
Outcomes of *Acinetobacter baumannii* Infection in Critically Ill Burned Patients

Vincent Trottier, MD,* Penelope Gonzalez Segura, MD,†
Nicholas Namias, MD, FACS, FCCM,* David King, MD,* Louis R. Pizano, MD,*
Carl I. Schulman, MD, MSPH*

The objective of this study was to determine the incidence of drug resistance among isolates of *Acinetobacter baumannii* from our Burn Intensive Care Unit (BICU), the rate of clinical cure, and the mortality rate. We undertook a retrospective review of all cases of infection from the BICU between January 2004 and November 2005. The group consisted of 24 men (80%) and 6 women with a mean age of 43 years (range, 17–76 years, ± 14.5 years). Mean TBSA burned was 43% (range, 9–75%, $\pm 19\%$). Mean BICU length of stay was 49 days (range, 5–118 days, ± 30 days). Patients developed their first infection after a mean of 16 days (5–73 days, ± 14 days). The initial site of infection was bronchoalveolar lavage in 21 (70%), blood in 6 (20%), central venous catheter tip in 2 (7%), and urine in 1 (3%). The isolates displayed resistance to imipenem in 87% of cases. No organism displayed resistance to colistin (polymixin E). Patients were treated with colistin in 20 cases (67%), with amikacin in 8 cases (27%), and with imipenem in 2 cases (7%). A total of 10 patients (33%) died, 1 from gastrointestinal bleeding and 9 from active infection, giving an infection related mortality of 30%. In 21 cases (70%), a cure was achieved with a mean duration of treatment of 16 days (range, 4–30 days, ± 7 days). The majority of *A. baumannii* isolates were multi-drug resistant; however, no isolate displayed resistance to colistin. Cure rate was 70% and infection-related mortality reached 30%. More investigation is warranted to improve prevention and to assess new therapeutic agents. (J Burn Care Res 2007;28:248–254)

Infection in the critically ill burned patient remains one of the most important contributors to morbidity and mortality. Despite advances in prevention, prophylaxis, and seemingly adequate therapeutic regi-

mens, serious life-threatening infections still plague the seriously burned patient during the critical phases of recovery.^{1–5} The most frequently encountered infections, including ventilator-associated pneumonia (VAP), catheter-related bloodstream infection, urinary tract infection, and wound infections, are generally caused by known nosocomial pathogens, with predictable drug sensitivities.² However, time has shown that the microbial environment of a critical care unit is a dynamic and complex system, and the most frequent pathogens are likely to change over time, as well as their respective drug sensitivities.⁶ *Acinetobacter baumannii* has emerged as a new threat to the burn patient population. Serious infections from this previously benign organism are reported with increasing frequency, and national infection surveillance programs now recognize it as a major component of nosocomial pathogens.^{6–11} Of additional concern is the changing drug sensitivities, which now display increasing drug resistance to conventional therapeutic agents. After encountering multiple cases of resistant *Acinetobacter* infection in the burn inten-

From the *Division of Burns, Trauma and Surgical Critical Care, University of Miami, Leonard Miller School of Medicine, Jackson Memorial Hospital, Ryder Trauma Center, Miami, Florida; and †Instituto Tecnológico de Santo Domingo, Santo Domingo, Dominican Republic.

Address correspondence to Vincent Trottier, MD, FRCSC, Fellow, Burns, Trauma and Surgical Critical Care, University of Miami, Leonard Miller School of Medicine, Jackson Memorial Hospital, Ryder Trauma Center, Division of Burns, Trauma and Surgical Critical Care, 1800 NW 10th Avenue, Suite T-215, Miami, Florida 33136.

Reprints: Nicholas Namias, MD, FACS, FCCM, Associate Professor of Surgery and Anesthesiology, C. Gillon Ward Endowed Chair in Burn Surgery, Chief, Division of Burns, DeWitt Daughtry Family Department of Surgery, Divisions of Burns and Trauma/Surgical Critical Care, Leonard Miller School of Medicine, Post Office Box 016960 (D-40), Miami, Florida 33101.

Copyright © 2007 by the American Burn Association.
1559-047X/2007

DOI: 10.1097/BCR.0B013E318031A20F

sive care unit (BICU) of our institution, we decided to review our experience dealing with this organism. The purpose of this study was to determine the incidence of multidrug resistance (MDR) among *A. baumannii* isolates from our institution, the cure rate of *A. baumannii* infection in critically ill burned patients, and the mortality associated with it. We defined *A. baumannii* as being MDR when displaying resistance to imipenem and one or more other drugs to which the organism is historically known to be sensitive. We also attempted to define the efficacy of the specific drug regimens used.

MATERIALS AND METHODS

We performed a retrospective review of all cases of *A. baumannii* infection from the BICU of our institution between January 2004 and November 2005. All documented infections during the study period were reviewed. Microbiological reports, electronic notes from the BICU attending, as well as laboratory data were reviewed.

For each patient, the primary site of infection was defined as the first positive culture for *A. baumannii*. The time between BICU admission and the first positive culture and the time between culture acquisition and initiation of adequate treatment was determined. Because this study was retrospective, we could not define strict clinical criteria that could be followed by the treating physician to determine clinical cure and end of treatment. In this context, we concluded that when an attending note documented that culture-directed treatment against *A. baumannii* was to be stopped, the patient had sufficient clinical and/or microbiological evidence that cure was achieved. The duration of treatment was recorded as well as the specific agent chosen and the route of administration. All-cause in-ICU and in-hospital mortality were recorded. We defined recurrent infection as a new positive culture at the initial site after a successful full course of culture-directed antibiotic treatment. Analysis was performed using descriptive statistics including means and standard deviations. Comparisons for individual variables were performed using z-test for proportions (Primer of Biostatistics, version 4.0, copyright 1996, McGraw Hill, New York, NY) and correlative analysis where appropriate. Univariate and multivariate analysis (logistic regression) was performed in an attempt to determine individual predictors of the outcome measures while controlling for potential confounders (NCSS 2004/PASS 2005, Kaysville, UT). A *P* value < .05 was considered significant.

RESULTS

We identified 35 patients that had a positive culture with *A. baumannii* in the BICU during the study period. Of these, we excluded 5 patients that harbored the organism on a single culture from the tip of a removed central venous catheter, and no treatment was deemed necessary in all cases. Two of those 5 patients died during the study period from noninfectious causes (1 cardiac failure, 1 multiple organ failure [MOF] without sepsis). The remaining 30 patients were included for analysis. The group consisted of 24 men (80%), with a mean age of 43 years (range, 17–76 years, ± 14.5 years). The mean TBSA burned was 43% (range, 9–75%, $\pm 19\%$). The mean BICU length of stay (LOS) was 49 days (range, 5–118 days, ± 30 days) and mean hospital LOS was 63 days (6–140 days, ± 37 days). The patients developed their first infection with *A. baumannii* after a mean of 16 days (range, 5–73 days, ± 14 days) in the BICU.

The initial site of infection was from bronchoalveolar lavage (BAL) in 21 patients (70%), from blood in 6 patients (20%), from central venous catheter tip in 2 patients (7%), and from urine in 1 patient (3%). A BAL was considered positive with greater than 10^4 colony-forming units (CFU)/ml, a blood culture when any growth was reported, a central venous catheter tip infection when greater than 15 CFU were present, and a urinary tract infection when greater than 10^5 CFU/ml of the organism was observed. The initial positive culture was polymicrobial in 17 cases of the 21 BAL (81%), with gram-positive organisms in 9 cases (6 oxacillin-sensitive *Staphylococcus aureus*, 2 methicillin-resistant *Staphylococcus aureus* and 1 *Streptococcus pneumoniae*), and gram-negative organisms in 8 cases (3 *Pseudomonas aeruginosa*, 3 *Enterobacteriaceae*, 1 *Proteus mirabilis*, and 1 *Klebsiella pneumoniae*). Patients had a positive culture with *A. baumannii* at more than one site during their BICU stay in 20 cases (67%).

The isolates displayed resistance to minocycline in 37% of cases, to amikacin in 63% of cases, to tobramycin in 80% of cases, and to imipenem in 87% of cases. Defining MDR as resistance to imipenem and one or more other drug tested, we found an incidence of 87% of MDR among the isolates of *A. baumannii* recovered. No organism displayed resistance to colistin. Patients were treated with colistin in 20 cases (67%), receiving the intravenous form in 9 cases (45%) and the nebulized form in 11 cases (55%). The intravenous dose was 2 mg/kg every 12 hours, adjusted to 2 mg/kg every 24 hours for creatinine clearance of 10 to 50 ml/min and to 2 mg/kg every 36 hours for creatinine clearance of less than 10 ml/min. Patients being dialyzed received 1 mg/kg after dialysis.

Table 1. Comparison of survivors and nonsurvivors

		Survivors	Nonsurvivors	P Value
	N	20	10	
	%	67%	33%	
Infection-related deaths	N		9	
	%		30%	
Age, years	Mean	40	49	0.025
	Range	17–71	24–76	
	SD	14	15	
Male sex	%	85%	78%	NS
TBSA	Mean	41%	45%	NS
	Range	9–75	10–75	
	SD	19	20	
Time in unit before infection, days	Mean	19	9	NS
	Range	6–73	5–13	
	SD	16	3	
Time to initiation of treatment, days	Mean	2	2	NS
	Range	0–4	0–7	
	SD	1.6	2.2	
Primary site of infection				
BAL	%	56%	75%	NS
Blood		33%	15%	
Catheter tip		11%	5%	
Urine		0%	5%	
Resistance to imipenem	%	85%	89%	NS
Treatment				
Colistin	%	56%	65%	NS
Amikacin		33%	30%	
Imipenem		11%	5%	
Duration of treatment, days	Mean	16	12	NS
	Range	4–30	1–38	
	SD	7	13	
BICU LOS, days	Mean	57	33	NS
	Range	13–118	5–91	
	SD	28	29	

BAL, bronchoalveolar lavage; BICU, burn intensive care unit; LOS, length of stay; NS, not significant.

We did not perform routine monitoring of the drug level. In the nebulized colistin group, the dosage used was 75 mg nebulized every 12 hours. The most frequent adverse events related to colistin are renal failure for the intravenous form and bronchorrea for the nebulized form. These events were not uniformly measured and, with the small number of patients in this study, it is difficult to draw conclusions regarding adverse events with colistin use. In nine cases, a combination of drugs were used based on drug sensitivities. Each of these nine cases had colistin and a second antibiotic (either minocycline, doxycycline, or amika-

cin). The remaining patients received amikacin alone in 8 cases (27%) and imipenem alone in 2 cases (7%). In 21 cases (70%), clinical cure was achieved during their BICU stay, with a mean duration of treatment of 16 days (range, 4–30 days, ± 7 days). Only three cases developed recurrent infection after a successful initial course of treatment.

A total of 10 patients (33%) died during their BICU stay, 1 from gastrointestinal bleeding and 9 from active infection creating septic shock and MOF, for an infection-related mortality of 30%. In the patients infected with the imipenem-sensitive organism,

one died (25%) and, in the MDR group, we found nine deaths, one from the gastrointestinal bleeding and eight from sepsis and MOF (31%). We found no significant differences between survivors and nonsurvivors in TBSA, time in BICU before development of infection, site of initial infection, pattern of resistance (MDR or non-MDR), duration of treatment, or time between obtaining the culture and initiation of treatment. However, patients in the nonsurvivor group were significantly older (49 vs 40 years, respectively, $P = .025$; Table 1). Multivariate regression did not reveal any independent predictors of survival, likely as a result of the small sample size.

One of the nonsurvivors deserves particular mention. The patient was a 41-year-old man who developed progressive cardiac failure in a septic context, with synchronous arrhythmias but without evidence of myocardial ischemia. His workup included transoesophageal echocardiography on two occasions, use of pulmonary artery catheter, and conventional tools for coronary artery disease and myocardial ischemia evaluation (electrocardiogram, cardiac enzymes). They revealed decreased cardiac output, global hypokinesia, small pericardial effusion, and no evidence of ischemia. The patient eventually died, and autopsy revealed the presence of a 95% stenosis of the left anterior descending artery and purulent bacterial pericarditis caused by a gram-negative organism, most likely *A. baumannii* because the patient was growing the organism repeatedly in his cultures. Unfortunately, no culture was sent by the medical examiner at the time of autopsy.¹² This demonstrates the potential ability of this very resistant organism to migrate to atypical clinical sites of infection.

DISCUSSION

Acinetobacter strains are nonfermenting aerobic gram-negative coccobacillary organisms, usually demonstrating diploid formations or chains. They can be found in soil and water as free-living saprophytes and are occasionally found colonizing skin, aero-digestive mucosa, and the gastrointestinal tract.¹³ Twenty-one DNA homology groups have been described based on DNA-DNA relationships within the *Acinetobacter* genus.¹⁴ Different species of the genus are predominant in different environments, and *A. baumannii* is the species most frequently encountered in the hospital setting.

In the medical environment, the organism has been cultured from multiple sources in either surveillance programs or investigation of epidemic outbreaks. *A. baumannii* has been found on inanimate surfaces such as pillows, bed mattresses, curtains, door han-

dles, and computer keyboards, even after cleaning with antiseptic solutions.¹⁵⁻¹⁸ It seems that the organism also prefers warm and moist environments, and it has been found on respiratory equipment, humidifiers, and sinks.¹⁹ However, the capacity of *Acinetobacter* to survive on dry surfaces and to sustain desiccation has also been demonstrated.^{17,18} Health care workers in contact with infected patients also have been shown to harbor the organisms on their hands and play a potential role in epidemic outbreaks through contamination of the environment and other patients.¹⁶

Numerous studies have attempted to identify potential risk factors predisposing to the nosocomial acquisition of *A. baumannii*. Most were retrospective studies and used univariate analysis. The most frequently identified risk factors were malignancy,²⁰ APACHE II score,^{20,21} mechanical ventilation,^{20,22-25} prior use of antibiotics, and placement of intravascular catheters^{20,22-24} among others. By multivariate analysis, severity of illness, burns, mechanical ventilation, male sex, duration of ICU stay before infection, and use of third-generation cephalosporins were found to be independent risk factors for acquisition of *A. baumannii* infection.^{20,23,24} In the present study, we unfortunately did not obtain data from all patients admitted to the BICU that would have allowed us to identify risk factors for the acquisition of the infection.

In early in vitro studies, the vast majority of *Acinetobacter* isolates were sensitive to ampicillin, cephalosporins, and aminoglycosides.²⁶⁻²⁸ Clearly, however, the resistance patterns have changed with the increased prevalence of infection and antibiotic use. In 1995, Lyytikäinen et al¹⁵ described their experience during the course of 4 years (1989-1993) and found the resistance to imipenem increased from 1.5% to 7% and resistance to tobramycin increased from 5% to 12%.¹⁵ Others have reported imipenem resistance in the range of 11% to 24% from more recently published data (2003-2005).²⁰ In the report by Hanberger in 1999 analyzing microbiological data from 5 European countries, *Acinetobacter* species were found to have the highest increase in resistance to antibiotics of all the gram-negative bacilli studied.¹¹ The report from Paul and colleagues from Israel found an increase in resistance to imipenem from 10% to 34% between 1997 and 2002.⁹

In our series, *A. baumannii* isolates displayed a much higher incidence of resistance to imipenem (87%). The explanation may lie in the frequent use of imipenem or piperacillin as the empiric regimen used for suspected gram-negative coverage in our institution. Weinbren and colleagues suggested that the use

of carbapenems in their BICU could be responsible for an increase in drug resistance, as they observed a significant increase (four to eightfold) in the minimal inhibitory concentration of imipenem for their *Acinetobacter* isolates under a policy of using meropenem for suspected gram-negative infections.²⁹ In contrast, LeFloch et al³⁰ described using a systematic antibiotic regimen composed of imipenem and tobramycin for suspected gram-negative infections. They found the incidence of *Acinetobacter* and *Pseudomonas* had decreased, but incidence of *Enterobacter* and *Klebsiella* as well as resistance to ticarcillin had increased.

With increasing drug resistance, clinicians are faced with difficult decisions regarding therapeutic choices. Colistin has been reintroduced as a treatment option, and a few published reports have described its use in cases of *Acinetobacter* and *Pseudomonas* infections.³¹⁻³⁸ However, the use of colistin in a nebulized form has been published more scarcely.^{33,39} Interestingly, we did not encounter resistance to colistin in any of our isolates. We used a daily dose of 4 mg/kg of colistin intravenously divided in two doses for the patients with normal renal function. The recommended dose is 2 to 5 mg/kg daily, divided in two doses, depending on the severity of the infection. We did not monitor for the drug levels, and the dose was adjusted to renal clearance in case of renal failure. The nebulized form was reserved for patients with isolated VAP and no evidence of bloodstream infection. In the burn population, published experience with colistin and evaluation of the pharmacokinetics is still lacking. Future development of our own experience will have to include research on the kinetics of the drug in our burn population and tissue levels measurement in wounds, blood and alveoli.

Newer agents have been recently introduced, including tigecycline, a glycylcycline, which shows in vitro and in vivo activity against *A. baumannii*.⁴⁰ This agent is presently approved by the Food and Drug Administration for skin and skin-structures infections as well as complicated intra-abdominal infections. More research is required to address the efficacy of this new agent in cases of nosocomial *A. baumannii* infection in ICUs. Nevertheless, it appears to be a promising option at this time.

The infection related mortality in our group was 30%, and we found similar rates in the recent literature. Bang et al⁴¹ found a 30% mortality in their 1998 report. Sengupta et al⁴² found a 38% mortality rate in their unit in 2001. Wisplinghoff et al⁴³ found a 31% total mortality rate in their group in 1999, but the infection related mortality rate was lower (7%). This lower rate of mortality may be related to the fact that all isolates in the study by Wisplinghoff were suscep-

tible to imipenem, whereas most of our isolates were resistant to imipenem. However, our small number of patients prevents us from identifying a significant difference in outcome between patients infected with the resistant and the susceptible strains. Two recent reports looked at the morbidity related to *A. baumannii* infection. Wilson et al⁴⁴ found that patients in their burn unit who developed a *A. baumannii* infection had a significantly higher mean hospital cost of \$98,575 per patient when compared with matched controls. Wong et al⁴⁵ found *A. baumannii* infection to be an independent risk factor for increased length of stay in the BICU in their retrospective analysis published in 2002.

All our cases of infection with *A. baumannii* were nosocomial. This pathogen has become endemic to the trauma intensive care unit of our institution, which shares a geographically adjacent space with the burn ICU. In the last 3 years, this pathogen has become encountered more frequently in the BICU as well as in the surgical ICU, and the study was aimed at acquiring further knowledge of the infection. Preventive measures have been put in place by the infection control department of our institution consisting of contact precautions for known cases, isolation of cases, education of healthcare workers to preventive measures, distribution of personal-size hand disinfectant to workers, and monitoring of new cases. Environmental measures also have been applied with installation of plastic curtains that can be cleaned with bactericidal solutions. Despite these measures implemented before and throughout the study period, the number of new cases found monthly has not declined and only stayed stable. *A. baumannii* is now the most frequently cultured gram-negative pathogen found both in the trauma ICU and the BICU of our institution. Further work is required in identifying strategies to reduce the number of new cases and to decontaminate our environment. A prospective observational study is presently underway in our institution to help identify the incidence of MDR organisms carriage in the population served by our resources. All trauma and burned patients admitted have stool samples collected upon admission and in the following weeks when hospitalized. We aim at finding the incidence of carriage and hopefully acquire data that could be correlated to clinical infections during their hospitalization.

CONCLUSION

We found an important number of *A. baumannii* infections in our BICU population during the 2-year duration of our study. The isolates showed resistance

to imipenem in 87% of cases but not to colistin. Mortality in this group of patient was high (30%). With increasing numbers of cases and increased resistance to antibiotics, it is now even more important to investigate and improve the prevention and treatment of this life-threatening organism.

REFERENCES

1. Pruitt BA, McManus AT. The changing epidemiology of infection in burn patients. *World J Surg* 1992;16:57-67.
2. Wurtz R, Karajovic M, Dacumos E, et al. Nosocomial infections in a burn intensive care unit. *Burns* 1995;21:181-4.
3. Lee JJ, Marvin JA, Heimbach DM, et al. Infection control in a burn center. *J Burn Care Rehabil* 1990;11:575-80.
4. Weber JM, Tompkins DM. Improving survival: infection control and burns. *AACN Clin Issues Crit Care Nurs* 1993;4:414-23.
5. Law EJ, Blecher K, Still JM. Enterococcal infections as a cause of mortality and morbidity in patients with burns. *J Burn Care Rehabil* 1994;15:236-9.
6. Dickama DJ, and the SENTRY Participants Group. Trends in antimicrobial susceptibility of bacterial pathogens isolated from patients with bloodstream infections in the USA, Canada and Latin America. *Int J Antimicrob Ag* 2000;13:257-71.
7. Jarvis WR, Martone WJ. Predominant pathogens in hospital infections. *J Antimicrob Chemother* 1992;29(Suppl A):19-24.
8. Vincent JL, Bihari DJ, Suter PM, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) study. EPIC International Advisory Committee. *JAMA* 1995;274:639-44.
9. Paul M, Weinberger M, Siegman-Igra Y, et al. *Acinetobacter baumannii*: emergence and spread in Israeli hospitals 1997-2002. *J Hosp Infect* 2005;60:256-60.
10. Minnangati VR, Cunha BA. *Acinetobacter baumannii*-associated arterial line infection. *Am J Infect Control* 2000;28:376-7.
11. Hanberger J, and the French and Portuguese ICU Study Group. Antibiotic susceptibility among aerobic gram-negative bacilli in ICU in 5 European countries. *JAMA* 1999;28:67-70.
12. King D, Namias N, Pizano LR, et al. An unusual cause of septicemia and death in a burn patient: discussion and review. *J Burn Care Rehabil* 2005;26:502-4.
13. Bergogne-Berezin E. The increasing significance of outbreaks of *Acinetobacter* spp.: the need for control and new agents. *J Hosp Infect* 1995;30(Suppl):441-52.
14. Schreckenberger PC, von Gravevenitz A. *Acinetobacter*, *Alcaligenes*, *Moraxella*, *Methylobacterium*, and other nonfermentative gram-negative rods. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Tenover RH, editors. *Manual of clinical microbiology*. Washington: ASM Press; 1999. p. 539-60.
15. Lyytikäinen O, Koljalg S, Harma M, et al. Outbreak caused by two multi-resistant *Acinetobacter baumannii* clones in a burn unit: emergence of resistance to imipenem. *J Hosp Infect* 1995;31:41-54.
16. Roberts SA, Findlay R, Lang SDR. Investigation of an outbreak of multi-drug resistant *Acinetobacter baumannii* in an intensive care burns unit. *J Hosp Infect* 2001;48:228-32.
17. Bergogne-Berezin E, Joly-Guillon ML, Vieu JF. Epidemiology of nosocomial infections due to *Acinetobacter calcoaceticus*. *J Hosp Infect* 1987;10:105-13.
18. Getchell-White SI, Donowitz LG, Groschel DHM. The inanimate environment of an intensive care unit as a source of nosocomial bacteria: evidence for long survival of *Acinetobacter calcoaceticus*. *Infect Control Hosp Epidemiol* 1989;10:402-7.
19. Cefai C, Richards J, Gould FK, et al. An outbreak of *Acinetobacter* respiratory tract infection, resulting from incomplete disinfection of ventilatory equipment. *J Hosp Infect* 1990;5:177-82.
20. Santucci SG, Gobara S, Santos CR, et al. Infections in a burn intensive care unit : experience of seven years. *J Hosp Infect* 2003;53:6-13.
21. Lortholary O, Fagon JY, Hoi AB, et al. Nosocomial acquisition of multiresistant *Acinetobacter baumannii*: risk factors and prognosis. *Clin Infect Dis* 1995;20:790-6.
22. Peacock JE, Sorrell L, Sottile FD, et al. Nosocomial respiratory tract colonization and infection with aminoglycoside-resistant *Acinetobacter calcoaceticus* var. *anitratus*: epidemiologic characteristics and clinical significance. *Infect Control Hosp Epidemiol* 1998;9:302-8.
23. Mulin B, Talon D, Viel JF, et al. Risk factors for nosocomial colonization with multiresistant *Acinetobacter baumannii*. *Eur J Clin Microbiol Infect Dis* 1995;14:569-76.
24. Scerpella EG, Wanger AR, Armitige L, et al. Nosocomial outbreak caused by a multiresistant clone of *Acinetobacter baumannii*: results of the case-control and molecular epidemiologic investigation. *Infect Control Hosp Epidemiol* 1995;16:92-7.
25. Vandembroucke-Grauls CM, Kerver AJ, Rommes JH, et al. Endemic *Acinetobacter anitratus* in a surgical intensive care unit : mechanical ventilators as reservoirs. *Eur J Clin Microbiol Infect Dis* 1998;7:485-9.
26. French GL, Casewell MW, Roncoroni AJ, et al. A hospital outbreak of antibiotic-resistant *Acinetobacter anitratus*: epidemiology and control. *F Hosp Infect* 1980;1:125-31.
27. Bergogne-Berezin E, Joly-Guillon ML. An underestimated nosocomial pathogen, *Acinetobacter calcoaceticus*. *F Antimicrob Chemother* 1985;16:535-8.
28. Glew RH, Moellering RC, Kunz LJ. Infections with *Acinetobacter calcoaceticus* (*Herellea vaginicola*). Clinical and laboratory studies. *Medicine* 1977;56:79-87.
29. Weinbren MJ, Johnson AP, Kaufmann ME. *Acinetobacter* spp. isolates with reduced susceptibility to carbapenems in a U.K. burns unit. *J Antimicrob Chemother* 1998;41:474-6.
30. LeFloch R, Arnould JF, Pilorget A. Effect of systematic empiric treatment with imipenem on the bacterial ecology in a burns unit. *Burns* 2005;31:866-9.
31. Garnacho-Montero J, Ortiz-Leyba C, Jimenez-Jimenez J, et al. Treatment of multidrug resistant *Acinetobacter baumannii* ventilator associated pneumonia (VAP) with intravenous colistin: a comparison with imipenem-susceptible VAP. *Clin Infect Dis* 2003;36:1111-8.
32. Levin AS, Barone AA, Penco J, et al. Intravenous colistin as therapy for nosocomial infections caused by multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. *Clin Infect Dis* 1999;28:1008-11.
33. Michalopoulos A, Kasiakou SK, Mastora Z, et al. Aerosolized colistin for the treatment of nosocomial pneumonia due to multidrug-resistant gram-negative bacteria in patients without cystic fibrosis. *Crit Care* 2005;9:R53-59.
34. Kwa ALH, Low CS, Low JGH, et al. Nebulized colistin in the treatment of pneumonia due to multidrug-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. *Clin Infect Dis* 2005;41:754-7.
35. Berlanda D, Llop JM, Fort E, et al. Use of colistin in the treatment of multiple-drug-resistant gram-negative infections. *Am J Health-Syst Pharm* 2005;62:39-47.
36. Michalopoulos AS, Tsiodras S, Rellos K, et al. Colistin treatment in patients with ICU-acquired infections caused by multiresistant gram-negative bacteria: the renaissance of an old antibiotic. *Clin Microbiol Infect* 2005;11:115-21.
37. Reina R, Estenssoro E, Saenz G, et al. Safety and efficacy of colistin in *Acinetobacter* and *Pseudomonas* infections: a pro-

- spective cohort study. *Intensive Care Med* 2005;31:1058–65.
38. Montero A, Ariza J, Corbella X, et al. Efficacy of colistin versus β -lactams, aminoglycosides and rifampin as monotherapy in a mouse model of pneumonia caused by multiresistant *Acinetobacter baumannii*. *Antimicrob Agents Chemother* 2002;46:1946–52.
 39. Michalopoulos A, Kasiakou SK, Mastora Z, et al. Aerosolized colistin for the treatment of nosocomial pneumonia due to multidrug-resistant gram-negative bacteria in patients without cystic fibrosis. *Crit Care* 2005;9:R53–9.
 40. Bradford PA, Weaver-Sands T, Petersen PJ. In vitro activity of tigecycline against isolates from patients enrolled in phase 3 clinical trials of treatment for complicated skin and skin-structure infections and complicated intra-abdominal infections. *Clin Infect Dis* 2005;41:S315–332.
 41. Bang RL, Gang RK, Sanyal SC, et al. Burn septicemia: an analysis of 79 patients. *Burns* 1998;24:354–61.
 42. Sengupta S, Kumar P, Ciraj AM, et al. *Acinetobacter baumannii*—an emerging nosocomial pathogen in the burns unit Manipal, India. *Burns* 2001;27:140–4.
 43. Wisplinghoff H, Perbix W, Seifert H. Risk factors for nosocomial bloodstream infections due to *Acinetobacter baumannii*: a case-control study of adult burn patients. *Clin Infect Dis* 1999;28:59–66.
 44. Wilson SJ, Knipe CJ, Zieger MJ, et al. Direct costs of multi-drug-resistant *Acinetobacter baumannii* in the burn unit of a public teaching hospital. *Am J Infect Control* 2004;32:342–4.
 45. Wong TH, Tan BH, Ling ML, et al. Multi-resistant *Acinetobacter baumannii* on a burns unit—clinical risk factors and prognosis. *Burns* 2002;28:349–57.