Nosocomial Urinary Tract Infections: Micro-organisms, Antibiotic Sensitivities and Risk Factors

L Savas[1], S Guvel[2], Y Onlen[1], N Savas[3], N Duran[4]

ABSTRACT

Objective: *Although urinary tract infections (UTIs) are the most common hospital-acquired infections, the epidemiology of these UTIs is not well defined in Turkey. The aim of this surveillance study was to determine micro-organisms responsible for UTI, their antibiotic sensitivities and to describe the incidence and risk factors of nosocomial urinary tract infections (NUTI).*

Subjects and Methods: *This was a prospective surveillance study including cases of NUTI in intensive care units and various inpatient clinics. This study was carried out between November 2000 and January 2002. The following information was recorded: patients' age, gender, type of infection (hospital-acquired), presence of urinary catheter, intensive care unit admission, duration of hospital stay, type of organisms isolated and their antimicrobial susceptibility. The diagnosis of NUTI was based on criteria established by the Centers for Disease Control, Atlanta. Mini Api and conventional culture methods were used to determine the causative agents. The agents were isolated on eosin methylene blue agar and 5% sheep blood agar. Statistical analyses of data were by chi-square test and logistic regression.*

Results: *In this study, 618 (2.1%) nosocomial infections (NIs) were determined in 29 778 patients, and 178 of these infections were NUTI (28.8%, 178/618). The mean age of NUTI patients was 61.0 ± 19.4 years (0–91 years) and 82 NUTI patients (46.1%) were male and 96 (53.9%) were female. The most frequently isolated micro-organism was* Escherichia coli *(31.4%) followed by* Candida spp *(21.3%),* Klebsiella spp *(10.6%) and* Enterococcus spp *(6.9%). Compared to the rate of other NIs, the rate of NUTI increased by 1.011 times per year of age, by 2.052 times in females and by 3.83 times in patients with urinary catheters ($p < 0.05$). The most effective antibiotics against Gram-negative bacteria were found to be imipenem and meropenem.*

Conclusions: *Important factors to prevent NUTI are to avoid unnecessary urethral catheterization, to choose narrow spectrum antibiotics according to antibiotic sensitivities, to investigate regularly the causative micro-organisms and their resistance patterns and to update the treatment protocols.*

Infecciones Nosocomiales del Tracto Urinario: Microorganismos, Sensibilidades Antibióticas y Factores de Riesgo

L Savas[1], S Guvel[2], Y Onlen[1], N Savas[3], N Duran[4]

RESUMEN

Objetivo: *Aunque las infecciones del tracto urinario (ITU) son las que con mayor frecuencia se adquieren en los hospitales, su epidemiología no se halla bien definida en Turquía. El objetivo de este estudio de vigilancia fue determinar los microorganismos responsables de la ITU, sus sensibilidades antibióticas, y describir la incidencia y los factores de riesgo de las infecciones del tracto urinario nosocomiales (ITUN).*

Sujetos Y Métodos: *Este fue un estudio prospectivo de vigilancia que incluyó casos de ITUN en unidades de cuidados intensivos y en varias clínicas de ingreso. El estudio se llevó a cabo entre noviembre de 2000 y enero de 2002. Se registró la siguiente información: edad del paciente, sexo, tipo de infección (adquirida en el hospital), presencia de catéter urinario, ingreso a la unidad de cuidados intensi-*

From: Departments of Infectious Diseases and Clinical Microbiology[1], Public Health[3], Microbiology and Clinical Microbiology[4], Mustafa Kemal University, Faculty of Medicine, Hatay, Turkey. Department of Urology[2], Baskent University, Faculty of Medicine, Adana Teaching and Medical Research Centre, Adana, Turkey.

Correspondence: Professor ND Duran, Sumerler Mahallesi, 16 Sokak, Arda Miskioglu Apt Kat 3, No 8, Antakya-Hatay, Turkey Fax: +90 326 214 1649, e-mail: nizamduran@hotmail.com

vos, duración de la estadía hospitalaria, y el tipo de organismo aislado así como su susceptibilidad antimicrobiana. El diagnóstico de ITUN se basó en criterios establecidos por los Centros de Control de Enfermedades, Atlanta. El sistema Mini Api y métodos de cultivo convencionales fueron usados con el propósito de determinar los agentes causantes. Los agentes causantes fueron aislados sobre agar-eosina-azul de metileno y agar sangre de oveja a 5%. El análisis estadístico de los datos se realizó usando la prueba de chi-cuadrado y regresión logística.

Results: *En este estudio, se determinaron 618 (2.1%) infecciones nosocomiales (IN) en 29 778 pacientes, y 178 de estas infecciones resultaron ser INTU (28.8%, 178/618). La edad media de los pacientes de INTU fue 61.0 ± 19.4 años (0–91 años) y 82 pacientes de INTU (46.1%) fueron varones y 96 (53.9%) fueron hembras. El micro-organismo más frecuentemente aislado fue* Escherichia coli *(31.4%), seguido por* Candida spp *(21.3%),* Klebsiella spp *(10.6%) y* Enterococcus spp *(6.9%). En comparación con la tasa de otras IN, la tasa de INTU aumentó 1.011 veces por año de edad, 2.052 veces en las hembras, y 3.83 veces en pacientes con catéteres urinarios ($p < 0.05$). Se halló que los antibióticos más efectivos contra las bacterias Gram-negativas fueron imipenema y meropenema.*

Conclusions: *Factores importantes para prevenir las INTU son: evitar cateterizaciones innecesarias de la uretra; escoger antibióticos de espectro estrecho de acuerdo con las sensibilidades antibióticas; investigar con regularidad los micro-organismos causantes y sus patrones de resistencia; y actualizar los protocolos de tratamiento.*

West Indian Med J 2006; 55 (3): 189

INTRODUCTION

Urinary tract infections are one of the most common community-acquired and nosocomial infections (NIs). Nosocomial urinary tract infections (NUTI) constitute 40–50% of all hospital infections (1, 2). Nosocomial urinary tract infections increase not only morbidity and mortality but also hospital costs (3, 4). The rate of NUTI is determined by the interactions of several factors such as primary disease and its severity, duration of hospitalization and treatment, and invasive interventions (1). Nosocomial urinary tract infections are associated with urinary catheters in 80% of the cases (5). Other risk factors include diabetes mellitus, long-term hospitalization, malignancy, immunosuppression and female gender (5–7).

Despite the widespread availablity of antibiotics, urinary tract infection (UTI) remains the most common bacterial infection in the human population. Antibiotics are usually given empirically before the laboratory results of urine culture are available. To ensure appropriate therapy, current knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory (8). The emergence of resistance to antimicrobial agents is a global public health problem, particularly so in pathogens causing nosocomial infections (9, 10). Antimicrobial resistance results in increased illness, death and healthcare cost (11). In the field of UTIs, there has been a steady increase in the level of resistance to commonly used antibiotics, including ampicillin and trimethoprim (12, 13). There have also been reports of resistance emerging to fluoroquinolones in some countries (14, 15). The distribution of pathogens causing nosocomial infections, especially antimicrobial-resistant pathogens, changes with time and varies among hospitals even different locations in the same hospital (16, 17). Since these rates of resistance to antibiotics differ from region to region, in making an appropriate choice of empiric or definitive therapy for UTI, it is useful to have information on prevailing levels of antimicrobial resistance among common urinary pathogens. One of the aims of this study was to determine whether there was a difference in antimicrobial resistance of uropathogens (such as *Escherichia coli, Proteus mirabilis*, *Klebsiella spp*, other Enterobacteriaceae, Staphylococci, enterococci and *Pseudomonas spp*).

In this study, the authors investigated the aetiologic agents of nosocomial UTIs, their susceptibility pattern to different antimicrobial agents and risk factors for NUTI, and thus determined measures for prevention of the infections.

METHODS

Specimens: This was a prospective cohort study of cases of NUTI. It was carried out from November 2000 to January 2002 at the Baskent University, Turkey. In the course of study, an infectious diseases specialist and a nurse visited the intensive care units, inpatient clinics and microbiology laboratory and filled in forms for hospital infections based on laboratory and clinical signs. All patients hospitalized at least for 72 hours throughout the study period were considered eligible for enrolment. This is the usual accepted duration of hospitalization required to develop a nosocomial infection. For each patient, a questionnaire was completed with the following data: age, gender, duration of stay in hospital, use of an indwelling catheter, duration of catheterization. Patients who were proven to have UTI were considered cases. The diagnosis of NUTI was based on Centers for Disease Control (CDC) definitions (18). **Criterion 1:** Patient has at least one of the following signs or symptoms with no other recognized cause: fever (> 38°C), urgency, frequency, dysuria, or suprapubic tenderness and a positive urine culture with colony counts equal to or more than 10^4 micro-organisms per cm^3. Bacterial counts less than this were considered insignificant (19). **Criterion 2:** Patient has at least two of the following

signs or symptoms with no other recognized cause: fever (> 38°C), urgency, frequency, dysuria, or suprapubic tenderness and at least one of the following; (a) pyuria (urine specimen with >10 wbc/mm^3); (b) organisms seen on Gram stain of unspun urine; (c) physician diagnosis of a UTI; (d) physician institutes appropriate therapy for a UTI. The urine specimens were transported to the bacteriology laboratory within two hours of collection or refrigerated for four hours before processing.

Culture: The urinary catheters were inserted and removed using standard aseptic precautions. After removal, the tip of each catheter was cut with a sterile blade and sent in a sterile tube for bacterial culture. The urinary catheter tip was flushed with one millilitre of glucose broth. A loopful of the broth was taken and inoculated on blood agar and eosin methylene blue (EMB) agar. The plates were incubated overnight. Mini Api and conventional culture methods were used for identification of causative micro-organisms (20). Simultaneously, a gram stained smear was also prepared. Specimens from which a single pathogen was isolated, were termed monomicrobial; and polymicrobial when two or more pathogens were isolated, growth of three or more types of organisms, or diphtheroids, was considered as contamination.

Antimicrobial susceptibility tests: All isolates were tested for susceptibility to antimicrobial agents on Mueller Hinton agar (Difco, USA) by the standard disc diffusion method recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (21). All Gram-negative bacilli were tested for susceptibility to the following 17 antimicrobials: ampicillin/sulbactam (10 + 10 µg/disc), amoxicillin (20 µg/disc) + clavulanic acid (10 µg/disc), amikacin (30 µg/disc), gentamycin (10 µg/disc), netilmicin (30 µg/ml), tobramycin (10 µg/ml), aztreonam (30 µg/disc), imipenem (10 µg/disc), meropenem (10 µg/disc), norfloxacin (10 µg/disc), ciprofloxacin (5 µg/disc), ceftriaxone (30 µg/disc), ceftazidime (30 µg/disc) and cefepime (30 µg/disc), cefoxitin (30 µg/disc), cefuroxime (30 µg/disc) and cotrimoxazole (125 + 23.75 µg/disc).

Statistical analyses: Chi-square test was used to determine the relation between NUTI and urinary catheterization and inpatient status. Stepwise logistic regression analysis was used to determine the difference in age, gender, wards/units where the patients were treated, malignancy, diabetes mellitus, immunosuppression and invasive procedures (urinary catheterization) between NUTI and other NIs. Male patients, patients without diabetes mellitus, malignancy and immunosuppression and those who did not undergo an operation or an invasive procedure *eg* haemodialysis and urinary catheterization, were considered without risk in the logistic regression analysis (5–7).

RESULTS

Of 29 778 patients studied, 24 251 (81.4%) were in various inpatient wards; 590 (1.9%) in the neonatal care unit, 127 (0.4%) in the burn care unit, 1293 (4.3%) in the intensive care unit (ICU) for surgical diseases, 805 (2.7%) in ICU for general internal medicine problems, 1069 (3.6%) in ICU for cardiovascular diseases and 1643 (5.5%) in ICU for coronary diseases. The mean length of stay in ICU for surgical conditions, for internal medicine, cardiovascular and coronary diseases were 3.2 ± 0.6 days, 4.7 ± 0.9 days, 2.9 ± 1.1 days, and 2.08 ± 0.4 days respectively.

In the current study, 618 (2.1%) NIs were determined in 29 778 patients, and 178 (28.8%, 178/618) of them were NUTI. The second most frequent NI was bacteraemia (145; 23.5%), followed by pneumonia (115; 18.6%), sepsis (62; 10.0%), surgical wound infection (40; 6.5%), superficial site infection (38; 6.1%), infection caused by catheter (20; 3.2%) and miscellaneous infections (20; 3.2%). The distribution of NI by inpatient wards/units is shown in Table 1.

The mean age of the patients with NUTI was 61.0 ± 19.4 years (0–91 years). Of 178 patients with NUTI, 96 (53.9%) were female, 108 (60.7%) were in the intensive care unit, 57 (32%) were from the internal medicine service and 13 (7.3%) were in the surgical clinics. There were 102 patients (57.3%) with only NUTI, 54 patients (30.7%) had NUTI and one accompanying NI and 22 patients (12.4%) had NUTI and two accompanying NIs.

A total of 216 nosocomial micro-organisms were cultured in urinary specimens from 178 patients with NUTI. The

Table 1: Distribution of nosocomial infections by inpatient clinics.

Nosocomial Infections	Intensive Care Units Number (%)*	Surgical Clinics Number (%)*	Departments of internal diseases Number (%)*	Total Number (%)**
NUTI	109 (61.2)	13 (7.3)	56 (31.5)	178 (28.8)
Bacteraemia	89 (61.4)	12 (8.3)	44 (30.3)	145 (23.5)
Pneumonia	98 (85.2)	5 (4.4)	12 (10.4)	115 (18.6)
Sepsis	52 (83.9)	1 (1.6)	9 (14.5)	62 (10.0)
Surgical wound infection	7 (17.5)	30 (75.0)	3 (7.5)	40 (6.5)
Superficial wound infection	34 (89.5)	–	4 (10.5)	38 (6.1)
Catheter infection	12 (60.0)	1 (5.0)	7 (35.0)	20 (3.2)
Other	14 (67.1)	2 (10.0)	4 (20.0)	20 (3.2)
Total	**415 (67.1)**	**64 (10.4)**	**139 (22.5)**	**618 (100)**

*Line Percentage **Column Percentage

mean duration of urinary catheterization was 3.3 ± 1.0 days in the NUTI patients. The most frequent micro-organism in patients with NUTI was *E coli* (68; 31.4%), followed by *Candida spp* (46; 21.3%), *Klebsiella spp* (23; 10.6%) and *Enterococcus spp* (15; 6.9%). The most frequent micro-organisms in patients with urinary catheters were *E coli* (53; 24.5%), *Candida spp* (21; 21.3%), *Klebsiella spp* (18; 8.3%) and *Pseudomonas spp* (14; 6.5%), (Table 2). In addition,

Table 2: Distribution of causative agents of NUTI by patients with or without a urinary catheter.

Microorganism	Patients with a catheter n (%)	Patients without a catheter n (%)	Total n (%)
E coli	53 (24.5)	15 (6.9)	68 (31.4)
Candida spp	46 (21.3)	–	46 (21.3)
Klebsiella spp	18 (8.3)	5 (2.3)	23 (10.6)
Enterococcus spp	13 (6.0)	2 (0.9)	15 (6.9)
Pseudomonas spp	14 (6.5)	–	14 (6.5)
Gram negative enteric rod	10 (4.6)	1 (0.5)	11 (5.1)
MRSA	5 (2.3)	2 (0.9)	7 (3.2)
MSSA	2 (0.9)	4 (1.9)	6 (2.8)
Streptococcus spp	4 (1.9)	1 (0.5)	5 (2.4)
Enterobacter spp	5 (2.3)	–	5 (2.3)
MRCNS	4 (1.9)	–	4 (1.9)
The others	10 (4.6)	2 (0.9)	12 (5.5)
Total	**184(85.2)**	**32(14.8)**	**216(100)**

MRSA = Methicillin-resistant *Staphylococcus aureus*
MSSA = Methicillin-susceptible *Staphylococcus aureus*
MRCNS = Methicillin-resistant coagulase negative staphylococci.

Candida spp, *Pseudomonas spp*, *Enterobacter spp* and methicillin-resistant coagulase negative Staphylococci were isolated only in patients with a urinary catheter. The sensitivities to antibiotics of Gram-negative bacteria isolated as causative micro-organisms of NUTI are shown in Table 3.

Table 3: Antibiotic sensitivities of most frequently detected micro-organisms in NUTI.

Antibiotics	*E coli* (%)	*Klebsiella spp* (%)	*Pseudomonas spp* (%)	Gr (-) Enteric rod (%)	*Enterobacter spp* (%)
Ampicillin/sulbactam	41.2	52.2	7.1	54.5	40.0
Amoxicillin/clavulanate	55.9	56.5	7.1	45.4	20.0
Amikacin	76.5	73.9	57.1	63.6	60.0
Gentamicin	48.5	47.8	28.6	54.5	40.0
Netilmicin	63.2	73.9	42.9	72.7	60.0
Tobramycin	48.5	43.5	50.0	63.6	40.0
Aztreonam	70.6	69.6	35.7	36.4	40.0
Imipenem	100.0	95.7	85.7	100.0	100.0
Meropenem	100.0	95.7	78.6	100.0	100.0
Norfloxacin	55.9	91.3	71.4	72.7	80.0
Ciprofloxacin	54.4	87.0	71.4	54.5	80.0
Ceftriaxone	63.2	60.9	28.6	63.6	40.0
Ceftazidime	70.6	69.6	50.0	63.6	60.0
Cefepime	72.1	73.9	71.4	72.7	80.0
Cefoxitin	72.1	78.3	14.3	36.6	20.0
Cefuroxime	42.6	43.5	7.1	54.5	40.0
Cotrimoxazole	42.6	60.9	14.3	45.4	20.0

Stepwise logistic regression analysis showed that compared to other NI, the rate of NUTI increased by 1.011 times per year of age, 2.052 times in females, 2.103 times in diabetics and 3.83 times in patients with a urinary catheter ($p < 0.05$) (Table 4). However, compared to the rate of other NIs,

Table 4: The relation between NUTI and age, sex, inpatient clinics, surgical operations, diabetes mellitus and urinary catheterization (Stepwise logistic regression analysis of risk factors).

Characteristics	Other NI n (%)	NUTI n (%)	B	*p*	Exp(B)
Age			0.011	0.041	1.011
Gender					
Male	187 (69.3)	83 (30.7)	0.719		2.052
Female	96 (50.3)	95 (49.7)		0.001	
Diabetes mellitus					
No	225 (68.0)	106 (32.0)	0.743		2.103
Yes	58 (44.6)	72 (55.4)		0.002	
Urinary catheter					
No	85 (75.2)	28 (24.8)	1.343		3.830
				0.000	
Yes	198 (56.9)	150 (43.1)			
Surgical operation					
No	146 (51.6) 1.208	137 (48.4)	–		0.299
				0.000	
Yes	137 (77.0)	41 (23.0)			
Inpatients clinics					
Intensive care units	180 (62.3)	109 (37.7)			
Surgical clinics	42(76.4)	13(23.6)	0.870		0.419
				0.004	
Internal medicine	61(52.1)	56(47.9)			

*B: Quotient
**Exp (B): Odds ratio

the rate of NUTI decreased by 0.299 times in patients who underwent an operation when they were hospitalized and by 0.419 times in patients who were treated in ICUs ($p < 0.005$). Malignancy, immunosuppression and haemodialysis had no significant effect on NUTI and other NIs ($p > 0.05$).

DISCUSSION

There are many factors which influence the incidence of NUTI and the micro-organisms which cause it. Studies on risk factors for NUTI have shown that the most important factor was urinary catheterization (22). It is reported that the risk of acquiring a UTI depends on the method and duration of catheterization, the quality of catheter care, and host susceptibility (23). Urinary tract infections were identified in approximately 30% of patients with urinary catheters within two weeks and virtually 100% at six weeks (24).

In the present series, a large proportion of the patients with NUTI (83.7%) had urinary catheters and the most frequent risk factor was the use of urinary catheters, followed by diabetes mellitus, female gender and advanced age, a finding consistent with the literature (5–7). Indeed, urinary catheterization increased the rate of NUTI by 3.83 times compared to the rate of other NIs. In addition, *Candida spp, Pseudomonas spp, Enterobacter spp* and methicillin-resistant coagulase negative staphylococci were isolated in specimens from patients with urinary cathe-ters but not in specimens from patients without a urinary catheter. Consistent with the results of numerous studies, this study revealed that Gram-negative bacteria and candida played an important role in development of NUTI, especially in patients with urinary catheters.

The results of this study showed that the rate of resistance to widely used antibiotics was high for gram-negative bacteria. The most effective antibiotics against gram-negative bacteria were imipenem and meropenem. Cefuroxime, cotrimoxazole, ampicillin-sulbactam**,** amoxicillin/clavulanate, gentamycin and tobramycin which are most frequently used for the treatment of community-based infections were the least sensitive antibiotics for the gram-negative micro-organisms. The most important reason for resistance to antibiotics is the widespread use of antibiotics in hospitals. Particularly the use of beta-lactam antibiotics, new generation cephalosporins and fluoroquinolones may cause multi-drug resistant micro-organisms (25, 26). The micro-organisms and their resistance patterns vary from hospital to hospital and even from clinic to clinic in the same hospital (27). In order to prevent or decrease resistance to antibiotics, the use of antibiotics should be kept under supervision, should be given in appropriate doses for an appropriate period of time and control programmes for hospital infections should be carried out. A multidisciplinary approach should be used to achieve the above mentioned goals. Haley *et al* (28) found that a surveillance programme decreased the incidence of UTIs. An active surveillance programme for NI is practised in our hospital and the hospital staff are informed regularly about micro-organisms detected and their sensitivities to antibiotics. In this study, the authors found the rate of NI as 2.1% (618/29778), which is compatible with that in the literature (29, 30).

It has been shown that the presence of an indwelling urethral catheter predisposes to urinary tract infection (6). Several studies have indicated that between 75% and 80% of all healthcare associated UTIs follow the insertion of a urinary catheter (31, 32). In the authors' opinion, one of the most important risk factors is the use of urinary catheters.

Therefore, urinary catheters should only be used when required, should be inserted under aseptic conditions and cleaned daily, should not be left in place for a long time, closed drainage systems should be used when possible and suprapubic catheters should be used in selected cases. Elderly patients, females and diabetics are prone to NUTI, so caution should be taken when a urinary catheter is inserted into such patients. In addition, culture results and antibiotic sensitivities should be taken into account when the treatment is planned and antibiotics with a narrow spectrum should be preferred. Furthermore, causative micro-organisms of NUTI and their resistance patterns should be regularly investigated and the treatment protocols should be updated accordingly. Each ICU should have an annual review of its microbial flora and its antibiotic susceptibility pattern, which would help in formulation of a rational antibiotic policy.

ACKNOWLEDGEMENTS

We would like to thank all the staff of Baskent University, Adana Training and Research Hospital, for their kind assistance during this study

REFERENCES

1. Saint S, Lipsky BA. Preventing catheter-related bacteriuria: should we? Can we? How? Arch Intern Med 1999; **159:** 800–8.
2. Merle V, Germain JM, Bugel H, Nouvellon M, Lemeland JF, Czernichow P et al. Nosocomial urinary tract infections in urologic patients: assessment of a prospective surveillance program including 10,000 patients. Eur Urol 2002; **41:** 483–9.
3. Givens CD, Wenzel RP. Catheter-associated urinary tract infections in surgical patients: A controlled study on the excess morbidity and costs. J Urol 1980; **124:** 646–8.
4. Medina M, Martinez-Gallego G, Sillero-Arenas M, Delgado-Rodriguez M. Risk factors and length of stay attributable to hospital infections of the urinary tract in general surgery patients. Enferm Infecc Microbiol Clin 1997; **15:** 310–4.
5. Mulhall AB, Chapman RG, Crow RA. Bacteriuria during indwelling urethral catheterization. J Hosp Infect 1988; **11:** 253–62.
6. Stamm WE. Nosocomial urinary tract infections. In: Bennett JV, Brachman PS (eds). Hospital Infections. Third ed. Boston: Little, Brown and Co, 1992: 597–610.
7. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH 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.
8. Grubenberg GN. Antibiotic sensitivities of urinary pathogens: 1971-1982. J Antimicrob Chemother 1984; **14:** 17–23.
9. Fridkin SK, Steward CD, Edwards JR, Pryor ER, McGowan JE Jr, Archibald LK et al. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. Project Intensive Care Antimicrobial Resistance Epidemiology (ICARE) hospitals. Clin Infect Dis 1999; **29:** 245–52.
10. Sahm DF, Marsilio MK, Piazza G. Antimicrobial resistance in key bloodstream bacterial isolates: electronic surveillance with the Sur-veillance Network Database-USA. Clin Infect Dis 1999; **29:** 259–63.
11. National Nosocomial Infections Surveillance (NNIS) System report, data summary from January 1990-May 1999, issued June 1999. Am J Infect Control 1999; **27:** 520–32.
12. Winstanley TG, Limb DI, Eggington R, Hancock F. A 10 year survey of the antimicrobial susceptibility of urinary tract isolates in the UK: The Microbe Base project. J Antimicrob Chemother 1997; **40:** 591–4.
13. Trienekens T, Stobberingh E, Beckers F, Knottnerus A. The antibiotic susceptibility patterns of uropathogens isolated from general practice patients in southern Netherlands. J Antimicrob Chemother 1994; **33:** 1064–6.
14. Garau J, Xercavins M, Rodriguez-Carballeria M, Gomez-Vera JR, Coll I, Vidal D et al. Emergence and dissemination of quinolone-resistant Eschenchia coli in the community. Antimicrob Agents Chemother 1999; **43:** 2736–41.

15. Aguiar JM, Chacon J, Canton R, Baquero F. The emergence of highly fluoroquinolone-resistant *Escherichia coli* in community-acquired urinary tract infections. J Antimicrob Chemother 1992; **29:** 349–50.
16. Beck-Sague CM, Jarvis WR. Secular trends in the epidemiology of nosocomial fungal infections in the United States, 1980-1990. National Nosocomial Infections Surveillance System. J Infect Dis 1993; **167:** 1247–51.
17. Schaberg DR, Culver DH, Gaynes RP. Major trends in the microbial etiology of nosocomial infection. Am J Med 1991; **91 (suppl 3B):** 72S-75S.
18. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988; **16:** 128–40.
19. Tolkoff-Rubin NE, Cotran RS, Rubin RH. Urinary tract infection, pyelonephritis and reflux nephropalhy. In: Brenner BM, (editor) Brenner & Rector's - The Kidney, 6th ed Vol 11 Philadelphia: WB Saunders; 2000: 1449–508.
20. Collee JG, Miles RS, Watt B. Tests for the identification of bacteria. In: Collee JG, Fraser AG, Marmion BP, Simmons A (editors). Mackie and McCartney. Practical Medical Microbiology 14th ed. London: Churchill Livingstone 1996: 131–45.
21. National committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility tests NCCLS document M2-A7, Approved Standard, 7th edition: Wayne, PA: NCCLS, 2000.
22. Bronsema DA, Adams JR, Pallares R, Wenzel RP. Secular trends in rates and etiology of nosocomial urinary tract infections at a university hospital. J Urol 1993; **150:** 414–6.
23. Wong ES. Guideline for prevention of catheter- associated urinary tract infection. Am J Infect Control 1983; **11:** 28–36.
24. Kirby RR, Taylor RW, Civetta JM. Nosocomial infection. In: Handbook of Critical Care. 2nd ed. Philadelphia (PA): Lippincott-Raven; 1997: 821–31.
25. Edmond MB, Wenzel RP. Organization for infection control. In: Mandell GL Bennett JE, Dolin R, eds. Principles and Practice of Infectious Diseases. 5th ed Philadelphia: Churchill Livingstone, 2000: 2988–91.
26. Khurana CM, Wojack BR. Prevalence of ciprofloxacin resistance in multi resistant Gram negative intensive care unit isolates. Infection 1994; **22 (Suppl 2):** S99–104.
27. Snydman DR. Clinical implications of multi-drug resistance in the intensive care unit. Scant J infect Dis 1991; **78:** 54–63.
28. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol 1985; **121:** 182–205.
29. Lizioli A, Privitera G, Alliata E, Antonietta Banfi EM, Boselli L, Panceri ML et al. Prevalence of nosocomial infections in Italy: result from the Lombardy survey in 2000. J Hosp Infect 2003; **54:** 141–8.
30. Leblebicioglu H, Esen S. Turkish Nosocomial Urinary Tract Infection Study Group. Hospital-acquired urinary tract infections in Turkey: a nationwide multicenter point prevalence study. J Hosp Infect 2003; **53:** 207–10.
31. Bryan CS, Reynolds KL. Hospital-acquired bacteraemic urinary infection: epidemiology and outcome. J Urol 1984; **132:** 494–8.
32. Turck M, Stamm W. Nosocomial infection of the urinary tract. Am J Med 1981; **70:** 651–4.