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<THE TOPIC OF THIS MONTH>

Invasive *Haemophilus influenzae* and *Streptococcus pneumoniae* infections, as of August 2014

The amendment of the Infectious Diseases Control Law on 1 April 2013 brought invasive *Haemophilus influenzae* disease/infection and invasive pneumococcal disease/infection into the category V infectious diseases. Physicians who have made the diagnosis of these infections must notify within 7 days of diagnosis (see <http://www.nih.go.jp/niid/images/iasr/34/401/de4011.pdf> and <http://www.nih.go.jp/niid/images/iasr/35/416/de4161.pdf> for notification criteria). Invasive infection is defined as infection of sterile sites.

Invasive *Haemophilus influenzae* disease (IHD)

H. influenzae is a gram-negative bacillus belonging to the genus *Haemophilus* in the *Pasteurellaceae* family. It causes invasive infections (e.g. meningitis and bacteremic pneumonia) and non-invasive infections (e.g. otitis media). Strains having capsular polysaccharide are resistance to phagocytosis by neutrophils in antibody-free conditions, and frequently cause invasive infections. *H. influenzae* having capsules are grouped into six serotypes, from a to f, determined by bacterial agglutination tests using polysaccharide antisera. Infection caused by the Hib strain with b type capsule is vaccine-preventable. Strains devoid of capsule are classified as “non-typable *H. influenzae* (NTHi)”.

National Epidemiological Surveillance of Infectious Diseases (NESID): From April 2013 to 20 August 2014, 235 IHD cases were reported (male to female ratio of 1.6:1). Children less than 5 years of age occupied 17% and those aged 65 years or older 57% of the reported IHD cases (Fig. 1). Among patients younger than 5 years, bacteremic pneumonia occupied 33% (13/39), meningitis 23% (9/39) and bacteremia 44% (17/39) of the cases. Relative to adults, meningitis was more frequent among children, particularly among infants less than 6 months of age (63%; 5/8). Bacteremic pneumonia occupied more than half of those older than 65 years (61%; 82/134). No clear seasonality was observed; there was a peak in June in 2013 and two peaks in January and in April in 2014 (Fig 2). Among 235 IHD cases, 16 died—13 cases were 65 years of age or older and 2 cases were less than 1 year of age. The incidence per 100,000 population was 0.13 for the total population, 0.52 for the population under 5 years of age and 0.29 for the population 65 years of age or older (Table).

Figure 1. Age distribution of invasive *Haemophilus influenzae* disease cases, April 2013–August 2014 (n=235)

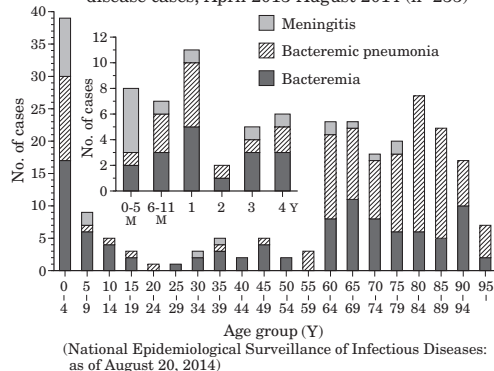


Figure 2. Monthly number of reported invasive *Haemophilus influenzae* disease cases, April 2013–August 2014 (n=235)

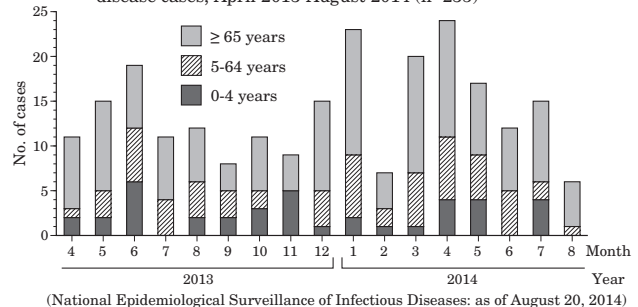


Table. Incidence of invasive *Haemophilus influenzae* disease & invasive pneumococcal disease, by age group, April 2013–March 2014, Japan

Age group (year)	Invasive <i>Haemophilus influenzae</i> disease		Invasive pneumococcal disease	
	Cases	per 100,000*	Cases	per 100,000*
0-4	27	0.52	331	6.32
5-14	9	0.08	40	0.36
15-64	33	0.04	366	0.46
≥65	92	0.29	768	2.41
Total	161	0.13	1,505	1.18

*Number of cases per 100,000 population of the age group indicated.

(National Epidemiological Surveillance of Infectious Diseases)

(THE TOPIC OF THIS MONTH-Continued)

Figure 3. Age distribution of invasive pneumococcal disease cases, April 2013-August 2014 (n=2,210)

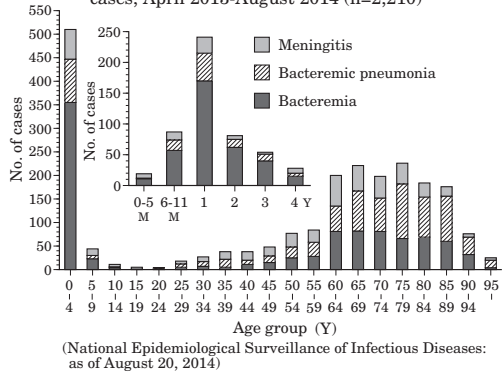
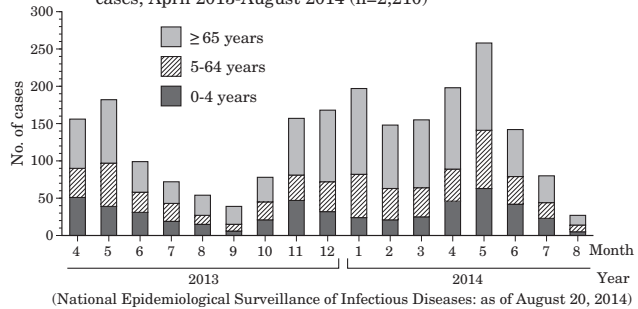


Figure 4. Monthly number of reported invasive pneumococcal disease cases, April 2013-August 2014 (n=2,210)



Vaccine: Vaccination for Hib vaccine for serotype b *H. influenzae* began in December 2008 on a voluntary basis for children less than 5 years of age; it was incorporated in the government supported "Program of accelerated vaccination with cervical cancer and other vaccines" in November 2010, and included in the routine immunization program in April 2013. According to "Research on evidence and recommended policies on better use of vaccinations" (Ihara-Kamiya Research Project that started in 2007), while the incidence per 100,000 population under 5 years of age of Hib-related meningitis was 7.71 and that of Hib-related non-meningitis was 5.15 before introduction of Hib vaccine (2008-2010), the respective figures fell to 0.17 and 0.10 after Hib vaccine introduction (2013) (see pp. 231 & 233 of this issue). Notably, with inclusion of IHD in the category V infectious diseases, reported data through NESID revealed that NTHi caused bacteremic pneumonia among adults (see p. 232 of this issue).

Invasive pneumococcal disease (IPD)

Streptococcus pneumoniae is a gram-positive diplococcus. It causes non-invasive infections among infants and the elderly (e.g. otitis media and non-bacteremic pneumonia). Once it enters the blood stream, it causes meningitis, bacteremic pneumonia, bacteremia/septicemia and other IPDs. The capsular polysaccharide is an important pathogenic factor, and *S. pneumoniae* is classified into more than 90 serotypes according to its antigenicity type.

NESID: From April 2013 to 20 August 2014, 2,210 IPD cases were reported (male to female ratio of 1.4:1). Children younger than 5 years of age occupied 23% (510/2,210), and adults aged 65 years or older occupied 50% (1,106/2,210) of the reported IPD cases (Fig. 3). Among patients younger than 5 years of age, bacteremia associated with pneumonia occupied 18% (92/510) and bacteremia unassociated with meningitis or pneumonia occupied 70% (355/510) of the cases. Among patients older than 65 years, bacteremic pneumonia occupied 46% (506/1,106) and meningitis 19% (206/1,106) of the cases. Among IPD patients 20-64 years of age, meningitis was most frequent (36%; 190/534). The number of IPD cases tended to slightly increase from winter to early summer (Fig 4). There were 154 fatal cases reported, among which 112 cases were older than 65 years of age and 3 cases younger than 5 years of age. The incidence of IPD was 1.18 per 100,000 total population, 6.32 for the population under 5 years of age and 2.41 for the population 65 years of age or older (Table).

Vaccine: Japan approved the heptavalent pneumococcal conjugate vaccine (PCV7) for children in February 2010 on a voluntary basis; it was incorporated in the government supported "Program of accelerated vaccination with cervical cancer and other vaccines" in November 2010 for children less than 5 years of age, and included into routine immunization program in April 2013. In November 2013, PCV7 was replaced with PCV13, which incorporated additional 6 serotype polysaccharide antigens.

For adults, a 23-valent pneumococcal polysaccharide vaccine (PPSV23) was approved in 1988. PCV13 was approved for immunization of adults aged 65 years or older in June 2014. Routine immunization of PPSV23 for adults 65 years or older is planned from October 2014 (see p. 240 of this issue).

According to the Ihara-Kamiya Research Project, while the incidence per 100,000 population under 5 years of age was 2.81 for meningitis IPD and 22.18 for non-meningitis IPD before the government supported implementation of PCV7 vaccination, after its incorporation into the routine vaccination program, respective incidences decreased to 1.10 and 9.71 (see p. 233 of this issue). With introduction of pneumococcal vaccines, the frequency of IPDs caused by the PCV7-covered serotypes was reduced from 77% (201/261) to 4% (4/94) in 2013. However, IPD due to serotypes that are not covered by the vaccines increased (serotype replacement) (see p. 234 of this issue).

According to a research project conducted in 10 prefectures, among the *S. pneumoniae* isolates detected since April 2013 during the past one year, serotypes covered by PCV13 occupied 46% (38/83) and those covered by PPSV23 60% (50/83) of the isolates (see p. 236 of this issue); prior to the introduction of PCV7 in 2006-2007, serotypes covered by PCV13 occupied 61% (185/301) and those covered by PPSV23 85% (257/301) of the isolates (Chiba N, *et al.*, *Epidemiol Infect* 138: 61-68, 2010). The proportion of serotypes included in PCV13 and PPSV23 are expected to further decline in 2014 and over the coming years. Serotype replacement, observed overseas among adult IPD cases following PCV introduction in children, is also becoming apparent in Japan (IASR 35: 179-181, 2014). Serotype replacement is similarly being observed among non-bacteremic pneumococcal pneumonia in adults (see p. 238 of this issue).

Conclusion: Since November 2010, the government has been supporting immunization of children with Hib vaccine and PCV. Starting in October 2014, vaccination of PPSV23 for adults 65 years or older will begin as a routine immunization. In addition to collection of epidemiological data of IHD and IPD, enhanced pathogen surveillance and analysis of serotypes will be important for assessing the vaccination program.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.