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National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare



## <THE TOPIC OF THIS MONTH>
## Meningococcal infection, 2005-October 2013, Japan

Table 1. History of notification related to *N. meningitidis* infections

| Name for notification | Acts (classification of infections) | Year (date) of enforcement |
|---|---|---|
| Epidemic cerebrospinal meningitis | Communicable Diseases Prevention Law (legal) | 1918 |
| Meningococcal meningitis | Infectious Diseases Control Law (category IV*) | 1999 April |
| Invasive meningococcal infection | Infectious Diseases Control Law (category V) | 2013 April |

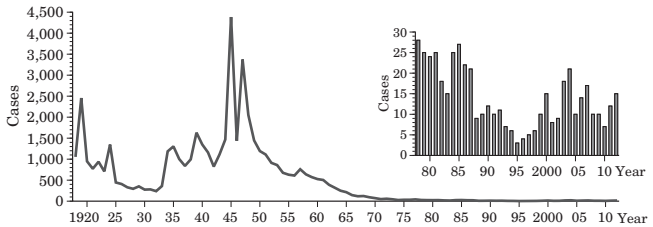
*Category was changed from IV to V in November 2003 under the revised the Infectious Diseases Control Law

*Neisseria meningitidis*, or meningococcus, is a gram-negative diplococcus that colonizes the nasopharynx of humans and spreads as respiratory droplets. Four invasive types are known: bacteraemia without causing sepsis, sepsis unassociated with meningitis (IASR 30: 158-159, 2009), meningitis (IASR 25: 207, 2004; IASR 27: 276-277, 2006) and meningoencephalitis. Prognosis of sepsis is poorer. Waterhouse-Friderichsen syndrome is an acute fulminant type of meningococcal infection accompanying adrenal bleeding and systemic shock. Noninvasive meningococcal infection includes pneumonia (see p. 368 of this issue), urethritis (see p. 370 of this issue), etc.

**History of surveillance for meningococcal infections**: Among meningococcal infections, "epidemic cerebrospinal meningitis" had been notified since before the World War II under the Communicable Diseases Prevention Law (Table 1). The epidemic peaked around 1945 amounting annually more than 4,000 cases. It subsided gradually; annual cases dropped to less than 100 cases in 1969, to less than 30 cases in 1978 and less than 10 in 1990s. The Infectious Diseases Control Law implemented in April 1999 classified meningococcal meningitis as a Category IV notifiable disease that needs notification of all the cases (Table 1). Since 1999, 7-21 cases were notified annually till March 2013 (Fig 1 & 2). In May 2011, there was a meningitis outbreak in a senior high school dormitory in Miyazaki Prefecture that included multiple non-meningitis infections, such as sepsis (IASR 32: 298-299, 2011; p. 367 of this issue). As a consequence, in April 2012, the School Health and Safety Act was modified to classify meningococcal meningitis as a category II school infectious disease under the Act.

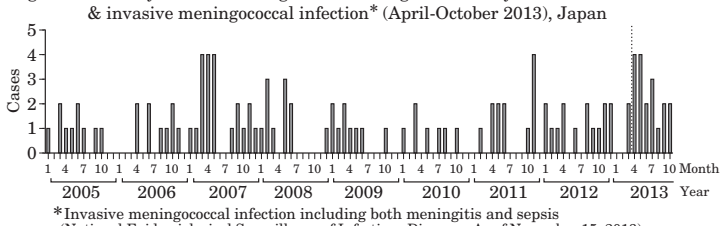
**Trends of invasive meningococcal infections (since April 2013)**: In April 2013, meningococcal meningitis and meningococcal sepsis together was classified as "invasive meningococcal infection", a Category V notifiable disease under the Infectious Diseases Control Law that needs notification of all the cases (http://www.nih.go.jp/niid/images/iasr/34/406/de4061.pdf). Since April 2013, 18 cases of invasive meningococcal infection have been notified; no infant case has been included (as of 15 November 2013, Table 2). The causative agents were detected from cerebrospinal fluid (2 cases), from blood (13 cases) and from the both (3 cases). Thirteen cases were notified from Kanto district, and ten of them were from Tokyo. There were no epidemiological links between them and none of them had travelled abroad. Three cases, 32-, 39- and 70-years old patients, died of septic shock. The calculated case-fatality rate was 17% (3/18).

Figure 1. Incidence of meningococcal meningitis in Japan, 1918-2012




Data from 1918 to March 1999 were based on "Statistics on Communicable Diseases in Japan."
Data after April 1999 were based on the reports under the National Epidemiological Surveillance of Infectious Diseases (As of November 15, 2013).

Figure 2. Monthly cases of meningococcal meningitis (January 2005-March 2013) & invasive meningococcal infection* (April-October 2013), Japan




*Invasive meningococcal infection including both meningitis and sepsis
(National Epidemiological Surveillance of Infectious Diseases: As of November 15, 2013)

**Gender and age distributions** (Fig. 3): Male to female ratio of patients reported from 2005 to October 2013 was 7:5. In 2005-2013 period, number of patients tended to be high among 20s and 50s-60s, while in 1999-2004 period it tended to be high in infants less than 4 years of age and people of 15-19 years of age (IASR 26: 33-34, 2005).

**Incidence according to serogroups**: *N. meningitidis* species are classified into 13 serogroups based

(Continued on page 362′)

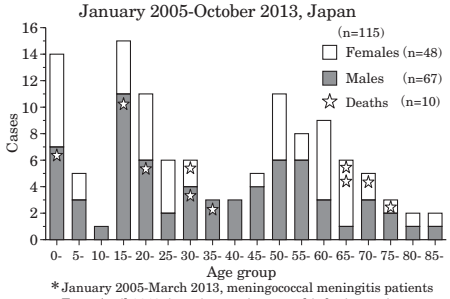
(THE TOPIC OF THIS MONTH-Continued)

Table 2. Reported cases of invasive meningococcal infection from April to October, 2013 (n=18)

| Month of diagnosis | Prefecture | Gender | Age | Pathogen detected specimen | | Sero-group | Severe Symptoms | Prognosis |
|---|---|---|---|---|---|---|---|---|
| Apr. | Okinawa | Female | 65 | | Blood | B | Meningitis | |
| Apr. | Tokyo | Male | 78 | CSF | Blood | | | |
| Apr. | Tokyo | Female | 54 | | Blood | | Shock, DIC, Petechiae | |
| Apr. | Tokyo | Male | 19 | CSF | | | Meningitis | |
| May | Saitama | Male | 32 | | Blood | Y | Shock, DIC, Purpura | Death |
| May | Hiroshima | Female | 70 | | Blood | | Shock, DIC | Death |
| May | Tokyo | Male | 64 | CSF | Blood | Y | Meningitis, DIC | |
| May | Mie | Male | 16 | CSF | | | | |
| Jun. | Tokyo | Male | 55 | CSF | Blood | | Meningitis, Shock, DIC | |
| Jun. | Tokyo | Male | 65 | | Blood | | | |
| Jul. | Chiba | Female | 93 | | Blood | | | |
| Jul. | Osaka | Male | 14 | | Blood | | Meningitis, Petechiae | |
| Jul. | Kanagawa | Male | 32 | | Blood | Y | | |
| Aug. | Tokyo | Male | 39 | | Blood | C | Shock | Death |
| Sep. | Tokyo | Male | 52 | | Blood | Y | | |
| Sep. | Tokyo | Male | 48 | | Blood | Y | Shock | |
| Oct. | Tokyo | Male | 71 | | Blood | | | |
| Oct. | Miyazaki | Male | 83 | | Blood | Y | Shock | |

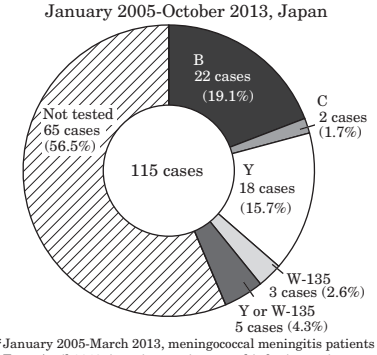
(National Epidemiological Surveillance of Infectious Diseases: As of November 15, 2013)

Figure 3. Age distribution of meningococcal infection cases*, January 2005-October 2013, Japan




*January 2005-March 2013, meningococcal meningitis patients
From April 2013, invasive meningococcal infection patients
(National Epidemiological Surveillance of Infectious Diseases: As of November 15, 2013)

Figure 4. Serogroup of *Neisseria meningitidis* isolates from meningococcal infection cases*, January 2005-October 2013, Japan




*January 2005-March 2013, meningococcal meningitis patients
From April 2013, invasive meningococcal infection patients
(National Epidemiological Surveillance of Infectious Diseases: As of November 15, 2013)

on differences in their capsular polysaccharides. Serogrouping provides important epidemiological information for vaccine planning in endemic areas. Among 115 cases that consisted of meningococcal meningitis reported from 2005 to March 2013 and invasive meningococcal infection reported from April to October of 2013 (Fig. 4), serogroup information was obtained from 50 cases. The most frequent was serogroup B (22 cases), followed by serogroup Y (18 cases), serogroup C (2 cases) and serogroup W-135 (3 cases); there were 5 cases indiscernible as to serogroup Y or serogroup W-135 (Fig. 4). Department of Bacteriology I, National Institute of Infectious Diseases (NIID) has been conducting molecular epidemiological analysis using the multilocus sequence typing (MLST) to make international database referencing possible. Analysis of 18 isolates obtained during 2005-2012 revealed that the Japanese isolates belonged to ST-23 complex, ST-41/44 complex and other known genotypes; there were small number of isolates of new ST types (see p. 363 of this issue).

**Treatment and vaccines**: The primary choice of treatment is intravenous administration of penicillin G or the third generation cephem antibiotics. To contacts, oral administration of rifampicin or new quinolone is recommended for prevention of further spread (see pp. 364, 365 & 366 of this issue), though guidelines for preventive administration is not yet ready. Currently, capsular antigen-specific vaccines against serogroups A, C, Y and W-135 are available, but they are not yet approved in Japan (see p. 371 of this issue).

**Epidemics abroad**: Meningococcal epidemics are reported continuously from the "Meningitis belt" in sub-Saharan Africa. Elsewhere, while it was mostly sporadic, outbreaks, such as, those in schools in the United States (IASR 33: 138 & 142, 2012), those among male homosexuals in Germany (IASR 34: 240, 2013) and those associated with Muslim pilgrimage to Mecca have been reported. International Health Regulation lists meningococcal disease in Annex 2 as an infection which is generally localized but has a potential of international spread (http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf).

Most epidemics have been due to serogroups A, B, C, Y and W-135, and among some of the developed countries serogroup B was dominant. More recently a new type serogroup X was reported from the meningitis belt (see p. 372 of this issue).

As most meningococcal patients notified in recent years have had no history of travelling abroad, public should be informed not only of infection risk abroad but also infection risk in Japan. Prompt notification, epidemiological investigation without delay and taking prompt countermeasures are required for preventing spread of infection, particularly when an outbreak is in dormitories or other places for communal life. Analysis of bacterial isolates is indispensable for finding routes of importation or domestic spread and for planning of countermeasures. Collaborations and networks between clinics, local governments, prefectural and municipal public health institutes and NIID should be further strengthened.

*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.*

**Infectious Disease Surveillance Center, National Institute of Infectious Diseases**
Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, JAPAN Tel (+81-3)5285-1111