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<THE TOPIC OF THIS MONTH>

Hepatitis A in Japan between 2015 and March 2019

Hepatitis A is an acute infectious disease caused by the hepatitis A virus (HAV), which belongs to the genus *Hepatitisvirus* of *Picornaviridae*. There is only one known serotype, which is classified into 6 genotypes, I-VI. Viruses of genotypes I to III are detected in humans, with each genotype further divided into subgroups A and B. HAV is transmitted through the ingestion of contaminated food or water, or by direct contact with an infected person. In developed countries with improved hygienic environments, such as water and sewage systems, large-scale outbreaks of hepatitis A are rare, but they have been reported among men who have sex with men (MSM) and persons who inject drugs (PWID).

HAV is a Category IV infectious disease under the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (Infectious Diseases Control Law) amended in November 2003. All diagnosed cases, including asymptomatic carriers, must be notified. The notification criteria can be found at <https://www.niid.go.jp/niid/images/iasr/36/419/de4191.pdf>.

The incubation period is 2–6 weeks (4 weeks on average). Early clinical symptoms include high fever (over 38°C), general malaise, anorexia, headache, myalgia, and abdominal pain, which are followed by the appearance of symptoms characteristic to hepatitis such as jaundice and hepatomegaly (see p. 149 of this issue). Its severity increase with age. Although no virus-specific therapy is available, the prognosis is generally good (case fatality rate <0.5%); it never becomes chronic and patients spontaneously recover in 2–3 months. Approximately 90% of infections in children under 5 years of age are asymptomatic, and 90% of adult infections are symptomatic. Once infected, life-long immunity is obtained. As HAV is excreted in the stool for long periods from approximately 2 weeks before onset to several months after, infected people can be a source of infection even before onset.

National Epidemiological Surveillance of Infectious Diseases

In Japan, an average of 266 cases (range of 115–502 cases) of hepatitis A patients per year have been notified since 2000 when information became available year round after the implementation of the Infectious Diseases Control Law, to 2017 (Fig. 1). In 2018, the number of notified cases reached 926 (tentative result) (see p. 150 of this issue). In 2019, 115 cases (tentative results) were notified as of March 2019 (as of week 13) (Table 1).

Suspected place of infection: Most (approximately 85%) of the 1,839 cases notified between 2015 and March 2019 were domestic infections (Fig. 2 in p. 148). Approximately 60 cases of infection outside of Japan are notified annually (Table 1). Among the cumulative 256 cases, the main destinations were the Philippines in 58, Thailand in 22 (including one multi-country visit), Taiwan in 20, Korea in 15, Indonesia in 14, Cambodia in 14, India in 13, Vietnam in 13, and Pakistan in 12.

Suspected route of infection: Of the 913 cases notified between 2015 and March 2019, excluding those notified in 2018, 660 cases (72%) were presumed to be oral infections, and 27 cases (3%) were reported to be due to homosexual contact. On the other hand, in 2018 (926 cases), 349 cases (38%) were orally infections, whereas 396 cases (43%) were due to homosexual contact, exceeding the number of cases due to oral infection.

Sex and age of the patients: Of the 1,556 patients notified between 2015 and March 2019, and considered to have been infected in Japan, 1,196 (77%) were males and 360 (23%) were females (Fig. 1). The increase in males was due to the overall increase in

Figure 1. Weekly number of notified hepatitis A cases, from January 2015 to March 2019, Japan

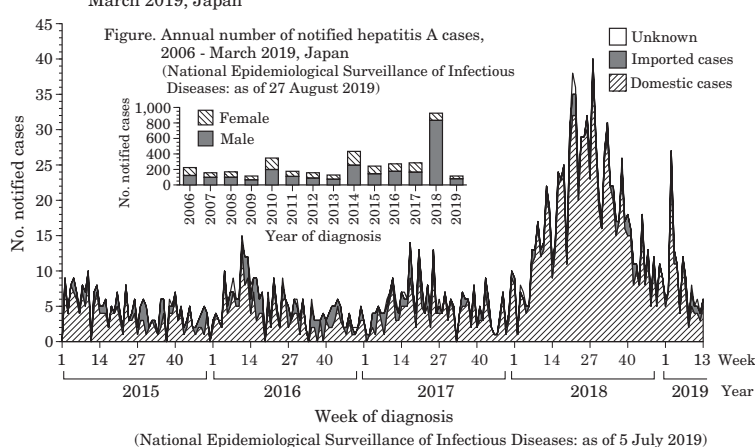


Table 1. Number of notified hepatitis A cases, January 2015-March 2019

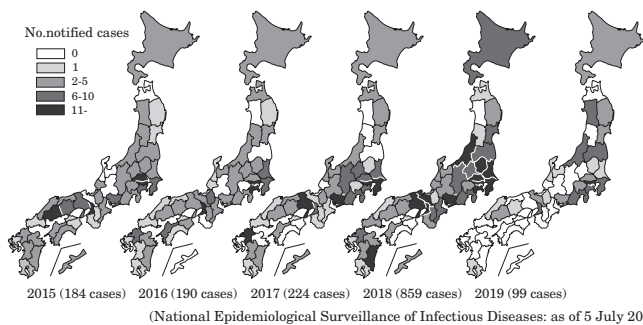
Year of diagnosis	Suspected place of infection			Total
	In Japan	Abroad	Unknown*	
2015	185	54	2	241
2016	192	69	11	272
2017	221	60	4	285
2018	859	59	8	926
2019	99	14	2	115
Total	1,556	256	27	1,839

*Infections could have been acquired domestically or abroad (National Epidemiological Surveillance of Infectious Diseases: as of 5 July 2019)

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Figure 2. Number of notified hepatitis A cases suspected to have been infected domestically, by prefecture, from January 2015 to March 2019, Japan (year of diagnosis)



infections due to homosexual contact in 2018 (833 males: 90%, 93 females: 10%). The median patient age was 46 years in 2015, 49 years in 2016, 40 years in 2017, 37 years in 2018, and 47 years in 2019 (as of week 13).

Summary of molecular epidemiology

Based on the notifications of April 26, 2010 and February 6, 2019, the Ministry of Health, Labour and Welfare (MHLW) requested local governments to ensure patient stool specimens for molecular epidemiological analysis and to cooperate in active surveillance (see p. 150 of this issue). In December 2018, the procedure manual for HAV detection was revised in order to support efficient surveillance nationwide. Based on HAV nucleotide sequence analysis conducted by the National Institute of Infectious Diseases (NIID) and Prefectural and Municipal Public Health Institutes (PHIs) (Table. 2), outbreaks

of the 2017 epidemic strain (genotype 1A) suspected to be associated with imported frozen clams were confirmed mainly in Tokyo, Nagano, and Miyazaki Prefectures (IASR 39: 25-26, 2018). This strain is still reported sporadically. The cause of the epidemic in 2018, the year with the most notifications in the past 20 years, was confirmed to be mainly the RIVM-HAV16-090 strain (genotype 1A) (see p. 150, 152, 153, and 154 of this issue), which has caused outbreaks in Taiwan and Europe since 2015 (see p. 151 of this issue). Although the number of individuals infected by this strain decreased in the latter half of 2018, it has not been fully eradicated. Between December 2018 and February 2019, the JP-HAV19-00758 strain (genotype 1A), which is classified into a cluster different from those reported previously, was transiently detected mainly in the Tohoku area (see p. 155 of this issue). MHLW, NIID, and PHIs cooperatively investigated the source of the outbreak, but they were unable to find identify common contaminated foods.

Preventive measures

As HAV is resistant to acid and drying, it is important to take measures against the source and route of infection by appropriate treatment of patient excrement and contaminated food, thorough hygiene management, including hand washing, sufficient cooking (85 °C, 1 minute or longer), and disinfection with chlorine agents.

Long-term prevention of hepatitis A can be expected by vaccines. There is no age limit for the administration of the inactivated hepatitis A vaccine approved in Japan, and it is recommended by the WHO for those aged one or older. The vaccination is strongly recommended for travelers going to HAV-endemic areas, medical practitioners, patients with chronic liver disease(s), and people with a higher risk of HAV infection such as MSM and PWID (see p. 157 of this issue).

According to a seroepidemiological survey in which blood samples of healthy Japanese were collected between 2013 and 2017, it was estimated that more than 80% of the Japanese population and 99% of those under 60 years old are sensitive to HAV infection (Fig. 3). The HAV outbreak in 2018 demonstrated the importance of intervention for susceptible groups in Japan. In response to this outbreak, on July 18, 2018, the MHLW issued a request for cooperation to local governments, medical associations, and infectious disease-related societies regarding alerts associated with the increase in the number of reports of HAV. In addition, medical institutions actively recommended HAV vaccination to MSM, and several workshops on hepatitis A were held by private organization(s) in collaboration with local governments (see p. 150 of this issue).

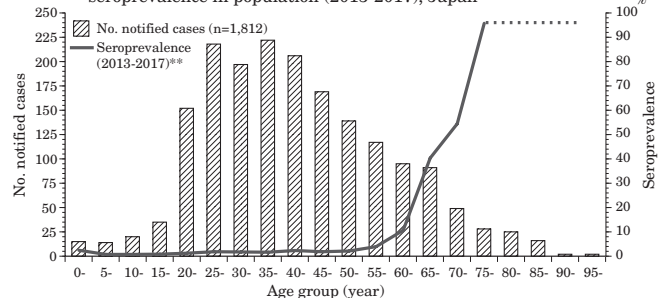
Due to the long incubation period of HAV, identifying the infection source or route has been difficult, but it is now possible to reinforce the estimation using molecular epidemiology. As the viral excretion period is also long, to prevent the spread of infection and respond quickly to outbreaks, it is essential that every patient is notified, guidance is provided to prevent secondary infections, and data are collected through interviews and active surveillance.

Table 2. Detected hepatitis A virus by genotype, 2015-2019

Sampled year	Hepatitis A virus genotype				Total
	1A	1B	III A	Not typed	
2015	57	4	4	10	75
2016	56	1	5	7	69
2017	58	1	14	8	81
2018	223	4	7	5	239
2019	44	0	3	3	50
Total	438	10	33	33	514
(%)	(85)	(2)	(6)	(6)	(100)

(Infectious Agents Surveillance System: as of 8 July 2019 from prefectural and municipal public health institutes)

Figure 3. Age distribution of hepatitis A cases* (January 2015-March 2019) and seroprevalence in population (2013-2017), Japan



*Exclude 27 cases whose the suspected place of infection could not be identified.

**Serum survey by Japanese Red Cross Society and The National Serum Reference Bank/Tokyo, National Institute of Infectious Diseases, Japan (National Epidemiological Surveillance of Infectious Diseases: as of 5 July 2019)

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 Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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