Clinical Infectious Diseases Advance Access published October 5, 2011

BRIEF REPORT

Post-Tsunami Outbreaks of Influenza in Evacuation Centers in Miyagi Prefecture, Japan

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We describe 2 post-tsunami outbreaks of influenza A in evacuation centers in Miyagi Prefecture, Japan, in 2011. Although containment of the outbreak was challenging in the evacuation settings, prompt implementation of a systemic approach with a bundle of control measures was important to control the influenza outbreaks.

On 11 March 2011, an earthquake measuring 9.0 on the Richter scale off the northeast coast of Honshu Island, Japan, produced a devastating tsunami that destroyed many towns and villages near the coast in Iwate, Miyagi, and Fukushima prefectures [1]. Miyagi Prefecture was the area most severely devastated by the tsunami, with extensive loss of life and property; hundreds of thousands of people lost their houses and were forced to move to evacuation areas.

In the days and weeks following devastating natural disasters, the threat of infectious disease outbreak is high [2]. However, there have been few reports describing outbreaks of influenza in disaster settings despite the potential for increased influenza transmission.

Here, we report 2 outbreaks of influenza A in different evacuation centers in Miyagi Prefecture and discuss the management of these outbreaks.

Received 8 June 2011; accepted 13 September 2011.

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Clinical Infectious Diseases

1058-4838/2011/00-0001$14.00
DOI: 10.1093/cid/cir752

Patients and Methods

Two outbreaks of influenza A occurred at different evacuation centers in Miyagi Prefecture. The first outbreak occurred at the Kesennuma City Gymnasium in Kesennuma, a large-scale evacuation center with 1360 evacuees (outbreak 1), and the second outbreak occurred at Tatekoshi Elementary School in Natori, a middle-scale evacuation center with 200 evacuees (outbreak 2). In both centers, evacuees spent time primarily sitting and lying on the floor in the overcrowded halls of the centers, where the distance between them was less than 1 or 2 meters. Other risk factors in these centers for the transmission of infectious diseases included inadequate air ventilation, poor hand hygiene due to the disrupted water supply, and the dysfunction of the public health system.

Influenza-like illness was defined as fever above 38.0°C with or without respiratory symptoms such as sore throat and cough, and surveillance for influenza-like illness among evacuees was performed once or twice daily, including close monitoring of evacuees within 2 m of the symptomatic patients.

Nasopharyngeal swab samples were obtained from febrile patients by a standard collection method and were submitted for rapid antigen tests for influenza: the Rapid Testa FLU Stick (Kyorin Pharmaceutical Co., Ltd., Tokyo) in Kesennuma and the Immuno Ace Flu test (Tauns Laboratories, Inc., Shizuoka) in Natori. Some samples were sent for real-time reverse-transcriptase polymerase chain reaction (RT-PCR) analysis to subtype the viruses.

In both outbreaks, nonpharmaceutical interventions and postexposure prophylaxis were actually implemented in a step-by-step manner depending on the availability of medical resources. Vaccination to the evacuees was not performed because influenza vaccines were not available. A therapeutic course of oseltamivir (75 mg twice daily for 5 days) was prescribed to patients with symptoms of influenza. Exposed persons who were defined as individuals within 2 m from a symptomatic patient, including close contacts and high-risk persons, received postexposure prophylaxis with oseltamivir (75 mg once daily for 5 days).

Results

Outbreak 1. On 21 March 2011, 2 evacuees presented to a temporary medical office established in the evacuation center with high fever, and both were diagnosed as having influenza. More cases occurred over the following 9 days, and in total, 25 patients were diagnosed as having influenza, with the attack rate of 1.8%; 15 patients had positive results for influenza A by

the rapid antigen test, and 10 patients were diagnosed clinically (Figure 1). The mean age was 50.2 (range 3–92 years), with a male-to-female ratio of 1:1.5. The mean body temperature at the initial evaluation was 38.0°C. Symptoms other than fever and the histories of influenza vaccination were not recorded.

A bundle of control measures was promptly implemented to control the outbreak. Symptomatic patients were kept in isolation rooms until 2 days after the resolution of fever. The surveillance for influenza-like illness among evacuees was performed. Because it was impossible for the evacuees to wash their hands due to the disruption of the water supply, bottles of alcohol-based hand sanitizer were installed at common sites in the center. Surgical masks were distributed for free not only to symptomatic persons and exposed persons but also to asymptomatic persons without exposure. Children were advised to rub their hands with hand sanitizer before and after playing in a play room, and symptomatic children were prohibited from entering the play room. Patients exhibiting signs and symptoms of influenza-like illness were triaged and sent to a medical examination room that was temporally set up outside of the usual medical office. A therapeutic course of oseltamivir was prescribed to all patients, and 50 individuals received the postexposure prophylaxis.

Outbreak 2. Twenty individuals were diagnosed with influenza at Tatekoshi Elementary School between 4 April and 18 April 2011, giving an attack rate of 10.0% (Figure 1). The suspected index case visited a medical clinic near the school with an influenza-like illness on 4 April. Fifteen cases had positive results for influenza A by the rapid antigen test, and a subtype of H3N2 was identified from a patient with the positive antigen test result. The mean age was 47.2 (range 7–80 years), with a male-to-female ratio of 1:1.2, and the mean body temperature was 38.2°C. All patients were treated with oseltamivir or zanamivir. There were 3 patients who had been vaccinated against influenza, 1 of whom had a positive result by the rapid antigen test for influenza A.

A systemic intervention with multiple control measures was also implemented to control the outbreak immediately, including patient isolation, active case finding, strong promotion of cough etiquette and hand hygiene, and the same postexposure prophylaxis as in outbreak 1 for 34 individuals.

Both outbreaks subsided without any complicated or fatal cases of influenza.

Discussion

Influenza outbreaks can be rapid in closed environments, and high illness attack rates have been reported in closed military

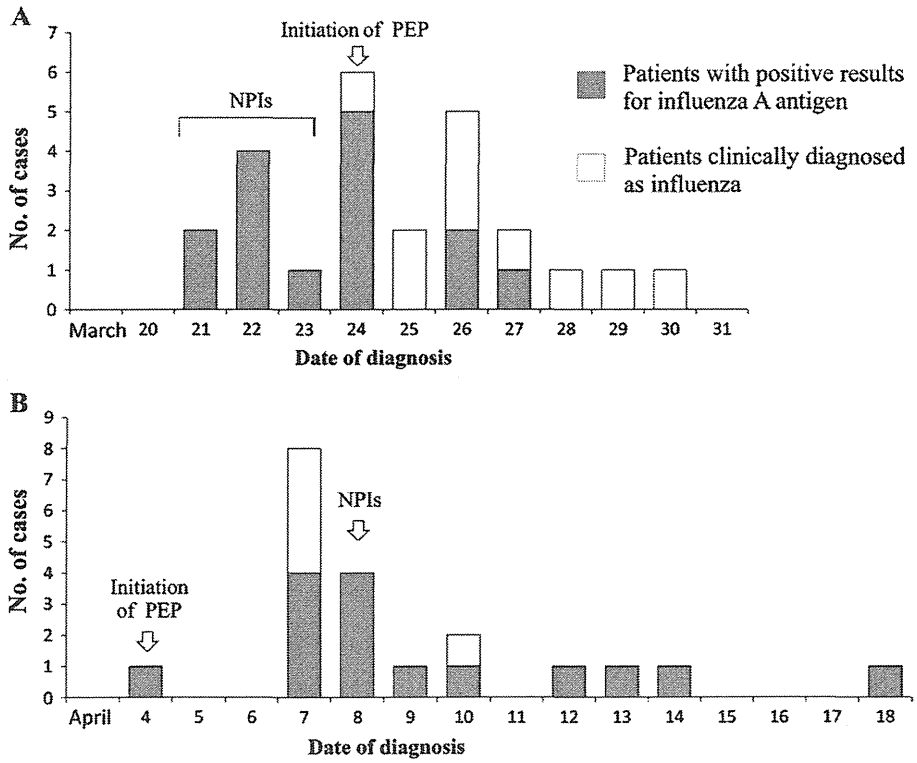

Figure 1. Epidemic curves for outbreaks of influenza in Kesennuma (*A*) and in Natori (*B*).
Abbreviations: NPIs, nonpharmaceutical interventions; PEP, postexposure prophylaxis.

settings and at enclosed schools; 22.0% in an outbreak of the 2009 pandemic influenza A (H1N1) virus on a Peruvian Navy ship [3], 42% in an influenza A (H3N2) outbreak on a U.S. Navy ship [4], and 35% in a New York City school outbreak of 2009 H1N1 influenza [5]. In both evacuation centers, there were several epidemic-prone factors other than overpopulation in semiclosed environments, but the low attack rates in our report may be attributable to several factors, including the rapid identification of cases, the swift implementation of several control measures, and partial immunity to the influenza A viruses.

More than half of the patients were diagnosed using the rapid antigen tests. The sensitivities of the rapid influenza antigen tests are generally 40%–70% compared with viral culture or RT-PCR [6], but their higher specificities (90%–95%) and short detection time (approximately 15 minutes or less) enabled us to provide timely treatment and implement prompt interventions.

Preventing the transmission of influenza virus within healthcare settings requires a multifaceted approach with nonpharmaceutical interventions, vaccination, and postexposure chemoprophylaxis with neuraminidase inhibitors [7, 8]. The same is true in nonhealthcare settings; the need for a multipartite approach for successful outbreak control has been reported in military settings and in a nursing school [3, 9, 10]. As to the postexposure chemoprophylaxis, we adopted a strategy of "ring chemoprophylaxis," which is simply based on spatial proximity and was shown to be effective in reducing the impact of outbreaks of 2009 H1N1 influenza in semiclosed military settings in Singapore [10], because of difficulties in identifying actual contacts and the practicalities of rapidly administrating chemoprophylaxis.

The findings in this report are subject to at least 3 limitations. First, we could not obtain a sufficient number of samples to subtype the influenza A virus. However, local surveillance data showed that H3N2 was the predominant subtype in Miyagi Prefecture after the disaster; 19 of 21 isolates were identified as H3N2 [11], which was the same subtype as that from a patient at the evacuation center in Natori. Second, we could not obtain sufficient information about influenza vaccination histories. The Ministry of Health, Labour and Welfare estimated that the vaccine coverage rate among entire Japanese population would be 38.9%–48.9% in 2010 [12], but there was no local data in the devastated region. Some evacuees had influenza despite having been vaccinated against influenza, which might suggest waning immunity against the prevalent influenza virus. Third, we could not prove clearly that the interventions terminated the outbreaks, as sporadic cases were still reported for a while after the initiation of the interventions. There might have been some cases where the influenza viruses were acquired outside the centers but were not detected by the surveillance, because there were constant comings and goings at the centers and H3N2 was prevalent in Miyagi Prefecture around the time of the disaster [11]. We, however, suppose that if it were not for the interventions, it would have taken longer time to terminate the outbreaks in the overcrowded circumstances.

Outbreaks of influenza after a severe natural disaster present unique challenges, and our report highlights the need for prompt implementation of a systemic approach with a bundle of control measures in evacuation settings, as in hospital settings.

Notes

Acknowledgments. We thank Dr Hayato Yamauchi (Saiki-Hoyouin, Oita), Dr Naoaki Tanno (TANNO Clinic, Natori), staff members of the public health centers in Kesennuma and Natori, and members of the Specific Disease and Infection Disease Policy Division, Miyagi Prefectural Government, for their dedicated efforts in terminating these outbreaks. We also thank Dr Akira Suzuki, Kentaro Tohma, and Kanako Otani (Department of Virology, Tohoku University Graduate School of Medicine) for identifying the subtype of the influenza A virus.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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CHEST

Original Research

CHEST INFECTIONS

Characteristics of Infectious Diseases in Hospitalized Patients During the Early Phase After the 2011 Great East Japan Earthquake

Pneumonia as a Significant Reason for Hospital Care

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Background: **Natural catastrophes increase infectious disease morbidity rates. On March 11, 2011, a 9.0-magnitude earthquake and associated Pacific coast tsunami struck East Japan. The aim of this study was to investigate the characteristics of patients with infectious diseases who needed hospitalization after this disaster.**

Methods: **We searched the medical records of 1,577 patients admitted to Tohoku University Hospital in the Sendai area within 1 month (March 11, 2011-April 11, 2011) after the disaster. We examined (1) changes in the rates of hospitalizations for infectious diseases over time and (2) the variety of infectious diseases.**

Results: **The number of hospitalized patients with infectious diseases increased after the first week to double that during the same period in 2010. Pneumonia comprised 43% of cases, and 12% consisted of skin and subcutaneous tissue infection, including tetanus. Pneumonia was prevalent in elderly patients (median age, 78 years) with low levels of serum albumin and comorbid conditions, including brain and nervous system disorders. Sputum cultures contained *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and *Haemophilus influenzae*, known pathogens of community-acquired pneumonia in Japan. In addition, 20.5% of patients had positive results for urinary pneumococcal antigen.**

Conclusions: **Among hospitalized patients, infectious diseases were significantly increased after the disaster compared with the same period in 2010, with pneumonia being prominent. The analyses suggest that taking appropriate measures for infectious diseases, including pneumonia, may be useful for disaster preparedness and medical response in the future.**

CHEST 2013; 143(2):349–356

Abbreviations: CAP = community-acquired pneumonia; ICD-10 = *International Statistical Classification of Diseases and Related Health Problems, 10th Revision*

On March 11, 2011, a 9.0-magnitude earthquake struck East Japan, and a tsunami washed away entire communities in the Pacific coastal area of Iwate, Miyagi, and Fukushima prefectures of the Tohoku district. This catastrophe killed 15,782 people, with >4,000 still missing 6 months after the disaster and seriously damaged health-care services and facilities. In the Pacific coastal region of Ishinomaki, Kesennuma, and part of the Sendai area, many hospitals collapsed or were flooded by the tsunami, and many health-care professionals were victims of the disaster. Thus, problems with the health-care system, including how to treat victims efficiently with limited resources, became critical issues in the aftermath.

For editorial comment see page 287

Several previous studies described the variety of illnesses that occur after natural disasters, including mega-earthquakes and tsunamis. After the 1995 Hanshin-Awaji earthquake, which struck southern Hyogo prefecture, Japan, the initial rash of illnesses was due to trauma and infectious diseases. Pneumonia was prominent, with the number of cases increasing within 1 month.[1,2] In the aftermath of the 2004 Indian Ocean tsunami in Thailand, acute diarrhea was predominant, followed by wound infection and respiratory illness.[3] Melioidosis, atypical mycobacterial, and polymicrobial bacterial infections were also reported in Thailand and Sri Lanka.[4,5] These reports indicate that infectious diseases are an important health issue after a natural disaster and that endemic background may influence infectious disease development in affected areas.

The aim of this study was to survey infectious disease trends in patients admitted to Tohoku University Hospital after the disaster. To our knowledge, it is the first to report changes in hospitalized patients with infectious diseases over a time course. We further identified the varieties of infectious diseases and conducted an analysis of pulmonary infection in the aftermath.

Materials and Methods

Background Medical Service Area and Population Before and After the Earthquake and Tsunami

Miyagi prefecture contains seven medical service areas. Tohoku University Hospital, one of the largest university hospitals in Japan with 1,300 beds for inpatient services, mainly served the Sendai area before the disaster. The coastal regions of Ishinomaki, Kesennuma, and Sendai were affected by the tsunami (Fig 1), with massive damage in Ishinomaki and Kesennuma. Ishinomaki contained seven secondary-care services and one tertiary-care service, and Kesennuma contained three secondary-care services. However, only one secondary-care service (Kesennuma City Hospital) and one tertiary-care service (Ishinomaki Red Cross Hospital) were available for inpatient services after the tsunami as designated disaster base hospitals, which play a central role in providing medical care during and after major disasters. Lack of essential utilities, food, and medicine limited inpatient service at these facilities. By contrast, the Sendai area had 30 secondary-care services and three tertiary-care services, including seven disaster base hospitals. The earthquake damaged these seven hospitals, including Tohoku University Hospital, but all except one were still available for inpatient care after the disaster. Among these six, Tohoku University Hospital sustained less damage and had much higher medical staffing and bed capacity than the other five. Thus, Tohoku University Hospital proactively received patients from Ishinomaki and Kesennuma in addition to those from Sendai.

We defined the background area of Tohoku University Hospital in the month after the 2011 disaster as Sendai, Ishinomaki, and Kesennuma, where an estimated 1,795,557 people lived. The background area during the same period in 2010 was Sendai, where an estimated 1,478,314 people lived (Fig 1).

Data Collection

We retrospectively reviewed medical charts and radiologic and laboratory findings for all available Tohoku University Hospital inpatient records during the first month after the earthquake and tsunami (March 11, 2011-April 11, 2011) and the same period of 2010. Including patients from the Ishinomaki and Kesennuma areas who were triaged once at Ishinomaki Red Cross Hospital or Kesennuma City Hospital, a total of 1,577 patients were admitted to our hospital during the month after the disaster. We classified the diseases of all hospitalized patients according to the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (ICD-10) and calculated the rate for each disease group based on background medical service population (e-Table 1). We extracted the patients with infectious diseases and new injuries after the disaster who required immediate medical treatment by specialists.

The physicians in charge of the patients conducted all clinical procedures and tests. Pneumonia was diagnosed through clinical evaluation, radiologic evaluation, and microbial testing according to community-acquired pneumonia (CAP) guidelines.[6,7] Pneumonia severity was evaluated by CURB-65 (confusion, urea >7 mmol/L, respiratory rate ≥ 30/min, low systolic [<90 mm Hg] or diastolic [≤ 60 mm Hg] BP, age ≥ 65 years).[8] This study was determined to be exempt from the requirement of institutional review board review because it was conducted as part of a public health investigation into retrospective data.

Microbiologic Tests

Pathogens in samples obtained from respiratory tracts were investigated. These samples were cultured semiquantitatively in sheep blood agar, chocolate agar, and potato dextrose agar. The Vitek 2 (bioMérieux sa) system was used to identify pathogens from blood, skin and wounds, and respiratory tracts. Upon positive identification of potentially drug-resistant pathogens, such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, and extended-spectrum β-lactamase-producing Enterobacteriaceae, drug resistance was defined according to Clinical and Laboratory Standards Institute guidelines.[9,10]

The BinaxNOW *S pneumoniae* test (Alere) and Check *Legionella* Urinary Antigen EIA (Alfresa Holdings Corp) were used for qualitative detection of *S pneumoniae* antigen and *Legionella pneumophila* serogroup 1 antigen, respectively, in human urine. The ESPLINE Influenza A&B-N (FUJIREBIO Inc) was used for

Manuscript received December 26, 2011; revision accepted July 9, 2012.
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Funding/Support: The authors have reported to *CHEST* that no funding was received for this study.
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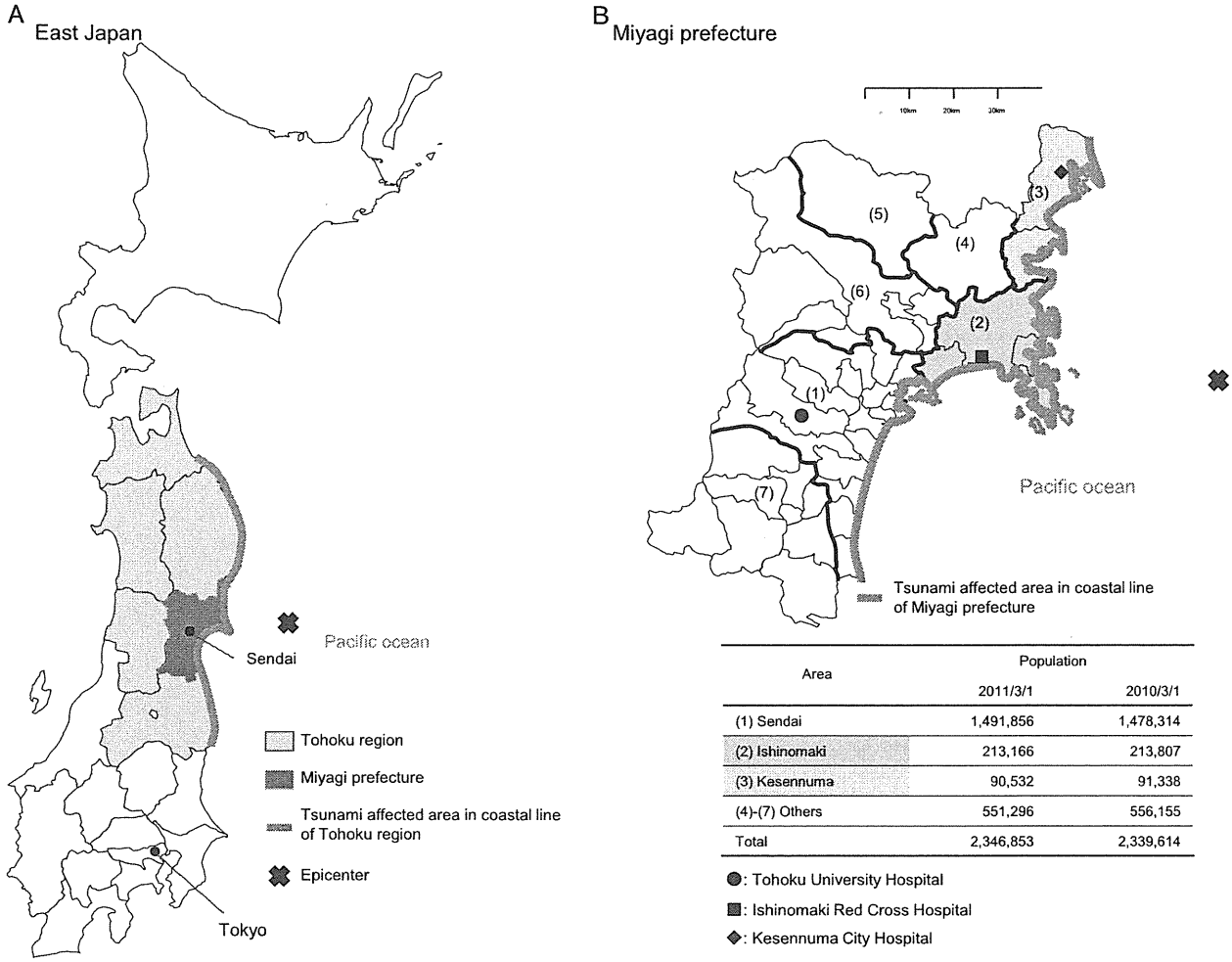
DOI: 10.1378/chest.11-3298



Area	Population	
	2011/3/1	2010/3/1
(1) Sendai	1,491,856	1,478,314
(2) Ishinomaki	213,166	213,807
(3) Kesennuma	90,532	91,338
(4)-(7) Others	551,296	556,155
Total	2,346,853	2,339,614

●: Tohoku University Hospital
■: Ishinomaki Red Cross Hospital
◆: Kesennuma City Hospital

FIGURE 1. Affected areas by the tsunami and patient background areas of Tohoku University Hospital before and after the disaster. A, The map shows the position of Miyagi prefecture and neighboring cities in East Japan, including the Tohoku region. B, The map of Miyagi prefecture shows medical service areas and the population served by Tohoku University Hospital before and after the tsunami. Note that the background areas of Tohoku University Hospital in 2011 were Sendai, Ishinomaki, and Kesennuma areas, whereas the background area in 2010 was only the Sendai area.

qualitative detection of influenza A and B nucleoprotein antigens in nasopharyngeal swabs.

Analysis

Data analysis was conducted using GraphPad Prism 5 (GraphPad Software, Inc) software. Statistical significance was evaluated by χ^2 test or Fisher test according to sample size, and $P < .05$ was considered significant.

RESULTS

Changes in Infectious Disease and Injury Rates During the Month

The population-based ratio of overall hospitalized patients was 87.8 and 104.8 per 100,000 population in 2011 and 2010, respectively (e-Table 1). The rate of hospitalized patients with infectious diseases in 2011 was doubled from that of 2010 (8.18 vs 4.47 per 100,000 population, $P < .0001$) (Table 1). We first evaluated the rates of hospitalized patients with infectious diseases within 1 month after the disaster, and the rate peaked 2 weeks after the disaster and then decreased to the 2010 level at 3 weeks (Fig 2).

ICD-10 disease classification of all admitted patients within 1 month after the disaster showed a significantly increased rate of injury (S00-T99) (2011 vs 2010, 7.7 vs 4.2 per 100,000 population; $P < .0001$) and diseases of the genitourinary system (N00-N99) (2011 vs 2010, 7.5 vs 3.1 per 100,000 population; $P < .0001$) (e-Table 1). However, > 90% of patients with diseases of the genitourinary system (N90-N99) were hospitalized for the purpose of hemodialysis.

In previous reports of natural disasters, the time trend of injuries differed from that of infectious diseases.[1,11-13] Thus, we also examined injury rate over time compared with that of infectious diseases. The injury rate increased

Table 1—*Variety of Infectious Diseases Within the First Month After the Earthquake and Tsunami (March 11, 2011-April 11, 2011, and 2010)*

ICD-10	Infectious Diseases	Rate/100,000 (No.) 2011	2012
	Certain infectious and parasitic diseases		
A00-A09	Intestinal infectious diseases	0.28 (5)	0.20 (3)
A15-A19	TB	0.00 (0)	0.14 (2)
A35	Tetanus	0.11 (2)	0.00 (0)
A41	Sepsis	0.50 (9)	0.28 (4)
A46	Erysipelas	0.00 (0)	0.07 (1)
A80-A89	Viral infections of the CNS	0.00 (0)	0.07 (1)
B00-B09	Viral infections characterized by skin and mucous membrane lesions	0.17 (3)	0.00 (0)
B20-B24	HIV disease	0.00 (0)	0.07 (1)
B35-B34	Other viral diseases	0.00 (0)	0.20 (3)
	Diseases of the nervous system		
G00	Bacterial meningitis	0.06 (1)	0.00 (0)
	Diseases of the eye and adnexa		
H00-H59	Disorders of conjunctiva	0.00 (0)	0.07 (1)
H15-H22	Disorders of sclera, cornea, iris, and ciliary body	0.00 (0)	0.07 (1)
	Diseases of the ear and mastoid process		
H60-H62	Diseases of external ear	0.00 (0)	0.07 (1)
	Diseases of the respiratory system		
J00-J06	Acute upper respiratory infections	0.11 (2)	0.28 (4)
J09-J18	Influenza and pneumonia	3.68[a] (66)	0.47 (7)
J20-J22	Other acute lower respiratory infections	0.44 (8)	0.14 (2)
J30-J39	Other diseases of upper respiratory tract	0.11 (2)	0.40 (6)
J40-J47	Chronic lower respiratory diseases	0.22 (5)	0.14 (2)
J60-J70	Lung diseases due to external agents	0.17 (3)	0.14 (2)
J80-J84	Other respiratory diseases principally affecting the interstitium	0.06 (1)	0.00 (0)
J95-J99	Other diseases of the respiratory system	0.06 (1)	0.14 (2)
	Diseases of the digestive system		
K00-K14	Diseases of the oral cavity, salivary glands, and jaw	0.00 (0)	0.07 (1)
K20-K31	Diseases of the esophagus, stomach, and duodenum	0.00 (0)	0.07 (1)
K35-K38	Diseases of the appendix	0.06 (1)	0.07 (1)
K65-K67	Diseases of the peritoneum	0.00 (0)	0.07 (1)
K80-K89	Disorders of the gallbladder, biliary tract, and pancreas	0.50 (9)	0.20 (3)
	Diseases of the skin and subcutaneous tissue		
L00-L08	Infections of the skin and subcutaneous tissue	0.56 (10)	0.40 (6)
L80-L99	Other disorders of the skin and subcutaneous tissue	0.22 (4)	0.00 (0)
	Diseases of the musculoskeletal system and connective tissue		
M00-M03	Infectious arthropathies	0.06 (1)	0.07 (1)
M40-M54	Dorsopathies	0.06 (1)	0.00 (0)
	Diseases of the genitourinary system		
N39	Urinary tract infection	0.33 (6)	0.14 (2)
N70-N77	Inflammatory diseases of female pelvic organs	0.11 (2)	0.00 (0)
	Pregnancy, childbirth, and the puerperium		
O20-O29	Other maternal disorders predominantly related to pregnancy	0.00 (0)	0.07 (1)
O85-O92	Complications predominantly related to the puerperium	0.00 (0)	0.07 (1)
P35-P39	Infections specific to the perinatal period	0.00 (0)	0.07 (1)
	Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified		
R00-R09	Symptoms and signs involving the circulatory and respiratory systems	0.06 (1)	0.14 (2)
R02	Gangrene, not elsewhere classified	0.06 (1)	0.00 (0)
	Injury, poisoning, and certain other consequences of external causes		
T79-T79	Certain early complications of trauma	0.00 (0)	0.07 (1)
T80-T88	Complications of surgical and medical care, not elsewhere classified	0.17 (3)	0.07 (1)
	Total	8.18[a] (147)	4.47 (66)

ICD-10 = *International Statistical Classification of Diseases and Related Health Problems, 10th Revision.*
[a]$P < .0001$.

and was significantly higher 1 week after the disaster in 2011 than during the same period in 2010 (Fig 2) and was reduced to the 2010 level 2 weeks after the disaster. The time trends of patients with infectious diseases and injuries in our hospital after the disaster were similar to previous reports.[1,11-13]

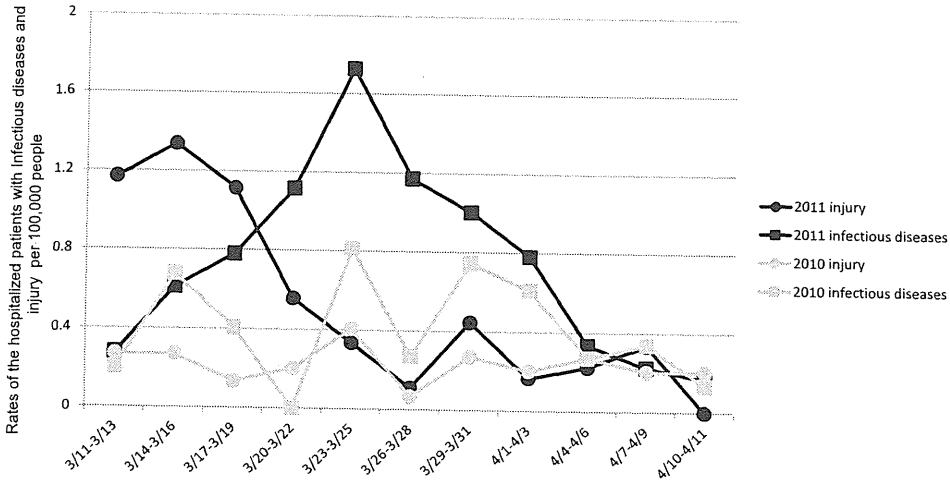


FIGURE 2. Time trends of the background population-based rates of infectious diseases and injuries of hospitalized patients at Tohoku University Hospital during the first month after the 2011 disaster as well as in the same period of 2010. The rates per 100,000 people of each background population are also shown.

Variety of Infectious Diseases

We then classified the infectious diseases of hospitalized patients according to the ICD-10. Respiratory infectious diseases (J00-J99) were found in 88 of 147 patients (60%), with pneumonia (J09-J18) accounting for 75% (66 of 88 patients) (Table 1). Skin and wound infections, including diseases of skin and subcutaneous tissue (L00-L99), tetanus (A35), and, viral infections characterized by skin and mucous membrane lesions (B00-B09), were found in 19 of 147 patients (13%) followed by nine (6%) with sepsis (A41) and nine (6%) with biliary duct infection (K80-K89). However, the rates of those infectious diseases, as well as other infectious diseases, did not differ statistically between 2011 and 2010.

In hospitalized patients with infectious diseases after the disaster, 13 of 147 (8.8%) were swept away by the tsunami directly, and 67 of 147 (46%) lost their houses because of the tsunami and were forced to live in an evacuation center. Among patients with respiratory infectious diseases, skin and wound infection, sepsis, and biliary duct infection, 12 of 88 (19%), one of 19 (5%), zero of nine (0%), and zero of nine (0%), respectively, were directly engulfed by the tsunami, and 49 of 88 (56%), four of 19 (21%), five of nine (56%), and five of nine (56%), respectively, lived in an evacuation center. Seventy-five percent of patients with respiratory infections experienced direct or indirect damage from the tsunami. These data suggest that after this disaster, respiratory infectious diseases were a significant cause of hospitalization among people in communities and evacuation centers.

Clinical Features of Pneumonia

Pneumonia (including J13-J15 and J18) was diagnosed by clinical evaluation, radiologic evaluation, and microbial testing in 64 patients. Twelve patients had been swept away by the tsunami and nearly drowned, and 40 of 64 patients (63%) lost their houses because of the tsunami and were forced to live in an evacuation center. We compared the characteristics of patients with pneumonia after the disaster with those during the same period in 2010 (Table 2), although the comparison was limited by the relatively small number of cases (seven) in 2010. The median age of the 2011 patients was 78 years (interquartile range, 69-84 years), which was not significantly different from that of the 2010 patients (median, 72 years; interquartile range, 67-84 years). Severe pneumonia, as indicated by a CURB-65 $\geq$ 4, did not differ between 2011 and 2010 (19% vs 14%). In 2011, 81% of patients with pneumonia had comorbid conditions, 36% with brain and nervous system disorders (cerebrovascular disease, Parkinson disease, and Alzheimer disease), whereas in 2010, all patients with pneumonia had underlying diseases but not brain and nervous system disorders. Serum albumin levels were lower in 2011 patients than in 2010 patients (2.4 g/dL vs 2.8 g/dL, $P < .05$). Sputum cultures were collected from 40 patients, and pathogens were isolated from 22 patients. Isolated microbes from sputum cultures included penicillin-susceptible *S pneumoniae*; methicillin-sensitive *S aureus*; methicillin-resistant *S aureus*, *M catarrhalis*, and *H influenzae* (Table 2). No significant differences in pathogens isolated from pneumonia sputum cultures were observed between 2011 and 2010. Urinary antigen assays revealed that nine of 44 patients (20.5%) had positive results for *S pneumoniae* antigen, and two had positive results for *L pneumophila* serogroup 1 antigen in 2011, whereas urinary antigen tests revealed no positive results in 2010. As of July 31, 2011, 59 patients had been cured and discharged. Five patients died while in the hospital, with three because of aggravation of

Table 2—*Comparison of Clinical Features of Patients With Pneumonia Admitted to Tohoku University Hospital Before and After the Earthquake and Tsunami (March 11, 2011-April 11, 2011, and 2010)*

Clinical Feature	2011	2010
Study population	64	7
Demographics		
Male sex	39 (61)	4 (57)
Age, y	78 (69-84)	72 (67-84)
Almost drowned	12 (19)	...
Lived in an evacuation center	40 (63)	...
Comorbidities	52 (81)	7 (100)
Cerebrovascular disease	13 (20)	0 (0)
Diabetes mellitus	7 (11)	5 (71)
COPD	7 (11)	1 (14)
Chronic heart failure	6 (9)	1 (14)
Hypertension	6 (9)	2 (29)
Parkinson disease	5 (8)	0 (0)
Alzheimer disease	5 (8)	0 (0)
Renal disease	5 (8)	2 (29)
Coronary artery disease	4 (6)	0 (0)
Liver disease	2 (3)	0 (0)
Hyperlipidemia	2 (3)	2 (29)
Immunosuppression[a]	4 (6)	2 (29)
Initial severity and management		
CURB-65 score		
0	1 (2)	0 (0)
1	16 (25)	0 (0)
2	16 (25)	2 (29)
3	19 (29)	3 (43)
4	10 (16)	1 (14)
5	2 (3)	0 (0)
Mechanical ventilation	7 (11)	1 (14)
Laboratory values		
WBC count, /L	9.2 (7.1-13.6)	9.3 (8.6-12.1)
BUN, mg/dL	23.4 (15.0-35.6)	23.0 (18.0-29.0)
Albumin, g/dL	2.4[b] (1.9-2.7)	2.8 (2.5-3.2)
Arterial pH < 7.35	6 (9)	0 (0)
Initial radiologic patterns		
Bilateral infiltrate	17 (27)	4 (57)
Multilobar infiltrate	38 (59)	2 (29)
Pleural effusion	5 (9)	1 (14)
Microbiologic test		
Patients examined by sputum culture	40 (64)	7 (100)
Patients with isolated pathogens from sputum	22 (55)	2 (29)
Methicillin-resistant *Staphylococcus aureus*	7 (18)	1 (14)
Penicillin-susceptible *Streptococcus pneumoniae*	5 (13)	0 (0)
Methicillin-susceptible *S aureus*	5 (13)	1 (14)
Moraxella catarrhalis	3 (8)	0 (0)
Haemophilus influenzae	2 (5)	0 (0)
Pseudomonas aeruginosa	2 (5)	0 (0)
Klebsiella pneumoniae	1 (3)	1 (1)
Legionella pneumophila	1 (3)	0 (0)
Others	2 (5)	0 (0)
Combined etiology	8 (20)	1 (14)
Urinary antigen assays		
Patients examined	44 (69)	2 (29)
S pneumoniae	9 (20.5)	0 (0)
L pneumophila serogroup 1	2 (4.5)	0 (0)
Rapid influenza antigen tests		
Patients examined	14 (25)	2 (29)
Influenza A	1 (2)	0 (0)
Influenza B	0 (0)	0 (0)
Outcomes (as of August 1, 2011)		
Cured and discharged	59 (92.2)	7 (100)
Died	5 (7.8)	0 (0)

Data are presented as No. (%) or median (interquartile range). CURB-65 = confusion, urea > 7 mmol/L, respiratory rate ≥ 30/min, low systolic (< 90 mm Hg) or diastolic (≤ 60 mm Hg) BP, age ≥ 65 y.
[a]Active cancer, HIV infection, long-term systemic corticosteroid use.
[b]$P < .05$.

comorbidities. One patient with severe pneumonia associated with *L pneumophila* serogroup 1 died of a massive brain infarction that developed during hospitalization.

Microbiologic Characteristics of Skin and Wound Infection, Sepsis, and Biliary Duct Infection

We also examined the causative pathogens of skin and wound infection (L00-L99), sepsis (A41), and biliary duct infection (K80-K89), which demonstrated relatively high rates (> 0.5 per 100,000 population) in 2011. No significant differences were observed in isolated pathogens from blood culture, bile ducts, and wounds between 2011 and 2010 (e-Table 2).

Discussion

Previous reports found that death rates among the East Japanese population caught in the tsunami were very high (50%-80%), with the tsunami-associated injury rate lower than the death rate.[14,15] The number of dead and missing was estimated at > 20,000 6 months later. Almost all victims were killed by the tsunami. One month after the earthquake and tsunami, total injuries numbered fewer than 5,000. However, about 150,000 people were forced to live in uncomfortable conditions without water, gas, or electricity during the winter. Previous studies have reported increased rates of infectious diseases, wound infection,[11-13] infectious enteritis,[3] and pneumonia[1,2] after natural disasters, and these diseases constituted a major public health problem. Therefore, we focused on whether the earthquake and tsunami damage influenced infectious disease rates during the early period after the disaster.

The most common early illnesses of natural disaster survivors (earthquake and tsunami) were reported as soft tissue wounds and orthopedic-related injuries.[11-13] No reports have described the time course of changes in injury and infectious diseases that lead to hospitalization

after a natural disaster. In our investigation, the injury rate among hospitalized patients increased 1 week after the disaster, whereas the infectious disease rate increased at 2 weeks after the disaster.

Wound infections during and after injury are high after natural disasters. Tetanus is a potential health threat after injury,[16] and wound infection with bacteria, such as *Pseudomonas*, Enterobacteriaceae, and *Aeromonas*, from soil and debris is a critical health issue.[17,18] We did not observe a significant increase in patients with wound infections, although two cases of tetanus occurred during the study period, which may highlight tetanus as another potential pathogenic health threat to survivors, as reported in previous natural disasters.

Several reports described increases in respiratory infection after natural disasters.[2,19] However, detailed analyses of the characteristics of pneumonia after disasters are limited. We observed that about 60% of admitted patients experienced infectious respiratory diseases, mainly pneumonia (> 40%), suggesting that pneumonia was a significant threat to the health of survivors in the areas affected by the earthquake and tsunami. However, no demographic differences were seen in hospitalized patients with pneumonia in 2011 and 2010.

Microbiologic etiology studies of CAP in Japan revealed *S pneumoniae* as the most common pathogen (23%-26%), followed by *H influenzae* (6%-19%), *M catarrhalis* (1%-4%), and *Klebsiella pneumoniae* (1%-2%).[20-23] Thus, the causative pathogens of pneumonia leading to hospitalization after the disaster were similar to those previously reported in Japan.

We could not examine bacterial culture tests for all patients with infectious diseases because testing instruments and utilities in our hospital were damaged by the earthquake and required 1 week for repair. However, urinary antigen assays, which were not affected by the disaster, revealed that 20% of patients tested positive for *S pneumoniae* antigen, similar to previous studies reporting that *S pneumoniae* accounts for 12% to 28% of causative pathogens in CAP.[20-23] One case of severe pneumonia caused by *L pneumophila* serogroup 1 was identified by both sputum culture and urinary antigen assay; this patient had aspirated soil-contaminated seawater. Presciently, the Centers for Disease Control and Prevention warned of possible *Legionella* pneumonia infections after disasters, although no cases of *Legionella* pneumonia were reported after previous earthquakes and tsunamis.[24]

In summary, this report is the first in our knowledge to describe the infectious diseases seen in inpatient services at Tohoku University Hospital in the month following the 2011 earthquake and tsunami in East Japan. The survey revealed pneumonia as prominent among infectious diseases in hospitalized patients after the disaster. Our observations suggest that improving living conditions as well as providing adequate healthcare services is necessary to protect people in affected areas, especially elderly and vulnerable persons, from infectious diseases, including pneumonia.

Acknowledgments

Author contributions: Drs Aoyagi and Yamada had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Dr Aoyagi: contributed to the study design, data analysis and interpretation, and writing and revision of the manuscript.
Dr Yamada: contributed to the study design, data analysis and interpretation, and writing and revision of the manuscript.
Dr Kunishima: contributed to the study concept and design, critical review of the manuscript, and approval of the final draft.
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Dr Yano: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Ishibashi: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Hatta: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Endo: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Arai: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Inomata: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Gu: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Kanamori: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Ms Kitagawa: contributed to the study concept and design, critical review of the manuscript, and approval of the final draft.
Dr Hirakata: contributed to the data collection and interpretation, critical review of the manuscript, and approval of the final draft.
Dr Kaku: contributed to the study design, data analysis and interpretation, and revision of the manuscript.
Financial/nonfinancial disclosures: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Additional information: The e-Tables can be found in the "Supplemental Materials" area of the online article.

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J Infect Chemother (2012) 18:609–620
DOI 10.1007/s10156-012-0434-3

SURVEILLANCE

Nationwide surveillance of bacterial respiratory pathogens conducted by the Surveillance Committee of Japanese Society of Chemotherapy, Japanese Association for Infectious Diseases, and Japanese Society for Clinical Microbiology in 2009: general view of the pathogens' antibacterial susceptibility

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Received: 13 February 2012 / Accepted: 10 May 2012 / Published online: 6 July 2012

Abstract For the purpose of nationwide surveillance of antimicrobial susceptibility of bacterial respiratory pathogens from patients in Japan, the Japanese Society of Chemotherapy (JSC) started a survey in 2006. From 2009, JSC continued the survey in collaboration with the Japanese Association for Infectious Diseases and the Japanese Society for Clinical Microbiology. The fourth-year survey was conducted during the period from January and April 2009 by the three societies. A total of 684 strains were collected from clinical specimens obtained from well-

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diagnosed adult patients with respiratory tract infections. Susceptibility testing was evaluable with 635 strains (130 *Staphylococcus aureus*, 127 *Streptococcus pneumoniae*, 4 *Streptococcus pyogenes*, 123 *Haemophilus influenzae*, 70 *Moraxella catarrhalis*, 78 *Klebsiella pneumoniae*, and 103 *Pseudomonas aeruginosa*). A maximum of 45 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), four 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 Standard Institute (CLSI). Incidence of methicillin-resistant *S. aureus* (MRSA) was as high as 58.5 %, and that of penicillin-intermediate and penicillin-resistant *S. pneumoniae* (PISP and PRSP) was 6.3 % and 0.0 %, respectively. Among *H. influenzae*, 21.1 % of them were found to be β-lactamase-non-producing ampicillin (ABPC)-intermediately resistant (BLNAI), 18.7 % to be β-lactamase-non-producing ABPC-resistant (BLNAR), and 5.7 % to be β-lactamase-producing ABPC-resistant (BLPAR) strains. A high frequency (76.5 %) of β-lactamase-producing strains has been suspected in *Moraxella catarrhalis* isolates. Four (3.2 %) extended-spectrum β-lactamase-producing *K. pneumoniae* were found among 126 strains. Four isolates (2.5 %) of *P. aeruginosa* were found to be metallo-β-lactamase-producing strains, including three (1.9 %) suspected multi-drug resistant strains showing resistance against imipenem, amikacin, and ciprofloxacin. Continuous national surveillance of the antimicrobial susceptibility of respiratory pathogens is crucial to monitor changing patterns of susceptibility and to be able to update treatment recommendations on a regular basis.

Keywords Surveillance · Susceptibility · Resistance · Respiratory tract infection

Introduction

To investigate comprehensively the antimicrobial susceptibility and resistance of bacterial respiratory pathogens, the Japanese Society of Chemotherapy (JSC) established a nationwide surveillance network in 2006. The first and second surveys were conducted during the period from January to August in 2006 and 2007 and the third survey was conducted during the period from January to April in 2008; we reported the trend of antimicrobial susceptibilities of bacterial species from patients with respiratory tract infections (RTIs) [1]. After a third year of study, we decided to continue this survey in association with JSC, the Japanese Association for Infectious Diseases, and the Japanese Society for Clinical Microbiology. Here we report the study in the fourth year of nationwide surveillance conducted by the three societies. The results obtained from this surveillance will be used as a set of controls for those conducted in future by the three societies and by other organizations as well.

Materials and methods

Strains and quality control

The causative bacteria from the patients with RTI were isolated from sputum, specimens collected by transtracheal

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aspiration, or bronchoscopy. Microbiological laboratory tests for respiratory pathogens were conducted by standard methods including Gram staining and quantitative culture of various respiratory samples at 46 medical institutions, as listed in Table 1. The isolated bacteria were identified to species level in each laboratory. The isolates were suspended in Micro-bank tubes (Asuka Junyaku, Tokyo, Japan) and transferred to the central laboratory of the Research Center for Anti-infective Drugs of the Kitasato Institute. The electronic uniform data sheets of each patient from whom these strains isolated were also completed at each institution and sent to the Center so that microbiological data obtained could be stratified under the settings and profiles of patients and under the diagnoses.

A total of 684 strains were received at the Center and kept at −80 °C until antimicrobial susceptibility testing was conducted. Re-identification and cultivation of the strains gave 635 evaluable strains consisting of 130 *Staphylococcus aureus*, 127 *Streptococcus pneumoniae*, 4 *Streptococcus pyogenes*, 123 *Haemophilus influenzae*, 70 *Moraxella catarrhalis*, 78 *Klebsiella pneumoniae*, and 103 *Pseudomonas aeruginosa*.

Accuracy of determination for minimum inhibitory concentration (MIC) of antibacterial agents was controlled according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) using 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 those of *S. pneumoniae* and *S. pyogenes*; *H. influenzae* ATCC49247 for *H. influenzae*; *E. coli* ATCC25922 for *K. pneumoniae* and *P. aeruginosa*; and *P. aeruginosa* ATCC27853 for *P. aeruginosa*. *E. coli* ATCC35218 was used as a control strain in case of MIC determination for β-lactam antibiotics combined with β-lactamase inhibitors.

Table 1 List of participating institutions contributing to our surveillance

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Japanese Red Cross Sendai Hospital, Sendai, Miyagi
Kagawa University Hospital, Kagawa, Mikicho
Kawasaki Medical School Hospital, Kurashiki, Okayama
Keio University Hospital, Shinjuku, Tokyo
Kyorin University Hospital, Mitaka, Tokyo
Muroran General Hospital, Muroran, Hokkaido
Nagasaki University School of Medicine, Nagasaki, Nagasaki
National Center for Global Health and Medicine, Shinjyuku, Tokyo
National Defense Medical College, Tokorozawa, Saitama
National Hospital Organization Tokyo Medical Center, Meguro, Tokyo
Niigata City General Hospital, Niigata, Niigata
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Osaka City General Hospital, Miyakojima, Osaka
Saka General Hospital, Shiogama, Miyagi
Sanyudo Hospital, Yonezawa, Sanyudo
Sapporo Medical Center NTT EC, Sapporo, Hokkaido
Shinrakuen Hospital, Niigata, Niigata
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Susceptibility testing and MIC determination

Susceptibility testing was performed according to CLSI (formerly NCCLS) standards M7-A7 for the micro-broth dilution method [2, 3]. 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 MIC against *S. aureus*, *M. catarrhalis*, *K. pneumoniae*, and *P. aeruginosa*. For determination of MIC of oxacillin, NaCl was added at 2 % to CA-MH broth. For measuring MICs against *S. pneumoniae*, *S. pyogenes*, and *H. influenzae*, 15 μg/ml nicotinamide, 5 mg/ml yeast extract, and horse blood at 5 % were added to CA-MH broth.

A 0.005-ml portion of test organism solution, grown to turbidity at McFarland number 0.5 and diluted tenfold with saline, was inoculated to CA-MH broth to make a final volume of 0.1 ± 0.02 ml. This solution was poured into a well on a microplate (Eiken Kagaku, Tokyo, Japan), serially diluted freeze-dried test agent was added, and the MIC

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was determined with the MIC2000 system (Eiken Kagaku, Tokyo, Japan).

Antibacterial agents

The susceptibilities of the bacterial strains were tested for the following 45 antimicrobial agents: four penicillins such as benzylpenicillin (PCG; Meiji Seika Kaisha), oxacillin (MPIPC; Meiji), ampicillin (ABPC; Meiji), and piperacillin (PIPC; Toyama Chemical); three penicillins in combination with β-lactamase inhibitors such as clavulanic acid-amoxicillin (CVA/AMPC; Glaxo SmithKline), sulbactam-ABPC (SBT/ABPC; Pfizer Japan), and tazobactam-PIPC (TAZ/PIPC; Toyama, TAZ/PIPC-1; tazobactam was fixed at 4 μg/ml; TAZ/PIPC-2; tazobactam/piperacillin was fixed at 1/8); four oral cephems such as cefaclor (CCL; Shionogi), cefdinir (CFDN; Astellas Pharma), cefcapene (CFPN; Shionogi), and cefditoren (CDTR; Meiji); eight parenteral cephems such as cefazolin (CEZ; Astellas), cefoxitin (CFX; Banyu Pharmaceutical), cefmetazole (CMZ; Daiichi-Sankyo), cefotiam (CTM; Takeda Pharmaceutical), ceftazidime (CAZ; Glaxo SmithKline), ceftriaxone (CTRX; Chugai Pharmaceutical), cefepime (CFPM; Meiji), and cefozopran (CZOP; Takeda); a monobactam aztreonam (AZT; Eisai); five carbapenems such as imipenem (IPM; Banyu), panipenem (PAPM; Daiichi-Sankyo), meropenem (MEPM; Dainippon Sumitomo Pharma), biapenem (BIPM; Meiji), and doripenem (DRPM; Shionogi); one penem such as faropenem (FRPM; Maruho); four aminoglycosides such as gentamicin (GM; Shionogi), tobramycin (TOB; J-dolph), amikacin (AMK; Banyu), and arbekacin (ABK; Meiji); four macrolides such as erythromycin (EM; Dainippon Sumitomo), clarithromycin (CAM; Toyama), azithromycin (AZM; Pfizer), and telithromycin (TEL; Sanofi-Aventis); a lincosamide clindamycin (CLDM; Dainippon Sumitomo.); a tetracycline minocycline (MINO; Wyeth/Takeda); two glycopeptides such as vancomycin (VCM; Shionogi) and teicoplanin (TEIC; Astellas); six fluoroquinolones such as ciprofloxacin (CPFX; Bayer-Yakuhin), levofloxacin (LVFX; Daiichi-Sankyo), tosufloxacin (TFLX; Toyama), moxifloxacin (MFLX; Shionogi), pazufloxacin (PZFX; Toyama) and garenoxacin (GRNX; Astellas), and an oxazolidinone linezolide (LZD; Pfizer). These antimicrobial agents were serially diluted and placed under the freeze-dried state into the respective microplate wells. 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 Nitorocefin disks (Kanto Chemical, Tokyo, Japan) were conducted according to the reference manual supplied by the manufacturer.

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

Statistical analysis

The categorical variables of the susceptibility of *S. pneumoniae* to PCG were summarized as percentages and compared using a chi-square test or Fisher's test when appropriate. A P value <0.05 was considered to be significant.

Results

Staphylococcus aureus

The in vitro antimicrobial susceptibilities, as MIC_{50}/MIC_{90} values, and the range of MICs for *S. aureus* isolates, are shown in Table 2. Among the total 130 strains of *S. aureus*, 76 strains (58.5 %) were found to be methicillin-resistant *S. aureus* (MRSA; MIC of MPIPC, ≥4 μg/ml).

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

The MIC_{90} of penicillins against 54 MSSA strains was 16 μg/ml; however, the MIC_{90} of penicillins in combinations with β-lactamase inhibitors (CVA/AMPC, SBT/ABPC, and TAZ/PIPC) decreased to 1.0–4.0 μg/ml. The MIC_{90}s of CCL, CAZ, CTRX, CFPM, and CFX ranged from 2.0 to 8.0 μg/ml and those of the other seven cephems from 0.25 to 1.0 μg/ml. Carbapenems showed the strongest activity, with MIC_{90}s ≤0.125 μg/ml. As for aminoglycosides, GM, TOB, AMK, and ABK showed MIC_{90} of 16.0, 8.0, 4.0, and 1.0 μg/ml, respectively. Among the macrolide-lincosamide antibiotics, TEL and CLDM showed relatively strong activity with MIC_{90} of 0.125 and 0.25 μg/ml, respectively, but the rest of the macrolides showed weak activity with MIC_{90} ≥128 μg/ml. Relatively strong activities of MINO, VCM, TEIC, and LZD were shown, with MIC_{90}s of 0.25–2.0 μg/ml. MIC_{90}s of the seven fluoroquinolones were within the range of 0.25–8.0 μg/ml.

Susceptibility of MRSA

Only four agents, ABK, VCM, TEIC, and LZD, showed strong activity against MRSA, with MIC_{90} ≤2.0 μg/ml.

Table 2 Antibacterial susceptibility of *Staphylococcus aureus* of the 130 strains of *S. aureus* to 44 antimicrobial agents measured

Antibacterial agent	All strains, $n = 130$			MRSA, $n = 76$			MSSA, $n = 54$		
	MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)		
	50 %	90 %	Range	50 %	90 %	Range	50 %	90 %	Range
PCG	16	32	≤0.06 to 128	16	64	8 to 128	0.25	16	≤0.06 to 64
MPIPC	64	≥256	0.125 to ≥256	128	≥256	16 to ≥256	0.25	0.5	0.125 to 2
ABPC	16	64	≤0.06 to 128	16	64	8 to 128	0.5	16	≤0.06 to 32
SBT/ABPC	8	32	0.125 to 128	16	32	4 to 128	0.25	2	0.125 to 4
CVA/AMPC	16	32	0.125 to ≥128	32	32	2 to ≥128	0.25	1	0.125 to 2
PIPC	64	128	0.5 to ≥256	128	≥256	32 to ≥256	1	16	0.5 to 64
TAZ/PIPC-1	32	128	0.5 to ≥256	64	≥256	4 to ≥256	1	2	0.5 to 2
TAZ/PIPC-2	32	128	0.5 to ≥256	64	128	8 to ≥256	1	4	0.5 to 8
CCL	64	128	0.5 to ≥256	128	≥256	8 to ≥256	1	2	0.5 to 4
CFDN	8	≥128	0.125 to ≥128	≥128	≥128	1 to ≥128	0.25	0.5	0.125 to 1
CFPN	≥256	≥256	0.5 to ≥256	≥256	≥256	4 to ≥256	1	1	0.5 to 2
CDTR	32	≥128	0.25 to ≥128	64	≥128	4 to ≥128	0.5	1	0.25 to 1
CEZ	64	≥256	0.25 to ≥256	128	≥256	1 to ≥256	0.25	0.5	0.25 to 1
CFX	32	≥128	1 to ≥128	≥128	≥128	8 to ≥128	2	4	1 to 8
CMZ	8	64	0.5 to ≥256	32	64	4 to ≥256	1	1	0.5 to 1
CTM	32	≥256	0.5 to ≥256	128	≥256	2 to ≥256	0.5	1	0.5 to 1
CAZ	≥128	≥128	8 to ≥128	≥128	≥128	16 to ≥128	8	8	8 to 16
CTRX	≥256	≥256	2 to ≥256	≥256	≥256	8 to ≥256	4	4	2 to 8
CFPM	64	≥256	1 to ≥256	128	≥256	8 to ≥256	2	4	1 to 4
CZOP	8	64	0.5 to ≥256	32	64	2 to ≥256	1	1	0.5 to 2
IPM	1	32	≤0.06 to ≥128	16	64	≤0.06 to ≥128	≤0.06	≤0.06	≤0.06
PAPM	1	16	≤0.06 to 128	8	32	0.125 to 128	≤0.06	≤0.06	≤0.06 to 0.125
MEPM	4	16	≤0.06 to 128	16	32	0.25 to 128	≤0.06	0.125	≤0.06 to 0.125
BIPM	4	32	≤0.06 to ≥256	16	64	0.125 to ≥256	≤0.06	≤0.06	≤0.06 to 0.125
DRPM	2	16	≤0.06 to ≥128	8	16	0.125 to ≥128	≤0.06	≤0.06	≤0.06
FRPM	2	≥256	≤0.06 to ≥256	128	≥256	0.125 to ≥256	0.125	0.125	≤0.06 to 0.25
GM	0.5	64	0.125 to ≥256	16	128	0.125 to ≥256	0.25	16	0.125 to 64
TOB	32	≥256	0.125 to ≥256	≥256	≥256	0.25 to ≥256	0.5	8	0.125 to 32
AMK	4	16	0.5 to ≥256	16	32	1 to ≥256	2	4	0.5 to 8
ABK	0.5	1	0.125 to 4	0.5	1	0.125 to 4	0.5	1	0.125 to 1
EM	≥256	≥256	0.125 to ≥256	≥256	≥256	0.25 to ≥256	0.25	≥256	0.125 to ≥256
CAM	≥128	≥128	0.125 to ≥128	≥128	≥128	0.25 to ≥128	0.25	≥128	0.125 to ≥128
AZM	≥128	≥128	0.25 to ≥128	≥128	≥128	0.5 to ≥128	0.5	≥128	0.25 to ≥128
TEL	≥128	≥128	≤0.06 to ≥128	≥128	≥128	≤0.06 to ≥128	0.125	0.125	≤0.06 to ≥128
CPFX	16	≥256	0.125 to ≥256	128	≥256	0.25 to ≥256	0.5	8	0.125 to ≥256
LVFX	4	≥256	≤0.06 to ≥256	16	≥256	0.125 to ≥256	0.25	4	≤0.06 to ≥256
TFLX	2	≥32	≤0.06 to ≥32	≥32	≥32	≤0.06 to ≥32	≤0.06	2	≤0.06 to ≥32
MFLX	1	32	≤0.06 to 64	4	32	≤0.06 to 64	≤0.06	1	≤0.06 to 32
PZFX	4	≥256	0.125 to ≥256	8	≥256	0.125 to ≥256	0.125	4	0.125 to ≥256
GRNX	0.5	32	≤0.06 to 64	1	64	≤0.06 to 64	≤0.06	0.5	≤0.06 to 64
MINO	0.25	16	≤0.06 to 16	16	16	0.125 to 16	0.125	0.25	≤0.06 to 16
CLDM	≥256	≥256	≤0.06 to ≥256	≥256	≥256	0.125 to ≥256	0.125	0.25	≤0.06 to ≥256
VCM	1	2	0.5 to 2	1	2	0.5 to 2	1	2	0.5 to 2
TEIC	0.5	1	0.125 to 4	0.5	2	0.125 to 4	0.5	1	0.25 to 2
LZD	2	2	1 to 4	2	2	1 to 4	2	2	1 to 4

The strains consist of 76 strains (58.5 %) of methicillin-resistant *Staphylococcus aureus* (MRSA) and 54 strains (41.5 %) of methicillin-susceptible *Staphylococcus aureus* (MSSA)

PCG benzylpenicillin, *MPIPC* oxacillin, *ABPC* ampicillin, *PIPC* piperacillin, *CVA/AMPC* clavulanic acid-amoxicillin, *SBT/ABPC* sulbactam-ABPC, *TAZ/PIPC* tazobactam-PIPC Toyama, *TAZ/PIPC-1* piperacillin with 4 μg/mL of tazobactam, *TAZ/PIPC-2* tazobactam : piperacillin = 1 : 8, *CCL* cefaclor, *CFDN* cefdinir, *CFPN* cefcapene, *CDTR* cefditoren, *CEZ* cefazolin, *CFX* cefoxitin, *CMZ* cefmetazole, *CTM* cefotiam, *CAZ* ceftazidime, *CTRX* ceftriaxone, *CFPM* cefepime, *CZOP* cefozopran, *AZT* aztreonam, *IPM* imipenem, *PAPM* panipenem, *MEPM* meropenem, *BIPM* biapenem, *DRPM* doripenem, *FRPM* faropenem, *GM* gentamicin, *TOB* tobramycin, *AMK* amikacin, *ABK* arbekacin, *EM* erythromycin, *CAM* clarithromycin, *AZM* azithromycin, *TEL* telithromycin, *CLDM* clindamycin, *MINO* minocycline, *VCM* vancomycin, *TEIC* teicoplanin, *CPFX* ciprofloxacin, *LVFX* levofloxacin, *TFLX* tosufloxacin, *MFLX* moxifloxacin, *PZFX* pazufloxacin, *GRNX* garenoxacin, *LZD* linezolide

MINO showed weak activity with MIC_{90} of 16 μg/ml. Other agents showed almost no activity, with MIC_{90} ≥32 μg/ml.

Streptococcus pneumoniae

The susceptibilities of the 127 strains of *S. pneumoniae* to PCG revealed that 119 strains (93.7 %), 8 strains (6.3 %), and 0 strains (0.0 %) were identified as penicillin-susceptible (PSSP), penicillin-intermediate (PISP), and penicillin-resistant strains (PRSP), respectively, with the breakpoint for PCG defined by the CLSI standards. However, with the previous susceptibility criteria for *S. pneumoniae* strains, 71 strains (55.9 %), 34 strains (26.8 %), and 22 strains (17.3 %) were classified as susceptible (MIC of PCG ≤0.06 μg/ml), intermediate (MIC of PCG 0.125–1 μg/ml), and resistant (MIC of PCG ≥2 μg/ml) strains, respectively.

Among the β-lactams, CCL, CAZ, and CMZ showed high MIC_{90}s (64, 8, and 16 μg/ml, respectively), while many of the other β-lactams, except for the carbapenems, showed potent activities, with MIC_{90}s of 1.0–4.0 μg/ml. All five carbapenems showed strong activities (MIC_{90} ≤0.25 μg/ml) against all *S. pneumoniae* strains, regardless of their different susceptibilities to PCG. Fluoroquinolones also showed potent activities against most of the strains with MIC_{90}s of ≤0.25–4 μg/ml, although 7 strains (2.6 %) were found to be resistant to LVFX. The glycopeptides (VCM and TEIC) and TEL showed strong activities (MIC_{90} ≤0.5 μg/ml). Aminoglycosides were substantially less active, with MIC_{90}s of 8.0–64.0 μg/ml. High frequencies of resistance against the macrolide antibiotics, EM, CAM, and AZM, were shown, with MIC_{90}s ≥64 μg/ml (Table 3).

Haemophilus influenzae

The susceptibilities of the 123 *H. influenzae* strains are summarized in Table 4. According to the CLSI breakpoint for ABPC, 67 (54.5 %) were found to be ABPC susceptible, 26 (21.1 %) to be ABPC intermediate, and 30 (24.4 %) ABPC resistant. With the use of the Nitrocephin disks, all ABPC-intermediate and 23 (18.7 %) ABPC-resistant strains were found to be β-lactamase-non-producing, and they were defined as BLNAI and BLNAR, respectively. The other 7 (5.7 %) ABPC-resistant strains were found to be β-lactamase-producing strains, designated as BLPAR. The MIC_{50} and MIC_{90} values of PCG and ABPC for BLPAR isolates were at least threefold 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 susceptibility to ABPC, all the *H. influenzae* strains were extremely susceptible to all six fluoroquinolones (MIC_{50}s ≤0.06 μg/ml). BLPAR strains showed high levels of resistance against PIPC, with MIC_{90} values ≥256 μg/ml, whereas TAZ/PIPC showed strong activities, with MIC_{90}s ≤0.125 μg/ml. Among the cephems, CDTR and CTRX showed the most potent activities, with MIC_{90}s of 0.25 μg/ml. Of the five carbapenem agents, MEPM showed the most potent acvitity against all types of *H. influenzae* strains. Among macrolides and the ketolide, AZM and TEL showed the most potent activity, with MIC_{90}s of 2 μg/ml.

Moraxella catarrhalis

The susceptibilities of 70 *M. catarrhalis* strains are shown in Table 5. For the penicillins, β-lactamase inhibitors restored the activities of penicillins; e.g., 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 0.125 μg/ml. Carbapenems showed strong activities, with MIC_{90}s ≤0.125 μg/ml. Fluoroquinolones also showed strong activities, with MIC_{90}s ≤0.06 μg/ml. Several cephems (CFDN, CFPN, CDTR, CAZ, and CMZ), four aminoglycosides (GM, TOB, AMK, and ABK), three macrolides (EM, CAM, and AZM), and the ketolide (TEL) also showed potent activities, with the MIC_{90}s of 0.125–1.0 μg/ml.

Klebsiella pneumoniae

The susceptibilities of 78 *K. pneumoniae* strains are shown in Table 6. Carbapenems showed strong activities, with MIC_{90}s ≤0.5 μg/ml; in particular, MEPM and DRPM showed the most potent activities, with MIC_{90}s ≤0.06 μg/ml. Of the cephems and the monobactam, CZOP showed the most potent activity, with MIC_{90}s ≤0.06 μg/ml, and CFDN, CTM, CAZ, CTRX, CFPM, and AZT also showed strong activities, with MIC_{90}s of 0.125–0.25 μg/ml. All fluoroquinolones we tested and three aminoglycosides (GM, TOB and ABK) showed potent activities, with MIC_{90}s of ≤0.25–0.5 μg/ml. β-lactamase inhibitors apparently restored the activities of penicillins; e.g., SBT decreased the MIC_{90} of ABPC from 128 to 8 μg/ml and TAZ decreased the MIC_{90} of PIPC from 8 to 4 μg/ml. Among 78 strains of *K. pneumoniae*, 1 strain (1.3 %) was found to be an ESBL producer.

Pseudomonas aeruginosa

A total 103 *P. aeruginosa* strains were tested for antimicrobial susceptibility (Table 7). Among the β-lactams, three carbapenems (MEPM, BIPM, and DRPM) showed potent activities, with MIC_{50}s of 0.25–0.5 μg/ml; however, these agents showed relatively higher MIC_{90} levels, 8.0–16 μg/ml. Among the fluoroquinolones, CPFX showed the most potent activity, with MIC_{50}s and MIC_{90}s of 0.25

Table 3 Antibacterial susceptibility of *Streptococcus pneumoniae*

Antibacterial agent	All strains, $n = 127$			PSSP, $n = 119$			PISP, $n = 8$		
	MIC (μg/ml)			MIC (μg/ml)			MIC (μg/ml)		
	50 %	90 %	Range	50 %	90 %	Range	50 %	90 %	Range
PCG	≤0.06	2	≤0.06 to 4	≤0.06	≤0.06	≤0.06 to 2	4	4	4 to 4
ABPC	≤0.06	2	≤0.06 to 8	≤0.06	≤0.06	≤0.06 to 4	2	8	2 to 8
SBT/ABPC	≤0.06	4	≤0.06 to 8	≤0.06	≤0.06	≤0.06 to 4	4	8	2 to 8
CVA/AMPC	≤0.06	1	≤0.06 to 8	≤0.06	≤0.06	≤0.06 to 2	4	8	0.5 to 8
PIPC	≤0.06	2	≤0.06 to 4	≤0.06	≤0.06	≤0.06 to 4	2	4	1 to 4
TAZ/PIPC-1	≤0.06	2	≤0.06 to 4	≤0.06	≤0.06	≤0.06 to 4	2	4	1 to 4
TAZ/PIPC-2	≤0.06	2	≤0.06 to 4	≤0.06	0.125	≤0.06 to 4	2	4	1 to 4
CCL	1	64	0.25 to 128	1.0	64	0.25 to 128	64	128	32 to 128
CFDN	0.25	4	≤0.06 to 32	0.25	4	≤0.06 to 16	8	32	4 to 32
CFPN	0.25	1	0.125 to 32	0.25	1	0.125 to 2	2	32	0.5 to 32
CDTR	0.125	0.5	≤0.06 to 4	0.125	0.5	≤0.06 to 2	0.5	4	0.5 to 4
CEZ	0.125	4	≤0.06 to 16	0.125	2	≤0.06 to 8	4	16	4 to 16
CMZ	0.5	16	≤0.06 to 32	0.5	8	≤0.06 to 32	16	32	8 to 32
CTM	0.25	4	≤0.06 to 16	0.25	4	≤0.06 to 8	8	16	4 to 16
CAZ	4	8	0.125 to 64	4	8	0.125 to 32	16	64	8 to 64
CTRX	0.25	1	≤0.06 to 8	0.25	1	≤0.06 to 2	1	8	0.5 to 8
CFPM	0.5	1	≤0.06 to 8	0.5	1	≤0.06 to 2	2	8	1 to 8
CZOP	0.25	1	≤0.06 to 16	0.25	1	≤0.06 to 2	2	16	1 to 16
IPM	≤0.06	0.25	≤0.06 to 0.5	≤0.06	0.125	≤0.06 to 0.5	0.25	0.5	0.125 to 0.5
PAPM	≤0.06	≤0.06	≤0.06 to 0.25	≤0.06	≤0.06	≤0.06 to 0.25	≤0.06	0.25	≤0.06 to 0.25
MEPM	≤0.06	0.25	≤0.06 to 0.5	≤0.06	0.25	≤0.06 to 0.5	0.25	0.5	0.125 to 0.5
BIPM	≤0.06	0.25	≤0.06 to 0.5	≤0.06	0.25	≤0.06 to 0.5	0.25	0.5	0.125 to 0.5
DRPM	≤0.06	0.25	≤0.06 to 0.5	≤0.06	0.125	≤0.06 to 0.5	0.25	0.5	0.125 to 0.5
FRPM	≤0.06	0.25	≤0.06 to 0.5	≤0.06	0.25	≤0.06 to 0.5	0.25	0.5	0.125 to 0.5
GM	4	8	2 to 16	4	8	2 to 16	4	16	4 to 16
TOB	16	16	4 to 32	16	16	4 to 32	16	32	8 to 32
AMK	32	64	16 to 128	32	64	16 to 128	32	64	32 to 64
ABK	16	32	8 to 64	16	32	8 to 64	16	64	16 to 64
EM	≥128	≥128	≤0.06 to ≥128	≥128	≥128	≤0.06 to ≥128	≥128	≥128	≤0.06 to ≥128
CAM	≥64	≥64	≤0.06 to ≥64	≥64	≥64	≤0.06 to ≥64	≥64	≥64	≤0.06 to ≥64
AZM	≥64	≥64	≤0.06 to ≥64	≥64	≥64	≤0.06 to ≥64	≥64	≥64	≤0.06 to ≥64
TEL	≤0.06	0.25	≤0.06 to 2	≤0.06	0.25	≤0.06 to 2	≤0.06	0.5	≤0.06 to 0.5
CPFX	1	2	≤0.06 to 64	1	2	≤0.06 to 64	1	2	0.25 to 2
LVFX	1	2	≤0.06 to 64	1	2	≤0.06 to 64	1	1	0.5 to 1
TFLX	0.125	0.25	≤0.06 to ≥16	0.25	0.25	≤0.06 to ≥16	0.125	0.25	≤0.06 to 0.25
MFLX	0.125	0.25	≤0.06 to 8	0.125	0.25	≤0.06 to 8	0.125	0.25	0.125 to 0.25
PZFX	2	4	1 to 128	2	4	1 to 128	2	4	2 to 4
GRNX	≤0.06	≤0.06	≤0.06 to 2	≤0.06	≤0.06	≤0.06 to 2	≤0.06	≤0.06	≤0.06 to ≤0.06
MINO	8	16	≤0.06 to 64	8	16	≤0.06 to 64	8	16	≤0.06 to 16
CLDM	64	≥128	≤0.06 to ≥128	64	≥128	≤0.06 to ≥128	≥128	≥128	≤0.06 to ≥128
VCM	0.25	0.5	0.125 to 0.5	0.25	0.5	0.125 to 0.5	0.5	0.5	0.25 to 0.5
TEIC	≤0.06	0.125	≤0.06 to 0.125	≤0.06	0.125	≤0.06 to 0.125	≤0.06	0.125	≤0.06 to 0.125
LZD	1	1	0.125 to 2	1	1	0.125 to 2	1	2	0.5 to 2

Susceptibilities of the 127 strains of *S. pneumoniae* to 42 antimicrobial agents were studied. The number of strains and proportion of penicillin-susceptible (PSSP), penicillin-intermediate (PISP), and penicillin-resistant (PRSP) are 119 (93.7 %), 8 (6.3 %), and 0 (0.0 %), respectively

Table 4 Antibacterial susceptibility of *Haemophilus influenzae*

Antibacterial agent	All strains, $n = 123$			BLNAS [ABPC ≤ 1, β-lactamase(−)], $n = 67$			BLNAI [ABPC = 2, β-lactamase(−)], $n = 26$			BLNAR [ABPC ≥ 4, β-lactamase(−)], $n = 23$			β-lactamase(+), $n = 7$		
	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	4	8	0.25 to ≥256	1	4	0.25 to 8	4	8	2 to 8	8	8	4 to 16	≥256	≥256	32 to ≥256
ABPC	1	4	0.125 to ≥256	0.5	1	0.125 to 1	2	2	2	4	8	4 to 8	≥256	≥256	32 to ≥256
SBT/ABPC	2	8	0.125 to 8	0.5	2	0.125 to 2	2	4	2 to 4	4	8	4 to 8	8	8	1 to 8
CVA/AMPC	2	8	0.25 to 16	0.5	2	0.25 to 8	4	8	1 to 8	8	8	2 to 16	8	8	1 to 8
PIPC	≤0.06	0.25	≤0.06 to ≥256	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.25	128	≥256	8 to ≥256
TAZ/PIPC-1	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.125
TAZ/PIPC-2	≤0.06	0.25	≤0.06 to 1	≤0.06	0.125	≤0.06 to 0.25	≤0.06	0.25	≤0.06 to 0.25	≤0.06	0.125	≤0.06 to 0.25	1	1	0.25 to 1
CCL	16	64	0.25 to 128	4	32	0.25 to 64	16	64	4 to 64	32	64	4 to 128	32	128	2 to 128
CFDN	2	8	≤0.06 to 16	0.5	4	≤0.06 to 8	2	8	0.5 to 8	4	8	1 to 16	2	4	0.25 to 4
CFPN	0.5	2	≤0.06 to 8	≤0.06	1	≤0.06 to 4	1	2	0.125 to 4	2	4	0.5 to 8	1	2	≤0.06 to 2
CDTR	≤0.06	0.25	≤0.06 to 0.5	≤0.06	≤0.06	≤0.06 to 0.25	0.125	0.25	≤0.06 to 0.5	0.25	0.25	≤0.06 to 0.5	0.125	0.25	≤0.06 to 0.25
CEZ	4	64	0.5 to ≥256	4	16	0.5 to 128	4	16	1 to 32	16	128	2 to ≥256	32	128	4 to 128
CMZ	8	16	0.25 to 64	4	8	0.25 to 32	8	16	2 to 32	16	32	4 to 64	8	16	2 to 16
CTM	4	32	0.25 to 64	2	16	0.25 to 64	8	32	1 to 64	32	64	4 to 64	16	64	1 to 64
CAZ	0.25	0.5	≤0.06 to 2	0.125	0.5	≤0.06 to 1	0.25	1	0.125 to 2	0.25	0.5	0.25 to 2	0.25	2	0.25 to 2
CTRX	0.125	0.25	≤0.06 to 0.5	≤0.06	0.25	≤0.06 to 0.5	0.25	0.25	≤0.06 to 0.25	0.25	0.25	≤0.06 to 0.5	0.25	0.5	≤0.06 to 0.5
CFPM	1	2	≤0.06 to 4	0.25	1	≤0.06 to 2	2	4	0.25 to 4	2	2	0.5 to 4	2	2	0.25 to 2
CZOP	4	16	≤0.06 to 32	0.25	8	≤0.06 to 8	8	16	1 to 16	8	16	2 to 32	8	32	0.25 to 32
IPM	0.5	2	≤0.06 to 4	0.5	1	≤0.06 to 4	0.5	2	0.125 to 4	1	2	0.5 to 4	1	4	0.5 to 4
PAPM	0.5	2	≤0.06 to 8	0.5	1	≤0.06 to 2	0.5	2	≤0.06 to 8	1	2	0.5 to 2	1	2	0.25 to 2
MEPM	≤0.06	0.25	≤0.06 to 1	≤0.06	0.125	≤0.06 to 0.25	0.125	0.25	≤0.06 to 0.5	0.25	0.5	≤0.06 to 1	0.125	0.25	≤0.06 to 0.25
BIPM	1	4	≤0.06 to 8	0.5	4	≤0.06 to 8	2	4	≤0.06 to 8	4	8	1 to 8	2	8	1 to 8
DRPM	0.125	1	≤0.06 to 2	0.125	0.25	≤0.06 to 1	0.25	1	≤0.06 to 2	1	2	≤0.06 to 2	0.5	0.5	0.125 to 0.5
FRPM	1	2	0.125 to 4	0.5	2	0.125 to 4	2	2	0.5 to 4	2	4	0.5 to 4	2	2	0.5 to 2
AZT	0.5	2	≤0.06 to 8	≤0.06	1	≤0.06 to 2	0.5	2	≤0.06 to 4	1	2	0.25 to 4	0.5	8	0.125 to 8
GM	1	1	0.125 to 4	1	1	0.125 to 4	1	1	0.25 to 2	1	1	0.5 to 2	1	2	0.5 to 2
TOB	2	2	0.5 to 8	2	2	0.5 to 8	2	2	0.5 to 4	2	2	1 to 4	2	4	1 to 4
AMK	4	8	0.5 to 8	4	8	0.5 to 8	4	8	1 to 8	4	8	2 to 8	4	8	2 to 8
ABK	2	4	0.5 to 8	2	4	0.5 to 8	2	4	1 to 4	2	4	1 to 4	2	4	1 to 4
EM	4	8	0.125 to 16	4	8	0.125 to 16	2	4	1 to 8	4	8	1 to 8	2	4	2 to 4
CAM	8	8	0.125 to 32	4	8	0.125 to 32	4	8	2 to 16	8	16	4 to 16	8	8	4 to 8
AZM	0.5	2	≤0.06 to 4	0.5	2	≤0.06 to 4	0.5	1	0.25 to 2	1	2	0.25 to 2	0.5	2	0.5 to 2

Table 4 continued

Antibacterial agent	All strains, $n = 123$			BLNAS [ABPC ≤ 1, β-lactamase(−)], $n = 67$			BLNAI [ABPC = 2, β-lactamase(−)], $n = 26$			BLNAR [ABPC ≥ 4, β-lactamase(−)], $n = 23$			β-lactamase(+), $n = 7$		
	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
TEL	1	2	0.125 to 4	1	2	0.125 to 4	1	2	0.5 to 4	1	2	1 to 4	1	2	1 to 2
CPFX	≤0.06	≤0.06	≤0.06 to 16	≤0.06	≤0.06	≤0.06 to 8	≤0.06	≤0.06	≤0.06 to 0.25	≤0.06	≤0.06	≤0.06 to 16	≤0.06	≤0.06	≤0.06
LVFX	≤0.06	≤0.06	≤0.06 to 32	≤0.06	≤0.06	≤0.06 to 8	≤0.06	≤0.06	≤0.06 to 0.25	≤0.06	≤0.06	≤0.06 to 32	≤0.06	≤0.06	≤0.06
TFLX	≤0.06	≤0.06	≤0.06 to ≥32	≤0.06	≤0.06	≤0.06 to ≥32	≤0.06	≤0.06	≤0.06	≤0.06	≤0.06	≤0.06 to 16	≤0.06	≤0.06	≤0.06
MFLX	≤0.06	≤0.06	≤0.06 to 16	≤0.06	≤0.06	≤0.06 to 4	≤0.06	≤0.06	≤0.06 to 0.25	≤0.06	≤0.06	≤0.06 to 16	≤0.06	0.125	≤0.06 to 0.125
PZFX	≤0.06	≤0.06	≤0.06 to 16	≤0.06	≤0.06	≤0.06 to 16	≤0.06	≤0.06	≤0.06 to 0.25	≤0.06	≤0.06	≤0.06 to 16	≤0.06	0.125	≤0.06 to 0.125
GRNX	≤0.06	≤0.06	≤0.06 to 8	≤0.06	≤0.06	≤0.06 to 8	≤0.06	≤0.06	≤0.06	≤0.06	≤0.06	≤0.06 to 8	≤0.06	≤0.06	≤0.06
MINO	0.5	1	0.125 to 2	0.5	1	0.125 to 2	0.5	1	0.25 to 1	0.5	1	0.25 to 1	1	1	0.5 to 1
CLDM	8	16	0.5 to 32	8	16	0.5 to 32	8	32	1 to 32	8	32	2 to 32	16	16	4 to 16

Susceptibilities of the 123 strains of *H. influenzae* to 40 antimicrobial agents were studied. The number of strains and proportion of β-lactamase-non-producing ampicillin-susceptible (BLNAS), β-lactamase-non-producing ampicillin (ABPC)-intermediately resistant (BLNAI), β-lactamase-non-producing ABPC-resistant (BLNAR), and β-lactamase-producing ABPC-resistant (BLPAR) are 67 (54.4 %), 26 (21.1 %), 23 (18.7 %), and 7 (5.7 %), respectively

and 8.0 μg/ml, respectively. Other fluoroquinolones also showed strong activities with MIC_{50}s of 0.5–4.0 μg/ml, whereas MIC_{90} levels (8.0 to ≥32 μg/ml) suggested partial resistance. Both PIPC and TAZ/PIPC showed potent activities, with MIC_{50}s of 4.0 μg/ml; the higher levels of MIC_{90}s (≥256 and 128 μg/ml) of these agents suggested resistance. The MIC_{50}s of the four aminoglycosides (GM, TOB, AMK, and ABK), three cephems (CAZ, CFPM, and CZOP), and the monobactam (AZT) were within the range 0.5–4.0 μg/ml. Among the 103 *P. aeruginosa* strains, we found 2 MBL-producing strains (1.9 %) and 3 multidrug-resistant strains (2.9 %).

Discussion

The JSC established a nationwide surveillance network in 2006 to establish the resource of information about antimicrobial susceptibility of bacterial pathogens in Japan. Our research focuses on major seven major bacterial respiratory pathogens, that is, *S. aureus*, *S. pneumoniae*, *S. pyogenes*, *H. influenzae*, *M. catarrhalis*, *K. pneumoniae*, and *P. aeruginosa*. It is desirable that analysis of antimicrobial susceptibility is carried out using the bacterial strains that actually cause the infections. To analyze the actual pathogens causing infections, we collected clinical isolates only from well-diagnosed adult patients with RTIs.

Our surveillance was conducted for 4 consecutive years from 2006. The total number of strains at surveillance conducted in 2006, 2007, 2008, and 2009 were 887, 1108, 987, and 635, respectively. Each species tested at surveillance in every year are as follows: *S. aureus* (205, 226, 189, and 130), *S. pneumoniae* (200, 257, 211, and 127), *H. influenzae* (165, 206, 187, and 123), *P. aeruginosa* (143, 171, 162, and 103), *M. catarrhalis* (91, 120, 106, and 70), *K. pneumoniae* (74, 122, 126, and 78), and *S. pyogenes* (9, 6, 6, and 4). The numbers of each species in each year of surveillance may generally reflect the trend of pathogens of respiratory infections in Japan, but we think we should increase the scope of the survey by reporting results with a greater number of pathogens.

With regard to *S. aureus*, 28 of 54 strains (51.8 %) of MSSA were thought to be penicillinase-producing strains because of their resistance to ABPC and susceptibility to SBT/ABPC and CCL, and 3 of 54 strains (5.6 %) of MSSA may be *emr*-harboring strains because of their resistance to the macrolides EM, CAM, and AZM and susceptibility to TEL (ketolide lacking *emr* resistance mechanism) [4]. The difference between resistance of MSSA against GM (11.1 %) and that against AMK (0 %) implied that major aminoglycoside-resistant strains were not *aad(4′, 4″)*-harboring AMK-resistant strains but *aac(6′)/aph(2″)*-harboring GM-resistant strains [5].