MAJOR ARTICLE

Risk Factors for Imipenem-Resistant *Pseudomonas aeruginosa* among Hospitalized Patients

Anthony D. Harris,[1,3] David Smith,[1] Judith A. Johnson,[2,3] Douglas D. Bradham,[1,3] and Mary-Claire Roghmann[1,3]

Departments of [1]Epidemiology and Preventive Medicine and [2]Pathology, University of Maryland, and [3]Veterans Affairs Maryland Health Care System, Baltimore, Maryland

Risk factors for the nosocomial recovery of imipenem-resistant *Pseudomonas aeruginosa* (IRPA) were determined. A case-control study design was used for the comparison of 2 groups of case patients with control patients. The first group of case patients had nosocomial isolation of IRPA, and the second group had imipenem-susceptible *P. aeruginosa* (ISPA). Control patients were selected from the same medical or surgical services from which case patients were receiving care when isolation of IRPA occurred. Risk factors analyzed included antimicrobials used, comorbid conditions, and demographic variables. IRPA was recovered from 120 patients, and ISPA from 662 patients. Imipenem (odds ratio [OR], 4.96), piperacillin-tazobactam (OR, 2.39), vancomycin (OR, 1.80), and aminoglycosides (OR, 2.19) were associated with isolation of IRPA. Vancomycin (OR, 1.64), ampicillin-sulbactam (OR, 2.00), and second-generation cephalosporins (OR, 2.00) were associated with isolation of ISPA. Antibiotics associated with ISPA are different from antibiotics associated with IRPA. The OR for imipenem as a risk factor for IRPA is less than that reported from studies in which control group selection was suboptimal.

Pseudomonas aeruginosa, a leading cause of nosocomial infections, was ranked fifth among all pathogens reported to the National Nosocomial Infection Surveillance (NNIS) System from January 1990 through March 1996 [1]. Infections due to this virulent organism are often difficult to treat because of the relatively limited choice of effective antimicrobial agents. The incidence of imipenem-resistant *P. aeruginosa* (IRPA) is increasing. The NNIS System reported a 32% increase in isolation of IRPA among nosocomially infected patients in intensive care units, in a comparison of related data from 1999 with NNIS System data from 1994–1998 [2].

The aim of this study was to identify risk factors for the nosocomial isolation of IRPA from clinical specimens. Potential risk factors of particular interest were previous antimicrobial drug exposures. The rationale for the study was that previous studies with the same aim had involved smaller numbers of case patients, thereby limiting the power to detect differences. Of more importance, the present study's refined control group selection is an improvement in epidemiologic methodology.

Received 5 June 2001; revised 23 August 2001; electronically published 26 December 2001.

Financial support: Unrestricted grants from Merck, Wyeth-Ayerst, and Bayer. The companies had no involvement in the study design, data analysis, or writing or editing of the manuscript.

Reprints or correspondence: Dr. Anthony Harris, Div. of Healthcare Outcomes Research, Dept. of Epidemiology and Preventive Medicine, University of Maryland School of Medicine–VA Maryland Health Care System, 10 N. Greene St. BT111, Baltimore, MD 21201 (aharris@epi.umaryland.edu); or Dr. Mary-Claire Roghmann, same address (mroghmann@epi.umaryland.edu).

Clinical Infectious Diseases 2002; 34:340–5

1058-4838/2002/3403-0007$03.00

METHODS

Case definition, control definition and study design. A case-case-control study design was used [3]. Two retrospective case-control studies were concurrently performed at the University of Maryland Medical System. The 609-bed acute-care hospital includes the R. Adams Cowley Shock Trauma Center and the Gree-

nebaum Cancer Center. The first group of case patients included patients who had nosocomial isolation of IRPA in clinical cultures. The second group included patients who had nosocomial isolation of imipenem-susceptible *P. aeruginosa* (ISPA) in clinical cultures.

The microbiology laboratory database was electronically searched to identify all *P. aeruginosa*–positive clinical cultures of samples obtained from patients admitted to the hospital from 1 January 1998 to 1 July 2000. Patients who had *P. aeruginosa* isolates recovered within 48 h of admission were excluded from the study, as were those who had isolates recovered from surveillance cultures. Patients in control group 1 were selected from among patients receiving care from the same medical or surgical services from which case patients were receiving care on the date that IRPA was isolated. Patients in control group 1 did not have IRPA isolated during their hospital stay. Selection of patients for control group 2 was identical to that for patients in control group 1, with the exception that patients with ISPA were also excluded from the study so that case patients would not be included in the control group. For each case patient with IRPA who was selected, 6 control patients were randomly chosen. The control patients were admitted to the hospital during the same 2.5-year period. Patients who were admitted for <48 h were excluded from the control groups.

The rationale for using a case-case-control study design was the advantage offered by the comparison of 2 multivariable models: risk factors for isolation of IRPA and risk factors for isolation of ISPA. The first model identifies risk factors for IRPA among nosocomially infected patients, compared with those receiving care from the same medical or surgical services, and the second model identifies risk factors for ISPA. The advantages of this design, compared with that of previous studies in which patients with IRPA were directly compared with control patients with ISPA, have been outlined elsewhere [3–5]. The study was approved by the institutional review board at the University of Maryland.

Risk factors that were investigated. Data were collected, by use of a relational database management system, from administrative, pharmacy, and laboratory computerized databases. The relational database is maintained by the Information Technology Group of the University of Maryland. Data in the pharmacy, microbiology, and medical demographics tables found in the relational database were validated against the data in the medical records of >400 patients admitted from October 1997 through January 2001. In addition, data for a 10% sample of the case patients and a 5% sample of the control patients included in this study were validated by examination of medical charts. The positive and negative predictive values of the data were >99%.

Variables analyzed as possible risk factors included age, sex, underlying diseases or comorbid conditions, Charlson score (the latter 2 variables were determined on the basis of the coding of the *International Classification of Diseases, Ninth Revision*) [6], intensive care unit (ICU) stay before nosocomial isolation of *P. aeruginosa* in culture (hereafter known as the "outcome of interest"), surgery before the outcome of interest, transfer from another hospital, number of hospital admissions during the previous year, length of hospital stay before the outcome of interest (for case patients, length of stay before isolation of *P. aeruginosa;* for controls, complete length of hospital stay), and treatment with antimicrobial drugs (analyzed individually and in combination; tables 1 and 2). With regard to antimicrobial data, only antimicrobial drugs administered within the hospital were analyzed. For case patients, antimicrobial drug treatment was included in the analysis only when such drugs were given during the 14 days before isolation of *P. aeruginosa* (for case group 1, within 14 days of isolation of IRPA; for case group 2, within 14 days of isolation of ISPA). For control patients, antimicrobial drug treatment administered during the 14 days before discharge from the hospital was included in the analysis.

The rationale behind the choice of a 14-day analysis period was to avoid analyzing data on antibiotics that patients received during the initial phase of a lengthy hospitalization. For example, if a patient was hospitalized for 40 days before nosocomial isolation of the resistant organism, we believed that antibiotics received early during hospitalization were unlikely to be related to isolation of resistant *P. aeruginosa.* However, because the 14-day period was chosen arbitrarily, statistical analysis was repeated with the use of data on antibiotics that were received during the *entire* time that the patient was at risk before the event (i.e., there was no 14-day limit to the period analyzed). Because the results obtained from analysis of the entire period of hospitalization were similar to results from the 14-day analysis period, only the data for the 14-day period are presented in the "Results" section.

Statistical analysis. All statistical analyses were performed using SAS software, version 7 (SAS Institute). Bivariate analyses were performed separately for each of the variables. ORs and 95% CIs were calculated for binomial variables. *P* values were calculated by use of Fisher's exact test, for binomial variables; by the χ^2 test, for categorical variables with > 2 subgroups; and by the Student's *t* test or the Wilcoxon rank-sum test, for continuous variables.

Variables for which the *P* value was <.1 in bivariate analysis were included in a logistic regression model for multivariable analysis. A forward selection process was used. Risk factors were checked for confounding and collinearity. Confounders were included in the multivariable models if inclusion of the covariate changed the coefficient of any statistically significant variable in the logistic regression model by ⩾10%. All tests were

Table 1. Bivariate risk factors for the isolation of imipenem-resistant *Pseudomonas aeruginosa*.

Risk factor	Control patients (n = 770)	Case patients (n = 120)	P value	OR (95% CI)
Demographic				
Age, mean years	49.3	50.7	.44	1.00 (0.99–1.02)
Male sex	302 (39.2)	47 (39.2)	.99	1.00 (0.68–1.49)
Comorbidity				
AIDS	18 (2.3)	5 (4.2)	.24	1.82 (0.66–4.99)
Cardiac disease	93 (12.1)	19 (15.8)	.25	1.37 (0.80–2.34)
Diabetes[a]	137 (17.8)	35 (29.2)	<.01	1.90 (1.23–2.94)
Malignancy	103 (13.4)	11 (9.2)	.20	0.65 (0.34–1.26)
Cerebrovascular injury	50 (6.5)	10 (8.3)	.45	1.31 (0.64–2.66)
Hepatic disease	13 (1.7)	4 (3.3)	.22	2.01 (0.64–6.26)
Renal disease	13 (1.7)	4 (3.3)	.22	2.00 (0.64–6.26)
Charlson comorbidity scale, mean	1.28	1.53	.19	1.06 (0.97–1.17)
Related to hospitalization				
Time at risk, days[a]	10.9	25.9	<.001	1.05 (1.04–1.06)
Intensive care unit stay[a]	312 (40.5)	102 (85)	<.001	8.32 (4.94–14.01)
Surgery	77 (10)	13 (10.8)	.77	1.09 (0.59–2.04)
Admissions during past year,[a] no.	0.58	1.13	.0004	1.21 (1.09–1.34)
Transfer[a]	107 (13.9)	33 (27.5)	.0001	2.35 (1.50–3.69)
Antibiotic				
Imipenem[a]	43 (5.6)	51 (42.5)	<.0001	12.50 (7.77–20.09)
Piperacillin-tazobactam[a]	91 (11.8)	40 (33.3)	<.0001	3.73 (2.41–5.78)
Ampicillin-sulbactam	59 (7.7)	12 (10)	.38	1.34 (0.70–2.57)
Vancomycin[a]	107 (13.9)	52 (43.3)	<.0001	4.74 (3.13–7.17)
Cephalosporin				
First generation[a]	224 (29.1)	16 (13.3)	.0003	0.38 (0.22–0.65)
Second generation	44 (5.7)	8 (6.7)	.68	1.18 (0.54–2.57)
Third generation[a]	81 (10.5)	25 (20.8)	.0012	2.24 (1.36–3.68)
Macrolide	28 (3.6)	6 (5)	.47	1.39 (0.57–3.44)
Aminoglycoside[a]	129 (16.8)	54 (45)	<.0001	4.07 (2.71–6.10)
Quinolone[a]	160 (20.8)	47 (39.2)	<.0001	2.45 (1.64–3.68)

NOTE. Data are no. (%) of patients, unless otherwise indicated.

[a] Risk factor for which $P < .05$.

2-tailed, and a P value of $< .05$ was considered significant in the multivariable model.

RESULTS

During the 2.5-year study, 120 patients with IRPA (case group 1) and 662 patients with ISPA (case group 2) were identified. A total of 770 control patients were included in control group 1. Of these control patients, 24 had ISPA isolated during hospitalization and therefore were not included in control group 2 (n = 746).

IRPA was most frequently recovered from respiratory secretions (50%). Recovery of IRPA from clinical culture of urine samples (15%), wound specimens (11%), and blood samples (7%) also occurred. ISPA was also most frequently recovered from respiratory secretions (37%), followed by urine samples (32%), wound specimens (12%), and blood samples (5%). The medical or surgical services from which patients with IRPA and ISPA were receiving care on the date that a positive culture result was obtained included medicine (22% and 13%, respectively), trauma (42% and 38%, respectively), and transplantation (16% and 11%, respectively) services as well as the cancer center (6% and 3%, respectively).

Results of bivariate analysis of risk factors for IRPA are outlined in table 1, whereas those for ISPA are outlined in table 2. The results of multivariable analyses of risk factors for IRPA

Table 2. Bivariate risk factors for the isolation of imipenem-susceptible *Pseudomonas aeruginosa*.

Risk factor	Control patients (n = 746)	Case patients (n = 662)	P value	OR (95% CI)
Demographic				
Age, mean years	49.4	55.7	<.0001	1.02 (1.01–1.03)
Male sex	292 (39.1)	259 (39.1)	.99	1.00 (0.81–1.24)
Comorbidity				
AIDS	18 (2.4)	13 (2.0)	.57	.81 (0.39–1.67)
Cardiac disease	90 (12.1)	102 (15.4)	.07	1.33 (0.98–1.80)
Diabetes[a]	134 (18.0)	136 (20.5)	.22	1.18 (0.91–1.54)
Malignancy	101 (13.5)	64 (9.7)	.024	.68 (0.49–0.95)
Cerebrovascular injury	44 (5.9)	101 (15.3)	<.0001	2.87 (1.98–4.16)
Hepatic disease	11 (1.5)	15 (2.3)	.27	1.55 (0.71–3.40)
Renal disease	13 (1.7)	13 (2.0)	.76	1.13 (0.52–2.45)
Charlson comorbidity scale, mean	1.29	1.39	.32	1.03 (0.97–1.09)
Related to hospitalization				
Time at risk, days[a]	10.2	13.2	<.0001	1.02 (1.01–1.03)
Intensive care unit[a]	289 (38.7)	485 (73.3)	<.0001	4.33 (3.45–5.43)
Surgery	77 (10.3)	139 (21)	<.0001	2.31 (1.71–3.12)
Admissions during past year,[a] no.	0.60	0.61	.79	1.01 (0.93–1.10)
Transfer[a]	103 (13.8)	117 (17.7)	.046	1.34 (1.01–1.79)
Antibiotic				
Imipenem[a]	38 (5.1)	20 (3)	.0508	.58 (.33–1.00)
Piperacillin-tazobactam[a]	89 (11.9)	120 (18.1)	.0011	1.63 (1.21–2.20)
Ampicillin-sulbactam	58 (7.8)	108 (16.3)	<.0001	2.31 (1.65–3.24)
Vancomycin[a]	95 (12.7)	136 (20.5)	<.0001	1.77 (1.33–2.36)
Cephalosporin				
First generation[a]	220 (29.5)	209 (31.6)	.40	1.10 (0.88–1.38)
Second generation	43 (5.8)	77 (11.6)	<.0001	2.15 (1.46–3.17)
Third generation[a]	78 (10.5)	94 (14.2)	.032	1.42 (1.03–1.95)
Macrolide	26 (3.5)	31 (4.7)	.26	1.36 (0.80–2.32)
Aminoglycoside[a]	123 (16.5)	115 (17.4)	.66	1.07 (0.81–1.41)
Quinolone[a]	148 (19.8)	106 (16)	.062	.77 (0.59–1.01)

NOTE. Data are no. (%) of patients, unless otherwise indicated.

[a] Risk factor for which $P < .05$.

are delineated in table 3, and those for ISPA are delineated in table 4.

Multivariable logistic regression analysis demonstrated that patients with nosocomial isolation of IRPA were more likely to have been exposed to the following antibiotics during the 14 days before the date that a positive culture result was obtained: imipenem (OR, 4.96; 95% CI, 2.88–8.57), piperacillin-tazobactam (OR, 2.39; 95% CI, 1.42–4.03), vancomycin (OR, 1.80; 95% CI, 1.09–2.96), and aminoglycosides (OR, 2.19; 95% CI, 1.35–3.56). The "time at risk," which was defined as the length of time from the date of hospital admission to the date that case patients received a positive culture result, was a significant risk factor (OR, 1.02; 95% CI, 1.01–1.04); for each extra day of hospitalization, the risk of isolation of IRPA increased by 2%. A previous stay in the ICU before the event of interest occurred (for case patients, a positive culture result; for controls, discharge from the hospital) was also a risk factor (OR, 3.26; 95% CI, 1.82–5.87).

Table 3 shows that patients with nosocomial isolation of ISPA were more likely to have been exposed to the following antibiotics during the 14 days before the date that a positive culture result was obtained: vancomycin (OR, 1.64; 95% CI, 1.20–2.26), ampicillin-sulbactam (OR, 2.00; 95% CI, 1.38–2.89), and second-generation cephalosporins (OR, 2.00; 95% CI, 1.30–3.06). Again, a previous stay in the ICU before the event of interest occurred was found to be a risk factor (OR, 3.53; 95% CI,

Table 3. Multivariable analysis of risk factors for imipenem-resistant *Pseudomonas aeruginosa*.

Risk factor	Estimate[a]	SE[b]	*P* value	OR (95% CI)
Imipenem	1.60	0.28	<.0001	4.96 (2.88–8.57)
Vancomycin	0.59	0.25	.02	1.80 (1.09–2.96)
Piperacillin-tazobactam	0.87	0.27	.0011	2.39 (1.42–4.03)
Aminoglycoside	0.78	0.25	.0015	2.19 (1.35–3.56)
Time at risk	0.02	0.007	.0006	1.02 (1.01–1.04)
Intensive care unit	1.18	0.30	<.0001	3.26 (1.82–5.87)

[a] Intercept, −3.91.
[b] Intercept, 0.27.

2.80–4.48). Age was also identified as a risk factor (OR, 1.02; 95% CI, 1.01–2.26).

DISCUSSION

In this study, we assessed the risk factors for IRPA and for ISPA. Our study differs from previous analyses of risk factors for IRPA in that (1) a larger number of cases led to increased power and, thus, the ability to identify additional risk factors with lower frequencies of exposures, and (2) the control group selection process was more refined. As outlined in previous studies, we believe that a refined control group selection process and the control of important confounding variables leads to greater validity of the risk factors identified [3–5].

We found that imipenem, piperacillin-tazobactam, vancomycin, and aminoglycosides were the antibiotics associated with isolation of IRPA. Vancomycin, ampicillin-sulbactam, and second-generation cephalosporins were associated with isolation of ISPA.

Imipenem has been identified as a risk factor for IRPA in previous studies [7, 8]. In these studies, patients with ISPA were included in the control group. Troillet et al. [7] identified imipenem as the only antibiotic that was a risk factor for IRPA (adjusted OR, 23.2; 95% CI, 4.1–132.7). The lower OR of imipenem noted in our study (OR, 4.96; 95% CI, 2.88–8.57) is likely to be more representative of the true OR, because our study design allowed for optimal selection of control patients [3–5].

The association between aminoglycosides, piperacillin-tazobactam, vancomycin, and IRPA has not been identified previously. Although logistic regression analyses do adjust for all other explanatory variables in the model, they do not necessarily identify causal associations; thus, these antibiotics may be statistically significant as a result of the fact that patients who develop resistant *Pseudomonas* strains receive a number of different antibiotics—often simultaneously—before a positive result for *P. aeruginosa* is obtained by clinical culture. Hence, these results will need to be validated by other studies. However, piperacillin-tazobactam may be a true causal risk factor, in that treatment with other β-lactam drugs has been thought to predispose for imipenem resistance by selecting for strains with stably depressed β-lactamase production; these selected strains could then be more likely to lose their porin OprD2 [9, 10].

The identification of vancomycin as a risk factor for both IRPA and ISPA is surprising. Again, it may be just a marker of associated antibiotic use. However, it may be a true causal risk factor. We hypothesize that vancomycin may help select for *Pseudomonas* species by destroying competing gram-positive bacteria that are part of the enteric or bronchial flora. This hypothesis is in keeping with the literature that identified antianaerobic agents as strong risk factors for vancomycin-resistant enterococci [11].

The identification of ICU stay and length of hospitalization as strong risk factors is not unexpected. They have been identified as risk factors in previous studies of antibiotic-resistant organisms [12–16].

A limitation of the present study is that we do not know the molecular mechanisms by which resistance was conferred in our study isolates. In addition, because the control patients were not screened by active surveillance culture for the presence of *P. aeruginosa,* it is possible that some of these patients actually might have been case patients. However, this type of misclassification would make the groups of case patients and control

Table 4. Multivariable analysis of risk factors for imipenem-susceptible *Pseudomonas aeruginosa*.

Risk factor	Estimate[a]	SE[b]	*P* value	OR (95% CI)
Imipenem	−1.00	0.31	.0010	.37 (0.20–0.67)
Vancomycin	0.50	0.16	.0022	1.64 (1.20–2.26)
Ampicillin-sulbactam	0.69	0.19	.0002	2.00 (1.38–2.89)
Cephalosporin[c]	0.69	0.22	.0015	2.00 (1.30–3.06)
Age	0.01	0.003	<.0001	1.02 (1.01–1.02)
Intensive care unit	1.26	0.12	<.0001	3.53 (2.80–4.48)

[a] Intercept, −1.86.
[b] Intercept, 0.19.
[c] Second generation.

patients more similar by including case patients in the control groups, and it would only serve to underestimate the associations noted in this study. Another limitation of the present study is that we were unable to assess the role of patient-to-patient transmission. However, not accounting for patient-to-patient transmission would likely bias toward the null hypothesis—that is, among patients who acquire the organism from other patients, the importance of antibiotics as causal components may be diminished. In addition, it has been shown that cross-infection with *P. aeruginosa* is a rare event [17].

In conclusion, this study is similar to other studies in its implication of imipenem as a risk factor for IRPA. However, in contrast to other studies, this study also identifies other antibiotics as risk factors for IRPA, which suggests that limiting the use of imipenem alone may not be sufficient to contain the increasing incidence of IRPA.

Acknowledgment

We thank Colleen Reilly for database maintenance and data extraction.

References

1. Centers for Disease Control and Prevention. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986–April 1996, issued May 1996. Am J Infect Control **1996**; 24:380–8.
2. National Nosocomial Infection Surveillance System. Selected antimicrobial resistant pathogens associated with nosocomial infections in ICU patients, comparison of resistance rates from January–December 1999 with 1994–1998, NNIS System [figure]. Available at: http://www.cdc.gov/ncidod/hip/NNIS/ar_surv99.pdf. Accessed 15 December 2001.
3. Kaye KS, Harris AD, Gold H, Carmeli Y. Risk factors for recovery of ampicillin-sulbactam–resistant *Escherichia coli* in hospitalized patients. Antimicrob Agents Chemother **2000**; 44:1004–9.
4. Harris AD, Karchmer TB, Carmeli Y, Samore MH. Methodological principles of case-control studies that analyzed risk factors for antibiotic resistance: a systematic review. Clin Infect Dis **2001**; 32:1055–61.
5. Harris AD, Samore MH, Carmeli Y. Control group selection is an important but neglected issue in studies of antibiotic resistance [letter]. Ann Intern Med **2000**; 133:159.
6. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol **1992**; 45:613–9.
7. Troillet N, Samore MH, Carmeli Y. Imipenem-resistant *Pseudomonas aeruginosa:* risk factors and antibiotic susceptibility patterns. Clin Infect Dis **1997**; 25:1094–8.
8. Krcmery V Jr, Trupl J, Kunova A, et al. Imipenem-resistant *Ps. aeruginosa* bacteraemia in cancer patients: risk factors, clinical features and outcome. Bratisl Lek Listy **1996**; 97:647–51.
9. Satake S, Yoneyama H, Nakae T. Role of OmpD2 and chromosomal beta-lactamase in carbapenem resistance in clinical isolates of *Pseudomonas aeruginosa.* J Antimicrob Chemother **1991**; 28:199–207.
10. Neu HC. Resistance of *Pseudomonas aeruginosa* to imipenem. Infect Control Hosp Epidemiol **1992**; 13:7–9.
11. Donskey CJ, Chowdhry TK, Hecker MT, et al. Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients. N Engl J Med **2000**; 343:1925–32.
12. Gaynes RP, Culver DH. Resistance to imipenem among selected gram-negative bacilli in the United States. Infect Control Hosp Epidemiol **1992**; 13:10–14.
13. Morrison AJ Jr, Wenzel RP. Epidemiology of infections due to *Pseudomonas aeruginosa.* Rev Infect Dis **1984**; 6(Suppl 3):S627–42.
14. Harris AD, Castro J, Sheppard DC, Carmeli Y, et al. Risk factors for nosocomial candiduria due to *Candida glabrata* and *Candida albicans.* Clin Infect Dis **1999**; 29:926–8.
15. Lucas GM, Lechtzin N, Puryear DW, et al. Vancomycin-resistant and vancomycin-susceptible enterococcal bacteremia: comparison of clinical features and outcomes. Clin Infect Dis **1998**; 26:1127–33.
16. Ostrowsky BE, Venkataraman L, D'Agata EM, Gold HS, De Girolami PC, Samore MH. Vancomycin-resistant enterococci in intensive care units: high frequency of stool carriage during a non-outbreak period. Arch Intern Med **1999**; 159:1467–72.
17. Olson B, Weinstein RA, Nathan C, Chamberlin W, Kabins SA. Epidemiology of endemic *Pseudomonas aeruginosa:* why infection control efforts have failed. J Infect Dis **1984**; 150:808–16.