patients demonstrated cure with carbapenem despite their isolates being carbapenemase producers. Why an antimicrobial that was likely inactive against the MDR KP isolate would result in cure is not clear. In this outbreak, renal transplant patients were more likely to relapse with MDR KP. Additional studies assessing treatment choices and outcomes would be beneficial.

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Risk Factors for Extended-spectrum Beta-lactamase (ESBL) Producing *Escherichia coli* and *Klebsiella* species in an Acute Care Hospital

**Laraine L. Washer, MD**, Daryl D. DePestel, PharmD, Melissa Halm, MPH, Elizabeth Rapa, MPH, Duane Newton, PhD, Clarise Rivera Starr, PhD, N. Cary Engleberg, MD, Jennifer Arndt, BS, Carol E. Chenoweth, MD.  
University of Michigan Health System, Ann Arbor, MI, USA.

**BACKGROUND:**

Resistance of Enterobacteriaceae to broad spectrum  $\beta$ -lactam antibiotics via ESBL production is an increasing problem worldwide. Beginning in 2004, we identified an increase in ESBL producing *Escherichia coli* and *Klebsiella* spp. in our hospitals.

**OBJECTIVE:**

To describe the epidemiology of ESBL producing *E.coli* and *Klebsiella* spp. and to identify risk factors for ESBL infections in our hospital.

**METHODS:**

We conducted a case-control study of hospitalized adults with clinical cultures positive for ESBL producing *E.coli* or *Klebsiella* spp. between January 1, 2004 and June 30, 2005. Controls were matched by age, gender, hospital unit, and length of stay prior to

culture or matched time point. Risk factors were analyzed for 3 months before the time of culture or matched time point. Sixteen available clinical isolates were conjugally mated with *E. coli* DH5 $\alpha$  and antibiotic resistance profiles and plasmid analysis was performed.

#### RESULTS:

Rate of ESBL isolation was 1.7 patients per 10,000 patient days during the 18 month study period. 49 isolates were identified among 47 hospitalized patients. Twenty-one (44.7%) patients had cultures with *E. coli*, 24 (51.1%) had cultures with *Klebsiella* spp and 2 patients had both *E. coli* and *Klebsiella* spp. Thirty-nine (83%) patients met criteria for infection. Significant infections included UTI in 15 (38.4%), pneumonia in 8 (20.5%), bloodstream infection in 4 (10.5%), and abdomen infection in 2 (5.3%). 63.3% of isolates were trimethoprim/sulfamethoxazole resistant and 83.7% were levofloxacin resistant. Risk factors for ESBL infection included hospitalization within 3 months (OR 2.38, p=0.04), pressure/vascular/diabetic ulcers within 3 months (OR 7.50, p=0.007), central venous catheter (CVC) within 3 months (OR 6.5, p=0.014), and long term care (LTC) stay within 3 months (OR=10.55, p=0.003). Mean antibiotic use in defined daily doses (DDD) was greater among cases (38.61 DDD) than controls (24.95 DDD) but was not statistically different (p=0.18). There was no difference in cephalosporin use but levofloxacin use within the prior 3 months was greater among cases than controls (p=0.07). With linear regression analysis, LTC stay and CVC within the prior 3 months remained significant risk factors. The ESBL phenotype was successfully transferred from 8 of 16 isolates with eight different plasmid profiles recovered. Levofloxacin resistance was not transferred.

#### CONCLUSION:

ESBL infections are increasing in our hospital and are associated with risk factors of LTC exposure and invasive CVCs. Plasmid analysis does not suggest clonal spread of ESBL infections in our hospital.

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### Risk Factors for Gastrointestinal Tract Colonization with Fluoroquinolone-Resistant *Escherichia coli* in Hospitalized Patients

**Ebbing Lautenbach, MD, MPH, MSCE, Joshua P. Metlay, MD, PhD, Mark G. Weiner, MD, Warren B. Bilker, PhD, Pam Tolomeo, MPH, Irving Nachamkin, DrPH, MPH, Xiangqun Mao, MD, Neil O. Fishman, MD.**  
University of Pennsylvania, Philadelphia, PA, USA.

#### Background:

The prevalence of fluoroquinolone (FQ) resistance in *Escherichia coli* has continued to rise in recent years. Understanding the factors that promote colonization with FQ-resistant *E. coli* (FQREC) in the gastrointestinal (GI) tract is critical for developing strategies to control the emergence of this resistant organism.

#### Objective:

To identify risk factors for GI tract colonization with FQREC among hospitalized patients.

#### Methods:

Institution-wide fecal surveillance surveys were conducted annually at two academic medical centers in 2002, 2003 and 2004. All fecal FQREC isolates (MIC  $\geq$ 8.0ug/mL to

levofloxacin) were identified. Cases (i.e., all subjects with FQREC colonization) were compared to controls (i.e., all subjects with no FQREC) to identify risk factors for FQREC colonization.

**Results:**

Of 789 total subjects, 99 (12.5%) were colonized with FQREC. On bivariable analyses, FQ use within the prior 30 days was associated with FQREC colonization [OR (95%CI) = 2.05 (1.25, 3.37); p=0.006]. In multivariable analyses, the adjusted association between FQ use and FQREC varied significantly by year of enrollment (table). Of note, a prior study of the molecular characteristics of these same isolates (*J Infect Dis* 2006;194:79-85) showed that the proportion of FQREC isolates demonstrating efflux overexpression as a mechanism of FQ resistance also significantly varied by year [49% in 2002; 48% in 2003; and 22% in 2004 (p=0.01)].

**Conclusions:**

The association between prior FQ use and FQREC colonization varied significantly by study year. While rarely studied, these results suggest that the clinical epidemiology of resistant organisms may change over time. In assessing these results in the context of other recent work, we found that prior FQ use was only associated with FQREC colonization during the year in which efflux overexpression was a less common mechanism of FQ resistance. Overexpression of efflux pumps can be elicited by many products (e.g., various antibiotics, detergents, dyes). Our results suggest that when efflux overexpression is less prevalent, FQ use (which elicits resistance primarily through mutations in the DNA gyrase and Topoisomerase IV genes) assumes a more prominent role in leading to FQ resistance. Finally, these findings indicate that clinical risk factors for resistance may vary depending on the underlying mechanism of resistance.

**Multivariable Model of Risk Factors for FQREC Colonization**

Association between FQ Use and FQREC Colonization*		
Enrollment Year	Adjusted OR (95%CI)	P value
2002	1.17 (0.38, 3.59)	0.78
2003	1.24 (0.50, 3.07)	0.65
2004	7.86 (3.04, 20.36)	<0.001

\*Adjusted for admitting hospital and duration of hospitalization

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**Increasing Prevalence of Gastrointestinal Colonization with Ceftazidime-Resistant Gram-negative Bacteria at a University Hospital.**

**Kerri A. Thom, MD<sup>1</sup>, Judith A. Johnson, PhD<sup>1</sup>, Sandra M. Strauss, BS, M(ASCP)<sup>1</sup>, Jon P. Furuno, PhD<sup>1</sup>, Eli N. Perencevich, MD, MS<sup>2</sup>, Anthony D. Harris, MD, MPH<sup>1</sup>.**

<sup>1</sup>University of Maryland, Baltimore, MD, USA, <sup>2</sup>VA Maryland Health Care System, Baltimore, MD, USA.

**Background:**

The occurrence of nosocomial infections due to third-generation cephalosporin-resistant Gram-negative bacteria is increasing and accounts for significant morbidity and mortality. The gastrointestinal tract is an important reservoir for the development of antibiotic resistance, and gastrointestinal colonization with antibiotic-resistant bacteria often precedes clinical infection.

**Objective:**

The goals of this study were: 1) to estimate the prevalence of colonization with ceftazidime-resistant Gram-negative bacteria among patients in the medical and surgical intensive care units at a university-affiliated tertiary care hospital during two distinct time periods and 2) to assess whether colonized patients had a positive clinical culture with the same organism found on surveillance during the index admission.

**Methods:**

We performed a cross-sectional study of adult intensive care patients admitted to the University of Maryland Medical Center from June 14, 2003, to July 14, 2003, and from June 14, 2006, to July 14, 2006. Perirectal surveillance cultures were obtained upon admission to the intensive care unit, weekly and at discharge. Each perirectal culture was plated onto MacConkey agar supplemented with 2 µg of ceftazidime per ml. Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method and results were interpreted according to the Clinical Laboratory Standards Institute's guidelines.

**Results:**

In 2003, 19% (33/176) of patients were colonized with ceftazidime-resistant Gram-negative bacilli. In 2006, the prevalence of ceftazidime-resistance increased to 31% (60/191),  $p = 0.0058$ . This increase in gastrointestinal colonization with ceftazidime-resistant Gram-negative bacilli was largely driven by an increase in ceftazidime-resistant *Klebsiella* species (from 6.4% in 2003 to 22.8% in 2006;  $p = 0.0044$ ). In 2003, 48% (16/33) of colonized patients had at least one positive clinical culture with the same organism found on perirectal surveillance culture compared to 37% (22/60) in 2006,  $p=0.2804$ .

**Conclusions:**

Our data suggest that gastrointestinal colonization with ceftazidime-resistant Gram-negative bacilli is common and increasing and may result in nosocomial infection.

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Risk Factors for Colonization and/or Infection with Carbapenem-Resistant *Klebsiella Pneumoniae* (CRKP)

David Kuhar, M.D.<sup>1</sup>, David Calfee, MD<sup>2</sup>.

<sup>1</sup>Emory University School of Medicine, Atlanta, GA, USA, <sup>2</sup>Mount Sinai School of Medicine, New York, NY, USA.

**Background:**

CRKP began to emerge as a significant nosocomial pathogen in our institution in 2004. Molecular testing determined that the mechanism of resistance was production of a *K. pneumoniae* carbapenemase (KPC). Because options for treatment of infections caused by these multidrug-resistant organisms are quite limited, prevention of transmission of CRKP is of critical importance.

**Objective:**

To identify risk factors for colonization and/or infection with CRKP in order to optimize control and prevention efforts.

#### Methods:

A case-control study was performed. A case was defined as a person from whom CRKP was isolated from a clinical specimen obtained between 1/1/04 and 6/15/05. Controls were selected from persons hospitalized for >48 hours matched to cases on the basis of age, sex, and date of admission. Demographic and clinical data were collected by retrospective review of medical records, laboratory data, and administrative data. Univariable and multivariable logistic regression analyses were performed.

#### Results:

69 cases and 69 matched controls were included in the analyses. Among cases, sites from which CRKP was first isolated included urine (45%), blood (20%), wounds (10%), intraabdominal sites (9%), catheter tips (7%), and sputum (7%). Cases and controls were similar in the prevalence of diabetes, cardiac disease, gastrointestinal disease, malignancy, and pulmonary disease. Variables that were associated with colonization and/or infection in univariable analyses are shown in the Table. Variables that were found to be independent predictors of CRKP colonization and/or infection included: length of stay (OR 1.05,  $p=0.02$ ) and presence of a central venous catheter (OR 106,  $p<0.0001$ ). ICU exposure (OR 5.3, 95% CI 0.84-33.8,  $p=0.08$ ) and nursing home residence (OR 14, 95% CI 0.94-209.8,  $p=0.056$ ) approached, but did not reach, statistical significance.

#### Conclusions:

The findings of this investigation suggest that the risk factors for colonization and/or infection with CRKP are similar to those identified for other healthcare-associated pathogens, such as prolonged hospital stay, higher severity of illness, and the presence of invasive devices such as central venous catheters. No single, specific risk factor for colonization and/or infection with CRKP was identified. Other factors, such as exposure to broad spectrum antibiotics, may also be important but the small size of this study prevented detection of such an association. Thus, adherence to routine infection control practices, Contact Precautions for affected patients, and prudent use of antibiotics are likely to be important in preventing spread of CRKP and minimizing the risk of transfer of the KPC-encoding plasmid to other organisms.

#### Results of Univariable Analysis

Characteristic	Cases (n=69)	Controls (n=69)	OR (p-value)
Length of stay (days)	Median: 32.2 Range: 4-140	Median: 10.3 Range: 3-80	NA (<0.0001)
Karnofsky Score	Median: 30 Range: 10-70	Median: 50 Range: 10-100	NA (<0.0001)
Skilled nursing facility resident	13 (19%)	1 (1%)	15.8 (0.0007)
ICU admission	44 (64%)	12 (17%)	8.4 (<0.0001)
Antibiotic exposure	67 (97%)	47 (68%)	15.7 (<0.001)
B-lactam/inhibitor	39 (56%)	10 (14%)	7.7 (<0.0001)
Carbapenem	22 (32%)	1 (1%)	31.8 (<0.0001)
3 <sup>rd</sup> gen cep	10 (14%)	3 (4%)	3.7 (0.04)
4 <sup>th</sup> gen cep	25 (36%)	3 (4%)	12.5 (<0.0001)
Fluoroquinolone	34 (49%)	15 (22%)	3.5 (0.0007)
Metronidazole	38 (55%)	10 (14%)	7.2 (<0.0001)
Vancomycin	43 (62%)	7 (10%)	14.6 (<0.0001)
CVC	52 (75%)	3 (3%)	67.3 (<0.0001)

Enteral tube	45 (65%)	7 (10%)	16.6 (<0.0001)
Urinary catheter	45 (65%)	31 (45%)	2.3 (0.02)
Mechanical vent.	35 (51%)	22 (32%)	2.2 (0.02)
Endoscopic procedure	24 (35%)	13 (19%)	2.3 (0.03)
Cirrhosis	19 (28%)	6 (9%)	4.0 (0.004)
ESRD	19 (28%)	2 (3%)	12.7 (<0.0001)

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### Use of Surveillance Cultures (SC) to Detect Colonization with Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP)

David Calfee, MD, Charlene Petrec, RN, Gene Kogan, MS, Sophie Labrecque, RN, Flora Samaroo, BA, Stephen Jenkins, PhD.  
Mount Sinai School of Medicine, New York, NY, USA.

#### Background:

CRKP has emerged as a significant nosocomial pathogen in the New York City area. When CRKP began to be detected at the Mount Sinai Hospital, SC to detect colonized ICU patients were introduced as one intervention intended to control its spread. SC have been shown to be of value in preventing transmission of several multidrug-resistant (MDR) pathogens, particularly MRSA and VRE, but data are limited regarding their use for MDR Gram-negative bacteria such as CRKP.

#### Objective:

To describe the findings of a program of SC for CRKP among ICU patients

#### Methods:

Microbiology and infection control data were reviewed. SC specimens (rectal swabs or sputum) were inoculated onto MacConkey agar with an ertapenem disk and incubated up to 48 hours. Organisms growing within 15mm of the disk were identified. Carbapenem resistance of *K. pneumoniae* isolates was confirmed by E-test.

#### Results:

The Table outlines the program timeline. Between 1/19/05 and 12/18/06, 355 patients were found to be colonized or infected with CRKP. 151 cases (43%) were detected in or attributable to the participating ICUs. CRKP was first identified by clinical microbiology culture (CMC) in 292 (82%) and by SC in 63 (18%). The median time from admission to a positive SC was 18 d (mean 22, range 0-111). When obtained upon admission and weekly thereafter, SC first identified 58% of colonized ICU patients as compared to just 20% when SC were obtained only upon admission. 36 (57%) patients detected by SC had at least one previous SC that did not yield CRKP. Most (84%) patients detected by SC had one or more CMC submitted prior to collection of the SC.

All patients detected by SC have reached an endpoint of either a positive CMC (n=32, 51%) or hospital discharge (n=31, 49%). 18 (58%) of the discharged patients had one or more CMC submitted after the positive SC. Among the 63 patients detected by SC, the length of time between the availability of the SC result and a positive CMC or hospital discharge ranged from 10-160 d (median: 10) and -2 to 77 d (median: 7), respectively. SC prevented a total of 1,109 days of unprotected CRKP exposures among staff and

patients.

Conclusions:

SC detect a substantial number of CRKP-colonized patients who would go completely undetected or who would be detected by CMC only after a substantial delay. Repeating SC periodically after admission appears to be important because it allows detection of those with a negative admission culture who later become culture-positive due to either new acquisition or increased bacterial burden resulting in conversion to culture positivity. Development of selective culture media to increase the sensitivity of SC and expansion of the program to other hospital units are in progress in efforts to further control this significant pathogen.

SC Program Timeline

ICU	Date Admission SC Begun	Date Weekly SC Begun
A	1/19/05	1/19/05
B	11/05	10/06
C	11/05	10/06
D	11/05	NA
E	11/05	NA
F	11/05	NA

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Risk Factors for Multi-Drug Resistant *Stenotrophomonas maltophilia* Transmission in a Surgical Intensive Care Unit: a Case Control Study

April Johnson, DVM, Charlene Ruse, BS, Mary Ann Gross, BS, Robert Kelly, RN, Michelle Forthofer, BS, Nabih Asal, PhD, Kenneth Rand, MD, Loretta Fauerbach, MS, CIC, Lennox K. Archibald, MD, FRCP.  
University of Florida, Gainesville, FL, USA.

Background:

During August 2004, Shands Hospital (SH) surgical intensive care unit (SICU) personnel noted increased numbers of multi-drug resistant *Stenotrophomonas maltophilia* (MDRSM) infections. SICU personnel thought that the increased numbers might be related to bronchoscopy. Thus, the SH Infection Control department was invited to assist in an investigation.

Objectives:

(i) to identify risk factors associated with transmission and acquisition of MDRSM infection; and (ii) institute preventive and control measures.

Methods:

To determine if there was a problem, we compared SICU MDRSM rates in the epidemic period (Aug-October 2004) versus the pre-epidemic period (Jan-July 2004). In addition, we conducted a retrospective case-control study. A case was defined as any adult SICU patient who acquired MDRSM infection during the epidemic period. Controls were randomly selected SICU patients matched to cases by time of admission but without MDRSM infection. We ascertained cases by review of medical and microbiology records. Also, we conducted epidemiologically-directed microbiology studies and evaluated the role, if any, played by SICU staffing levels. We calculated odds ratio (OR) and 95%

confidence interval (CI).

#### Results:

Infection rates in epidemic and pre-epidemic periods were 11.3 per 100 discharges versus 1.6 per 100 discharges, respectively ( $p < 0.00001$ ). Twelve patients met the case definition; 20 controls were identified. The median age of case-patients was 62 years; 6 (50%) were male. Infection sites included the respiratory tract (10), biliary tract (1), and wound (1). Case and controls were similar for surgeon, co-morbidities, biochemistry, and survival. In contrast, cases were significantly more likely to be older (median age: 62 vs. 45 years,  $p < 0.05$ ), to have had abdominal surgery (OR: 20.0, CI: 2.2-192), TPN (OR: 5.6, CI: 1.2-27), prolonged mechanical ventilation ( $p < 0.05$ ), raised white count ( $p < 0.01$ ), or to have been treated with a cephalosporin ( $p < 0.01$ ) or penicillin ( $p < 0.05$ ) during the previous month. On multivariate analysis, abdominal surgery and high white count were the two independent risk factors. There was no correlation between monthly rate of infection and the nursing-hours/patient-day ratio. Cultures of bronchoscopes were negative for bacterial and fungal growth.

#### Conclusions:

Older SICU patients who were severely ill and had undergone abdominal surgery were at particular risk of acquiring MDRSM infection. Bronchoscopy was not a risk factor as was previously thought by SICU personnel. The mode of transmission was likely mediated by one or more SICU healthcare workers at the time of surgery. Interventions included review of infection control practices and procedures used in the management of patients who had undergone abdominal procedures; review of SICU hand care protocols; use of false fingernails; and enhancement of handwashing.

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### Risk Factors for Invasive Infection Due to Cephalosporin Resistant Enterobacter

**Vera P. Luther, MD**, Zachary E. Smith, PAC, Victor Varela, John C. Williamson, PharmD, Tobi B. Karchmer, MD, Elizabeth Palavecino, MD, Christopher A. Ohl, MD. Wake Forest University School of Medicine, Winston Salem, NC, USA.

#### Background:

Enterobacter spp. are common health-care associated pathogens and increasingly associated with multi-drug resistance (MDR). Previous studies showed that intensive care unit (ICU) care, invasive procedures, and prior use of selected antimicrobials, particularly 3rd generation cephalosporins, were risk factors for infection by antibiotic-resistant Enterobacter.

#### Objective:

To better understand the characteristics of and risk factors for health-care associated infection due to cephalosporin-resistant and MDR-Enterobacter.

#### Methods:

Setting: 850 bed tertiary care medical center. Study design: Retrospective case control study. From Oct. 2000 to Jun. 2003 sequential non-duplicate isolates of Enterobacter spp. from sterile body fluid or catheter tip culture were obtained from the clinical laboratory that had ceftazidime (CAZ) MICs  $\geq 2$  by micro-broth dilution (MBD). Isolates were retested by MBD to selected antimicrobials from each antimicrobial class. Pulse-field gel electrophoresis (PFGE) was performed. Clinical data was obtained from patient

medical records. Controls were selected from the entire hospital population, matched by age and length of hospitalization at the time of culture positivity. Collected data included patient and culture demographics, invasive devices, surgical procedures, immunosuppression, Apache II score, comorbid illnesses, site of care, and previous exposure to antibiotics measured by days of antibiotic therapy. Antibiotics were defined as narrow (NS) or broad spectrum (BS) based on activity against gram-positive, gram-negative, or anaerobic bacteria (BS having activity against  $\geq 2$  organism groups). Data was analyzed using logistic linear regression.

**Results:**

45 culture isolates were collected: catheter tip (42%), blood (36%), CSF (4%), other body fluid (13%), bone (4%). 70% of the isolates were resistant to  $\geq 4$  classes of tested antibiotics. 44% were resistant to ciprofloxacin and none to carbapenems. Risk factors for acquisition of Enterobacter with reduced susceptibility to CAZ are shown in the table. PFGE demonstrated the majority of isolates to be polyclonal.

**Conclusions:**

Enterobacter sp. with reduced susceptibility to CAZ is frequently MDR. Risk factors for infection or colonization include invasive procedures, ICU care and duration of antibiotic therapy. Perhaps due to a high proportion of resistance, prior fluoroquinolone use was not protective.

	Univariate (OR, 95%CI, p)	Multivariate (OR, 95%CI, p)
Indwelling Foley catheter	5.7 (2.0-16.1, 0.001)	9.5 (1.6-57.3, 0.01)
Endotracheal intubation/ventilation	3.7 (1.5-8.9, 0.004)	6.1 (1.1-35.3, 0.04)
Central Venous Catheter	8.9 (3.3-24.5, <0.0001)	7.7 (1.8-33.0, 0.006)
Surgical Procedure	2.7 (1.1-6.6, 0.03)	Not significant
ICU Site of Care	5.7 (2.1-15.4, 0.0006)	Not significant
Total ABX Days	2.8 (1.7-4.7, 0.0002)	3.1 (1.25-7.6, 0.01)
BS ABX Days	2.0 (1.3-3.0, 0.002)	Not significant
NS ABX Days	1.8 (1.3-2.6, 0.0005)	Not significant
Fluoroquinolone ABX Days	2.0 (1.2 - 3.3, 0.005)	Not significant