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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>
Acute hepatitis C, April 2006-October 2020

Acute hepatitis C is caused by infection of the hepatitis C virus (HCV), which belongs to the *Flaviviridae* family, genus *Hepacivirus*. After a latency period of 15-160 days (average 7 weeks), acute hepatitis develops with multiple symptoms such as general fatigue, cold-like symptoms, anorexia, chills, nausea, or vomiting; in 30-40% of patients, the virus becomes undetectable and the patient is cured, but the remaining 60-70% become HCV carriers and often progress from acute to chronic hepatitis. Asymptomatic carriers infected with HCV who have no symptoms account for 20-30% of HCV-infected individuals. The probability of spontaneous remission from chronic hepatitis is very low, at approximately 0.2%, and 10-16% of patients are thought to develop cirrhosis after an average of 20 years after the initial infection. Moreover, patients with cirrhosis develop hepatocellular carcinoma at a high rate of greater than 5% per year. The total number of deaths due to liver cancer used to exceed 30,000 a year, but has been on a downward trend since around 2000 (Cancer statistics in Japan, National Cancer Center, 1958-2018). The HCV carrier rate has also decreased since 2000 (see p.3 of this issue). Hepatitis C cases are diagnosed mostly via the combination of anti-HCV antibody and quantification of HCV RNA. Since 2014, direct acting antivirals (DAAs) have been used instead of interferon, which has problems with effectiveness and side effects; more than 95% of treated patients achieve sustained virological response (SVR), i.e., undetectable HCV RNA in the blood, 24 weeks after the end of the treatment (see p.5 of this issue).

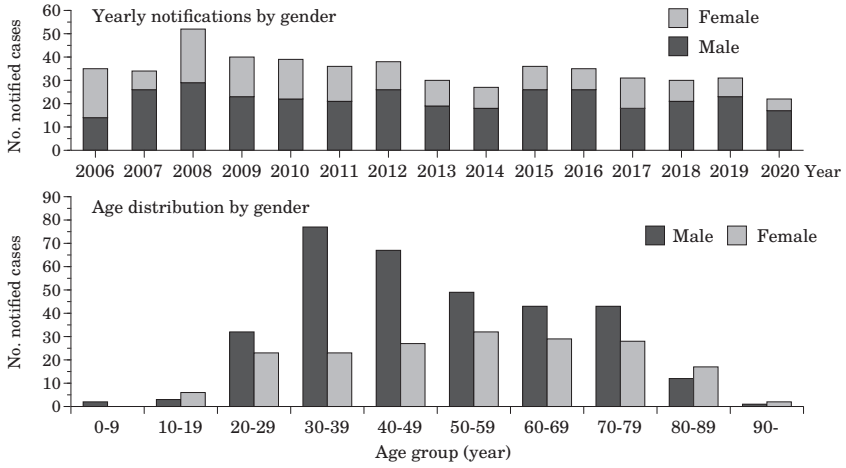
Notifications under National Epidemiological Surveillance of Infectious Diseases (NESID)

Acute hepatitis C surveillance was added to the infectious disease surveillance program (a budgeted activity of the Ministry of Health, Labour and Welfare) in 1987 and initiated as a program based on monthly reports from 500 sentinel hospitals nationwide. Later, in April 1999, the Infectious Diseases Control Law was enacted and acute hepatitis C was classified into the category of "acute viral hepatitis", a category IV Infectious Disease that requires notification of all diagnosed cases. In November 2003, the law was amended and acute hepatitis C was reclassified into "viral hepatitis (excluding hepatitis A and E)", a category V Infectious Disease, with its trend being monitored accordingly. Only acute hepatitis is subject to notification, and chronic hepatitis, cirrhosis, and liver cancer are not included. All physicians who diagnose a case of acute hepatitis C are required to submit a notification form to the public health center within seven days of diagnosis (https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-02.html). This report summarizes the acute hepatitis C cases diagnosed and reported from April 2006, when the notification form was revised under the Infectious Diseases Control Law, through October 2020. Among the notifications of "viral hepatitis (excluding hepatitis A and E)" during this period, there were 516 cases of hepatitis C (as at November 10, 2020). The annual number of acute hepatitis C diagnoses notified ranged from 23-58 cases (male: 14-31 cases, female: 5-27 cases) (Fig. 1).

Gender and Age distribution

Of these 516 cases, 329 were in males and 187 were in females, with a male to female ratio of 1.8. The male/female ratio increased over time, from 0.7 in 2006 to 3.6 in 2020 (Fig. 1). By age group, males exhibited a peak in their 30s, whereas females were similarly distributed from their 20s to 70s with no clear peak. There were few reports of children younger than 10 years of age or the elderly in their 90s (Fig. 1).

Figure 1. Yearly number of notified acute hepatitis C cases, April 2006 to October 2020, Japan (n=516)



(National Epidemiological Surveillance of Infectious Diseases: as at 10 November 2020)

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(THE TOPIC OF THIS MONTH-Continued)

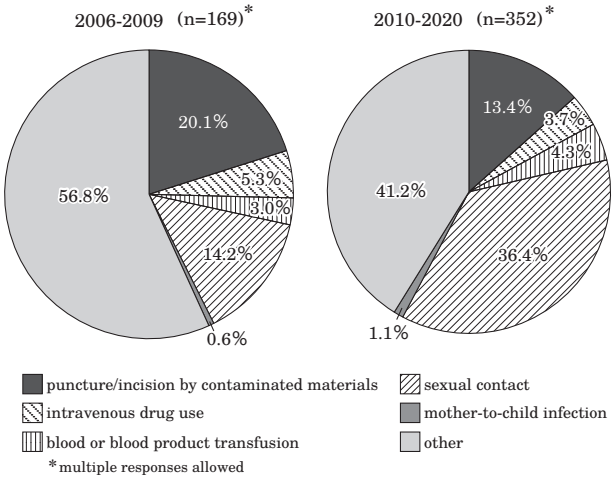
Table. Number of notified acute hepatitis C cases by prefecture, April 2006 to October 2020, Japan

Prefecture	Notified cases	per 1 million population*	Prefecture	Notified cases	per 1 million population*
Hokkaido	16	2.97	Shiga	5	3.54
Aomori	1	0.76	Kyoto	12	4.60
Iwate	1	0.78	Osaka	74	8.37
Miyagi	5	2.14	Hyogo	20	3.61
Akita	0	0.00	Nara	7	5.13
Yamagata	1	0.89	Wakayama	10	10.37
Fukushima	5	2.61	Tottori	1	1.75
Ibaraki	8	2.74	Shimane	1	1.44
Tochigi	9	4.56	Okayama	27	14.05
Gunma	11	5.58	Hiroshima	20	7.03
Saitama	18	2.48	Yamaguchi	2	1.42
Chiba	10	1.61	Tokushima	1	1.32
Tokyo	113	8.36	Kagawa	3	3.07
Kanagawa	24	2.63	Ehime	6	4.33
Niigata	2	0.87	Kochi	7	9.62
Toyama	2	1.88	Fukuoka	29	5.68
Ishikawa	2	1.73	Saga	0	0.00
Fukui	5	6.35	Nagasaki	6	4.36
Yamanashi	1	1.20	Kumamoto	1	0.56
Nagano	6	2.86	Oita	2	1.72
Gifu	1	0.49	Miyazaki	8	7.25
Shizuoka	9	2.43	Kagoshima	8	4.85
Aichi	11	1.47	Okinawa	3	2.09
Mie	2	1.10	Total	516	4.06

*Population based on 2015 census data

(National Epidemiological Surveillance of Infectious Diseases: as at 10 November 2020)

Figure 2. Infection route of acute hepatitis C cases, April 2006 to October 2020, Japan



(National Epidemiological Surveillance of Infectious Diseases: as at 10 November 2020)

Notifications by prefectures

Of the 516 cases, Tokyo Prefecture had the highest number of notifications with 113 cases, followed by Osaka Prefecture with 74 cases, and 23 prefectures had 5 or fewer cases (Table). The number of reports per 1,000,000 population was highest in Okayama Prefecture (14.05), followed by Wakayama Prefecture (10.37) and Kochi Prefecture (9.62).

Symptoms

Among the 516 cases, 435 (84%) had liver dysfunction, 264 (51%) had general fatigue, 177 (34%) had jaundice, and 4 (0.8%) had fulminant hepatitis (multiple responses allowed). One case of death was reported over the period from April 2006 to October 2020.

Transmission routes

Among the 516 cases, the transmission route was classified as confirmed in 47 and presumed in 450, whereas it was unknown in 19. Of the presumed cases, 209 were recorded as "unknown". Excluding 288 cases with unknown status, the causes/routes of infection was reported in 489 cases, and including multiple responses, there were 120 cases (25%) recorded as sexual contact; 81 cases (17%) recorded as puncture/incision by contaminated materials; 22 cases (4.5%) recorded as intravenous drug use; 20 cases (4.1%) recorded as blood or blood product transfusion; 5 cases (1.0%) recorded as mother-to-child infection; and 241 cases recorded as "other". When the causes/routes of infection (including multiple responses) of the 516 cases were separated into two periods from April 2006 to December 2009 (earlier period) and from January 2010 to October 2020 (latter period), "other" accounted for 57% in the earlier period, and although sexual contact increased to 36%, "other" still accounted for 41% of the cases in the latter period (Fig. 2).

Summary (Challenges ahead)

The number of acute hepatitis C notifications in recent years has been stable in the range of 23-58 cases each year. The liver is called the "silent organ", and it is possible that there are many infected persons without symptoms who are unaware of their infection, and the number of notifications to the NESID system may not reflect the actual number of infected individuals. It is strongly recommended that people who have never been tested for hepatitis be tested during health checkups even if they do not have any symptoms, and if positive, they should visit a healthcare facility as soon as possible. Physicians are also expected to promptly (within seven days) report to NESID when they diagnose a patient with acute viral hepatitis due to HCV, as mandated by the Infectious Diseases Control Law. The information collected through NESID is important in the consideration of developing preventive measures.

The risk of HCV transmission through blood transfusion and contaminated medical equipment was substantially reduced thanks to eliminating the practice of reusing medical equipment and the introduction of a highly sensitive nucleic acid amplification test (NAT) as a screening test for blood used for transfusion. Furthermore, laboratory diagnosis methods using HCV antibody and HCV RNA quantification tests have been established, and treatment using DAAs effective against HCV infection even at the chronic phase has made it possible to achieve SVR in approximately 95% of patients. Hepatitis C is becoming a "curable disease".

The World Health Organization (WHO) aims to eliminate viral hepatitis by 2030. In Japan, hepatitis countermeasures are promoted through cooperation among the national government, local governments, and medical institutions by ensuring a system in which many people undergo hepatitis tests, access medical institutions if an infection is suspected, receive standard treatment as necessary, and continue to receive regular checkups in consideration of the risk of developing liver cancer (see p.6 of this issue). In addition, "hepatitis coordinators" (see p.8 of this issue) are trained to coordinate these activities. On the other hand, although SVR can now be achieved in approximately 95% of patients, countermeasures against carcinogenesis after SVR (see p.9 of this issue), and effective methods to prevent prejudice and discrimination against those infected with the hepatitis virus, are also issues that must be resolved (see p.11 of this issue).

Furthermore, three researchers (including one from the National Institutes of Health (NIH) in the United States) received the Nobel Prize in Physiology or Medicine in 2020 (see p.12 of this issue). They were recognized for their discovery of the hepatitis C virus, which clarified the cause of many chronic hepatitis cases, enabled tests to be performed for blood transfusions, and paved the way for the development of highly effective therapeutic drugs.

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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