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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>
Hepatitis A in Japan, 2010-2014, as of November 2014

Hepatitis A is an acute infectious disease caused by hepatitis A virus (HAV), which belongs to genus *Hepatovirus* of *Picornaviridae*. There is only one serotype known, which is classified into 6 genotypes, I-VI. Genotypes I-III have been detected from man so far, with each of these genotypes further grouped into A or B. HAV is shed via the infected person's stool, and spreads fecal-orally through contaminated food or water causing occasionally large outbreaks. According to the WHO Fact Sheet (N° 328, June 2014, http://www.who.int/mediacentre/factsheets/fs328/en/), globally an estimated 1.4 million hepatitis A cases occur each year. The improved water supply and sewage system, along with improved environmental hygiene, have greatly reduced the number of large-scale HAV outbreaks in developed countries. Nevertheless, Japan continuously reports more than 100 HAV infections per year (Fig. 1).

HAV infection is a category IV infectious disease under the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infectious Diseases (the Infectious Diseases Control Law) amended in November, 2003. All diagnosed cases, including asymptomatic carriers, must be notified. The notification criteria are found in http://www.nih.go.jp/niid/images/iasr/36/419/de4191.pdf.

The incubation period is 2-6 weeks (average of 4 weeks). Early clinical signs and symptoms include high fever (38°C or above), general malaise, headache, anorexia, myalgia, and abdominal pain, which is followed by appearance of signs characteristic of hepatitis, such as jaundice and hepatomegaly. Fulminant type or death is rare, though its frequency increases with age particularly among those with no anti-HAV antibody. The prognosis is generally good (case fatality rate <0.5%); it does not becomes chronic and patients recover in 2-3 months. No specific therapeutics are available and patients are kept in rest and treated symptomatically. Among children under five years of age, 90% are asymptomatic. Among adults, 90% are symptomatic and 60% among them develop jaundice. Once infected, symptomatically or asymptomatically, life-long immunity is acquired.

HAV infected cases release virus from 1 week after infection to several months after the onset, during which time they remain as the infectious source.

National Epidemiological Surveillance of Infectious Diseases

HAV epidemiology in Japan used to display seasonality with the high season during winter to spring (January-May). With reduced notifications since 2004, the clear seasonality has become restricted to peak years (see IASR 31: 284-285, 2010 for data before 2004).

From 2004 to 2014, there were three such years, 2006, 2010 and 2014, which respectively reported 320, 347 and 421 (as of week 48) cases; number of reported cases during other years during this period ranged from 115-176 (Fig. 1). During 2010 to 2014 (as of week 48), twenty asymptomatic cases (ranging from 2 to 6 cases per year) and six fulminant hepatitis cases (ranging in age from 56-67 years) were reported.

Suspected place of infection: There was no regional clustering of the hepatitis A cases (Fig. 2). The majority of patients (80%) were infected in Japan, though there were also annually 40-50 cases infected abroad (Table 1). Among 228 patients suspected to have been infected abroad, reported travel countries included the Philippines (n=34), India (n=33), Pakistan (n=17), the Republic of Korea (n=14) and Indonesia (n=12).

Suspected route of infection: Among 1,229 cases that were notified from 2010 to the 48th week of 2014, 987 were attributed to foodborne routes, among which 41% (405/987) were due to

Figure 1. Weekly number of reported hepatitis A cases, from week 1 of 2009 to week 48 of 2014, Japan (National Epidemiological Surveillance of Infectious Diseases: as of December 3, 2014)

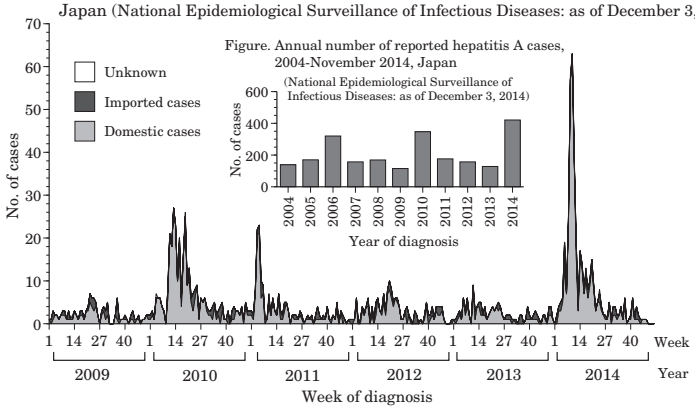
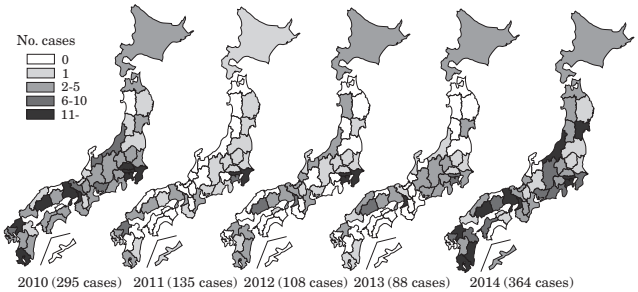


Figure 2. Number of reported hepatitis A cases suspected to have been infected domestically, by prefecture, 2010-2014, Japan



(National Epidemiological Surveillance of Infectious Diseases: As of December 3, 2014)

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(THE TOPIC OF THIS MONTH-Continued)

Table 1. Number of reported hepatitis A cases, January 2010-November 2014

Year of diagnosis	Suspected place of infection			Total
	In Japan	Abroad	Unknown*	
2010	295	50	2	347
2011	135	40	1	176
2012	108	48	1	157
2013	88	40	-	128
2014	364	50	7	421
Total	990	228	11	1,229

*Includes 8 cases whose infections could have been acquired domestically or abroad

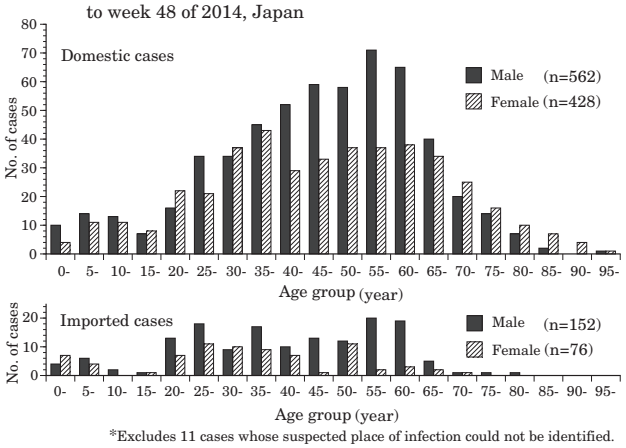
(National Epidemiological Surveillance of Infectious Diseases: as of December 3, 2014)

Table 2. Detected Hepatitis A virus by genotype, 2010-2014

Sampled year	Hepatitis A virus genotype				Total
	IA	IB	IIIA	Not typed	
2010	8	-	4	53	65
2011	1	-	-	53	54
2012	21	2	4	8	35
2013	17	1	1	5	24
2014	128	3	15	9	155
Total	175	6	24	128	333
(%)	(53)	(2)	(7)	(38)	(100)

[Infectious Agents Surveillance Report: as of December 8, 2014 from prefectural and municipal public health institutes (PHIs)]

Figure 3. Age distribution of hepatitis A cases* by gender, week 1 of 2010 to week 48 of 2014, Japan



*Excludes 11 cases whose suspected place of infection could not be identified.

(National Epidemiological Surveillance of Infectious Diseases: as of December 3, 2014)

ingestion of contaminated oyster or other shellfish and seafood products. The infection source was unknown for 49% (486/987) of cases. There were 9 cases suspected of transmission via sexual routes.

Sex and age distribution of cases: As shown in Fig. 3, 59% (723/1,229) of cases were male and 41% (506/1,229) female. The cases' age distribution ranged broadly from 20 to 60 years, with a large proportion of cases occurring among those 40-64 years of age, particularly among males. The median age of cases has been rising; from 41 years in 2000, 44 years in 2004, 47 years in 2010, and 49 years in 2014 (as of week 48).

Laboratory diagnosis and detected genotypes: Laboratory confirmation of cases notified from 2010 to the 48th week of 2014 consisted of IgM antibody detection (1,205 cases, 98%) and HAV genome detection by PCR (105 cases, 9%) (some cases were tested for more than one method). Specimens used for PCR detection were stool (65 cases), blood (38 cases) and both stool and blood (2 cases). Among 333 cases reported to the Infectious Agents Surveillance Report (IASR), 175 cases were genotype IA (as of 8 December 2014) (Table 2). The proportion of cases that were genotyped increased remarkably since 2012.

Epidemiologic situation in 2014

Concerned by the sudden increase of HAV cases in February 2014, the Ministry of Health, Labour, and Welfare (MHLW) issued a note "Trends in hepatitis A infections and a warning regarding the hepatitis A epidemic" on 14 March 2014. MHLW asked the local governments, according to the notice on 26 April 2010 (IASR 31: 140, 2010) to ensure collection of stool specimens from notified cases for molecular epidemiological investigations and to conduct active surveillance. National Institute of Infectious Diseases (NIID) and prefectural and municipal public health institutes (PHIs) jointly genotyped HAV specimens obtained from 159 cases in 2014, and found that 137 cases were IA, 18 cases IIIA, and 4 cases IB (see pp. 3 to 7 of this issue). Seventy-five percent of the IA type isolates obtained, ranging from Miyagi prefecture in the north to the southern prefecture of Kagoshima, shared almost identical nucleotide sequences, which was named "2014 Japan epidemic strain (2014JapanEPM)". As the "2014JapanEPM" gave false negative results when assayed by using the real-time PCR method described in the HAV detection manual (August 2006), conventional RT-PCR or a real-time PCR using modified primers is now recommended (see p. 7 of this issue, IASR 35: 154-156, 2014).

Preventive measures

Special attention should be paid to the fact that HAV is resistant to acid or drying, and cases' discharges and foods contaminated by HAV should be handled with care. Implementation of hand washing and other hygienic practices, sufficient heating of foods (85°C for at least 1 minute), and disinfection using chlorine agents are indispensable for interrupting transmission.

Long-term protection against hepatitis A can be achieved by three shots of the available vaccine. Inactivated HAV vaccine produced in Japan had been used for vaccinating adults (16 years of age or above) on a voluntary basis, but since March 2013, voluntary vaccination was expanded to children younger than 16 years of age (see p. 10 of this issue). The vaccination, though voluntary, is strongly recommended for those with higher risk of HAV infection, such as long-term travelers going to HAV endemic areas, medical practitioners with a high chance of coming in contact with HAV patients, people with underlying chronic hepatic disease(s) without HAV antibody, and men who have sex with men.

According to the 2003 national serological survey, while more than 70% of the Japanese population aged 70 years or older have anti-HAV antibody, almost none of those 50 years or younger have immunity (http://idsc.nih.go.jp/iasr/31/368/graph/df36811.gif). Therefore, a large proportion of the Japanese population is at risk of HAV infection. Among reported cases, an estimated 10% of the HAV infections occurred among household members (does not necessarily mean person-to-person transmission and may include exposure to a common infection source) (see p. 8 of this issue). Due to HAV's long incubation period, identifying the infection source or route is difficult, but using molecular epidemiology tools are helpful for analysis (IASR 32: 78-79, 2011; and IASR 34: 311-312, 2013). Due to long-term shedding of the virus, notification of cases and information-sharing among medical institutions, health centers, PHIs and NIID is important for interrupting HAV transmission.

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