Hospital acquired urinary tract infections in urology departments: pathogens, susceptibility and use of antibiotics: Data from the PEP and PEAP-studies

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on behalf of the PEP and PEAP-study investigators and the board of the European Society of Infections in Urology[1]

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Abstract

Data from two internet-based studies on NAUTI in hospitalized urological patients are presented together: the Pan European Prevalence (PEP) study, which was a 1-day prevalence study in November 2003; and the Pan Euro-Asian Prevalence (PEAP) study, which was carried out in November 2004. Overall, 93 and 101 hospitals from the two studies, respectively, completed the hospital questionnaires and provided patient information for the present study. NAUTI was diagnosed according to the Centres for Disease Control and Prevention (CDC) criteria in 727 of the 6033 patients hospitalized on study days in urological departments. The most commonly reported pathogen was *Escherichia coli* (31%), followed by species of *Pseudomonas* (13%), *Enterococcus* (10%), *Klebsiella* (10%), *Enterobacter* (6%) and *Proteus* (6%). *Candida* spp. and *Pseudomonas* spp. occurred significantly more frequently as causative agents in urosepsis than in other types of infections. The resistance of *E. coli*, *Klebsiella* and *Proteus* spp. was below 45% for the most commonly used antibiotics. *Enterococcus* spp. and *Pseudomonas* spp. however, had resistance rates above 70% to most antibiotics. A total of 56% of the hospitalized urological patients were receiving antimicrobial therapy on the study day; 46% for prophylaxis, 26% for microbiologically proven UTI, 21% for only clinically suspected UTI and 7% for other infections. The most commonly used antibiotics were fluoroquinolones (35%), cephalosporins (27%), penicillins (16%), aminoglycosides (15%), and co-trimoxazole (9%). Differences between countries and regions were highly significant. There is an urgent need for continuous surveillance of NAUTI and improvement of antibiotic policy to counteract the widespread increase of antimicrobial resistance.

Keywords: Urinary tract infection (UTI), Prevalence study, Antibiotic resistance, Antibiotic use

1. Introduction

Urinary tract infections (UTIs) are among the most common community-acquired infection; the types of pathogens and the susceptibility of pathogens are well described [1]. In some regions, however, a rising resistance rate is a cause of concern [2]. UTIs are also the most common nosocomially acquired infection [3], [4]. The spectrum and susceptibility of these infections is different from that of community-acquired infections and they are more difficult to treat. Most published data of UTIs are in patients in intensive care units [5]. Nosocomially acquired UTIs (NAUTI) occurring in urological departments may be even more difficult to treat due to complicating factors such as urinary tract obstruction, stones, and reduced kidney function. Although UTIs may occur as a complication of any type of surgery, the detrimental effect on the outcome of surgery is of particular importance in urology. Little is known about the spectrum and the susceptibility of pathogens in urology departments in an international perspective. Pathogens may spread between patients, and health personnel may act as carriers [6]. Since pathogens do not respect national boundaries, and the transport of patients and health personnel is increasing, we decided to study this on an international level [7]. The aim of this paper is to present the data on pathogens, susceptibility, and use of antibiotics from the Pan European Prevalence (PEP) and the Pan Euro-Asian Prevalence (PEAP) studies. More detailed results on the internet application, the data collection, and the prevalence of NAUTI in regard to clinical aspects, regions and countries are reported elsewhere [8].

2. Materials and methods

2.1. Protocol and organisation

The studies were initiated and organized by the board of the European Society of Infections in Urology (ESIU), which is a scientific section within the European Association of Urology (EAU). Both studies were fully sponsored by the EAU. Both studies were carried out in collaboration with the European Study Group on Nosocomial Infections (ESGNI), a working group of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID); the International Society of Chemotherapy for Infection and Cancer (ISC); the Federation of European Societies for Chemotherapy and Infection (FESCI); and the Asian Association of UTI/STD (sexually transmitted diseases) in the PEAP study.

The study protocols were prepared by the board of the ESIU and accepted by the EAU and the collaborating associations. The studies were announced during ESIU and EAU meetings, through European Urology Today (The newspaper of the EAU), through mass mailings to members of the collaborating organisations and personal E-mails.

The question of ethical approval was the responsibility of each study centre. Since all patient data were reported anonymously to the study database, no investigator decided to ask for a formal approval of the protocol by the regional ethical committees.

The first study (PEP-study) was carried out as a 1-day prevalence study on one of two Wednesdays in November 2003. The investigators were free to choose the study day that best fitted themselves. The second study (PEAP-study) was carried out as a 1-day prevalence study on one of three Wednesdays in November 2004. The study organizers wanted the registration to take place in the middle of a regular working week. Several study days could be chosen because of national variations in terms of scientific meetings and holidays.

The PEP and PEAP-studies used the definitions of NAUTI worked out by the Centres for Disease Control and Prevention (CDC) in the USA [9].

2.2. Data assembly and Internet application

Patients with NAUTI were identified by local urologists or microbiologists. Hospital characteristics, risk factors and use of antibiotics were registered and reported according to two questionnaires; one characterizing the hospital and another characterizing each patient with NAUTI. Details on risk factors are elaborated elsewhere [8]. Risk factors such as urinary catheters were only registered if present on study days.

All microbiological cultures were analysed in the local laboratories. Colony counts and standards used for susceptibility testing are presented in the results section.
The study was carried out electronically by means of Uroweb, the Internet portal of the EAU. The Internet application and the system for data assembly have been reported previously [7]. The study application has a predefined workflow. After registration, the respondent fills in the 'hospital report form'. When this form has been submitted, the 'patient reply form' becomes available. The system allows the investigators to fill in only a part of the 'patient report form', save the patient information, and come back at a later time to complete their work before submitting the forms. Investigators were also given the opportunity to submit handwritten report forms, which were later entered into the study database by the study organizers. Handwritten forms were only submitted by three investigators.

2.3. Evaluation of patients, specimens and countries

On the study day, the urological investigator evaluated all hospitalized patients in the urology department for NAUTIs, according to the CDC criteria, i.e. infections not present at the time of the patient's admission to hospital [9]. Patient data were not reported to the study database until all results of culture tests were available. Deadline for data entry was the last day of the corresponding study year.

Investigators from 216 hospitals registered for the PEP study, Investigators from 93 hospitals completed the registration form and were included in the study. Investigators from 210 hospitals registered for the PEAP study. Investigators from 101 hospitals filled in the registration form and were included in the study. Data from 194 hospitals, 42 of which were included in both studies, were eligible for the final analysis that comprised of 727 cases of NAUTI. When calculating the antibiotic usage of all hospitalized patients in the urology departments, each department was only included once. For departments that participated in both the PEP and PEAP studies, only data from the PEAP study were used. Overall, 4706 patients from a total of 6033 patients hospitalized on the study day in all departments were included in the analyses. This was done to avoid regimes of departments participating in both studies and thereby weighing more than those departments participating in one only study. The regional recruitment of investigators is listed in the

Appendix. In order to obtain groups of hospitals suitable for regional comparisons, the countries with the greatest recruitment, such as Turkey, Hungary, Germany and Russia, were considered as separate units, while the Asian countries were assembled in one group called 'Asia', and the other European countries were assembled in another group called 'Europe'.

2.4. Data processing and statistics

Study data were imported from the web-based survey into Microsoft Access. They were reorganized and imported into SPSS 13.0. The data were then coded and analysed in SPSS 13.0. This article mainly presents observed frequencies. Where dichotomous data are compared, the odds ratios (OR) and 95% confidence intervals (CI) have been computed alongside P-values from Chi-square tests and Fischers exact tests. When comparing other categorical data, the Chi-square test is used. To assess the most important risk factors for infections with the different pathogens, a logistic regression was used. To compare continuous variables for different regions and hospital types, ANOVA with Bonferroni as post-hoc test was used.

3. Results

3.1. Pathogens

3.1.1. Types of pathogens and numbers of colony forming units (CFU)/mL in urine

A total of 727 cases with NAUTI were reported, of which 527 (74%) were declared by the investigators to be microbiologically proven. The diagnosis of microbiologically proven infections in these 527 patients was based on 495 urine cultures (91%), 38 blood cultures (7%) and 12 cultures from other sources (2%). However, only in 486 patients were urinary pathogens specified. In 83/486 patients (17%), a second pathogen was also reported. The amount of bacteriuria (CFU/mL) reported for the first pathogen was 105/mL

for 79% of pathogens, 104/mL for 13%, 103/mL for 6% and 102/mL for 2%, and for the second pathogen, the amount of bacteriuria was 105/mL for 73%, 104/mL for 17%, 103/mL for 4% and 102/mL for 5% of pathogens. The most common pathogen was E. coli followed by species of Pseudomonas, Enterococcus, Klebsiella, Enterobacter and Proteus. Candida sp. and coagulase-negative staphylococci (CNS) were mainly found in mixed cultures. The relative distribution of the pathogens is shown in Table 1.

Species	**Germany**	**Hungary**	**Russia**	**Turkey**	**Europe**[a]	**Asia**	**Total**
	N(%)	*N(%)*	*N(%)*	*N(%)*	*N(%)*	*N(%)*	*N(%)*
Escherichia coli	20(27)	49(30)	35(36)	22(49)	25(21)	24(35)	175(31)
Pseudomas	5(7)	24(15)	17(17)	5(11)	15(12)	9(13)	75(13)
Enteroccus	8(11)	20(12)	3(3)	4(9)	18(15)	6(9)	59(10
Klebsiella	7(10)	10(6)	12(12)	7(16)	12(10)	8(12)	56(10)
Enterobacter	8(11)	12(7)	3(3)	1(2)	4(3)	5(7)	33(6)
Proteus	3(4)	9/6)	20(20)	1(2)	1(1)	1(1)	35(6)
CNS[b]	6(8)	13(8)	0(0)	2(4)	5(4)	1(1)	27(5)
Candida	4(5)	6(4)	0(0)	0(0)	(8/7)	4(6)	87(15)
Others	12(16)	20(12)	8(8)	3(7)	33(27)	11(16)	87(15)
TOTAL	73(100)	153(100)	98(100)	45(100)	121(100)	69(100)	569(100)

a Other European countries.
b CNS, coagulase-negative staphylococci.

Table 1. Distribution of microbial species in various regions and countries in 486 patients with nosocomially acquired urinary tract infection (83 patients had two urinary pathogens)

3.1.2. Pathogens and risk factors

All 727 (100%) patients with the diagnosis of NAUTI were considered for determining the frequency of risk factors. However, the odds ratios were only calculated from the 486 patients where pathogens were reported. This was done to counter the fact that a causative pathogen was reported significantly more often in patients with risk factors than in those without.

The following risk factors were correlated with the presence of specific pathogens: UTI during the previous 12 months; urinary tract obstruction; urinary stones; antibiotic therapy during the previous 3 months; hospitalization during the previous 6 months; and urinary catheter.

3.1.3. UTI during the previous 12 months

Overall, 312 patients (44%) were reported as having a previous UTI as a risk factor. For patients having had a UTI during the previous 12 months, there was a significantly increased risk of having a *Klebsiella* sp. as a causative pathogen ($P = 0.03$, OR 1.9; 95% CI 1.1–3.5).

3.1.4. Urinary tract obstruction

A total of 353 patients (49%) were considered as having a significant urinary tract obstruction at any level according to evaluation by the local urologist. For patients with a significant urinary tract obstruction, there was a significantly reduced risk of having a *Proteus* sp. as a causative pathogen ($P = 0.01$, OR 0.39; 95% CI 0.19–0.82).

3.1.5. Urinary stones

In total, 143 patients (20%) were reported as having a urinary stone as a risk factor for developing NAUTI.

For the group as a whole, there were no significant differences in the occurrence of pathogens. For patients having stones in the ureter, there was an increased risk of having a *Pseudomonas* sp. as a causative pathogen ($P = 0.02$, OR 2.4, 95% CI 1.1–5.5).

3.1.6. Antibiotic therapy during the previous 3 months

A total of 307 patients (43%) had received antibiotics for any reason during the previous 3 months. For these patients, the risk of having a *Candida* sp. ($P = 0.05$, OR 2.6; 95% CI 1.0–6.4) or a *Klebsiella* sp. ($P = 0.04$, OR 1.8; 95% CI 1.0–3.3) as causative pathogens was increased, while the risk of having *E. coli* as a causative pathogen was reduced ($P = 0.05$, OR 0.67; 95% CI 0.46–0.98).

3.1.7. Hospitalization during the previous 6 months

Overall, 323 patients (45%) had been hospitalized for any reason during the previous 6 months. For these patients, there was a significantly increased risk of having a *Klebsiella* sp. ($P = 0.004$, OR 2.5; 95% CI 1.4–4.5) as well as a *Pseudomonas* sp. ($P = 0.02$, OR 1.8; 95% CI 1.1–3.0) as causative pathogens, and a reduced risk of having *E. coli* as a causative pathogen ($P = 0.04$, OR 0.66; 95% CI 0.46–0.97).

3.1.8. Urinary catheter

A total of 537 patients (74%) had some kind of urinary catheter on study day. The median duration of catheter use was 6 days for urethral catheters, 9.5 days for suprapubic catheters, 11 days for ureteral and 13 days for nephrostomy tubes. For patients with urinary catheter of any type, there was a significantly increased risk of a *Pseudomonas* sp. as a causative pathogen ($P = 0.02$, OR 2.7; 95% CI 1.2–6.0). There was an increased risk of a *Proteus* sp. as a causative pathogen in patients with suprapubic catheter ($P = 0.05$, OR 2.4; 95% CI 1.0–5.5), and an increased risk of a *Candida* sp. as a causative pathogen in patients with ureteral stent ($P = 0.03$, OR 3.2; 95% CI 1.2–8.7).

The duration of catheter use was divided into three categories: no catheter use; use <5 days; and use ≥6 days. The duration of catheter use resulted in a significant linear increase in the occurrence of *Candida* sp. ($P = 0.05$), *Enterococcus* sp. ($P = 0.04$) and *Proteus* sp. ($P = 0.02$), and a significant linear decrease in the occurrence of *E. coli* ($P = 0.02$) and an *Enterobacter* sp. ($P = 0.02$).

3.1.9. Multiple risk factors

In total, 65 patients had none of the risk factors listed above. However, 119 patients had one risk factor, 146 had two, 121 had three, 260 had more than three and 16 patients had missing data. For patients having more than three risk factors, there was a significantly increased risk of having a *Candida* sp. as a causative pathogen ($P = 0.02$, OR 2.8; 95% CI 1.2–6.8) as well as *Klebsiella* ($P = 0.008$, OR 2.2; 95% CI 1.2–3.8) and a *Pseudomonas* sp. ($P = 0.01$, OR 2.0; 95% CI 1.2–3.2), when compared to those patients with three or less risk factors.

3.1.10. Relation to type of urological intervention and contamination status

A surgical intervention was reported to have aetiological importance for the development of NAUTI in 588 patients (81%). The surgical intervention could have taken place at any time during the present hospital stay. Overall, 27 patients underwent more than one procedure. The most common interventions were endoscopic procedures (38%) and open surgery (30%). A total of 43% of all procedures were clean, and 28% were contaminated or infected. More details concerning surgical interventions are presented elsewhere [8]. There was no significant association between the type of surgery or the contamination status and the distribution of any bacterial species.

3.1.11. Logistic regression analysis of risk factors and pathogens

A logistic regression analysis was used to assess the most important risk factors for detecting a certain causative pathogen. The findings for each pathogen were analysed with forward logistical regression. Risk factors, contamination status of surgical intervention, age and gender were included in the analysis.

The only significant risk factor for detecting *E. coli* was catheter duration category (no catheter; ≤5 days; >5

days) (P = 0.17, OR 0.72; 95% CI 0.54–0.94 per level). The occurrence of *E. coli* as a causative pathogen decreased with the period of catheterization. The odds of having an infection with *E. coli* was reduced by 0.72 for each level of increased catheter duration compared to no catheter.

The factors that significantly predicted a *Candida* sp. were laparoscopic intervention (P = 0.010, OR 9.5; 95% CI 1.7–53.1) and having an increased number of risk factors (P = 0.011, OR 1.5; 95% CI 1.1–2.1 per risk factor).

The only significant factor predicting an *Enterobacter* sp. was catheter duration category (P = 0.027, OR 0.58; 95% CI 0.36–0.94 per level). The odds of having an infection with an *Enterobacter* sp. was reduced by 0.58 for each level of increased catheter duration compared to no catheter.

Endoscopic intervention (P = 0.034, OR 0.51; 95% CI 0.27–0.954) was the only significant factor predicting an *Enterococcus* sp. Hospitalization during the last 6 months (P = 0.011, OR 2.2; 95% CI 1.2–4.1) was the only significant factor predicting a *Klebsiella* sp.

The factors that significantly predicted a *Proteus* sp. were hospitalization for any reason within the last 6 months (P = 0.012, OR 3.6; 95% CI 1.3–9.8), suprapubic catheter (P = 0.019, OR 2.9; 95% CI 1.2–7.1), other catheter types, i.e. not urethral, suprapubic, ureteral stent or nephrostomy catheters (P = 0.038, OR 5.9; 95% CI 1.1–31.3), and increasing number of risk factors (P < 0.001, OR 0.52; 95% CI 0.36–0.74).

The factors that significantly predicted a *Pseudomonas* sp. were catheter of any kind (P = 0.032, OR 4.9; 95% CI 1.1–20.6) and increasing number of risk factors (P = 0.010, OR 1.3; 95% CI 1.1–1.5 per risk factor).

3.1.12. Relation to clinical presentation of the NAUTI

The clinical diagnosis of a urogenital infection was given to 686 of 727 (94%) patients with NAUTI. Asymptomatic bacteriuria was the most common type of NAUTI, accounting for 29%, followed by cystitis (26%), pyelonephritis (21%), urosepsis (12%) and others (12%).

A *Candida* sp. occurred significantly more frequently as a causative agent in patients with urosepsis (13%) than in those with other types of infections (2–5%) (P = 0.05). The distribution of causative pathogens in patients with urosepsis was most similar to those causing asymptomatic UTIs. The occurrence of pathogens for each clinical diagnosis is presented in Table 2.

Type of NAUTI	***E. coli***	***Pseudomonas***	***Enterococcus***	***Klebsiella***	***Proteus***	**Enterobac-ter**	**Candida**
	N (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Asymptomatic (*N* = 157)	56 (36)	26 (17)	22 (14)	11 (7)	15 (10)	6 (4)	7 (5)
Cystitis (*N* = 127)	49 (39)	15 (12)	15 (12)	12 (9)	8 (6)	12 (9)	3 (2)
Pyelonephritis (*N* = 97)	35 (37)	16 (17)	9 (9)	17 (18)	7 (7)	7 (7)	3 (3)
Urosepsis (*N* = 61)	19 (31)	14 (23)	10 (16)	9 (15)	2 (3)	2 (3)	8 (13)
Others (*N* = 39)	12 (31)	4 (10)	1 (3)	5 (13)	3 (8)	4 (10)	1 (3)
Unknown (*N* = 5)	2 (40)	0 (0)	2 (40)	1 (20)	0 (0)	1 (20)	0 (0)
Total (*N* = 486)	173 (36)	75 (15)	59 (12)	55 (11)	35 (7)	32 (18)	22 (5)

E. coli, *Escherichia coli*.

Table 2. Distribution of the most common microbial species related to the clinical diagnosis of nosocomially acquired urinary tract infection (NAUTI) in 486 patients (83 patients had two urinary pathogens)

3.1.13. Comparison between regions and countries

When all types of infections were considered together, the distribution of *E. coli* varied from 21% in Europe to 49% in Turkey, but the differences were not significant. The most significant difference in regional distribution was seen for *Proteus* sp., which was reported in 20% of cases in Russia and in only 1–6% of cases in the other regions studied ($P < 0.001$). *Enterococcus* sp. was the causative agent in 3% of cases in Russia and varied from 9% to 15% in the other regions ($P = 0.032$). *Candida* sp. was seen in 7% of cases in 'other European countries', but was not seen at all in Russia or Turkey ($P = 0.009$). The relative occurrence of the most important pathogens is shown in Table 1. When the different regions were added to the list of risk factors in the logistical regression analysis, a significant effect of the regions was observed on the occurrence of *Enteroccous* sp. and *Proteus* sp. There was a significant difference between regions in the reported frequency of a second pathogen, varying from 24% in Europe, 22% in Germany, to 10% in Turkey.

The proportion of microbiologically proven infections, based on a first pathogen count of 105/mL, varied from 70% in Russia to 83% in Hungary. For a pathogen count of 104/mL this proportion varied from 10% in Hungary to 20% in Turkey. A pathogen count of 103/mL was reported in 11% of cases from Russia, 8% in Turkey and 7% in Asia. In Europe, 5% of cases had a pathogen count of 102/mL. A pathogen count of <103/mL was rarely (<5% of the cases) used in the other regions. No significant statistical differences were found between regions in the use of pathogen counts.

3.2.Susceptibility

Information about the standard used for susceptibility testing was provided for 451 of the 486 cases with reported susceptibility results. The National Committee for Clinical Laboratory Standards (NCCLS) was used in 69% of cases, the Deutsches Institut für Normung (DIN) standard in 25% and 'other standards' in 6% of cases. DIN was most frequently used in Germany (69%) but was not used in Russia. NCCLS was most frequently used in Russia (99%) and Turkey (92%) and least frequently in Germany (18%). 'Other standards' were described as 'quantified', 'automated' or 'bioassay'.

The susceptibility rates of all bacterial pathogens (Candida sp. and other fungi were excluded) to the most commonly used antimicrobials are shown in Table 3. These rates varied from 79% in Turkey (resistance to co-trimoxazole) to 17% in Germany (resistance to ampicillin/amoxicillin + β-lactamase inhibitor). In general, there were higher resistance rates in Europe, Asia and Turkey than in either Germany, Hungary or Russia. This was particularly the case for ampicillin/amoxicillin and co-trimoxazole.

Country/region	N	*Escherichia coli*			N	Total bacterial spectrum		
		S (%)	I (%)	R (%)		S (%)	I (%)	R (%)
A. Ampicillin/amoxicillin + β-lactamase inhibitor								
Germany	11	6 (55)	5 (45)	0 (0)	35	21 (60)	8 (23)	6 (17)
Hungary	35	24 (69)	2 (6)	9 (26)	97	59 (61)	4 (4)	34 (35)
Russia	35	16 (46)	13 (37)	6 (17)	77	30 (39)	28 (36)	19 (25)
Turkey	11	2 (18)	1 (9)	8 (73)	25	4 (16)	3 (12)	18 (72)
Europe[a]	11	8 (73)	1 (9)	2 (18)	44	19 (43)	2 (5)	23 (52)
Asia	23	11 (48)	3 (13)	9 (39)	49	17 (35)	6 (12)	26 (53)
Total	126	67 (53)	25 (20)	34 (27)	327	150 (46)	51 (16)	126 (39)
B. Susceptibility to cefuroxime (or second generation cephalosporins)								
Germany	17	16 (94)	0 (0)	1 (6)	47	33 (70)	2 (4)	12 (26)
Hungary	37	31 (84)	2 (5)	4 (11)	98	59 (60)	3 (3)	36 (37)
Russia	29	14 (48)	9 (31)	6 (21)	59	24 (41)	21 (36)	14 (24)
Turkey	17	8 (47)	0 (0)	9 (53)	25	9 (36)	1 (4)	15 (60)

Europe[a]	19	14 (74)	2 (11)	3 (16)	45	22 (49)	5 (11)	18 (40)
Asia	11	4 (36)	4 (36)	3 (27)	28	7 (25)	7 (25)	14 (50)
Total	130	87 (67)	17 (13)	26 (20)	302	154 (51)	39 (13)	109 (36)
C. Susceptibility to cefotaxime/cetriaxone (or third generation cephalosporins)								
Germany	10	10 (100)	0 (0)	0 (0)	36	28 (78)	1 (3)	7 (19)
Hungary	33	29 (88)	2 (6)	2 (6)	86	54 (63)	6 (7)	26 (30)
Russia	33	26 (79)	5 (15)	2 (6)	76	46 (61)	10 (13)	20 (26)
Turkey	13	6 (46)	0 (0)	7 (54)	29	9 (31)	0 (0)	20 (69)
Europe[a]	14	11 (79)	1 (7)	2 (14)	48	22 (46)	3 (6)	23 (48)
Asia	18	11 (61)	2 (11)	5 (28)	46	24 (52)	6 (13)	16 (35)
Total	121	93 (77)	10 (8)	18 (15)	321	183 (57)	26 (8)	112 (35)
D. Susceptibility to ciprofloxacin								
Germany	14	12 (86)	0 (0)	2 (14)	50	34 (68)	2 (4)	14 (28)
Hungary	42	29 (69)	2 (5)	11 (26)	120	78 (65)	6 (5)	36 (30)
Russia	34	24 (71)	6 (18)	4 (12)	93	40 (43)	18 (19)	35 (38)
Turkey	16	2 (13)	1 (6)	13 (81)	35	8 (23)	2 (6)	25 (71)
Europe[a]	20	14 (70)	0 (0)	6 (30)	70	32 (46)	4 (6)	34 (49)
Asia	21	6 (29)	3 (14)	12 (57)	49	12 (24)	7 (14)	30 (61)
Total	147	87 (59)	12 (8)	48 (33)	417	204 (49)	39 (9)	174 (42)
E. Susceptibility to co-trimoxazole								
Germany	19	13 (68)	2 (11)	4 (21)	58	42 (72)	3 (5)	13 (22)
Hungary	35	28 (80)	1 (3)	6 (17)	82	48 (59)	3 (4)	31 (38)
Russia	29	8 (28)	13 (45)	8 (28)	55	11 (20)	22 (40)	22 (40)
Turkey	13	3 (23)	0 (0)	10 (77)	29	4 (14)	2 (7)	23 (79)
Europe[a]	20	10 (50)	1 (5)	9 (45)	77	27 (35)	5 (6)	45 (58)
Asia	16	2 (13)	0 (0)	14 (88)	39	9 (23)	2 (5)	28 (72)
Total	132	64 (48)	17 (13)	51 (39)	340	141 (41)	37 (11)	162 (48)

A.Other European countries; N, total number of strains; S, susceptible; I, intermediate; R, resistant.

Table 3. Susceptibility of Escherichia coli and of the total bacterial spectrum to the most commonly used antibiotics

For the most commonly used antimicrobials, Russia and Asia had a significantly higher proportion of reported intermediate resistance than the other regions/countries, indicating a difference in practice among microbiological laboratories.

The most favourable sensitivity for all bacterial pathogens when taken together was for imipenem, with rates of 98% in Russia, 92% in Turkey, 91% in Hungary, 89% in Germany, 84% in Asia and 83% in Europe.

3.2.1. Individual pathogens

The susceptibility of *E. coli*, *Klebsiella* sp. and *Proteus* sp. to the most commonly used antimicrobials showed resistance rates below 45% for most antibiotics. However, *Enterococcus* sp. and *Pseudomonas* sp. had resistance rates that were greater than 70% to most antibiotics, with the exception of *Enterococcus* sp., which had a resistance rate of 25% to ampicillin/amoxicillin. The number of cultures that were tested for susceptibility to a specific antibiotic varied from 147 (for *E. coli* susceptibility to ampicillin) to 14 (for *Enterococcus* sp. susceptibility to ampicillin + β-lactamase inhibitor) cultures. The average number of cultures tested was 49.

Detailed information on the susceptibility of *E. coli* and the other pathogens was obtained from 121 to 147 and 14–51 cultures, respectively, from the different regions. Thus, only data for *E. coli* allowed for a stratification of susceptibility between regions. However, for individual countries, the numbers of samples were still rather small, i.e. the number of samples tested for co-trimoxazol was only 13 in Turkey. Nevertheless, the differences between countries and regions were highly significant ($P < 0.001$). For most antibiotics tested, there seems to be an increasing resistance as one moves from west to east in the regions/countries studied, as illustrated by the lowest (6%) resistance to cefuroxime in Germany and the highest (88%) resistance to co-trimoxazol in Asia for *E. coli*. Turkey and Asia had the highest resistance rates to all of the most commonly used antimicrobials. The regional susceptibility for *E. coli* and for the total bacterial spectrum is shown in Table 3.

3.3. Use of antibiotics

3.3.1. Patients receiving antibiotics on study day

Of the 4706 hospitalized patients on study day, 2617 were receiving antibiotics (56%). There were no significant differences between the hospitals in terms of the percentage of patients receiving antibiotics on study day. The percentage of patients receiving antibiotics in Turkey was 70%, followed by 66% in Asia, 59% in Russia, 55% in the rest of Europe, 49% in Hungary and 47% in Germany. The use of antibiotics in Turkey was statistically different from that of Hungary and Germany ($P < 0.001$).

Of the 2617 patients receiving antibiotics on study day, 26% of the antibiotic use was for a microbiologically proven UTI, 21% for a clinically suspected, but not microbiologically proven UTI, 7% for other infections, and 46% for prophylaxis. Comparison between regions and countries showed significant differences, with 53% of patients in Russia receiving antibiotics for a suspected UTI, compared to 13% in Germany and 11% in Turkey. While 59% of Asian patients and 58% of Turkish patients received antibiotics for prophylaxis, only 19% of Russian patients received antibiotics for this reason. Details are shown in Table 4.

Indication	Region (*N*)						
	Germany (496)	Hungary (354)	Russia (276)	Turkey (301)	Europe[a] (1044)	Asia (146)	Total (2617)
Proven UTI	27	32	26	26	26	17	26
Suspected UTI	13	25	53	11	18	17	21
Other infections	9	3	2	6	8	7	7
Prophylaxis	51	39	19	58	48	59	48
Total	100	100	100	100	100	100	100

a. Other European countries; UTI, urinary tract infection

Table 4. Indications for use of antibiotics on study day in percent of all hospitalized patients receiving antibiotics per region

When antibiotic use was evaluated by considering the regimen of each department, and by doing the

calculation based on the percent of patients given each regimen, Turkish urology departments used antibiotics for prophylaxis significantly more often than urologists in the other regions except Asia ($P < 0.05$, ANOVA with Bonferoni as post-hoc test). Russia used antibiotics for suspected UTI significantly more often than all other regions and countries ($P < 0.03$, ANOVA with Bonferoni as post-hoc test).

In total, 367 of 673 (55%) patients were receiving antimicrobials at a time when a culture was also taken. There were significant differences between the regions in the frequency of antibiotic use when cultures were taken, ranging form 64% in Asia, 57% in Russia and Hungary, 55% in Turkey, 54% in the rest of Europe to 37% in Germany ($P = 0.01$). 282/367 (77%) cultures were positive with one or two pathogens specified. In total 250 cases of susceptibility testing on the pathogens found in the 367 patients were done on the same antimicrobials given at the time of culture. 103 (41%) were sensitive for the antimicrobials, 29 (12%) were intermediate and 118 (47%) were resistant.

3.3.2. Antibiotics given for treatment of the current episode of NAUTI

Antibiotics given for the treatment of the current episode of NAUTI were reported for 681 of the 727 (94%) patients with NAUTI. For these 681 patients, the most commonly used antibiotics were fluoroquinolones in 35% of cases, followed by cephalosporins, which were administered in 27% of the cases. First generation cephalosporins were only used in 4% of cases while second and third generation cephalosporins were used in 12% and 14% of the cases, respectively. Sixteen percent of the patients received penicillins, of which aminopenicillins with β-lactamase inhibitor were the most commonly used. Aminoglycosides were used in 15% of patients and co-trimoxazol in 8%. Trimethoprim alone was given in less than 1% of cases. Other antibiotics given were imipenem (6%), vancomycin (2%), antifungal drugs (2%) and tetracyclins (2%).

Combinations of antibiotics were most frequently used in Russia, where fluoroquinolones were given to 42% of patients. Aminoglycosides were also most frequently used in Russia (26%), while cephalosporins were mostly used in Asia (53%). Only 5% of German patients received aminoglycosides for treatment. Differences between countries were highly significant. Details of antibiotic usage are shown in Table 5.

	Region (*N*)						
	Germany (81)	Hungary (200)	Russia (123)	Turkey (78)	Europea (112)	Asia (87)	Total (681)
Penicillins	22	15	22	5	23	9	16
Cephalosporins	20	20	36	32	12	53	27
Aminoglycosides	5	12	26	12	13	17	15
Fluoroquinolones	33	40	42	32	29	29	35
Co-trimoxazole /Trimethoprim	17	12	2	6	10	3	9

a Other European countries.

** Based on the 681 patients where antibiotics given were reported. Numbers indicate percent of all patients in each country/region. Some patients received more than one antibiotic.*

*Table 5. Use (%) of the most common antibiotics for treatment of the current episode of nosocomially acquired urinary tract infection (NAUTI)**

Of all the patients known to have an *Enterococcus* sp. as a causative agent, 31% received a penicillin derivative as treatment for the current episode, and 28% of those with a *Pseudomonas* sp. received one of the fluoroquinolones.

The route of antibiotic administration was reported for 660 of the 681 patients with reported antibiotic use for the current NAUTI. A total of 53% of all treatments were administered orally, 38% parenterally, and 9% by both routes. There were highly significant differences ($P < 0.001$) between regions. Details of

administration of antibiotics are given in Table 6.

	Region (*N*)						
	Germany (79)	Hungary (196)	Russia (118)	Turkey (76)	Europe[a] (109)	Asia (82)	Total (660)
Oral	77	73	26	41	52	35	53
Parenteral	15	22	57	57	41	48	38
Both	8	5	17	3	6	17	9
Total	100	100	100	100	100	100	100

a Other European countries.

Table 6. Routes of administration of antibiotic treatment for current nosocomially acquired urinary tract infection (NAUTI) per region or country for all 660 patients with reported administration

4. Discussion

4.1. Methods

There are several weak points in the methodology of this kind of Internet-based study, as has been discussed elsewhere [8]. There was no central laboratory for culturing pathogens. We also did not register in detail the number of antibiotic courses and the specific agents administered during the previous time period that would have enabled a more thorough evaluation of antibiotic usage on the rates of resistance between regions. The two groups 'Europe' and 'Asia' that were established for comparison are very heterogeneous. Additionally, local hospitals also had the sole responsibility for the data reported in other studies on NAUTI [4], [5], [10], [11]. All investigators in our studies used the same definition of NAUTI according to CDC criteria, and most microbiological laboratories used accepted standards for susceptibility testing. We therefore believe that our data from 486 patients, from whom pathogens were reported, give a reliable overview of pathogens, susceptibility and use of antibiotics in nosocomial infections in urology departments in the study areas. To our knowledge, these studies are the first to be carried out on an intercontinental basis in a single medical speciality. However, the results presented here should not be interpreted as representative for the participating countries. In Hungary, Turkey, Germany and Russia, significantly more centres took part in the studies than in other countries. The infection control is usually better in hospitals where doctors are aware of the prevalence and resistance rates, so the situation might well be worse in countries with a poor participation in the PEP and PEAP-studies.

The questionnaires used in the studies asked about 'first' and 'second' pathogen identified by culture. In the clinical situation, the results of culture are usually not known when treatment is started. Our presentation of susceptibility data for first and second pathogens is an attempt to mimic the clinical situation. We believe this information has clinical as well as didactic importance.

4.2. Most important findings

Our most important findings are the regional differences in the distribution of pathogens and the susceptibility patterns, and the differences in the use of antibiotics for prophylaxis and treatment. The high proportion of *Enterococcus* sp., *Pseudomonas* sp. and *Candida* sp. as causative agents in asymptomatic bacteriuria and urosepsis is remarkable. The occurrence of these pathogens is highest in Europe, while the resistance figures for most pathogens are highest in the eastern regions. A similar distribution of pathogens was found in the ESGNI-04-study, which compared the situation in the European Union including Eastern Europe [10].

The pathogens causing NAUTI may come from the patients themselves, from the hospital personnel or neighbouring patients [6]. Significant regional differences have been reported for the susceptibility pattern in community-acquired UTIs [1]. This may be explained by differences in national antibiotic policy. In some countries, antimicrobials are advertised among the public and freely sold over the counter in pharmacies, often upon the recommendation by poorly educated people. There is no doubt that there is overlap between populations of pathogens causing community acquired and hospital acquired infections. Our study provides data about the use of antimicrobials inside urological departments that, to some extent, may explain differences in resistance rates. *Enterococcus* sp. and *Pseudomonas* sp. both have less favourable resistance figures than more conventional pathogens. Most of these pathogens are probably hospital strains developed as opportunists under considerable antibiotic pressure over a longer period of time [12], [13] The increased frequency of these pathogens is a cause of concern and should be monitored on a regular basis.

4.3. Perspectives

Candidal infections are well known in critically ill patients in intensive care units, but have been not previously reported with such a high frequency in urology departments [3]. We believe that one important reason is that major urological surgery is being undertaken with increasing frequency in older patients, many of whom require a longer stay in the intensive care or observation unit. This is supported by the fact that the risk of *Candida* sp. increased with the number of risk factors and that *Candida* sp. was most frequently reported as a causative pathogen in urosepsis compared with the other types of NAUTI. In the ESGNI-study, *Candida* sp. was the causative pathogen in 16.4% of patients with a urinary catheter [10]. Usually, the diagnosis and susceptibility testing of *Candidal* infections need more time, the administration of antimicrobials is more difficult, and the treatment has more side effects. The high frequency of *Candidal* infections is also a cause of concern. With Candiduria it is sometimes difficult to differentiate between infection (treatment) and colonization (no treatment).

The resistance rates to the most commonly used antimicrobials observed in our study are strong arguments for a critical antimicrobial policy as long as there are a limited number of upcoming new antibiotics. Key questions are: What should be copied from the countries with the best rates?; and What should be omitted in countries with unwanted distribution patterns and resistance rates? It is not possible to administer all antibiotics based on culture results. In many cases empiric therapy has to be initiated and then adjusted when microbilogical results become available, which again is only possible if a culture was taken before. From the results obtained from patients reveiving antimicrobials whan a culture was taken it can be seen, that in about half of the cases adjustment would have been necessary; in other words, empiric therapy was only “correct” in about half of the patients. Therefore, it is necessary to base both prophylaxis and treatment on a continuous surveillance of pathogens causing NAUTI in each urology department. This means that one would be able to foresee with greater likelihood which pathogen is the ‘leading pathogen’. In many departments this would require a significant increase in the number of cultures taken. There was a wide range between 5.8 cultures per patient admission and 7 cultures per 1000 patient admissions [8]. A close collaboration between urologists and microbiologists is decisive for good infection control. Facilities for preliminary culture of pathogens inside the urological ward may provide valuable information on a short notice [14].

Almost all cases of NAUTI were considered clinically significant and treated with antibiotics. When antibiotics are administered for treatment there seems to be a good balance between the choice of antimicrobials and the susceptibility patterns of the most common pathogens in most regions. The high use of fluoroquinolones is balanced by a low resistance rate in most regions. However, in Turkey, 29.8% of patients are treated with fluoroquinolones while the reported resistance rate of *E. coli* to this antibiotic was above 80%. Furthermore, in Hungary, Russia and Turkey, the profile of antibiotic use for treatment is quite similar to the profile used for prophylaxis. German urologists give fluoroquinolones to treat a large percentage of patients, but less often (9%) for prophylaxis. Germany has the lowest resistance rates of *E. coli* to fluoroquinolones of all regions. The German practice is in accordance with the recommendations on prophylaxis given in the EAU-guidelines [13]. Protocols on antimicrobial prophylaxis should be based on a regular monitoring of resistance in every hospital.

Because of a possible spread of resistant community-acquired strains to hospitals, urologists should also be concerned with national treatment recommendations for community-acquired UTIs.

The regional differences found in our study should precipitate a new discussion about classification,

reporting of culture results and the use of antimicrobials for prophylaxis and treatment of nosocomial UTIs.

5. Conclusions

In conclusion, 727 cases of NAUTI were reported, of which 527 (72%) were microbiologically proven, and for 486 patients, the pathogens were specified. In 83 of 486 patients (17%), a second pathogen was also reported. The most common pathogen was *E. coli* (31%) followed by species of *Pseudomonas* 13%, *Enterococcus* 10%, *Klebsiella* 10%, *Enterobacter* 6%, and *Proteus* (6%). *Candida* (9.4%) and *Pseudomonas* sp. (23%) occurred significantly more frequently as causative agents in urosepsis (9.4%) than in the other types of infections.

The resistance of the bacterial pathogens to the most commonly used antimicrobials varied from 75% to ampicillin/amoxicillin + β-lactamase inhibitor in Turkey, to 16% resistance to cefotaxime in Germany. In general, there were higher resistance rates in Europe, Asia and Turkey than in Germany, Hungary and Russia.

The resistance of *E. coli*, *Klebsiella* sp. and *Proteus* sp. to the most commonly used antimicrobials was below 45% for most antibiotics. *Enterococcus* sp. and *Pseudomonas* sp., however, had resistance rates to most antibiotics above 70%, with the exception of 25% resistance of *Enterococcus* sp. to ampicillins.

Only data for *E. coli* allowed for a stratification of susceptibility between regions. For most antibiotics tested there seemed to be increasing resistance as one moves from west to east, as illustrated by the lowest resistance to cefuroxime in Germany (6%) and the highest resistance to co-trimoxazole (88%) in Asia. Turkey and Asia had the highest resistance to all of the most commonly used antimicrobials.

In 681 patients, the use of antibiotics for the treatment of the current episode of NAUTI, based on culture results, was reported. The most commonly used antibiotics for this treatment were fluoroquinolones in 35% of cases, cephalosporins in 27%, penicillins in 16%, aminoglycosides in 15% and co-trimoxazol in 9%. Other antibiotics given were imipenem 6%, vancomycin 2%, antifungal drugs in 2% and tetracyclins in 2% of cases.

Combinations of antibiotics were most frequently used in Russia, where fluoroquinolones were given to 42% of patients. Aminoglycosides were also most frequently used in Russia (26%), while cephalosporins were mostly used in Asia (53%). Only 5% of German patients received aminoglycosides for treatment. Differences between countries were highly significant. Overall, the study demonstrates an urgent need for continuous surveillance of NAUTI and improvement of antibiotic policy to counteract the widespread increase of antimicrobial resistance.

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Appendix

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	x	Germany	Bad Soden	Kliniken MTK	Urology	W.		Kramer	wkramer@kliniken-mtk.de
	x	Germany	Bad Wildungen	Klinik Wildetal	Urology	Thomas		Gilbert	der-urologe@web.de
x		Germany	Berlin	Charite Medical School	Urology	Markus	Daniel	Sachs	markus.sachs@charite.de
	x	Germany	Berlin	Berlin NeukÃ¶lln	Urology	Thomas		Zegenhagen	thomas.zegenhagen@vivantes.de
x	x	Germany	Bocholt	St.-Agnes-Hospital	Urology	Dietmar		Bach	urologie@st-agnes-bocholt.de
	x	Germany	Bonn	UniversitÃ¤t Bonn	Urology	Kai Frederik		Schierbaum	schierbaum@aol.com
	x	Germany	Brandenburg an der Havel	Stadtisches Klinikum Brandenburg	Urology	Frank		Benzing	mainzerfb@gmx.de
	x	Germany	Coburg	Klinikum Coburg	Urology	Andreas	Alexander	Weinbuch	walterstrohmaier@klinikum-coburg.de
	x	Germany	Deggendorf	Klinikum Deggendorf	Urology	Michael		Wiese	Michael.Wiese@klinikum-deggendorf.de

Appendix Contd.

PEP-study	PEAP-study	Region	Country	City	Hospital name	Department	First name	Middle name	Last name	E-mail
x			Germany	Dortmund	Klinikum Dortmund gGmbH	Urology	Hans	Jurgen	Knopf	knopfhjwit@t-online.de
	x		Germany	Essen	Universitatsklinikum Essen	Urology	Marcus		Schenck	marcus.schenck@uni-essen.de
x	x		Germany	Frankfurt	Nordwest Krankenhaus	Urology	Daniel		Kappler	d.kappler@gmx.de
x			Germany	Fulda	Klinikum Fulda	Urology	Christoph		Greb	t.kaeble.uologie@klinikum-fulda.de
x	x		Germany	Garmisch-Partenkirchen	Klinikum Garmisch-Partenkirchen	Urology	Petra		Egelhof	petra.egelhof@klinikum-gap.de
x			Germany	Gelsenkirchen	Marienhospital Gelsenkirchen	Urology	Stefan		Becker	U.Rabs@St-Augustinus.de
x	x		Germany	Gera	Waldklinikum Gera	Urology	Lothar		Hoffmann	urologie@waldklinikumgera.de
x			Germany	Giessen	University Hospital Giessen	Urology	Martin		Ludwig	martin.ludwig@chiru.med.uni-giessen.de
	x		Germany	Gotha	Helios-Klinik Gotha/Ohrdruf	Urology	Marco		Teichmann	mteichmann@gotha.helios-kliniken.de
x			Germany	Hamburg	University Hospital Hamburg Eppendorf	Urology	Uwe	H.G.	Michl	michl@uke.uni-hamburg.de
x			Germany	Hameln	Kreiskrankenhaus Hameln	Urologische Klinik	Michael		Baumann	baumann@kreiskrankenhaus-hameln.de
	x		Germany	Hof	Klinikum Hof	Urology	Dagmar		Hoelscher	dagmar_hoelscher@web.de
	x		Germany	Homburg/Saar	Saarland University	Urology	Jan	Erik	Lehmann	Jan.Lehmann@uniklinik-saarland.de
x			Germany	Munchen	Klinikum rechts der Isar	Urology	Ulrich		Sachse	Sachseuli@yahoo.com
x			Germany	Nuernberg	Martha- Maria Hospital	Urology	Orlin	Stojcev	Savov	OSavov@aol.com
x	x		Germany	Regensburg	Krankenhaus St. Josef	Urology	Jens		Lunz	jelu@gmx.de
	x		Germany	Schwedt	Klinikum Uckermark	Urology	Ruediger		Heicappell	ruediger.heicappell@klinikum-uckermark.de
x	x		Germany	Straubing	St. Elisabeth	Urology	Florian	ME	Wagenlehner	wagenlehner@aol.com
x			Germany	Ulm	Military Hospital of Ulm/Germany	Urology	Mathias	Philip	Keilberth	Keilberth-Mathias@t-online.de
	x		Germany	Wuppertal	HELIOS Klinikum Wuppertal	Urology	Theo		Luetgen	tluetgen@wuppertal.helios-kliniken.de
x	x		Hungary	Baja	Baja Hospital	Urology	Levente		Rosztoczy	rosztoczyl@bajakorhaz.hu
x	x		Hungary	Budapest	Uzsoki Hospital	Urology	Andras		Paczelt	apaczelt@uzsoki.hu
x	x		Hungary	Budapest	Semmelweis University	Urology	Imre		Romics	romimre@urol.sote.hu
x	x		Hungary	Budapest	Jahn Ferenc South-Pest	Urology	Peter		Tenke	tenkep@chello.hu
	x		Hungary	Budapest	Bajcsy-Zsilinszky	Urology	Gabor		Prekopp	prekopp.gabor@bajcsy.hu
	x		Hungary	Budapest	National Health Center	Andrology and Urology	Ferenc		Szabo	szaboferenc@freemail.hu
	x		Hungary	Budapest	Karolyi Sandor Hospital	Urology	Geza		Boszormenyi	bng@enternet.hu
x	x		Hungary	Debrecen	Kenezy County Hospital	Urology	Barnabas		Szoke	laczkoi@gizi.dote.hu

GERMANY

HUNGARY

x	x		Hungary	Debrecen	University of Debrecen Medical and Health Science Center	Urology	Antal		Farkas	anfarkas@freemail.hu
	x		Hungary	Dombovar	Szent Lukacs Hospital	Urology	Fel		Pal	eukhtdombovar@axelero.hu
x			Hungary	Dunaujvaros	Szent Pantaleon Hospital	Urology	Lajos		Hazay	messie@westel900.net
x			Hungary	Kaposvar	Kaposi Mor County Hospital	Urology	Istvan		Rakasz	rakasz@kmmk.hu
x	x		Hungary	Kiskunhalas	Semmelweis Hospital	Urology	Endre		Holman	holmane@axelero.hu
x	x		Hungary	Nagykanizsa	M.J.V. Hospital	Urology	Zoltan		Florian	drflorian@nkkorhaz.hu
x	x		Hungary	Papa	GEK	Urology	Istvan		Nagy	papaurol@freemail.hu
x	x		Hungary	Pecs	PTE AOK	Urology	Arpad		Szanto	szantorp@freemail.hu
x	x		Hungary	Sopron	Erzsebet Hospital	Urology	Laszlo		Koranyi	erdeik@sopkorh.elender.hu
x			Hungary	Szeged	Szeged University	Urology	Laszlo		Pajor	pajor@comser.szote.u-szeged.hu
	x		Hungary	Szeged	Szeged County Hospital	Urology	Istvan		Szalay	szalayi@westel900.net
	x		Hungary	Szekszard	Tolna County Hospital	Dept. of Hygiene	Istvan		Almasi	almasi.istvan@tmkorhaz.hu
x	x		Hungary	Szentes	Szentes Hospital	Urology	Akos		Lakatos	gyovaig@szentes.hu
x	x		Hungary	Szombathely	Markusovszky Hospital	Urology	Karoly		Konyves	kon06@freemail.hu
x	x		Hungary	Veszprem	Csolnoky Ferenc Hospital	Urology	Sandor		Gecs	gecssandor@sednet.hu
	x		Russia	Krasnodar	City Hospital â„–2	Clinical Pharmacology	Asya	Igorevna	Ponomareva	kl_farm@mail.ru
x			Russia	Moscow	â„–20 of Moscow	Urological	Iskander	Ilfakovich	Abdullin	urolog1974@mail.ru
x			Russia	Moscow	S.R.State Institute of Urology	Clinic Farmacology	Tamara	Perepanova	Perepanova	Perepanova2003@mail.ru
x	x		Russia	Moscow	Hospital 50	Urology	Andrew	Vladimirovich	Zaitcev	zaitcevandrew@mtu-net.ru
x			Russia	Moskow	Municipal clinical hospital named after S.P.Botkin	Urology	Sinakova	Alexandrovna	Lubov	Den@xforce.ru
x			Russia	Saint-Petersburg	Leningrad Regional Oncological Hospital	Uro-oncology	Ivan	Lvovitch	Pouline	pouline@mail.ru
x	x		Russia	Smolensk	Smolensk Regional Hospital	Urology	Vladimir	Vitaliy	Rafalsky	raf@antibiotic.ru
x	x		Russia	Smolensk	Railway Hospital	Urology & Nephrology	Mstislav	Valentinovich	Morozov	morozov@antibiotic.ru
x	x		Turkey	Adana	University	Urology	Yildirim		Bayazit	bayazit@cukurova.edu.tr
x			Turkey	Ankara	Mevki Military Hospital	Urology	Muharrem	Murat	Yildiz	ozelurology@hotmail.com
	x		Turkey	Ankara	med-art medical center	Urology	Muharrem	Murat	Yildiz	ozelurology@hotmail.com
x			Turkey	Ankara	Gata	Urology	Bedreddin		Seckin	bseckin@gata.edu.tr
x			Turkey	Aydin	Adnan Menderes University Medicine Faculty	Urology	Adnan		Kocak	ikocak_99@yahoo.com

RUSSIA

Appendix Contd.

PEP-study	PEAP-study	Region	Country	City	Hospital name	Department	First name	Middle name	Last name	E-mail
x	x		Turkey	Diyarbakir	Dicle University Hospital	Urology	Hayrettin		Sahin	hsahin@dicle.edu.tr
x			Turkey	Edirne	Trakya university medical faculty	Urology	Bulent	Hasan	Alagol	alagol@superonline.com
x	x		Turkey	Isparta	Suleyman Demirel University Hospital	Urology	Sedat		Soyupek	drtaylanoksay@yahoo.com
x			Turkey	Istanbul	Numune	Urology I.	Ahmet	Ruknettin	Aslan	aslanar@ttnet.net.tr
x			Turkey	Istanbul	BakirkoyTeaching Hospital	Urology	Necati		Gurbuz	nctgrbz@yahoo.com
	x		Turkey	Istanbul	BakÄ±rkÃ¶y Dr. Sadi Konuk EÄŸitim ve AraÅŞtÄ±rma Hastanesi	Urology	Necati		Gurbuz	nctgrbz@yahoo.com
x	x	**TURKEY**	Turkey	Istanbul	Taksim Teaching Hospital	Urology	Mete		Cek	cekmd@doruk.net.tr
x			Turkey	Istanbul	Kartal Training & Research Hospital	2nd. Clinic of Urology	Onder		Canguven	ocanguven@yahoo.com
x	x		Turkey	Istanbul	SSK Istanbul	Urology	Mahmut	Gokhan	Toktas	canello1989@yahoo.com
x			Turkey	Izmir	SSK Tepecik Education Hospital	Urology	Oguz		Mertoglu	tepecikuro@superonline.com
x	x		Turkey	Izmir	Ege University	Urology	Oktay		Nazli	nazli@med.ege.edu.tr
	x		Turkey	Konya	Selcuk Universty Meram Medical Faculty	Urology	Ahmet		Ozturk	ahoztr@yahoo.fr
x	x		Turkey	Manisa	Celal Bayar University Hospital	Urology	Cagri		Asan	www.cagriasan@yahoo.com
x			Turkey	Samsun	Ondokuz Mayis University, School of Medicine	Urology	Ramazan		Asci	rasci@omu.edu.tr
x			Turkey	Uludag	Bursa University	Department of Urology	Ismet Yavascaoglu		Yavascaoglu	
	x		Turkey	Zonguldak	Zonguldak Karaelmas University Hospital	Urology	Ilker		Seckiner	iseckiner@yahoo.com
x			Turkey	Zonguldak	Karaelmas University medical Faculty Hospital	Urology	Cetin		Yesilli	cyesilli@hotmail.com