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Nationwide surveillance of bacterial respiratory pathogens conducted by the Japanese Society of Chemotherapy in 2007: general view of the pathogens' antibacterial susceptibility

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Abstract For the purpose of a nationwide surveillance of the antimicrobial susceptibility of bacterial respiratory pathogens in patients in Japan, the Japanese Society of Chemotherapy conducted their second year survey, during the period from January to August, 2007. A total of 1178 strains were collected from clinical specimens obtained from adult patients with well-diagnosed respiratory tract infections. Susceptibility testing was evaluable for 1108 strains (226 *Staphylococcus aureus*, 257 *Streptococcus pneumoniae*, 6 *Streptococcus pyogenes*, 206 *Haemophilus influenzae*, 120 *Moraxella catarrhalis*, 122 *Klebsiella pneumoniae*, and 171 *Pseudomonas aeruginosa*). A total of 44 antibacterial agents, including 26 β-lactams (four penicillins, three penicillins in combination with β-lactamase inhibitors, four oral cephems, eight parenteral cephems, one monobactam, five carbapenems, and one penem), three aminoglycosides, four macrolides (including ketolide), one lincosamide, one tetracycline, two glycopeptides, six fluoroquinolones, and one oxazolidinone were used for the study. Analysis was conducted at the central reference laboratory according to the method recommended by the Clinical and Laboratory Standards Institute (CLSI). The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) was high, at 59.7%, and the incidences of penicillin-intermediate-resistant and -resistant *Streptococcus pneumoniae* (PISP and PRSP) were 30.4% and 5.1%, respectively. Among *Haemophilus influenzae strains*, 19.9% of them were found to be β-lactamase-non-producing ampicillin (ABPC)-intermediately-resistant (BLNAI), 29.1% to be β-lactamase-non-producing ABPC-resistant (BLNAR), and 6.7% to be β-lactamase-producing ABPC-resistant (BLPAR) strains. Extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* was not isolated. Two isolates (1.2%) of *Pseudomonas aeruginosa* were found to be metallo-β-lactamase-producing strains, including one (0.6%) suspected multidrug-resistant strain showing resistance to imipenem, amikacin, and ciprofloxacin. These data will be a useful reference for future periodic surveillance studies and for investigations to control resistant infections as well. Continued surveillance is required to prevent the further spread of these antimicrobial resistances.

Key words Surveillance · Susceptibility · Resistance · Respiratory tract infection

Introduction

In order to investigate trends and changes in bacterial pathogens and the emergence of resistance among them, the Japanese Society of Chemotherapy (JSC) established a nationwide surveillance network in 2006. The first survey was conducted during the period from January to August, 2006, with the cooperation of 32 medical institutions throughout Japan, and we reported trends in the antimicrobial susceptibilities of bacterial species from patients with respiratory tract infections (RTIs).[1] The first surveillance, with a total of 924 strains, revealed the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) as 63.4%, penicillin-intermediate-resistant and -resistant

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Streptococcus pneumoniae (PISP and PRSP) as 35.0% and 4.0%, respectively, and β-lactamase-non-producing ABPC-resistant (BLNAR) and β-lactamase-producing ABPC-resistant (BLPAR) strains of *Haemophilus influenzae* as 29.1% and 4.8%, respectively. The incidence of extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* was low, at 2.7%; and 2.1% of *Pseudomonas aeruginosa* were found to be metallo-β-lactamase-producing strains.

Here we report the study of the second year nationwide surveillance conducted by the JSC. The results obtained from this surveillance will be used as a set of controls for surveillance studies to be conducted in the future by the JSC and by other organizations as well.

Materials and methods

Strains and quality control

The causative bacteria from patients with RTI were isolated from sputum, specimens collected by transtracheal aspiration, or bronchoscopy. Identification of a causative pathogen of RTI was evaluated by quantitative culture and Gram staining, or by other means, at the 39 participating medical institutions (listed in Table 1). These bacteria were identified at the species level, suspended in preservation-broth contained in Micro-bank tubes (Asuka Junyaku, Tokyo, Japan) at each institution, and sent to the central laboratory, the Research Center for Anti-infective Drugs of the Kitasato Institute (hereafter referred to as the Center), in containers kept at –20°C. Electronic uniform data sheets for each patient from whom these strains were isolated were also completed at each institution and sent to the Center so that the microbiological data obtained were able to be stratified according to the settings and profiles of the patients and the diagnoses.

A total of 1178 strains were received at the Center and kept at –80°C until the antimicrobial susceptibility testing was conducted. Re-identification and cultivation of the strains gave 1108 evaluable strains, consisting of 226 *S. aureus*, 257 *S. pneumoniae*, 6 *S. pyogenes*, 206 *H. influenzae*, 120 *M. catarrhalis*, 122 *K. pneumoniae* and 171 *P. aeruginosa.*

The accuracy of the determination of the minimum inhibitory concentrations (MICs) of antibacterial agents was controlled according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI), using

Table 1. List of participating institutions contributing to our surveillance[a]

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Shinrakuen Hospital, Niigata, Niigata
South Miyagi Medical Center, Ogawara, Miyagi
Tokyo Metropolitan Toshima Hospital, Toshima, Tokyo
Tottori University Hospital, Yonago, Tottori
Toyama Prefectural Central Hospital, Toyama, Toyama
Yamagata Saisei Hospital, Yamagata, Yamagata
Yamanashi Red Cross Hospital, Fujikawaguchiko, Yamanashi

[a] City and prefecture locations are shown

the following control strains, respectively: *S. aureus* ATCC29213 and *Escherichia coli* ATCC35218 for clinical isolates of *S. aureus* and *M. catarrhalis*; *S. pneumoniae* ATCC49619 for clinical isolates of *S. pneumoniae* and *S. pyogenes*; *H. influenzae* ATCC49247, ATCC49766, and *E. coli* ATCC35218 for clinical isolates of *H. influenzae*; *E. coli* ATCC25922 and ATCC35218 for clinical isolates of *K. pneumoniae*; and *P. aeruginosa* ATCC27853, *E. coli* ATCC25922, and ATCC35218 for clinical isolates of *P. aeruginosa*. *E. coli* ATCC35218 was used as a control strain for the determination of the MICs of β-lactam antibiotics combined with β-lactamase inhibitors.

Susceptibility testing and MIC determination

Susceptibility testing was performed according to the CLSI (formerly NCCLS) standards M7-A7[2] for the microbroth dilution method. In brief, cation-adjusted Mueller-Hinton broth (25 mg/L Ca^{2+} and 12.5 mg/L Mg^{2+}; CA-MH broth) was used to measure MICs against *S. aureus*, *M. catarrhalis*, *K. pneumoniae*, and *P. aeruginosa*. For the determination of the MIC of oxacillin, 2% NaCl was added to CA-MH broth. For the determination of MICs against *S. pneumoniae* and *S. pyogenes*, 3.3% lysed horse blood (LHB) was added to the CA-MH broth. *Haemophilus* Test Medium (HTM) broth was used for *H. influenzae*.

A 0.005-ml portion of test organism solution, grown to turbidity of MacFarland number 0.5 and diluted tenfold with saline, was inoculated to either CA-MH broth or HTM broth to make a final volume of 0.1 ± 0.02 ml. The broth was poured into a well in a microplate where the serially diluted freeze-dried test agent was placed, and the MIC was determined by using the MIC2000 system (Eiken Kagaku, Tokyo, Japan).

Antibacterial agents

Susceptibilities of the bacterial strains were tested for the following 44 antimicrobial agents: four penicillins: benzylpenicillin (PCG; Meiji Seika, Tokyo, Japan), oxacillin (MPIPC; Meiji), ampicillin (ABPC; Meiji), and piperacillin (PIPC; Toyama Chemical, Tokyo, Japan); three penicillins in combination with β-lactamase inhibitors: clavulanic acid-amoxicillin (CVA/AMPC; Glaxo SmithKline, Japan, Tokyo, Japan), sulbactam-ABPC (SBT/ABPC; Pfizer Japan, Tokyo, Japan), and tazobactam-PIPC (TAZ/PIPC; Toyama); four oral cephems: cefaclor (CCL; Shionogi, Tokyo, Japan), cefdinir (CFDN; Astellas Pharma, Tokyo, Japan), cefcapene (CFPN; Shionogi), and cefditoren (CDTR; Meiji); eight parenteral cephems: cefazolin (CEZ; Astellas), cefoxitin (CFX; Banyu Pharmaceutical, Tokyo, Japan), cefmetazole (CMZ; Daiichi-Sankyo, Tokyo, Japan), cefotiam (CTM; Takeda Pharmaceutical, Tokyo, Japan), ceftazidime (CAZ; Glaxo SmithKline), ceftriaxone (CTRX; Chugai Pharmaceutical, Tokyo, Japan), cefepime (CFPM; Meiji), and cefozopran (CZOP; Takeda); a monobactam: aztreonam (AZT; Eisai, Tokyo, Japan); five carbapenems: imipenem (IPM; Banyu, Tokyo, Japan), panipenem (PAPM; Daiichi-Sankyo), meropenem (MEPM; Dainippon Sumitomo Pharma, Tokyo, Japan), biapenem (BIPM; Meiji), and doripenem (DRPM; Shionogi); one penem: faropenem (FRPM; Maruho, Tokyo, Japan); three aminoglycosides: gentamicin (GM; Shionogi), amikacin (AMK; Banyu), and arbekacin (ABK; Meiji); four macrolides: erythromycin (EM; Dainippon Sumitomo), clarithromycin (CAM; Toyama), azithromycin (AZM; Pfizer), and telithromycin (TEL; Sanofi-Aventis, Tokyo, Japan); a lincosamide: clindamycin (CLDM; Dainippon Sumitomo); a tetracycline: minocycline (MINO; Wyeth, Madison, NJ, USA/Takeda); two glycopeptides: vancomycin (VCM; Shionogi) and teicoplanin (TEIC; Astellas); six fluoroquinolones: ciprofloxacin (CPFX; Bayer Yakuhin, Tokyo, Japan), levofloxacin (LVFX; Daiichi-Sankyo), tosufloxacin (TFLX; Toyama), gatifloxacin (GFLX; Kyorin Pharmaceutical, Tokyo, Japan), moxifloxacin (MFLX; Shionogi), and pazufloxacin (PZFX; Toyama); and an oxazolidinone: linezolid (LZD; Pfizer). These antimicrobial agents were serially diluted and placed in a freeze-dried state in the respective wells of microplates. The stability of the antimicrobial agent-containing microplates was guaranteed by the manufacturer (Eiken Kagaku) for 9 months.

Detection of β-lactamases

To detect β-lactamases in *H. influenzae*, tests with Nitrocefin disks (Kanto Chemical, Tokyo, Japan) were conducted according to the reference manual supplied by the manufacturer.

A recently established rapid detection method, Cica-Beta Test 1 (Kanto Chemical), designed to detect extended-spectrum β-lactamase (ESBL) and metallo-β-lactamase (MBL) directly in colonies of Gram-negative rods,[3,4]) was employed to identify *K. pneumoniae* and *P. aeruginosa* strains which produce such β-lactamases.

Results

Findings for *Staphylococcus aureus*

S. aureus was the species with the greatest number (226/1108; 20.4 %) among the evaluable strains in this investigation. The in-vitro antimicrobial susceptibilities, given as MIC_{50} /MIC_{90} values and MIC ranges, for *S. aureus* isolates are shown in Table 2. The susceptibility of these *S. aureus* strains against 43 antibacterial agents revealed that 135 strains (59.7%) were methicillin-resistant *S. aureus* (MRSA; MIC of MPIPC ≥ 4 μg/ml).

Susceptibility of methicillin-susceptible S. aureus *(MSSA)*

The MIC_{90}s of penicillins, except for oxacillin, against 91 MSSA strains were 16–32 μg/ml; however, the MICs in combinations with β-lactamase inhibitors (CVA/AMPC,

Table 2. Antibacterial susceptibility of *Staphylococcus aureus*

Antibacterial agent	All strains $n = 226$			MSSA (MPIPC ≦2 μg/ml) $n = 91$			MRSA (MPIPC ≧4 μg/ml) $n = 135$		
	MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)		
	50%	90%	Range	50%	90%	Range	50%	90%	Range
PCG	16	32	≦0.06–128	0.25	16	≦0.06–64	16	64	4–128
ABPC	16	64	0.125–128	1	16	0.125–64	32	64	8–128
SBT/ABPC	8	32	0.125–64	0.5	2	0.125–4	16	32	2–64
CVA/AMPC	16	32	0.125–≧128	0.5	1	0.125–8	32	64	2–≧128
PIPC	64	≧256	0.5–≧256	2	32	0.5–128	128	≧256	16–≧256
TAZ/PIPC	64	128	0.25–≧256	0.5	2	0.25–4	64	128	4–≧256
CCL	64	≧256	0.5–≧256	1	2	0.5–8	128	≧256	8–≧256
CFDN	≧128	≧128	0.125–≧128	0.25	0.25	0.125–0.5	≧128	≧128	0.5–≧128
CFPN	≧256	≧256	0.25–≧256	1	1	0.25–2	≧256	≧256	2–≧256
CDTR	64	≧128	0.25–≧128	0.5	0.5	0.25–1	64	≧128	2–≧128
CEZ	128	≧256	0.25–≧256	0.5	0.5	0.25–2	≧256	≧256	1–≧256
CTM	128	≧256	0.25–≧256	0.5	1	0.25–1	≧256	≧256	2–≧256
CAZ	≧128	≧128	4–≧128	8	8	4–16	≧128	≧128	16–≧128
CTRX	≧256	≧256	2–≧256	4	4	2–8	≧256	≧256	8–≧256
CFPM	128	≧256	0.5–≧256	2	4	0.5–4	128	≧256	4–≧256
CZOP	16	64	0.5–≧256	0.5	1	0.5–2	32	64	2–≧256
CMZ	32	64	0.5–128	1	2	0.5–4	32	128	4–128
IPM	16	64	≦0.06–≧128	≦0.06	0.125	≦0.06–0.25	32	64	≦0.06–≧128
PAPM	8	32	≦0.06–≧256	≦0.06	0.125	≦0.06–0.5	16	32	0.125–≧256
MEPM	8	32	≦0.06–64	0.125	0.125	≦0.06–0.25	16	32	0.25–64
BIPM	16	64	≦0.06–128	≦0.06	≦0.06	≦0.06–0.125	32	64	0.125–128
DRPM	4	16	≦0.06–32	≦0.06	≦0.06	≦0.06–0.125	8	32	0.125–32
FRPM	128	≧256	0.125–≧256	0.125	0.25	0.125–0.5	≧256	≧256	0.25–≧256
GM	0.5	128	0.25–≧256	0.5	8	0.25–≧256	16	128	0.25–≧256
AMK	4	16	1–≧256	2	4	2–64	16	32	1–≧256
ABK	0.5	1	0.25–8	0.5	0.5	0.25–8	0.5	2	0.25–4
CPFX	8	128	0.125–≧256	0.25	1	0.125–64	128	128	0.25–≧256
LVFX	4	≧256	0.125–≧256	0.25	0.5	0.125–16	32	≧256	0.25–≧256
TFLX	4	≧32	≦0.06–≧32	≦0.06	0.125	≦0.06–≧32	≧32	≧32	≦0.06–≧32
GFLX	1	64	≦0.06–≧256	≦0.06	0.125	≦0.06–4	8	64	≦0.06–≧256
PZFX	4	≧256	0.125–≧256	0.25	0.25	0.125–8	8	≧256	0.125–≧256
MFLX	1	32	≦0.06–64	≦0.06	0.125	≦0.06–4	4	32	≦0.06–64
MINO	0.5	16	≦0.06–16	0.125	0.125	≦0.06–16	8	16	0.125–16
EM	≧256	≧256	0.5–≧256	0.5	≧256	0.5–≧256	≧256	≧256	0.5–≧256
CAM	≧128	≧128	0.125–≧128	0.25	≧128	0.125–≧128	≧128	≧128	0.25–≧128
AZM	≧128	≧128	0.25–≧128	0.5	≧128	0.25–≧128	≧128	≧128	0.5–≧128
TEL	≧64	≧64	≦0.06–≧64	0.125	0.25	≦0.06–≧64	≧64	≧64	0.125–≧64
CLDM	≧256	≧256	≦0.06–≧256	0.25	0.25	≦0.06–≧256	≧256	≧256	0.125–≧256
VCM	1	2	0.5–2	1	1	0.5–2	1	2	0.5–2
TEIC	**1**	2	0.125–4	1	1	0.25–2	1	2	0.125–4
LZD	**2**	2	1–4	2	4	1–4	2	2	1–4
MPIPC	128	≧256	0.125–≧256	0.25	0.5	0.125–2	≧256	≧256	4–≧256
CFX	128	≧256	2–≧256	2	4	2–4	128	≧256	8–≧256

Susceptibilities of the 226 strains of *S. aureus* to 43 antimicrobial agents were measured. The strains consisted of 135 strains (59.7%) of MRSA and 91 strains (40.3%) of MSSA

SBT/ABPC, and TAZ/PIPC) decreased to 1.0–2.0 μg/ml. The MIC_{90}s of CCL, CAZ, CTRX, CFPM, and CMZ ranged from 2.0 to 8.0 μg/ml and those of the rest of the six cephems ranged from 0.25 to 1.0 μg/ml. Carbapenems showed the strongest activity, with MIC_{90}s of ≤0.125 μg/ml. As for the aminoglycosides, GM, AMK, and ABK showed MIC_{90s} of 8.0, 4.0, and 0.5 μg/ml, respectively. Among the macrolide-lincosamide antibiotics, TEL and CLDM showed relatively strong activity, with an MIC_{90} of 0.25 μg/ml, but the rest of the macrolides showed weak activity, with MIC_{90}s of ≥128 μg/ml. Relatively strong activities of MINO, VCM, TEIC, and all six fluoroquinolones, with MIC_{90}s of 0.125–1.0 μg/ml, were noted.

Susceptibility of MRSA

Only 4 of the 43 antibacterial agents tested, ABK, VCM, TEIC, and LZD, showed appreciable activity against MRSA, with MIC_{90s} of ≤2.0 μg/ml. The other 39 agents showed weak or almost no activity, with MIC_{90}s of 16–≥256 μg/ml against these MRSA strains.

Findings for *Streptococcus pneumoniae*

The susceptibilities of the 257 strains of *S. pneumoniae* to 40 antimicrobial agents were measured, and 166 (64.6%) of

them were identified as penicillin-susceptible (PSSP), 78 (30.4%) as penicillin-intermediate (PISP), and 13 (5.1%) as penicillin-resistant strains (PRSP) according to the breakpoint for PCG defined by the CLSI standards.[2]

The Food and Drug Administration (FDA) has amended the breakpoints for penicillin in the treatment of pneumococcal pneumonia, as follows: the MICs of susceptible (S), intermediate (I), and resistant (R) strains are ≤2, 4, and ≥8 μg/ml, respectively. With the new criteria for breakpoint MICs, the 257 pneumococcal strains were classified as 256 (99.6%) susceptible strains, and only 1 (0.4%) intermediate strain. We did not find resistant pneumococcal strains that showed MIC ≥ 8 μg/ml.

Two cephems, CFPN and CDTR, all five carbapenems, both glycopeptides, TEL, and three fluoroquinolones (TFLX, GFLX, and MFLX) showed strong activities (MIC_{90} ≤ 0.5 μg/ml) against these *S. pneumoniae* strains, regardless of their different susceptibilities to PCG. On the other hand, aminoglycosides were substantially less active, as expected, against *S. pneumoniae*, with MIC_{50s} of 8.0–64 μg/ml (Table 3). Except for 2 isolates, 164 strains (98.8%) of PSSP were susceptible to IPM, whereas 39 strains (50.0%) of PISP and 10 strains (76.9%) of PRSP were IPM-resistant (including intermediate resistance). Regarding macrolide resistance, 77.1% of PSSP, 84.6% of PISP, and all strains of PRSP were EM-resistant.

Susceptibility of PSSP

Among the β-lactams, CCL and CAZ showed high MIC_{90s} (4.0 and 8.0 μg/ml, respectively) while the MIC_{90}s of the other β-lactams were ≤1.0 μg/ml. Particularly, TAZ/PIPC and all carbapenems showed markedly strong activities, with MIC_{90}s of ≤0.06 μg/ml. With regard to the fluoroquinolones, CPFX, LVFX, and PZFX showed moderate activities (MIC_{50s} of = 2.0–4.0 μg/ml), though TFLX, GFLX, and MFLX were very active.

Susceptibility of PISP

Penicillins, including combinations with β-lactamase inhibitors, were relatively weak against PISP, with MIC_{90}s of 1.0 or 2.0 μg/ml. Among the oral cephems, CFPN and CDTR showed relatively strong activities, with MIC_{90}s of 1.0 and 0.5 μg/ml, respectively, while CCL and CFDN were less active, with MIC_{90}s of 64 and 4.0 μg/ml, respectively. The activities of parenteral cephems were found to be moderate to relatively weak, with MIC_{90}s ranging from 1.0 to 8.0 μg/ml. The MIC_{90}s of four carbapenems, IPM, MEPM, BIPM, and DRPM, were ≤0.5μg/ml.

With regard to the fluoroquinolones, the MIC_{90s} of TFLX, GFLX, and MFLX were 0.25, 0.5, and 0.25 μg/ml, respectively, while that of CPFX, LVFX, and PZFX was 2.0 μg/ml. The activities of macrolide-lincosamide antibiotics against PISP were found to be very weak (MIC_{90}s of ≥128 μg/ml), except that TEL showed strong activity (MIC_{90} of 0.25 μg/ml).

Susceptibility of PRSP

Although the number of PRSP strains examined in this study was small (13 strains), some tendencies in susceptibility were noted. The strains were highly susceptible to PAPM, MEPM, BIPM, DRPM, FRPM, TFLX, GFLX, MFLX, TEL, and VCM (MIC_{90s} of 0.25–0.5 μg/ml), but they were relatively less susceptible to CFDN, CEZ, CTM, CAZ, CMZ, and MINO (MIC_{50s} of 8.0–32 μg/ml).

Findings for *Haemophilus influenzae*

Susceptibilities of 206 *H. influenzae* strains to 39 antibacterial agents were determined. The results of susceptibility testing of *H. influenzae* isolates are summarized in Table 4. According to the CLSI breakpoint for ABPC,[2] 91 *H. influenzae* strains (44.2%) were found to be ABPC-susceptible, 41 (19.9%) to be ABPC-intermediate, and 74 (35.9%) to be ABPC-resistant strains. With the use of the Nitrocefin disks, all ABPC-intermediate and 60 (29.1%) ABPC-resistant strains were found to be β-lactamase-non-producing, and they were defined as BLNAI and BLNAR, respectively. The remaining 14 ABPC-resistant strains were found to be β-lactamase-producing and were designated as BLPAR. The MIC_{50} and MIC_{90} values of PCG and ABPC for BLPAR isolates were at least fivefold higher than those for BLNAR isolates. However, there were no differences in the MIC_{50} and MIC_{90} values of SBT/ABPC and CVA/AMPC among BLNAR isolates and BLPAR isolates. Regardless of their susceptibility to ABPC, all of the *H. influenzae* strains were extremely susceptible to all six fluoroquinolones (MIC_{50}s ≤ 0.06 μg/ml).

Susceptibility of ABPC-susceptible strains

Of the 33 antibacterial agents other than fluoroquinolones, 11 agents (PIPC, TAZ/PIPC, CFPN, CDTR, CAZ, CTRX, CFPM, AZT, MEPM, DRPM, and MINO) showed strong activities, with MIC_{90}s of ≤0.5 μg/ml.

Susceptibility of BLNAI and BLNAR strains

The BLNAI and BLNAR strains were found to be substantially susceptible (MIC_{90} ≤ 0.5 μg/ml) to PIPC, TAZ/PIPC, CDTR, CTRX, MEPM, and MINO. Among the cephems, CCL, CEZ, CTM, CZOP, and CMZ were less or not active against BLNAI and BLNAR, showing MIC_{90}s of 64 and 64, 64 and 128, 64 and 64, 8 and 16, and 16 and 32 μg/ml, respectively.

Susceptibility of BLPAR strains

Although the number of BLPAR was small (eight strains), some tendencies in susceptibility were noted. β-Lactamase inhibitors markedly restored the activities of penicillins against these strains: SBT decreased the MIC_{90} of ABPC from ≥256 to 8.0 μg/ml and TAZ decreased the MIC_{90} of

Table 3. Antibacterial susceptibility of *Streptococcus pneumoniae*

Antibacterial agent	All strains *n* = 257			PSSP (PCG ≦ 0.06 μg/ml) *n* = 166			PISP (PCG ≧ 0.125 μg/ml, ≦1 μg/ml) *n* = 78			PRSP (PCG ≧ 2 μg/ml) *n* = 13		
	MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)		
	50%	90%	Range	50%	90%	Range	50%	90%	Range	50%	90%	Range
PCG	≦0.06	1	≦0.06–4	≦0.06	≦0.06	≦0.06–≦0.06	0.5	1	0.125–1	2	2	2–4
ABPC	0.125	2	≦0.06–8	0.125	0.125	≦0.06–0.5	1	2	0.25–8	4	4	2–8
SBT/ABPC	0.125	2	≦0.06–8	0.125	0.125	≦0.06–0.25	1	2	0.125–8	4	4	1–8
CVA/AMPC	≦0.06	1	≦0.06–8	≦0.06	0.125	≦0.06–0.25	0.5	1	0.125–4	1	2	0.5–8
PIPC	≦0.06	2	≦0.06–4	≦0.06	0.125	≦0.06–1	1	2	≦0.06–2	2	4	1–4
TAZ/PIPC	≦0.06	1	≦0.06–4	≦0.06	0.125	≦0.06–0.5	1	2	≦0.06–2	2	4	1–4
CCL	1	32	≦0.06–≧256	0.5	4	≦0.06–8	16	64	0.5–128	64	128	32–≧256
CFDN	0.25	4	≦0.06–16	0.125	1	≦0.06–2	2	4	≦0.06–16	4	8	2–8
CFPN	0.25	0.5	≦0.06–4	0.125	0.5	≦0.06–2	0.5	1	≦0.06–2	0.5	1	0.5–4
CDTR	0.125	0.5	≦0.06–1	≦0.06	0.25	≦0.06–1	0.25	0.5	≦0.06–1	0.5	1	0.25–1
CEZ	0.25	2	≦0.06–32	0.125	0.5	≦0.06–1	2	2	0.25–4	4	8	2–32
CTM	0.25	4	≦0.06–16	0.25	1	≦0.06–2	2	4	0.25–8	4	8	2–16
CAZ	4	8	≦0.06–32	2	8	≦0.06–32	4	8	0.25–32	8	16	4–32
CTRX	0.25	1	≦0.06–4	0.25	1	≦0.06–2	0.5	1	0.125–2	1	2	0.5–4
CFPM	0.25	1	≦0.06–2	0.25	1	≦0.06–2	0.5	1	0.125–2	1	2	0.5–2
CZOP	0.25	1	≦0.06–4	0.125	1	≦0.06–2	0.5	1	≦0.06–2	1	2	0.5–4
CMZ	0.5	8	≦0.06–32	0.5	1	≦0.06–2	4	8	0.5–32	8	32	8–32
IPM	≦0.06	0.25	≦0.06–2	≦0.06	≦0.06	≦0.06–0.25	0.125	0.5	≦0.06–0.5	0.25	1	0.125–2
PAPM	≦0.06	0.125	≦0.06–1	≦0.06	≦0.06	≦0.06–0.25	≦0.06	0.25	≦0.06–0.5	0.25	0.5	≦0.06–1
MEPM	≦0.06	0.25	≦0.06–2	≦0.06	≦0.06	≦0.06–0.25	0.25	0.5	≦0.06–0.5	0.5	0.5	0.25–2
BIPM	≦0.06	0.25	≦0.06–2	≦0.06	≦0.06	≦0.06–0.125	0.125	0.25	≦0.06–0.5	0.25	0.5	0.125–2
DRPM	≦0.06	0.25	≦0.06–1	≦0.06	≦0.06	≦0.06–0.125	0.125	0.25	≦0.06–0.5	0.25	0.5	0.125–1
FRPM	≦0.06	0.25	≦0.06–1	≦0.06	≦0.06	≦0.06–0.25	0.25	0.5	≦0.06–0.5	0.25	0.5	0.25–1
GM	4	8	1–16	4	8	1–16	4	8	2–8	4	8	4–8
AMK	32	64	8–128	32	64	8–128	32	64	16–128	64	64	32–128
ABK	16	32	2–64	16	32	2–64	16	32	4–32	16	32	8–32
CPFX	1	2	≦0.06–64	1	2	≦0.06–32	1	2	0.25–64	1	2	0.5–2
LVFX	1	2	0.5–64	1	2	0.5–32	1	2	0.5–64	1	2	0.5–2
TFLX	0.25	0.25	≦0.06–≧32	0.25	0.25	≦0.06–≧32	0.125	0.25	≦0.06–≧32	0.125	0.25	0.125–0.25
GFLX	0.25	0.5	≦0.06–16	0.25	0.5	≦0.06–8	0.25	0.5	0.125–16	0.25	0.25	0.25–0.5
PZFX	2	4	≦0.06–128	2	4	≦0.06–64	2	2	1–128	2	2	2–4
MFLX	0.25	0.5	≦0.06–8	0.25	0.5	≦0.06–4	0.25	0.25	0.125–8	0.25	0.25	0.25–0.5
MINO	8	16	≦0.06–64	4	16	≦0.06–64	8	8	≦0.06–32	8	16	0.5–16
EM	≧256	≧256	≦0.06–≧256	≧256	≧256	≦0.06–≧256	≧256	≧256	≦0.06–≧256	≧256	≧256	2–≧256
CAM	128	128	≦0.06–≧128	128	128	≦0.06–≧128	128	128	≦0.06–≧128	128	128	1–≧128
AZM	≧128	≧128	≦0.06–≧128	≧128	≧128	≦0.06–≧128	≧128	≧128	≦0.06–≧128	≧128	≧128	1–≧128
TEL	≦0.06	0.25	≦0.06–4	≦0.06	0.25	≦0.06–4	≦0.06	0.25	≦0.06–1	0.125	0.5	≦0.06–0.5
CLDM	64	≧256	≦0.06–≧256	64	≧256	≦0.06–≧256	32	≧256	≦0.06–≧256	16	≧256	≦0.06–≧256
VCM	0.25	0.25	≦0.06–0.5	0.25	0.25	≦0.06–0.5	0.25	0.25	0.125–0.5	0.25	0.25	0.25–0.25
LZD	0.5	1	0.25–2	0.5	1	0.25–2	1	1	0.25–2	1	1	0.5–1

Susceptibilities of the 257 strains of *S. pneumoniae* to 40 antimicrobial agents were studied. The number of strains and proportions of PSSP, PISP, and PRSP were 166 (64.6%), 78 (30.4%), and 13 (5.1%), respectively

Table 4. Antibacterial susceptibility of *Haemophilus influenzae*

Antibacterial agent	All strains $n = 206$			BLNAS (ABPC ≦ 1 μg/ml, β-lactamase(−)) $n = 91$			BLNAI (ABPC = 2 μg/ml, β-lactamase(−)) $n = 41$			BLNAR (ABPC ≧ 4 μg/ml, β-lactamase(−)) $n = 60$			BLPAR (ABPC ≧ 4 μg/ml, β-lactamase(+)) $n = 14$		
	MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)		
	50%	90%	Range	50%	90%	Range	50%	90%	Range	50%	90%	Range	50%	90%	Range
PCG	2	8	≦0.06–≧256	0.25	2	≦0.06–16	4	8	2–8	4	8	2–16	128	≧256	8–≧256
ABPC	2	8	0.25–≧256	0.5	1	0.25–1	2	2	2–2	4	8	4–16	128	≧256	16–≧256
SBT/ABPC	2	8	≦0.06–16	0.25	1	≦0.06–1	2	2	1–4	4	8	2–8	4	8	2–16
CVA/AMPC	2	8	0.25–32	0.5	2	0.25–8	2	4	1–8	8	16	2–16	8	16	1–32
PIPC	≦0.06	0.25	≦0.06–≧256	≦0.06	0.125	≦0.06–1	0.125	0.25	≦0.06–0.5	0.125	0.25	≦0.06–0.5	128	≧256	16–≧256
TAZ/PIPC	≦0.06	0.125	≦0.06–1	≦0.06	≦0.06	≦0.06–1	≦0.06	0.25	≦0.06–0.5	≦0.06	0.125	≦0.06–0.5	≦0.06	0.25	≦0.06–0.25
CCL	8	64	0.25–128	2	16	0.25–32	16	64	4–128	32	64	4–128	16	64	4–128
CFDN	1	8	≦0.06–16	0.25	1	≦0.06–4	2	8	0.5–16	4	8	1–16	2	8	0.25–16
CFPN	0.5	2	≦0.06–8	≦0.06	0.125	≦0.06–1	1	2	≦0.06–4	2	4	0.125–4	0.5	4	≦0.06–8
CDTR	0.125	0.25	≦0.06–2	≦0.06	≦0.06	≦0.06–2	0.125	0.25	≦0.06–0.25	0.25	0.25	≦0.06–0.5	0.125	0.25	≦0.06–2
CEZ	8	64	0.25–≧256	4	16	0.25–64	8	64	1–≧256	32	128	1–≧256	8	64	2–128
CTM	4	64	0.25–128	1	8	0.25–32	16	64	4–64	32	64	2–128	4	64	2–128
CAZ	0.25	0.5	≦0.06–4	0.125	0.25	≦0.06–0.5	0.25	1	0.125–2	0.5	1	0.125–4	0.25	1	≦0.06–2
CTRX	0.125	0.25	≦0.06–0.5	≦0.06	≦0.06	≦0.06–0.5	0.25	0.25	≦0.06–0.5	0.25	0.5	≦0.06–0.5	0.125	0.5	≦0.06–0.5
CFPM	0.5	2	≦0.06–16	0.125	0.25	≦0.06–2	1	2	0.25–4	2	4	0.5–4	1	4	0.125–16
CZOP	4	8	≦0.06–64	0.125	1	≦0.06–4	8	8	0.5–32	8	16	2–64	4	32	0.125–32
CMZ	4	16	0.5–64	2	8	0.5–16	8	16	2–32	8	32	4–64	4	8	2–32
AZT	0.25	2	≦0.06–16	≦0.06	0.25	≦0.06–0.5	0.5	2	≦0.06–4	1	2	0.125–16	0.5	2	≦0.06–2
IPM	1	2	≦0.06–8	0.5	2	≦0.06–4	0.5	2	≦0.06–4	1	4	≦0.06–8	1	4	0.25–4
PAPM	0.5	2	≦0.06–4	0.5	1	≦0.06–2	0.5	2	≦0.06–2	1	4	≦0.06–4	1	2	0.125–4
MEPM	0.125	0.25	≦0.06–1	≦0.06	0.125	≦0.06–0.25	0.125	0.25	≦0.06–0.5	0.25	0.5	≦0.06–1	0.125	0.5	≦0.06–1
BIPM	1	4	≦0.06–8	0.5	2	≦0.06–8	2	4	≦0.06–4	4	8	≦0.06–8	2	4	0.25–8
DRPM	0.125	1	≦0.06–2	≦0.06	0.25	≦0.06–0.5	0.25	0.5	≦0.06–1	0.5	1	≦0.06–2	0.25	2	≦0.06–2
FRPM	1	2	0.125–4	0.5	2	0.125–2	2	2	0.25–4	2	4	0.25–4	2	2	0.25–4
GM	1	2	≦0.06–2	1	2	0.125–2	1	2	0.5–2	1	2	≦0.06–2	1	2	0.5–2
AMK	4	8	0.5–8	4	8	0.5–8	4	8	2–8	4	8	2–8	4	4	2–8
ABK	4	4	0.5–4	4	4	0.5–4	4	4	1–4	4	4	1–4	2	4	1–4
CPFX	≦0.06	≦0.06	≦0.06–16	≦0.06	≦0.06	≦0.06–4	≦0.06	≦0.06	≦0.06–16	≦0.06	≦0.06	≦0.06	≦0.06	0.125	≦0.06–1
LVFX	≦0.06	≦0.06	≦0.06–8	≦0.06	≦0.06	≦0.06–4	≦0.06	≦0.06	≦0.06–8	≦0.06	≦0.06	≦0.06	≦0.06	0.125	≦0.06–4
TFLX	≦0.06	≦0.06	≦0.06–≧32	≦0.06	≦0.06	≦0.06–1	≦0.06	≦0.06	≦0.06–≧32	≦0.06	≦0.06	≦0.06	≦0.06	≦0.06	≦0.06–0.5
GFLX	≦0.06	≦0.06	≦0.06–8	≦0.06	≦0.06	≦0.06–2	≦0.06	≦0.06	≦0.06–8	≦0.06	≦0.06	≦0.06	≦0.06	≦0.06	≦0.06–2
PZFX	≦0.06	≦0.06	≦0.06–32	≦0.06	≦0.06	≦0.06–2	≦0.06	≦0.06	≦0.06–32	≦0.06	≦0.06	≦0.06–0.125	≦0.06	≦0.06	≦0.06–4
MFLX	≦0.06	≦0.06	≦0.06–8	≦0.06	≦0.06	≦0.06–4	≦0.06	≦0.06	≦0.06–8	≦0.06	≦0.06	≦0.06–0.125	≦0.06	0.125	≦0.06–2
MINO	0.25	0.5	0.125–8	0.25	0.5	0.125–2	0.25	0.5	0.125–1	0.25	0.5	0.125–1	0.5	8	0.125–8
EM	4	8	0.25–32	4	4	0.25–16	4	8	1–16	4	8	0.5–32	4	4	2–8
CAM	8	16	0.5–64	8	8	2–32	8	32	2–32	8	16	0.5–64	4	32	2–32
AZM	0.5	1	0.125–4	0.5	1	0.25–4	0.5	2	0.25–4	1	1	0.125–4	0.5	1	0.125–1
TEL	2	4	0.25–8	1	2	0.25–8	2	4	0.5–8	2	4	0.25–8	1	2	0.5–4
CLDM	8	16	0.5–128	4	16	0.5–64	8	16	1–128	8	16	2–32	8	64	2–64

Susceptibilities of the 206 strains of *H. influenzae* to 39 antimicrobial agents were studied. The number of strains and proportions of BLNAS, BLNAI, BLNAR, and BLPAR were 91 (44.2%), 41 (19.9%), 60 (29.1%), and 14 (6.7%), respectively

PIPC from ≥256 to 0.25 μg/ml. Among the cephems, CDTR and CTRX showed appreciable activity, with MIC_{90}s of 0.25 and 0.5 μg/ml, respectively.

Findings for *Moraxella catarrhalis*

Susceptibilities of 120 *M. catarrhalis* strains to 39 antibacterial agents were tested. β-Lactamase inhibitors restored the activities of penicillins against these strains: SBT decreased the MIC_{90} of ABPC from 16 to 0.25 μg/ml and TAZ decreased the MIC_{90} of PIPC from 16 to ≤0.06 μg/ml. Although AMPC was not included in the panel, CVA was thought to restore the activity of AMPC, because the MIC_{90} of CVA/AMPC was low (0.5 μg/ml). Four of five carbapenems (PAPM, MEPM, BIPM, and DRPM), AZM, MINO, and all six fluoroquinolones showed strong activities, with MIC_{90}s of ≤0.06–0.125 μg/ml. The activities of IPM, CAM, and TEL were also strong, with MIC_{90}s of 0.25 μg/ml. Several cephems (CFDN, CFPN, CDTR, CTRX, CAZ, and CMZ), three aminoglycosides (GM, AMK, and ABK), and EM showed MIC_{90}s of 0.25–1.0 μg/ml (Table 5).

Findings for *Klebsiella pneumoniae*

Susceptibilities of 122 *K. pneumoniae* strains to 34 antibacterial agents were determined. The agents that showed very strong activity (MIC_{90}s ≤ 0.06 μg/ml) were MEPM and DRPM. Two oral cephems, CFDN and CDTR, five parenteral cephems (CTM, CAZ, CTRX, CFPM, and CZOP), three carbapenems (IPM, PAPM, and BIPM), two aminoglycosides, GM and ABK, and four fluoroquinolones (CPFX, TFLX, GFLX, and PZFX), showed relatively strong activities, with MIC_{90}s of 0.125–0.5 μg/ml (Table 6).

Findings for *Pseudomonas aeruginosa*

The antibacterial activities of 22 agents against 171 *P. aeruginosa* strains were measured. Two aminoglycosides, GM and ABK, and one of six fluoroquinolones, CPFX, showed moderate activities, with MIC_{90}s of 4.0 μg/ml. Two carbapenems, MEPM and DRPM, and two fluoroquinolones, LVFX and PZFX, showed MIC_{90}s of 8.0 μg/ml. The MIC_{90}s of three parenteral cephems (CAZ, CFPM, and CZOP), two carbapenems, IPM and BIPM, and two fluoroquinolones, TFLX and GFLX, were 16 μg/ml, while the MIC_{90}s of the remainder of the agents ranged from 32 to ≥256 μg/ml.

Only one strain was identified as multidrug-resistant *P. aeruginosa* (MDRP) from its profile of resistance to IPM, AMK, and CPFX (Table 7).

Cica-Beta Test (Kanto Chemical) in *K. pneumoniae* and *P. aeruginosa*

No ESBL-producing strain was detected in the 122 *K. pneumoniae* strains by the Cica-beta test. In the 171 *P. aeruginosa* strains, the test revealed two strains of MBL-producing *P. aeruginosa*, including one multidrug-resistant strain.

Table 5. Antibacterial susceptibility of *Moraxella catarrhalis*

Antibacterial agent	MIC (μg/ml)		
	50%	90%	Range
PCG	16	32	≦0.06–64
ABPC	8	16	≦0.06–64
SBT/ABPC	0.25	0.25	≦0.06–0.5
CVA/AMPC	0.25	0.5	≦0.06–0.5
PIPC	8	16	≦0.06–64
TAZ/PIPC	≦0.06	≦0.06	≦0.06
CCL	2	8	0.25–32
CFDN	0.25	0.5	≦0.06–2
CFPN	0.5	0.5	≦0.06–1
CDTR	0.25	1	≦0.06–2
CEZ	4	8	0.25–32
CTM	1	2	0.25–4
CAZ	0.125	0.25	≦0.06–0.5
CTRX	0.5	1	≦0.06–4
CFPM	1	4	0.125–4
CZOP	2	4	0.125–8
CMZ	0.5	1	≦0.06–2
AZT	2	2	0.25–4
IPM	≦0.06	0.25	≦0.06–0.5
PAPM	≦0.06	0.125	≦0.06–0.25
MEPM	≦0.06	≦0.06	≦0.06
BIPM	≦0.06	≦0.06	≦0.06–0.25
DRPM	≦0.06	≦0.06	≦0.06
FRPM	0.25	0.5	≦0.06–1
GM	0.25	0.25	≦0.06–0.25
AMK	0.5	1	0.25–2
ABK	0.25	0.25	0.125–0.5
CPFX	≦0.06	≦0.06	≦0.06–0.5
LVFX	≦0.06	0.125	≦0.06–1
TFLX	≦0.06	≦0.06	≦0.06
GFLX	≦0.06	≦0.06	≦0.06–0.25
PZFX	≦0.06	≦0.06	≦0.06–0.5
MFLX	0.125	0.125	≦0.06–0.25
MINO	0.125	0.125	≦0.06–0.5
EM	0.5	0.5	0.125–≧256
CAM	0.125	0.25	≦0.06–≧128
AZM	≦0.06	≦0.06	≦0.06–64
TEL	0.125	0.25	≦0.06–≧64
CLDM	4	8	0.5–≧256

Susceptibilities of the 120 strains of *M. catarrhalis* to 39 antimicrobial agents were studied

Discussion

Because there was no accessible public database of the susceptibility of bacterial pathogens to contemporaneously used antibacterial agents in Japan, the Japanese Society of Chemotherapy (JSC) established a nationwide surveillance network in 2006 so that the data obtained through the surveillance would enable the JSC to construct a database.

Our research focuses on major bacterial respiratory infections, so the collection of bacterial strains was limited to the seven species *S. aureus*, *S. pneumoniae*, *S. pyogenes*, *H. influenzae*, *M. catarrhalis*, *K. pneumoniae*, and *P. aeruginosa.* It is desirable that the analysis of antimicrobial susceptibility is conducted with those bacterial strains that really caused the infection. Therefore, we collected the

Table 6. Antibacterial susceptibility of *Klebsiella pneumoniae*

Antibacterial agent	MIC (μg/ml)		
	50%	90%	Range
ABPC	64	≧256	1–≧256
SBT/ABPC	4	8	0.5–128
CVA/AMPC	2	4	1–32
PIPC	8	16	0.5–≧256
TAZ/PIPC	2	4	0.25–≧256
CCL	0.5	1	0.25–≧256
CFDN	0.125	0.25	≦0.06–64
CFPN	0.5	1	0.125–4
CDTR	0.25	0.5	≦0.06–32
CEZ	1	2	0.5–128
CTM	0.125	0.5	≦0.06–64
CAZ	0.125	0.25	≦0.06–64
CTRX	≦0.06	0.125	≦0.06–8
CFPM	≦0.06	0.125	≦0.06–2
CZOP	≦0.06	0.125	≦0.06–8
CMZ	0.5	2	0.5–16
AZT	≦0.06	0.125	≦0.06–64
IPM	0.25	0.5	≦0.06–1
PAPM	0.25	0.5	≦0.06–1
MEPM	≦0.06	≦0.06	≦0.06–0.125
BIPM	0.25	0.5	≦0.06–1
DRPM	≦0.06	≦0.06	≦0.06–0.25
FRPM	0.5	1	0.25–4
GM	0.25	0.5	0.125–128
AMK	1	2	0.25–2
ABK	0.5	0.5	0.25–1
CPFX	≦0.06	0.5	≦0.06–8
LVFX	0.125	1	≦0.06–4
TFLX	≦0.06	0.25	≦0.06–4
GFLX	≦0.06	0.5	≦0.06–8
PZFX	≦0.06	0.25	≦0.06–2
MFLX	0.25	1	≦0.06–16
MINO	2	4	0.25–64
AZM	8	8	1–32

Susceptibilities of the 122 strains of *K. pneumoniae* to 34 antimicrobial agents were studied

Table 7. Antibacterial susceptibility of *Pseudomonas aeruginosa*

Antibacterial agent	MIC (μg/ml)		
	50%	90%	Range
PIPC	8	128	0.25–≧256
TAZ/PIPC	4	64	≦0.06–≧256
CAZ	2	16	0.125–≧128
CTRX	64	≧256	0.5–≧256
CFPM	4	16	0.25–≧256
CZOP	2	16	0.125–≧256
AZT	4	32	≦0.06–128
IPM	2	16	0.25–≧128
PAPM	8	32	0.25–≧256
MEPM	1	8	≦0.06–≧256
BIPM	0.5	16	≦0.06–128
DRPM	0.5	8	≦0.06–≧128
GM	2	4	≦0.06–64
AMK	4	8	0.25–128
ABK	2	4	0.125–64
CPFX	0.25	4	≦0.06–128
LVFX	1	8	≦0.06–≧256
TFLX	0.5	16	≦0.06–≧32
GFLX	1	16	≦0.06–≧256
PZFX	0.5	8	≦0.06–≧256
MFLX	2	16	0.25–≧256
MINO	16	64	0.5–≧256

Susceptibilities of the 171 strains of *P. aeruginosa* to 22 antimicrobial agents were analyzed

clinical isolates from adult patients with well-diagnosed respiratory tract infections.

The first year that surveillance was conducted the survey was done with the limited scope of respiratory tract infections in adults during the period from January to August, 2006. A total of 952 strains were collected at 32 institutions throughout Japan, and 887 strains (93.2%) were found to be evaluable, via re-identification and cultivation at the central reference laboratory, for their susceptibilities to antibacterial agents.

The total numbers of strains we used for the first and second yearly surveillance studies were 887 and 1108, respectively. The reason for the increase in the number of strains may be the increase in the number of participating institutions, from 32 in the first year to 39 in the second year. The numbers of each species tested in the first period and the second yearly surveillance were as follows: *S. aureus* (205, 226), *S. pneumoniae* (200, 257), *H. influenzae* (165, 206), *P. aeruginosa* (143, 171), *M. catarrhalis* (91, 120), *K. pneumoniae* (74, 122), and *S. pyogenes* (9, 6). These results suggest that the numbers of each species in the second yearly surveillance had generally increased by 10% to 30% compared to the numbers in the first surveillance period. We noticed that the increase in the number of *K. pneumoniae* strains at 64.8%, was the highest among these species. Although we cannot give any clear reason for this difference, we think we should observe further changes in the types of respiratory pathogens.

With regard to *S. aureus* strains, their susceptibilities were analyzed according to their classification as MSSA and MRSA. Approximately 55% of MSSA were thought to be penicillinase-producing strains because of their resistance to ABPC and susceptibility to SBT/ABPC and CCL, and 10.9% of them were thought to be *emr*-harboring strains because of their resistance to macrolides – EM, CAM, and AZM – and susceptibility to TEL (so-called ketolide lacking a sugar moiety to be recognized by *emr* resistance mechanism).[5] The difference between the resistance of MSSA to GM (10.9%) and that to AMK (1.1%) implied the coexistence of *aac*(*6′*)/*aph*(*2″*)-harboring GM-resistant strains with *aad*(*4′*, *4″*)-harboring AMK-resistant strains.[6]

The incidence of MRSA was high, at 59.7%, a finding that is similar to the data reported by Mochizuki et al.[7] according to analyses via WHONET 5. These MRSA strains were susceptible to ABK, VCM, TEIC, and LZD, except that a few strains were somewhat less susceptible (MIC 8.0 μg/ml) to ABK; these strains may possess both the *aph*(*3′*)-*III* and *aac*(*6′*)/*aph*(*2″*) genes, as reported recently.[6] Although the emergence of MRSA resistant to VCM, TEIC, or LZD has already been reported in Japan, such a resistant strain was not detected in the present surveillance.

Regarding *S. pneumoniae*, the proportion of PSSP/PISP/PRSP was found to be 65: 30: 5. The proportion of each group of strains remained at a level similar to that in the

first year of surveillance (61: 35: 4). More than 60% of the PSSP were thought to be *emr*-harboring strains because of their resistance to macrolides (EM, CAM, and AZM) and CLDM, and their susceptibility to the ketolide TEL. As for PISP, their incidence (30%) in this survey of adult RTI was much lower than that (50.8%) reported in pediatric infections.[8–10] In general, the antimicrobial susceptibilities of PISP were somewhat lower than those of PSSP: the activities of penicillins, including those combined with β-lactamase inhibitors, against PISP were 8 to 32 times less than those against PSSP; among the cephems, CCL, CFDN, CEZ, CTM, and CMZ showed activities 8 to 16 times less than those against PSSP, while CDTR, CAZ, CTRX, CFPM, CFPN, and CZOP showed 2 to 4 times less activity against PISP than against PSSP; the activities of carbapenems against PISP were 4 times less than those against PSSP. The activities of fluoroquinolones, glycopeptides, and LZD against PISP were the same as those against PSSP.

The incidence of PRSP was very low (5.0%) in the present surveillance of adult RTI, as compared with the incidence (16.9%-49.0%) reported in pediatric infections.[8–10] This difference is thought to be attributable to the excess usage of oral penicillins and cephems for the treatment of children, because fluoroquinolones (except for norfloxacin) are contraindicated in children in Japan. The pattern of susceptibility of PRSP strains somewhat resembled that of PISP, however, PRSP were substantially susceptible (MIC_{90}s ≤ 0.5 μg/ml) only to carbapenems, except for IPM, TFLX, GFLX, MFLX, TEL, and VCM.

The FDA has raised the concentration at which *S. pneumoniae* is considered to be susceptible to penicillin for the treatment of pneumonia, although the susceptibility breakpoint for meningitis remains unchanged (0.06 μg/ml). With the new criteria for breakpoint MICs, only 1 (0.4%) of the 257 *S. pneumoniae* strains in the present study was found to be intermediate-resistant, and the remainder (256 strains; 99.6%) were classified as susceptible strains. These results suggest that penicillin is still effective against community-acquired pneumonia caused by *S. pneumoniae*.

Concerning *H. influenzae*, half of the strains showed decreased susceptibility to ABPC without production of β-lactamase; BLNAI (19.9%) and BLNAR (29.1%). The incidence of BLNAI in adults is thought to be somewhat lower than that in children (30.4%).[11]

All six fluoroquinolones demonstrated extremely strong activity (MIC_{90} ≤ 0.06 μg/ml) against *H. influenzae* strains, regardless of the strains' ABPC-susceptibility. Of the rest of the agents, PIPC, TAZ/PIPC, CDTR, CTRX, MEPM, and MINO showed strong activities (MIC_{90}s of 0.125–0.5 μg/ml) against BLNAI and BLNAR, and TAZ markedly restored the activity of PIPC against BLPAR (MIC_{90} decreased from ≥256 μg/ml to 0.25 μg/ml).

By means of a recently established method, the Cica-Beta Test 1 (Kanto Chemical), for the detection of extended-spectrum β-lactamases (ESBL) and metallo-β-lactamases (MBL), two strains of *P. aeruginosa* were identified to be MBL-producing, although we did not find ESBL-producing *K. pneumoniae*. Such a low incidence of ESBL- and MBL-producing strains may be attributable to the target of our surveillance being limited to adult RTI; a higher incidence of such strains was reported in clinical isolates from urinary tract infections.[12]

The information on the patients' backgrounds and clinical settings supplied by the participating institutions enabled the JSC Surveillance Committee to analyze the collected pathogens in more detail; the results of this analysis will be published elsewhere.

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