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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 Flaccid Paralysis in Japan as of December 2019

Acute flaccid paralysis (AFP) is medically a broad term for disorders presenting with acute flaccid motor paralysis of the extremities (see p. 19 of this issue). AFP develops when the anterior horn cells of the spinal cord, along with the peripheral nerves or muscles, are damaged. Typical diseases causing AFP include Guillain-Barré syndrome (GBS), acute poliomyelitis (polio), and acute flaccid myelitis (AFM).

Global Polio Eradication Initiative and AFP Surveillance: The World Health Organization (WHO) is promoting the Global Polio Eradication Initiative to terminate the spread of wild-type polioviruses from all countries and regions worldwide (see pp. 20 and 21 of this issue). Although the global eradication of wild-type poliovirus type 2 was declared in September 2015 and type 3 in October 2019, cases of AFP due to vaccine-derived polioviruses (VDPV) have been reported in a broad area of Africa. In the WHO Western Pacific Region (WPR), which includes Japan, outbreaks due to VDPV have also recently occurred in countries such as Laos, Papua New Guinea, and the Philippines. From the perspective of countermeasures against polio, the WHO has been monitoring AFP cases in patients under the age of 15 in each country and has established a system for AFP pathogen surveillance by conducting virological tests (virus isolation from two stool specimens collected at least 24 hours apart) on patients aged under 15 years in many countries to grasp the situation (see p. 20 of this issue).

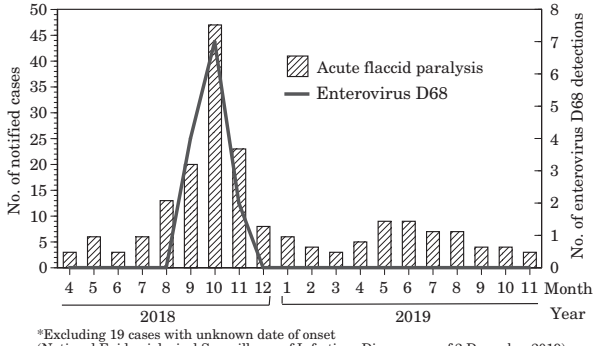
National Epidemiological Surveillance of Infectious Diseases (NESID): In Japan, the need for early detection of AFM and collection of epidemiologic information was pointed out due to the high incidence of AFM in the autumn of 2015. In addition, although Japan was the only country in the WPR that did not conduct AFP surveillance, AFP (except for acute poliomyelitis) was added to the list of category V notifiable infectious diseases on May 1, 2018. Any physician who diagnoses AFP is required to notify the jurisdictional public health center within 7 days of the diagnosis. In addition, specimens must be collected for the pathogen test after the diagnosis to differentiate it from polio and authorities must notify the occurrence as soon as possible without waiting for the result of the pathogen test. If poliovirus (including vaccine-derived strains) is detected after notification, the notification of "AFP" under category V infectious diseases must be withdrawn and changed to "acute poliomyelitis" as a category II infectious disease.

Between May 1, 2018 and November 17, 2019, 209 AFP cases were notified. An epidemic curve, excluding 19 patients whose onset month is unknown, is shown (Fig. 1). The number was high from September to November 2018, with a peak in October 2018. Based on the frequency of GBS, the WHO estimates the incidence of AFP to be 1 per 100,000 children aged under 15 years and recommends it as a sensitivity index for AFP surveillance. However, there were only 16 prefectures in 2018 and 8 prefectures in 2019 where the number of notifications exceeded 1 per 100,000 children (Fig. 2).

By age, the peak age was 1 year with a median age of 3 years in 2018. In 2019, there was no evident peak and the median age was 7 years (Fig. 3 in p.18). By gender, 105 male and 104 female children were notified.

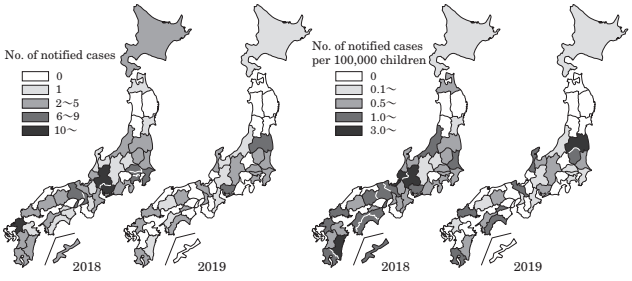
The symptoms of 216 AFP cases notified NESID between May 1, 2018 and November 17, 2019 included monoplegia in 52 patients (24%), paraplegia in 90 patients (upper extremity in 23 patients, lower extremity in 67 patients) (42%), triplegia in 15 patients (7%), quadriplegia in 42 patients (19%), respiratory muscle paralysis in 17 patients (8%), facial paralysis in 23 patients

Figure 1. Monthly number of notified acute flaccid paralysis (AFP) cases* and enterovirus D68 detections**, 1 May 2018- 17 November 2019, Japan



*Excluding 19 cases with unknown date of onset
(National Epidemiological Surveillance of Infectious Diseases: as of 2 December 2019)
**Including 4 cases with multiple detections
(Infectious Agents Surveillance System: as of 2 December 2019)

Figure 2. Number of cases and cases per 100,000 children aged under 15 years of acute flaccid paralysis (AFP), by prefecture, 2018 & 2019, Japan

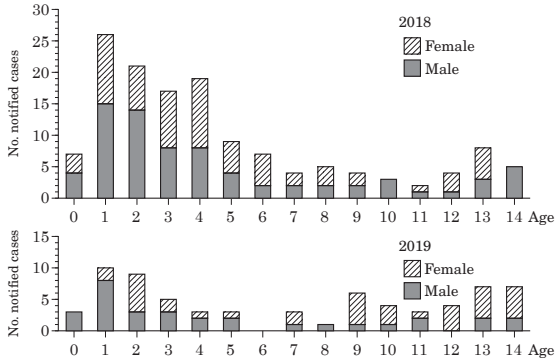


(National Epidemiological Surveillance of Infectious Diseases: as of 2 December 2019)

(Continued on page 18′)

(THE TOPIC OF THIS MONTH-Continued)

Figure 3. Age and gender distribution of notified acute flaccid paralysis (AFP) cases, 1 May 2018- 17 November 2019, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 2 December 2019)

Table. Type of pathogen reported to the Infectious Agents Surveillance System as acute flaccid paralysis (AFP) cases, 1 May 2018- 17 November 2019

Pathogen detected	No. of detections	Positive sample (isolation/detection)*						
		Stool	Sputum/ tracheal aspirate	Throat swab	Blood	Cerebrospinal fluid	Urine	Other
Enterovirus NT	1(1)	-	-	-	1	-	-	-
Coxsackievirus A2	1	1	-	-	-	-	-	-
Coxsackievirus A4	3	2	-	-	1	1	-	-
Coxsackievirus A5	1	1	-	-	-	-	-	-
Coxsackievirus A6	3(1)	3	-	1	-	1	-	-
Coxsackievirus A9	1	1	-	-	-	-	-	-
Coxsackievirus A10	1	1	-	-	-	-	-	-
Coxsackievirus A16	3(1)	3	-	3	1	1	1	1
Coxsackievirus B4	1(1)	1	-	-	-	-	-	-
Echovirus 11	2	2	-	2	1	-	-	-
Echovirus 30	1(1)	1	-	1	-	-	-	-
Enterovirus D68	13(4)	4	1	10	-	1	-	-
Parechovirus NT	1(1)	1	-	-	-	-	-	-
Parechovirus 1	2(1)	2	-	-	-	-	-	-
Parechovirus 3	2(2)	2	-	1	1	-	-	1
Rhinovirus	15(6)	2	-	15	-	-	-	-
Adenovirus 2	2(2)	2	-	1	-	-	-	-
Adenovirus 5	1	1	-	1	1	-	-	-
Cytomegalovirus	6(4)	-	-	3	1	1	4	-
Human herpes virus 6	6(3)	1	-	5	-	1	-	-
Human herpes virus 7	6(3)	-	1	5	-	-	-	-
Epstein-Barr virus	4(2)	-	-	3	1	-	-	-
Parvovirus B19	1(1)	1	-	1	1	-	-	-
Total	77(34)	32	2	52	9	6	5	2

( ): Multiple detections NT: Not typed
*Includes cases where the same pathogen was detected in different specimens
(Infectious Agents Surveillance System: as of 2 December 2019)

(11%), and bladder and rectal disturbance in 37 patients (17%). No pupillary dilatation suggestive of botulism was reported (see p. 23 of this issue).

Acute Flaccid Myelitis (AFM): AFM was frequent in North America during the 2014 epidemic season of enterovirus D68 (EV-D68) and in Japan during the 2015 EV-D68 epidemic (see p. 19 of this issue). Symptoms including pyrexia and respiratory manifestations developed first, and paralysis frequently exhibited bilaterally asymmetry. T2-weighted magnetic resonance imaging (MRI) demonstrated the characteristics of long-sized longitudinal lesions predominantly of the gray matter, with high signal intensity and contrast effects on the cauda equina. Electrophysiological examination revealed motor neuropathy and a mild increase in white blood cell count, predominantly by mononuclear cells, that peaked within 5 days after the onset of paralysis was observed on the cerebrospinal fluid test (see p. 19 of this issue).

Although the relationship between EV-D68 infection and the development of central nervous system disease in humans is unclear, at the animal experimental level, when respiratory disease-derived EV-D68 was inoculated intracerebrally into neonatal mice, flaccid paralysis developed from the front limbs and viral antigens were observed in large neurons in the anterior horn of the cervical spinal cord. After inflammation, loss of large neurons and replacement with astroglia were observed, suggesting that the infection pathology is similar to that of polio (see p. 25 of this issue).

Pathogen Test in AFP Cases: Pathogens detected in AFP cases reported to NESID between May 1, 2018 and November 17, 2019 are listed (Table). Pathogens were most commonly detected from throat swabs, followed by stool. Although the items of pathogen tests differed depending on the prefectural and municipal public health institutes (PHIs), approximately half of the PHIs conducted pathogen tests. When other PHIs, the National Institute of Infectious Diseases (NIID), and PHIs that commissioned universities to conduct the tests were included, pathogen tests were performed for all AFP cases that were notified (see p. 27 of this issue). Polioviruses were not detected and the peak of AFP notification coincided with the peak of EV-D68 detection (Fig. 1 in p.17).

Polio was only able to be excluded based on the WHO criteria in 7% of the cases of AFP that were notified to the NESID, and there were many cases in which it was unknown whether a test for poliovirus was performed or in which specimen collection was inappropriate (see p. 23 of this issue). In the AFP notification form, it is necessary to include a column for the results of poliovirus tests and the types of specimens tested.

In April 2018, the Health and Labour Sciences Research Group created “Guidelines on Surveillance, Diagnosis, Examination, and Treatment of Diseases with AFP” concerning the detection of AFP and notification of all cases to public health centers for notifiable disease surveillance, the importance of securing specimens in the acute phase, the laboratory procedures, in addition to the diagnosis, examination, and treatment of AFM cases. Detection of EV-D68 from the cerebrospinal fluid is difficult, and the viruses are most frequently obtained from specimens of respiratory origin in the acute phase. Polioviruses and enterovirus A71 are neurotropic viruses, but their detection from cerebrospinal fluid is difficult. The viruses are most frequently obtained from stool specimens (see p. 28 of this issue). For the diagnosis of AFP pathogens, it is important to secure specimens, such as throat swabs, stools (it is required to collect two separate specimens), blood, and cerebrospinal fluid, in the acute phase, and prior preparation and cooperation in the field are essential (see p. 29 of this issue).

Future Measures: AFP surveillance began in Japan in May 2018. However, as of 2019, the number of cases reported has not reached one or more per 100,000 children, which is recommended as a sensitivity index of surveillance. In addition, under the Global Polio Eradication Initiative, it is required that two stool specimens collected at least 24 hours apart within 14 days from the onset of paralysis be tested for poliovirus. To confirm the maintenance of poliovirus eradication and detect AFP pathogens, cooperation among medical institutions, public health centers, PHIs, and NIID is indispensable.

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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