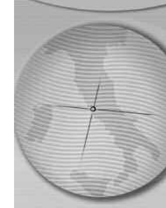

Molecular epidemiology of nosocomial infections in an intensive care unit: results of a one-year surveillance study

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Abstract

Background. Nosocomial infections contribute substantially to increased morbidity, mortality and resource expenditure in Intensive Care Units (ICUs).

Methods. A one-year prospective surveillance study was performed using epidemiological and microbiological methods to quantify the frequency of infections and the antimicrobial usage, microbiological environmental sampling and molecular typing of clinical and environmental isolates.

Results. The frequency of ICU-acquired infections was comparable to other Italian ICUs. Most of these infections were caused by few epidemic clones of *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumannii*. The survival advantage of these epidemic clones over the sporadic isolates may be related to the multi-resistant profile of the epidemic clones and to the high usage of some antibiotics in the ICU. Hand contamination of ICU personnel is a likely factor for dissemination of epidemic clones within the ICU.

Conclusions. The integrated surveillance approach described in this study is able to clarify the complex epidemiology of ICU-acquired infections and can provide important cues for prevention and control activities.

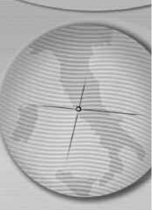
Key words: molecular epidemiology, surveillance, nosocomial infections, intensive care units

Introduction

Nosocomial infections (NI) contributed substantially to increased morbidity, mortality and resource expenditure throughout the hospital setting, particularly in the Intensive Care Units (ICUs). ICUs house patients most likely to have decreased host defences, who are undergoing invasive diagnostic and therapeutic procedures, and receiving intensive nursing and medical care with a high risk of person-to-person spread of infection.[1] Moreover, the wide usage of antibiotics strongly promotes the emergence of antimicrobial resistance and ensures the survival of nosocomial multi-resistant pathogens.[2,3] Nosocomial infections in the ICUs may be endogenous or exogenous – with the latter being more amenable to infection control practices reinforcing barrier precautions – and the relative importance of these two is the subject of much debate.[4-10]

Surveillance of nosocomial infections is an essential element of an infection control program. The landmark SENIC (Study on the Efficacy of Nosocomial Infection Control) conducted in the 1970s in the U.S. provided the scientific basis for surveillance of hospital infections while showing that hospital which are effective in lowering their infection rates also have an organized surveillance system.[11] Since then, significant changes in the complexity of acute hospital care and in the epidemiology of NI have occurred, such as for example the increase in the number of ICUs beds and the epidemic spread of antibiotic resistance.[12] Surveillance methods need to be continuously updated to adequately address these new challenges and should incorporate new technical tools, such as the use of device-day infection rates to control over main confounding factors, as well as procedures to evaluate antimicrobial use and methods for molecular typing of microrganisms.

This report describes the results of a one-year surveillance programme for adult ICU-acquired infections in an university hospital in Italy. The surveillance was carried out employing epidemiological and microbiological methods to quantify the frequency of infections and the antimicrobial usage, microbiological environmental sampling and molecular typing of clinical and



environmental isolates. This approach was able to provide standardized rates of infections and antimicrobial use, to distinguish between exogenous and endogenous infections and to define the most likely epidemiological patterns of transmission.

Methods

Setting

The teaching hospital of the University "Federico II" of Naples is built on a site of 40,000 m^2 and consists of 1,470 beds housed in 19 buildings, each consisting of one or more departments, connected by tunnels and passages. The ICU is located in one of these buildings and cares for all of the medical-surgical patients transferred from other units, with the exception of cardiac surgery and neurosurgery. The ICU has 16 beds and consists of one room with a maximum capacity of six patients and five rooms with two beds in each. Sinks are available in each room and gloves are used routinely.

Surveillance procedures

Nosocomial infections surveillance in the ICU was performed using the protocol of the National Nosocomial Infections Surveillance (NNIS) ICU component and the standard definitions of nosocomial infections according to Centers for Disease Control (CDC).[13] Surveillance of nosocomial infections after discharge was not performed. All infection rates, including patient and patient-day and device-associated infections, were calculated according to the formulas of the NNIS system. Antimicrobial use was evaluated though the calculation of the usage density rate for each antibiotic (number of defined daily doses or DDDs per 1,000 patients days), adopting the DDD definitions of the Intensive Care Antimicrobial Resistance Epidemiology (ICARE) Project.[14,15] The infection surveillance reported here covers the period from October 1998 to October 1999.

Microbiological methods

Clinical specimens were cultured when indicated and processed using standard methods. Air sampling was performed with a Surface Air System sampler (PBI), whereas other environmental sites were sampled with swabs moistened in saline 0.9% or by the direct contact method. Isolates were identified using VITEK and API 20 systems (bioMerieux, Morey-L'Etoile, France) and stored at -80°C with glycerol for subsequent phenotypic and genotypic typing. Only first patient isolates were included in the analysis.

Antimicrobial susceptibilities

Antimicrobial resistance was determined by the disk diffusion method, according to NCCLS document M2-A5.[16] The following antibiotics were tested: ampicillin/sulbactam (10/10 μg), amoxicillin/clavulanic acid (20/10 μg), mezlocillin (75 μg), piperacillin (100 μg), ticarcillin (75 μg), ticarcillin/clavulanic acid (75/10 μg), cephalothin (30 μg), cefamandole (30 μg), cefoxitin (30 μg), cefotaxime (30 μg), ceftazidime (30 μg), ceftriaxone (30 μg), cefoperazone (30 μg), imipenem (10 μg), aztreonam (30 μg), vancomycin (30 μg), teicoplanin (30 μg), ciprofloxacin (5 μg), ofloxacin (5 μg), gentamicin (10 μg), amikacin (30 μg), tobramycin (10 μg), kanamycin (30 μg), netilmicin (30 μg), chloramphenicol (30 μg), trimethoprim/sulfamethoxazole (1.25/23.75 μg), erythromycin (15 μg), rifampin (30 μg) and tetracycline (30 μg). Susceptibility or resistance was defined using NCCLS criteria.[17] Isolates showing an intermediate level of susceptibility were classified as resistant.

Preparation of chromosomal DNA for pulsed-field gel electrophoresis (PFGE) and restriction digestion

The preparation of chromosomal DNA of staphylococci, acinetobacter and pseudomonas was performed as previously described.[18-21] DNA restriction was done with *Sma*I (staphylococci), *Apa*I (acinetobacter) and *Xba*I (pseudomonas), according to the manufacturer's recommendations (New England Biolabs).

Pulsed-field gel electrophoresis

PFGE gels were run in a CHEF-DR II apparatus (BioRad) using the following conditions: for staphylococci, temperature 11.8°C, voltage 200 V, pulse times of 1-30 sec for 23 h; for acinetobacter, temperature 14°C, voltage 200 V, pulse times of 5-13 sec for 20 h; for pseudomonas, temperature 14°C, voltage 200 V, pulse times of 4-8 sec for 12 h and 10-15 sec for 12 h.

Results

ICU nosocomial infections and antimicrobial usage

A total of 444 patients, 235 men (52.9%) and 209 women (47.1%) with an age range of 14 to 95 years (average = 58.8; SD = 18.4), were included in the study. These patients spent a total 3,890 days in the ICU (average = 8.8; SD = 17.3) with device utilization ratios of 0.70, 0.89 and 0.88 for ventilator, central line and urinary catheter, respectively. The total mortality rate in the study population was 34.2% (152 of 444).

Overall, 112 infections occurred in 79 patients, with a cumulative incidence of 17.8 per 100

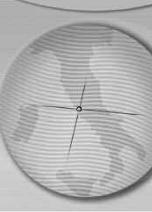
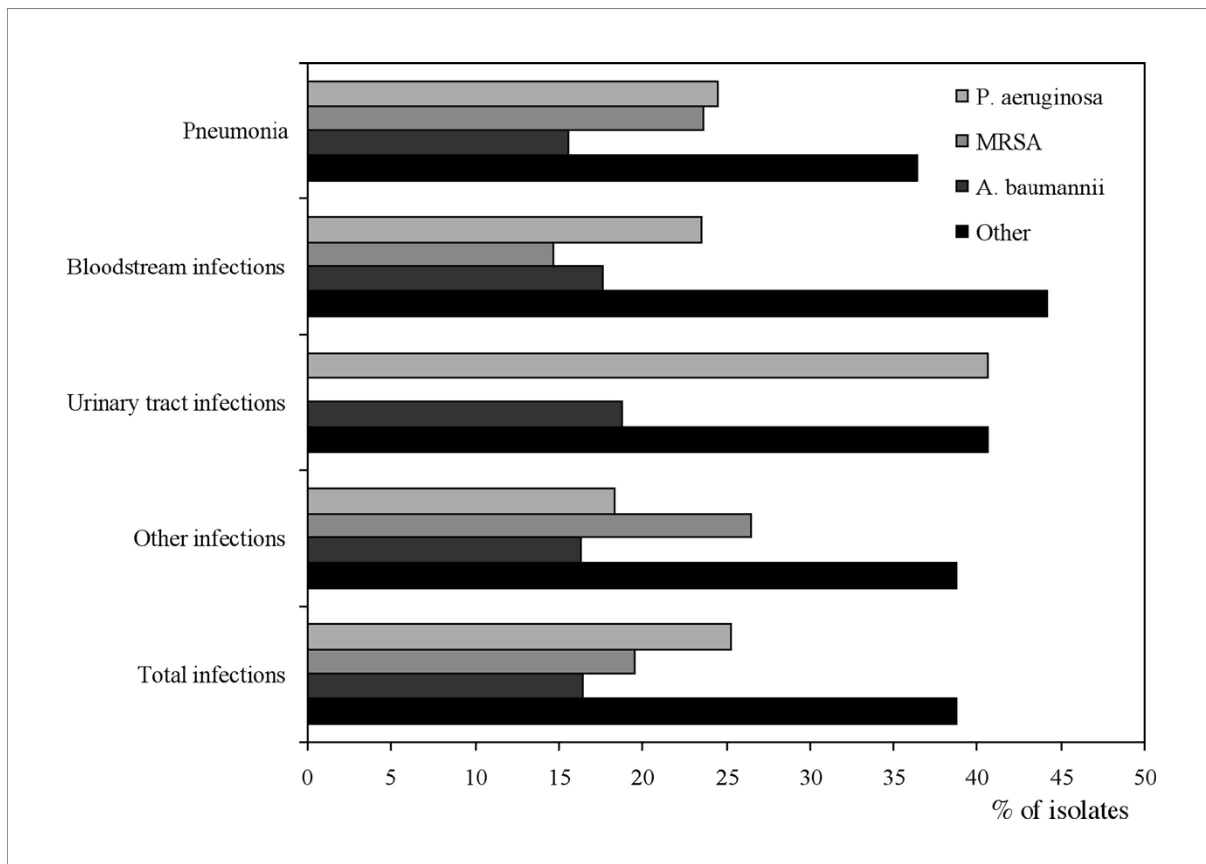


Figure 1. Percentages of *P. aeruginosa*, methicillin-resistant *S. aureus* (MRSA) and *A. baumannii* isolates in the ICU of University "Federico II", by site of infection. Other microorganisms include mainly *C. albicans* (13.8% of the isolates).



patients and an incidence rate of 28.8 per 1000 patient days. Pneumonia developed in 41 patients (36.6% of all nosocomial infections), bloodstream infections in 22 (19.6%) and urinary tract infections in 29 (25.9%). Of the total 112 infections, 79 were primary infections (70.5%), whereas 33 (29.5%) occurred in patients who already had a previous infection episode. The ventilator-associated pneumonia rate, central line-associated bloodstream infection rate and the urinary catheter associated infection rate were 15.1, 6.4 and 8.4 per 100 device-days, respectively.

In all, 225 pathogens were responsible for the 112 infections that occurred during the study period. The most common bacterial pathogens were *Pseudomonas aeruginosa* (25.3%), methicillin-resistant S*taphylococcus aureus* (MRSA) (19.6%) and *Acinetobacter baumannii* (16.4%) (Figure 1). *Candida albicans* accounted for a significant part of the isolates (13.8%). Pneumonia was caused primarily by *P. aeruginosa* (24.5%), MRSA (23.6%) and *A. baumannii* (15.4%). *P. aeruginosa* was also the most frequently identified pathogen for bloodstream infections (23.5%, followed by coagulase-negative staphylococci, *A. baumannii* and MRSA) and for urinary tract infections (40.6%, followed by *A. baumannii* and *C. albicans*).

The antimicrobial usage was high (Figure 2). Glycopeptides were the most frequently used group of antibiotics (33.7% of the total consumption), followed by carbapenems (16.3%). Teicoplanin and imipenem were administered more commonly than vancomycin and meropenem, respectively. Cephalosporins and aminoglycosides accounted for 15.3% and 12.8% of the total consumption, respectively. Ampicillins (ampicillin and amoxicillin/clavulanic acid), antipseudomonal penicillins (ticarcillin/clavulanic acid) and fluoroquinolones (ciprofloxacin) were used less frequently.

Molecular epidemiology of nosocomial infections

P. aeruginosa infections. Fifty-two of the 57 *P. aeruginosa* isolates involved with infection were available for molecular typing. The strains originated mainly from bronchial aspirate (50.0%), urine (23.1%) and blood (15.4%). All of these strains were typed with macrorestriction analysis for chromosomal DNA with *Xba*I and PFGE (Figure 3). Assuming that a single base mutation in the chromosomal DNA could

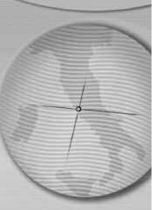


Figure 2. Antimicrobial usage rates (DDD/1000 patient-days) in the ICU of University "Federico II", by different antibiotics.

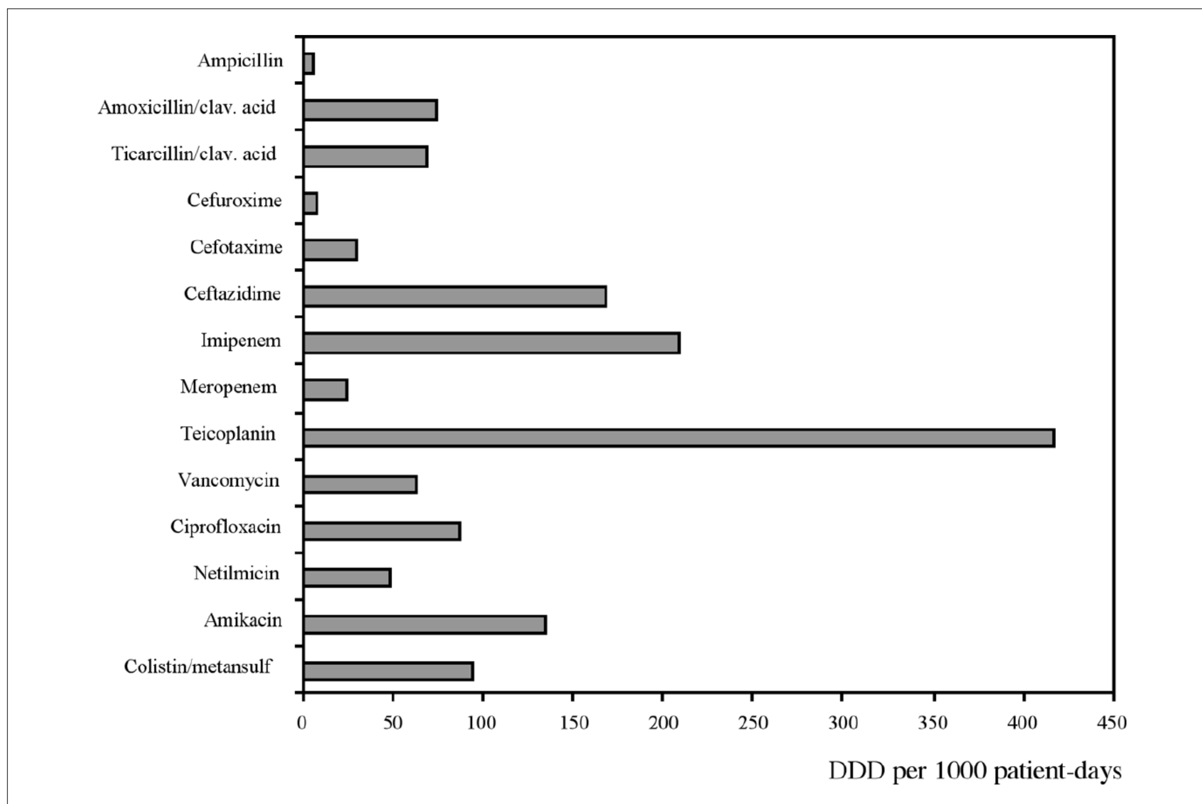
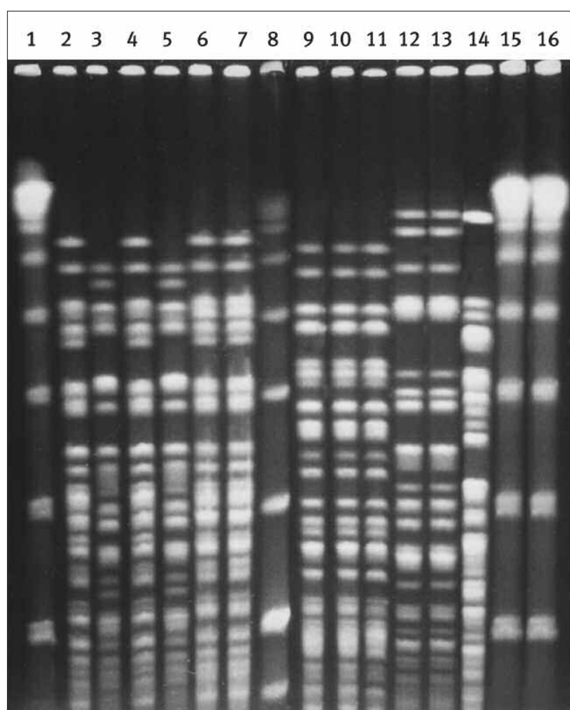
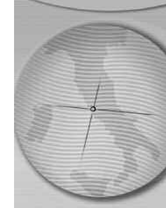


Figure 3. XbaI PFGE patterns of *P. aeruginosa* isolates in the ICU of University "Federico II". Lanes 2, 4, 6 and 7, PFGE pattern H1; lanes 9, 10, 11, PFGE pattern I1; lanes 12 and 13, PFGE pattern G1; lanes 3 and 5, PFGE pattern A1; lanes 1, 8, 15 and 16, molecular weight markers (bacteriophage lambda ladder).



introduce a maximum of a three-fragment difference in the restriction pattern [22], strains showing more than three-fragment variations were assumed to represent major patterns (assignment of capital letters), while one-to three-fragment differences were considered to represent subtypes (represented by capital letters with numerical subcodes). Using these criteria, 17 major patterns (A to R except J and K) were identified. However, two PFGE types (H and I) actually represented approximately two-thirds of the isolates (34 out of 52, 65.4%). PFGE type H had 24 strains isolated during the period January 1999 – October 1999 (46.1%), whereas PFGE type I, had only two subtypes (I_1 and I_2), which appeared in 10 strains, isolated during the period March 1999 – October 1999 (19.2%). PFGE type G occurred in three strains and another two PFGE types (A and C) contained two strains each. The remaining PFGE patterns were found only in single isolates.

P. aeruginosa isolates were tested with 15 antibiotics (piperacillin, ticarcillin, ticarcillin/ clavulanic acid, ceftazidime, ceftriaxone, cefoperazone, imipenem, aztreonam, ciprofloxacin, gentamicin, amikacin, tobramycin, netilmicin, chloramphenicol and trimethoprim/ sulfamethoxazole). Resistance phenotypes were defined through a number (representing the number of antibiotics to which the strain was



resistant) with a letter subcode (indicating the particular combination of antibiotics to which the isolate was resistant). Altogether, 15 distinct resistance phenotypes were found, all of which correlated poorly with the clonal types as defined by the PFGE (Table 1). Isolates belonging to the two main clones found in this study appeared definitively more resistant to antibiotics than the other strains. PFGE pattern H was resistant to all antibiotics in 16 isolates (66.7%) and susceptible only to netilmicin in 8 isolates (33.3%). Analogously, isolates with PFGE pattern I were resistant to all antibiotics in 50% of the cases, susceptible to only imipenem in four cases (40%) and susceptible to netilmicin and chloramphenicol in one case.

MRSA infections. All 44 MRSA isolates responsible for infection were available for genotyping. The most frequent source of isolation was bronchial aspirate (59.1%), followed by blood (11.4%). Macrorestriction analysis of genomic DNA with *Sma*I and PFGE was performed to determine the extent of clonal spread of MRSA. Different patterns were defined by a variation in migration of at least four fragments between strains.[22] A total of 10 profiles (A to L except J and K) were identified, with three PFGE patterns (B, A and C) being displayed by the majority of isolates (36 out of 44 strains, 81.8%) (Figure 4). PFGE pattern B was present in 16 isolates and was subdivided into three subtypes (B_1, B_2 and B_3). PFGE pattern A included 15 isolates and could be further classified into three subtypes (A_1, A_2 and A_3). PFGE pattern C, which had two subtypes (C_1 and C_2), was seen in five isolates. All other PFGE patterns were observed in single isolates, with the exception of PFGE pattern E which was present in two of the isolates. All major PFGE patterns occurred throughout the entire study period.

MRSA isolates were tested with 11 antibiotics (ceftazidime, vancomycin, teicoplanin, ciprofloxacin, gentamicin, amikacin, netilmicin, chloramphenicol, trimethoprim/sulfamethoxazole, erythromycin and rifampin). All isolates were susceptible to vancomycin and teicoplanin. Strains with the PFGE pattern B were always susceptible also to rifampin and trimethoprim sulfamethoxazole, whereas susceptibility to netilmicin and chloramphenicol was detected in only 87.5% and 50% of the isolates, respectively. Susceptibility to rifampin, trimethoprim/ sulfamethoxazole and netilmicin was shown by all isolates with PFGE pattern A, with a variable rate of susceptibility to amikacin and chloramphenicol (66.7% and 13.3%, respectively). Analysis of phenotype resistance, defined using the same criteria as above, showed a total of 12 different antibiotypes, with a poor correlation to the clonal types as defined by PFGE. Once again, strains with the predominant PFGE patterns appear to be resistant to more antibiotics than sporadic strains (Table 1).

A. baumannii infections. The 37 *A. baumannii* responsible for ICU infections were isolated mainly from bronchial aspirates (45.9%), blood (16.2%) and urine (16.2%). PFGE after restriction with *Apa*I divided the genomic DNA of these isolates into nine major PFGE patterns, which we named from A to I using the same criteria as above (Figure 5). Two major PFGE profiles were identified: PFGE pattern D, which generated three subtypes (D_1, D_2 and D_3) in 20 isolates (54.1%) and PFGE pattern B, which had two subtypes (B_1 and B_2), displayed in seven isolates. Strains with PFGE pattern B were isolated mainly during the first part of the study period (October 1998 – June 1999), whereas PFGE pattern D was the predominant clone isolated during the last five months of the study. PFGE patterns A (with two subtypes) and C were seen in three and two isolates, respectively. All other PFGE patterns were observed in single isolates.

A. baumanni isolates were tested with 18 antibiotics (ampicillin/sulbactam, amoxicillin/ clavulanic acid, mezlocillin, piperacillin, ticarcillin, ticarcillin/clavulanic acid, cephalothin, cefamandole, cefoxitin, cefotaxime, ceftazidime, ceftriaxone, imipenem, aztreonam, ciprofloxacin, ofloxacin, amikacin, kanamycin, chloramphenicol and tetracycline). All isolates with PFGE pattern D were susceptible only to imipenem, whereas strains belonging to PFGE pattern B were susceptible to imipenem and ampicillin/sulbactam. It is interesting to note that isolates with PFGE patterns A and C shared resistance phenotypes with isolates belonging to the major PFGE patterns. Sporadic isolates show less resistant phenotypes compared to epidemic strains (Table 1).

Environmental investigations. A total of 70 environmental investigations were undertaken in the ICU on two occasions (June and September 1999). Sites screened included air (6 samples), room surfaces (16), sinks (6), mattresses (6), in-use disinfectants (8), respirators (6), infusion pumps (6), monitors (6), aspiration pumps (6) and staff hands (4). *P. aeruginosa*, MRSA and *A. baumannii* were isolated on five occasions, always from areas frequently handled by healthcare personnel (infusion pumps, monitor and aspiration pumps).

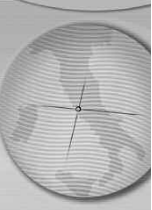


Table 1. ***P. aeruginosa*, methicillin-resistant *S. aureus* (MRSA) and *A. baumannii* clones identified in the ICU of University "Federico II".**

Bacterial pathogen	PFGE pattern[a] (*n*)[b]	Resistance phenotypes[a,c] (*n*)[b]	Sites of isolation (*n*)[b]
P. aeruginosa	H (24)	15_a(16)	bronchial aspirate (12); blood (1); urine (2); other sites (1)
		14_b(8)	bronchial aspirate (6); blood (1); urine (1)
	I (10)	15_a(5)	bronchial aspirate (2); blood (1); urine (2)
		14_a(4)	bronchial aspirate (2); blood (1); urine (1)
		13_a(1)	other sites(1)
	G (3)	4_c (1)	blood (1)
		3_a(1)	other sites(1)
		2_a(1)	urine (1)
	A (2)	2_a(2)	bronchial aspirate (1); urine (1)
	C (2)	4_a(2)	blood (1); urine (1)
	B (1)	7_a(1)	urine (1)
	E (1)	10_a(1)	blood (1)
	D (1)	13_a(1)	bronchial aspirate (1)
	F (1)	7_b(1)	other sites (1)
	L (1)	6_a(1)	blood (1)
	M (1)	10_a(1)	bronchial aspirate (1)
	N (1)	5_a(1)	other sites (1)
	O (1)	4_b(1)	bronchial aspirate (1)
	P (1)	10_b(1)	other sites (1)
	Q (1)	10_b(1)	urine (1)
	R (1)	4_a(1)	urine (1)
MRSA	B (16)	5_a(8)	bronchial aspirate (4); blood (1); other sites (3)
		6_a(6)	bronchial aspirate (4); blood (1); other sites (1)
		7_a(2)	bronchial aspirate (1); other sites (1)
	A (15)	5_b(10)	bronchial aspirate (6); blood (1); other sites (3)
		5_a(2)	other sites (2)
		6_b(3)	bronchial aspirate (2); blood (1)
	C (5)	5_a(2)	bronchial aspirate (1); other sites (1)
		7_a(1)	blood (1)
		7_b(1)	bronchial aspirate (1)
		6_a(1)	bronchial aspirate (1)
	D (1)	0_a(1)	other sites (1)
	E (2)	3_a(1)	bronchial aspirate (1)
		1_a(1)	bronchial aspirate (1)
	F (1)	1_b(1)	bronchial aspirate (1)
	G (1)	2_a(1)	bronchial aspirate (1)
	H (1)	0_a(1)	bronchial aspirate (1)
	I (1)	0_a(1)	bronchial aspirate (1)
	L (1)	4_a(1)	other sites (1)
A. baumannii	D (20)	17_a(20)	bronchial aspirate (11); blood (2); urine (3); other sites (4)
	B (7)	16_a(7)	bronchial aspirate (2); blood (2); urine (1); other sites (2)
	A (3)	17_a(2)	bronchial aspirate (1); blood (1)
		16_a(1)	urine (1)
	C (2)	16_a(2)	bronchial aspirate (1); other sites (1)
	E	8_a(1)	other sites (1)
	F	12_a(1)	blood (1)
	G	11_a(1)	bronchial aspirate (1)
	H	6_a(1)	urine (1)
	I	12_a(1)	bronchial aspirate (1)

[a,c] *See text for definitions*
[b] *n, number of strains*

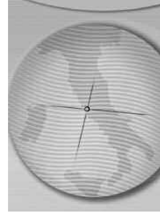


Figure 4. SmaI PFGE patterns of methicillin-resistant *S. aureus* (MRSA) isolates in the ICU of University "Federico II". Lanes 5 to 10, PFGE pattern B1 and lane 11, PFGE pattern B2; lanes 2, 3 and 4, PFGE pattern A1; lanes 13, 14 and 15, PFGE pattern C1; lanes 1, 12 and 19, molecular weight markers (bacteriophage lambda ladder).

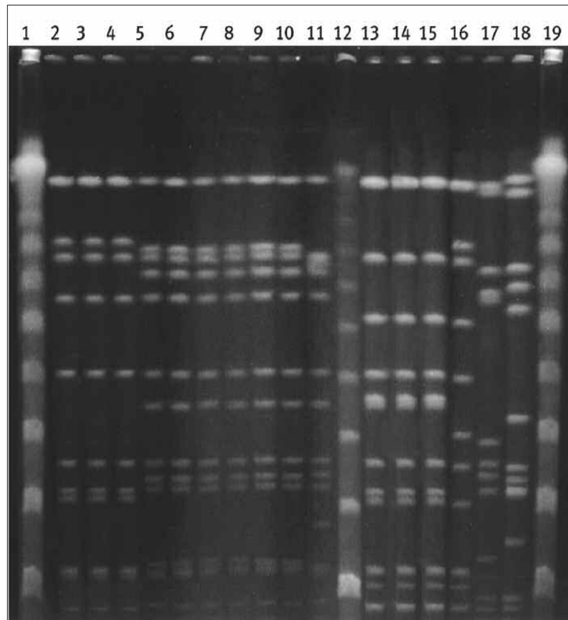
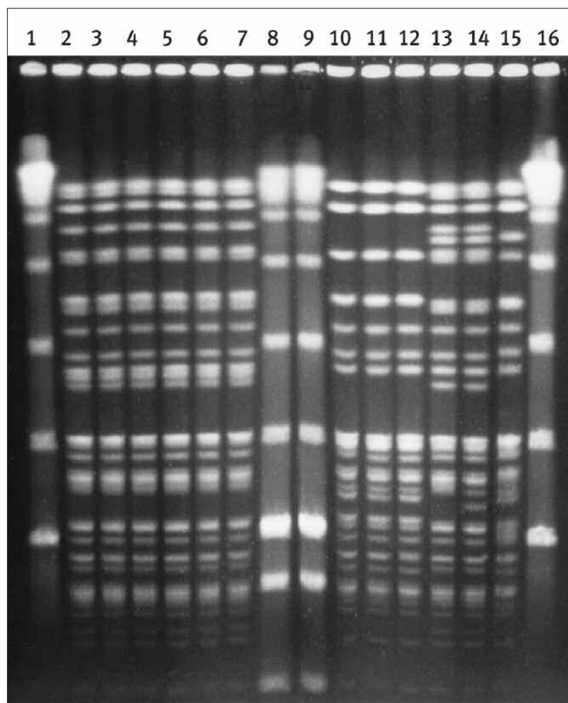


Figure 5. ApaI PFGE patterns of *A. baumannii* isolates in the ICU of University "Federico II". Lanes 2 to 7, PFGE pattern D1 ; lanes 10, 11 and 12, PFGE pattern B1; lanes 13 and 14, subtypes of PFGE pattern A; lanes 1, 8, 9 and 16, molecular weight markers (bacteriophage lambda ladder).

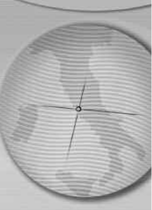


In four of the cases isolates belonged to the major PFGE clones responsible for ICU infections (PFGE pattern H for *P. aeruginosa*, PFGE pattern B for MRSA and PFGE pattern D for *A. baumannii)*.

Discussion

Prevalence surveys recently performed in Italy confirmed that the frequency of nosocomial infections is particularly high in ICUs.[23-25] Their results agree with the EPIC study that, in 1992, documented an overall prevalence of 21% in 1,417 western European ICUs.[26] The advantage of prospective studies is that they can provide standardized incidence rates that make comparisons feasible over time and throughout different hospitals. When compared with the incidence data generated by the NNIS System, infection rates found in this study were within the benchmarks for major teaching medical-surgical ICUs (with the exception of the rate for pneumonia if compared with the most recent NNIS data),[27] but they are similar to those reported in other Italian medical-surgical ICUs.[28,29] It is interesting to note that also the use of devices was more frequent in our ICU (as well as in other Italian ICUs) than in U.S. hospitals. The higher device utilization ratios found in Italian ICUs may result from differences in patient characteristics and case mix, in staffing or in procedures, but the available data was not sufficient to examine these possibilities.

The distribution of the major sites of infection found in this study is similar to that reported in Europe and in the U.S.[26,30] since nosocomial pneumonias were most frequent, followed by urinary tract infections and bloodstream infections. By contrast, the pathogen distribution among ICU-acquired infections appeared somewhat different: three pathogens (*P. aeruginosa*, MRSA and *A. baumannii*) were responsible for more than 60% of infections that occurred in the unit during the study period. Whereas the importance of *P. aeruginosa* and MRSA is well established in European and U.S. ICUs, the relative major impact of *A. baumannii* had already been reported in Italian ICUs.[20,29] The molecular characterization of clinical isolates clearly indicated the existence of a clonal spread within the ICU, since most infections that occurred in our ICU were caused by few epidemic clones rather than by several different strains and may thus be attributable to transmission among patients. Knowledge about the relative importance of exogenous and endogenous routes of infection is essential in order to design targeted strategies for infection



prevention, since measures to prevent cross-infections are likely to have a significant impact only on exogenous pathogens.

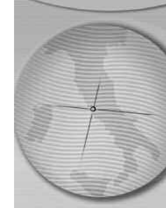
The success of the predominant clones circulating in our ICU may be related to several yet uncharacterized factors that provide the microrganisms with advantages in colonization or in their ability to infect patients. One of these factors is the antibiotic resistance, since the major clones found in this study were more resistant than sporadic strains, with most isolates of *P. aeruginosa* belonging to the two major PFGE patterns resistant to all of the antimicrobial agents that are usually tested. The antimicrobial use in the ICU was high, particularly for glycopeptides and carbapenems. The use of these antibiotics, justified by the high frequency of infections sustained by MRSA and *A. baumannii*, was much higher compared to other ICUs in U.S.A. and Europe.[14,15,31] This high antimicrobial use is likely to facilitate the clonal spread of multi-resistant strains, particularly when combination therapy is not administered appropriately. For example, the use of glycopeptides to treat MRSA may enhance the diffusion of *P. aeruginosa* and *A. baumannii*, whereas the use of imipenem and meropenem gives a selective advantage to *P. aeruginosa* to become resistant to carbapenems. It is important to note that the same ICU described in this study subsequently experienced an outbreak of imipinem-resistant *A. baumanni*, as described elsewhere.[32]

Surveillance cultures of the hospital environment once were advocated on a routine basis. During the 1970s, studies found these programs to be of minimal value in infection control; by the 1980s, most institutions took the approach that routine environmental culturing should be severely limited, and further studies have supported this selective approach.[33] However, environmental surveys may be useful while investigating specific problems or in an epidemic context. In this study, some of the predominant clones in the ICU were found specifically at points typically handled by healthcare personnel, such as infusion pumps, monitors and aspiration pumps. Even if these findings represent secondary contamination rather than identifying the source of contamination, they strongly suggest that one important pattern of transmission of the major epidemic clones within the ICU could be through transient carriage on the hands of personnel. Failing to wash hands before and between contacts with patients was recently documented among healthcare workers in Italian ICUs.[34]

The most important finding of this study, however, is that an integrated surveillance approach using the NNIS system, methods to quantify antimicrobial usage, microbiological cultures of the hospital environment and molecular typing of clinical and environmental isolates can provide quite clear picture of the complex epidemiology of ICU-acquired infections. In our experience, this approach was able to clarify that the frequency of ICU-acquired infections was higher than that reported in U.S. hospitals and comparable to other Italian ICUs and that most of these infections were caused by a few epidemic clones. The survival advantage of these epidemic clones over the sporadic isolates may be related to the multi-resistant profile of the epidemic clones and to the high use of some antibiotics in the ICU. Finally, hand contamination of ICU personnel is likely to be an important factor in the dissemination of epidemic clones within the ICU.

Surveillance for nosocomial infections is the focus of any evidence-based infection control and prevention program. In a recent publication, the CDC reported a decrease in all 3 site-specific, risk-adjusted infection rates (respiratory tract, urinary tract and bloodstream) monitored in NNIS ICUs from 1990 through 1999.[35] Similar findings were reported in other countries, such as Germany, where a nationwide surveillance project was implemented.[36] Several studies with observational or experimental designs have documented the positive effects of surveillance and comparative data feedback on the frequency of ICU-acquired infections.[37,38] Providing data to physicians about the antimicrobial use and the antimicrobial resistance in the ICU may help them to optimize prophylactic, empiric and therapeutic antibiotic use.[39] Properly disseminating, among staff members, the results of molecular typing may play a fundamental role in the education of staff regarding cross-transmission mechanisms and the appropriate measures to be taken in order to control the spread of epidemic clones within the ICU.[40] It may be argued that the integrated surveillance approach described in this study is time, labour and financially intensive, however the higher costs might be justified by considering the fact that ICUs might now be considered as factories that create and amplify antibiotic resistance and can serve as reservoirs for the dissemination of multi-resistant isolates in other wards of the hospital, as well as in the community.[3]

Effective surveillance should provide a stimulus to keep prevention and control activities moving



rapidly ahead and in the correct direction. It should be pointed out, however, that there is not much evidence about effective interventions to prevent nosocomial infections and antimicrobial resistance in the ICU. Intervention trials are strongly needed, particularly in the presence of confirmed cross-transmission without a definable common source. Prime areas for investigation include the preferential use of alcohol-based products that may be superior to other products for the removal of microrganisms from hands, universal gloving with or without gowns for the care of patients who are intubated and receiving mechanical ventilation, prescribing of reduced or narrower spectrum antibiotics or shorter courses of therapy to decrease the risk of subsequent colonization or infection and private rooms with or without special ventilation to isolate patients colonized or infected with multi-resistant microrganisms. Much uncertainty also exists around the effectiveness of selective digestive contamination, particularly when systemic antibiotics are added systematically to non-absorbable ones. A recent randomized study comparing two units in the same department of a hospital in the Netherlands showed significant survival advantages without increasing antimicrobial resistance.[41] This study, however, was performed in a country in which the resistance level is very low and it is unclear what would happen in units where the resistance level is very high.

In conclusion, the integrated surveillance approach adopted in this study was able to clarify that the majority of ICU-acquired infections were caused by a few epidemic strains of *P. aeruginosa*, MRSA and *A. baumanni*. Even if evidence-based corrective actions to the epidemiological situation described in this study are largely lacking, there is no doubt that control strategies should depend on identifying the major driving forces in the selection and in the dissemination of the major epidemic clones. The results of this study underline the importance of two main mechanisms: selection by antibiotic treatment of multi-resistant organisms and dissemination of resistant clones within the ICU. While the intense selective pressure of antimicrobial use gives multi-resistant clones an important survival advantage over the sporadic strains, the inconsistent application of basic infection control procedures by hospital personnel accounts largely for the spread of resistant clones in the ICU. Given the reduction of therapeutic options and the possible dissemination of multi-resistant microrganisms into other hospital wards and into the community, rational and limited use of antimicrobials as well as reinforcing barrier precautions should be among the primary strategic goals of health care delivery in ICUs.

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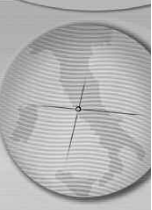

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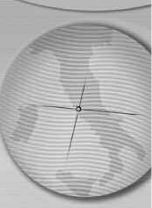

ERRATUM

Molecular epidemiology of nosocomial infections in an intensive care unit: results of a one-year surveillance study

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Volume 2, no.1, p. 39-48. Page 41, column 1, line 12:
"...per 100 device days..." should read "...per 1000 device-days..."