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The nationwide surveillance of bacterial urinary pathogens conducted by the Japanese Society of Chemotherapy (JSC)

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Introduction

JSC conducted the first nationwide surveillance of bacterial urinary pathogens in 2008.

Materials and Methods:

1) Surveillance period: January – June 2008.
2) Cooperative institutes: 28 medical institutions throughout Japan.
3) Strains tested: A total of 715 strains belonging to six clinically relevant bacterial species were collected from adult patients with well-diagnosed complicated urinary tract infections (C-UTIs).
4) Antibacterial agents tested: 41 Agents as listed in Table. 1.
5) Susceptibility test: Conducted at the central laboratory (The Kitasato University, Anti-infective Drugs Research Center) according to CLSI standards for broth micro dilution methods.
6) Determination of β-lactamase: Nitrocefin method and Cica-Beta Test [Kanto Chemicals, Tokyo; for detection of expanded spectrum β-lactamase (ESBL) and metallo β-lactamase (MBL)].
7) Referring to the CLSI breakpoint, the susceptibility of each pathogen was classified into the following categories:
S: sensitive, I: intermediate, R: resistant

Bacterial strains

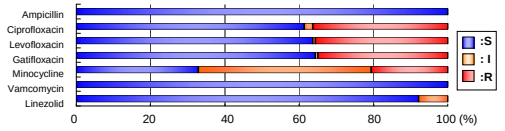
	Enterococcus faecalis	*Escherichia coli*	*Klebsiella pneumoniae*	*Proteus mirabilis*	*Serratia marcescens*	*Pseudomonas aeruginosa*	Total
Numbers collected	147	263	98	45	46	116	715
Numbers tested	140	255	93	42	44	114	688

Results

Background of Patients

	Total : 688
Inpatients	31.4%(216)
Outpatients	68.6% (472)
Male	50.1% (345)
Female	49.6% (341)
Age (yrs)	
20 – 29	2.0% (14)
30 – 39	2.2% (15)
40 – 49	2.8% (19)
50 – 59	10.2% (70)
60 – 69	18.8% (129)
70 – 79	34.3% (236)
80 –	29.8% (205)
Underlying disease	
Neuropathic bladder	50.3% (346)
Prostatomegaly	17.4% (120)
Bladder cancer	12.1% (83)
Hydronephrosis	5.4% (37)
Nephrolith	4.9% (34)
Prostate cancer	4.8% (33)
Ureterolithiasis	3.5% (24)
Ureterostenosis	3.1% (21)
Cystolithiasis	2.5% (17)
Vesical diverticulum	1.0% (7)
Vesicoureteral reflux	1.0% (7)
Nephrocystosis	0.7% (5)
Others	18.9% (130)

Fig. 1 Susceptibility of *E. faecalis* to 7 antibacterial agents (μg/mL)

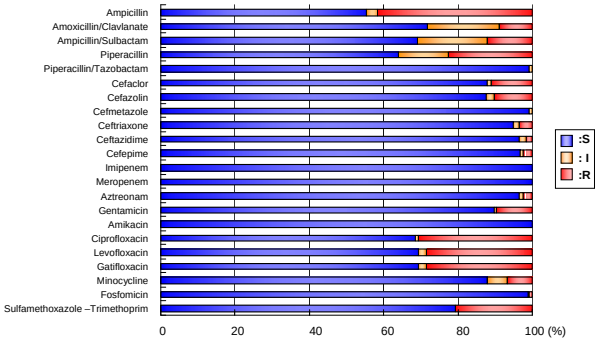


In a susceptibility distribution of 140 *E. faecalis*, Ampicillin and Vancomycin were relatively active, but 11 strains (7.8%) were intermittent to Linezolid.
The proportion of Fluoroquinolone(FQ)-resistant strains was about 35%.

Table. 1 Susceptibility of 6 urinary pathogens to antibacterial agents (μg/mL)

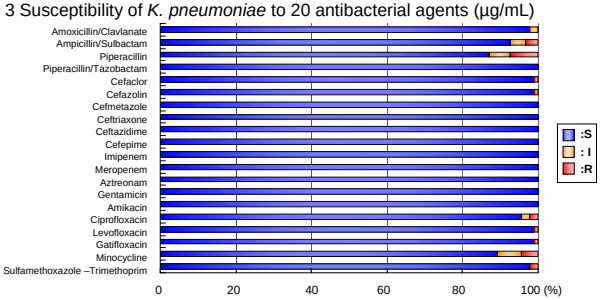
	1) *Enterococcus faecalis* (N=140)			2) *Escherichia coli* (N=255) ESBL: 13			3) *Klebsiella pneumoniae* (N=93) ESBL: None			4) *Proteus mirabilis* (N=42) ESBL: 5			5) *Serratia marcescens* (N=44)			6) *Pseudomonas aeruginosa* (N=114) MDRP: 2 MBL: 3		
Antibacterial agent	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}
Ampicillin	0.25 – 8	2	4	0.5 – ≥ 256	8	≥ 256				0.5 – ≥ 256	2	≥ 256						
Amoxicillin /Clavlanate				0.25 – ≥ 128	8	16	0.5 – 16	2	4	0.5 – 16	0.5	8						
Ampicillin /Sulbactam	0.25 – 8	2	4	≤ 0.06 – 128	4	32	0.5 – 64	4	8	0.5 – 32	1	8						
Piperacillin	0.5 – 16	4	4	0.25 – ≥ 256	2	≥ 256	1 – ≥ 256	4	64	0.125 – ≥ 256	0.5	≥ 256	0.5 – 128	4	64	1 – ≥ 256	8	128
Piperacillin /Tazobactam	0.5 – 16	4	4	0.25 – 64	2	4	0.5 – 16	2	4	0.125 – 64	0.25	1	0.5 – 128	2	128	0.5 – ≥ 256	8	128
Cefaclor				0.125 – ≥ 256	2	32	0.125 – 32	0.5	0.5	0.5 – ≥ 256	1	≥ 256						
Cefdtorene				≤ 0.06 – ≥ 128	0.25	2	≤ 0.06 – 4	0.25	0.5	≤ 0.06 – ≥ 128	≤ 0.06	≥ 128	0.25 – ≥ 128	2	≥ 128			
Cefcapene				≤ 0.06 – ≥ 256	0.5	2	≤ 0.06 – 4	0.25	1	≤ 0.06 – 64	≤ 0.06	16	≤ 0.06 – ≥ 256	2	32			
Cefazolin				0.5 – ≥ 256	2	32	0.5 – 128	1	2	2 – ≥ 256	4	≥ 256						
Cefmetazole				0.125 – 32	0.5	2	0.25 – 8	0.5	2	1 – 8	2	2	2 – ≥ 256	8	128			
Cefotiam				≤ 0.06 – ≥ 256	0.25	2	≤ 0.06 – 8	0.25	0.5	0.25 – ≥ 256	0.25	≥ 256	2 – ≥ 256	≥ 256	≥ 256			
Flomoxef				≤ 0.06 – 32	≤ 0.06	0.25	≤ 0.06 – 0.25	≤ 0.06	0.125	0.125 – 0.5	0.25	0.25	0.25 – ≥ 256	4	32			
Cefiriaxone				≤ 0.06 – ≥ 256	≤ 0.06	0.25	≤ 0.06 – 8	≤ 0.06	0.125	≤ 0.06 – ≥ 256	≤ 0.06	32	≤ 0.06 – 64	0.25	64	2 – ≥ 256	64	≥ 256
Ceftazidime				≤ 0.06 – 64	0.125	0.5	≤ 0.06 – 0.5	0.125	0.25	≤ 0.06 – 4	≤ 0.06	0.25	≤ 0.06 – ≥ 128	0.25	4	0.5 – ≥ 128	2	32
Cefpirome	0.5 – ≥ 256	8	64	≤ 0.06 – ≥ 256	≤ 0.06	0.125	≤ 0.06 – 2	≤ 0.06	0.125	≤ 0.06 – ≥ 256	≤ 0.06	≥ 256	≤ 0.06 – 128	0.125	2	1 – ≥ 256	8	64
Cefepime				≤ 0.06 – 64	≤ 0.06	0.125	≤ 0.06 – 1	≤ 0.06	0.125	≤ 0.06 – ≥ 256	≤ 0.06	128	≤ 0.06 – ≥ 256	0.125	4	0.5 – ≥ 256	4	32
Imipenem	0.125 – 4	0.5	2	≤ 0.06 – 0.5	0.125	0.25	≤ 0.06 – 0.5	0.125	0.25	0.125 – 8	2	4	0.125 – 2	0.5	1	0.125 – ≥ 128	1	8
Panipenem	≤ 0.06 – 8	1	2	≤ 0.06 – 0.25	0.125	0.25	≤ 0.06 – 0.25	0.125	0.25	0.125 – 4	2	4	0.125 – 8	0.25	1	0.25 – ≥ 256	4	16
Meropenem	0.25 – 16	4	8	≤ 0.06 – 0.25	≤ 0.06	≤ 0.06	≤ 0.06	≤ 0.06	≤ 0.06	≤ 0.06 – 0.5	≤ 0.06	0.25	≤ 0.06 – 2	≤ 0.06	0.125	≤ 0.06 – ≥ 256	0.5	8
Biapenem	0.25 – 16	4	8	≤ 0.06 – 1	≤ 0.06	≤ 0.06	≤ 0.06 – 1	0.125	0.5	0.5 – 4	2	4	0.125 – 4	0.5	1	≤ 0.06 – ≥ 256	0.25	4
Doripenem	0.25 – 8	2	8	≤ 0.06 – 0.125	≤ 0.06	≤ 0.06	≤ 0.06 – 0.125	≤ 0.06	0.125	≤ 0.06 – 2	0.25	0.5	≤ 0.06 – 2	0.125	0.25	≤ 0.06 – ≥128	0.25	8
Faropenem	0.25 – 16	1	4	0.125 – 4	0.5	1	0.5 – 2	0.25	1	0.25 – 4	1	2	0.5 – 128	8	64			
Aztreonam				≤ 0.06 – 128	≤ 0.06	0.5	≤ 0.06 – 4	≤ 0.06	0.125	≤ 0.06 – 16	≤ 0.06	0.125	≤ 0.06 – 16	0.125	8	0.25 – ≥ 256	4	32
Gentamicin				0.125 – 128	0.5	8	0.125 – 0.5	0.25	0.25	0.25 – 64	0.5	2	0.125 – 32	0.5	1	0.125 – ≥ 256	2	4
Isepamicin				0.25 – 8	1	2	0.25 – 1	0.5	0.5	2 – 8	4	4	0.25 – 16	1	4	0.25 – ≥ 256	4	8
Amikacin				0.5 – 16	2	4	0.5 – 2	1	2	1 – 8	4	4	0.5 – 64	2	16	0.25 – 128	4	8
Ciprofloxacin	0.25 – 128	1	32	≤ 0.06 – 128	≤ 0.06	32	≤ 0.06 – 8	≤ 0.06	0.25	≤ 0.06 – ≥ 256	≤ 0.06	16	≤ 0.06 – ≥ 256	≤ 0.06	16	≤ 0.06 – ≥ 256	0.25	64
Levofloxacin	0.5 – 128	2	64	≤ 0.06 – 128	0.125	16	≤ 0.06 – 8	≤ 0.06	0.5	≤ 0.06 – ≥ 256	0.125	8	≤ 0.06 – ≥ 256	0.125	16	≤ 0.06 – ≥ 256	1	128
Tosufloxacin	0.125 – ≥ 32	0.25	≥ 32	≤ 0.06 – ≥ 32	≤ 0.06	≥ 32	≤ 0.06 – 16	≤ 0.06	0.25	≤ 0.06 – ≥ 32	0.125	≥ 32	≤ 0.06 – ≥ 32	0.125	≥ 32	≤ 0.06 – ≥ 32	0.5	≥ 32
Gatifloxacin	0.25 – 64	0.5	32	≤ 0.06 – 128	0.125	16	≤ 0.06 – 16	≤ 0.06	0.5	0.125 – ≥ 256	0.25	32	≤ 0.06 – ≥ 256	0.25	16	≤ 0.06 – ≥ 256	2	128
Prulifloxacin	0.5 – ≥ 64	1	≥ 64	≤ 0.06 – ≥ 64	≤ 0.06	8	≤ 0.06 – 4	≤ 0.06	0.25	≤ 0.06 – ≥ 64	≤ 0.06	8	≤ 0.06 – ≥ 64	≤ 0.06	8	≤ 0.06 – ≥ 64	0.25	32
Pazufloxacin	1 – ≥ 256	2	128	≤ 0.06 – 64	≤ 0.06	8	≤ 0.06 – 4	≤ 0.06	0.25	≤ 0.06 – ≥ 256	≤ 0.06	2	≤ 0.06 – ≥ 256	0.125	8	≤ 0.06 – ≥ 256	0.5	64
Minocycline	≤ 0.06 – 32	8	16	0.125 – ≥ 256	0.5	8	0.5 – 16	2	8	4 – ≥ 256	16	32	0.5 – 32	4	8	4 – ≥ 256	16	64
Fosfomicin				0.125 – ≥ 256	0.5	4				0.5 – ≥ 256	4	128	2 – ≥ 256	8	≥ 256	2 – ≥ 256	64	≥ 256
Sulfamethoxazole –Trimethoprim	0.0078 – ≥ 16	0.06	≥ 16	0.015 – ≥ 16	0.06	≥16	0.031 – ≥ 16	0.125	0.5	≤ 0.06 – ≥ 16	0.25	≥ 16						
Vamcomycin	0.5 – 4	1	4															
Linezolid	0.5 – 4	2	2															
Colistin				0.125 – 1	0.25	0.25	0.125 – 1	0.25	0.5	≥ 64	≥ 64	≥ 64	0.5 – ≥ 64	≥ 64	≥ 64	0.125 – 2	0.5	0.5
Polymyxin B				0.125 – 2	0.25	0.5	0.25 – 4	0.5	1	32 – ≥ 256	≥ 256	≥ 256	0.5 – ≥ 256	≥ 256	≥ 256	0.25 – 2	0.5	1

Fig. 2 Susceptibility of *E. coli* to 22 antibacterial agents (μg/mL)



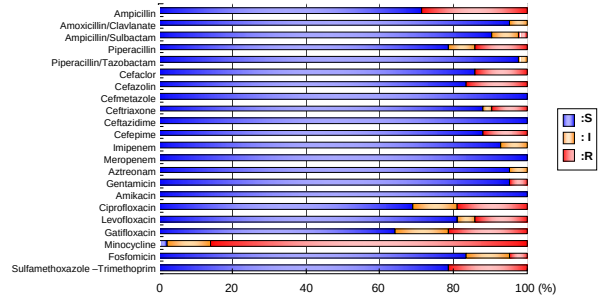
The MIC90s of FQs against the 225 *E. coli* strains were 8-32mg/L and the FQ-resistant rate was also near 30%.

Fig. 3 Susceptibility of *K. pneumoniae* to 20 antibacterial agents (μg/mL)



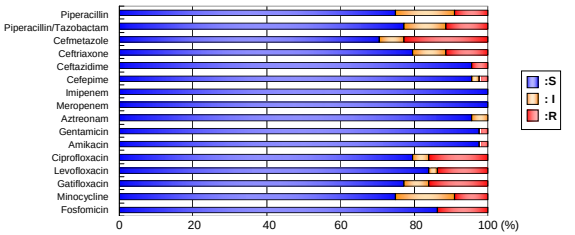
K. pneumoniae was susceptible to all agents.

Fig. 4 Susceptibility of *P. mirabilis* to 22 antibacterial agents (μg/mL)



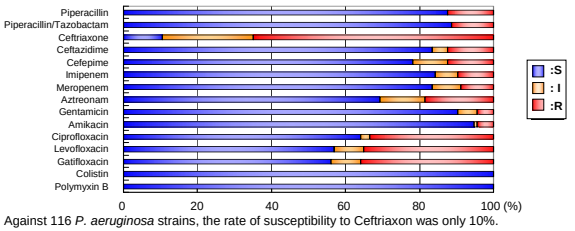
Five (12%) of 42 *P. mirabilis* strains were suspected of producing extended-spectrum beta-lactamase (ESBL).

Fig. 5 Susceptibility of *S. marcescens* to 16 antibacterial agents (μg/mL)



No strain was identified as ESBL-producing or multidrug–resistant *S. marcescens*.

Fig. 6 Susceptibility of *P. aeruginosa* to 15 antibacterial agents (μg/mL)



Against 116 *P. aeruginosa* strains, the rate of susceptibility to Ceftriaxon was only 10%.
The resistant rate to Carbapenems, Aminoglycosides, and FQs was 10%, 4%, and 35%, respectability.
Three (2.6%) of all strains were found to be multidrug- resistant strain (MDRP).

Conclusion and Discussion:

* In a susceptibility distribution of 140 *E. faecalis*, Ampicillin and Vancomycin were relatively active, but 11 strains (7.8%) were intermittent to Linezolid . The proportion of FQ-resistant strains was about 35%.
* The MIC90s of FQ against the 225 *E. coli* strains were 8-32mg/L and the FQ-resistant rate was also near 30%.
* *K. pneumoniae* was susceptible to all agents.
* Five (12%) of 42 *P. mirabilis* strains were suspected of producing ESBL.
* No strain was identified as ESBL-producing or multidrug–resistant *S. marcescens*.
* Against 116 *P. aeruginosa* strains, the rate of susceptibility to Ceftriaxon was only 10%. The resistant rate to Carbapenems, Aminoglycosides, and FQs was 10%, 4%, and 35%, respectability. Three (2.6%) of all strains were found to be multidrug- resistant strain (MDRP).

* Surveillance data of the current antimicrobial agents are essential for the optimal management of patients with urinary tract infection. We can expect the best result if the empirical therapy to which the organism is susceptible is applied on the day when infection is clinically suspected. These data will be a useful reference for future periodic surveillance studies, as well as for investigations to control antimicrobial-resistant pathogens.