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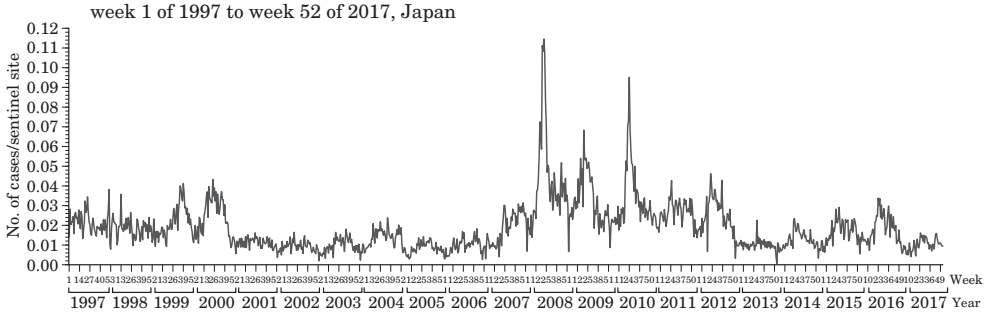
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

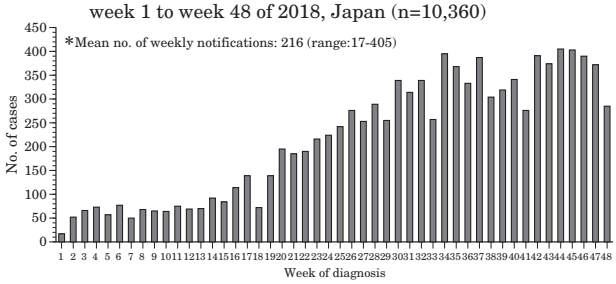
<THE TOPIC OF THIS MONTH>
Pertussis in Japan, as of November 2018

Figure 1. Weekly number of reported pertussis cases per pediatric sentinel site, week 1 of 1997 to week 52 of 2017, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 5 December 2018)

Figure 2. Number of notified pertussis cases by diagnosis week, week 1 to week 48 of 2018, Japan (n=10,360)



(National Epidemiological Surveillance of Infectious Diseases: as of 5 December 2018)

Pertussis is defined as "acute respiratory tract infection caused by *Bordetella pertussis*" under the Japanese Infectious Diseases Control Law. The main symptom is a prolonged cough, and the severity is greater when newborns or infants are infected. Vaccination is important, and in Japan, in addition to the "adsorbed diphtheria-tetanus-acellular pertussis (DPT) vaccine", the diphtheria-tetanus-acellular pertussis (DPT)-inactivated polio virus (IPV) vaccine, DPT-IPV, was added as a routine immunization in November 2012. The immunization schedule for DPT-IPV in Japan is composed of a primary series and a booster dose. For the primary series, three subcutaneous injections are administered with an interval of at least 20 days between each dose (recommended interval is 20-56 days) for those 3-12 months of age. For the subsequent booster, a subcutaneous injection is administered at least 6 months after the third dose of the primary series (recommended interval is 12-18 months after the third dose of the primary series) (http://www.niid.go.jp/niid/images/vaccine/schedule/2016/EN20161001.pdf: Routine/Voluntary Immunization Schedule in Japan, October 1, 2016). Immunity acquired by vaccination wanes 4-12 years after vaccination, and as the time since the last vaccination increases, those vaccinated may also become infected and develop disease onset. To protect infants from pertussis, some countries recommend and/or implement administration of a booster dose of the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine for adults, including adolescents and pregnant women (see p.14 of this issue). In developed countries, there have been concerns regarding unvaccinated infants who become infected and have severe outcomes, attributed to infections from adults and young adults who serve as a source of infection. In Japan, pertussis cases had until recently been reported from pediatric sentinel sites, and because the epidemiology of pertussis (including adult cases) could not be understood in a timely and accurate manner, the possibility of a delay in response existed.

For this reason, since January 1, 2018, pertussis was amended as a category V notifiable infectious disease under the Infectious Diseases Control Law (IASR 39: 13-14, 2018). As a result, all pertussis cases to be notified to the National Epidemiological Surveillance of Infectious Diseases (NESID) system require clinical manifestations of pertussis and, as a rule, confirmation by laboratory diagnosis.

Laboratory diagnosis of pertussis: For the laboratory diagnosis of pertussis, bacterial isolation, serological tests, and gene detection are available (IASR 38: 33-34, 2017). Isolation of the bacteria has excellent specificity, but it requires special culture medium and has a low detection rate. Serological diagnosis using anti-PT IgG is used globally, but the World Health Organization (WHO) does not recommend its use for infants whose immune system is immature or for those who were vaccinated less than a year ago. In Japan, a serological diagnosis method detecting IgM and IgA antibodies against *B. pertussis* became available and covered by insurance in 2016. Gene detection has the highest sensitivity and the real-time PCR method is used as a rapid detection method worldwide. The highly specific loop-mediated isothermal amplification (LAMP) method was developed in Japan, which is more rapid and simple to perform than real-time PCR, and became covered by insurance in November 2016. Each laboratory diagnosis method has its respective

(Continued on page 2′)

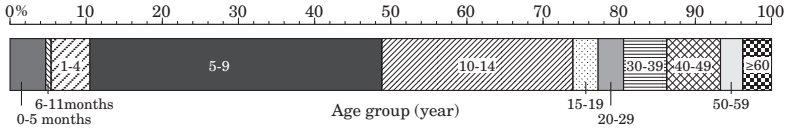
(THE TOPIC OF THIS MONTH-Continued)

optimal timing for testing based on the time from onset. Thus, to make a correct diagnosis, it is important to choose the appropriate diagnosis method depending on the time of specimen collection.

Pertussis reports/notifications under the NESID system: Trends in the number of clinically diagnosed cases reported weekly from approximately 3,000 pediatric sentinel sites in Japan from 1997 to 2017 (Fig. 1 in p. 1) and the weekly number of cases notified from all medical facilities from January 1 to November 30 in 2018 are presented (Fig. 2 in p. 1). The annual number of reported cases per sentinel site fluctuated with increases and decreases every few years. In the year 2018 when all-case reporting began, the number of notified cases started to increase around week 16, and the cumulative number of cases reached 10,360 on December 5, 2018.

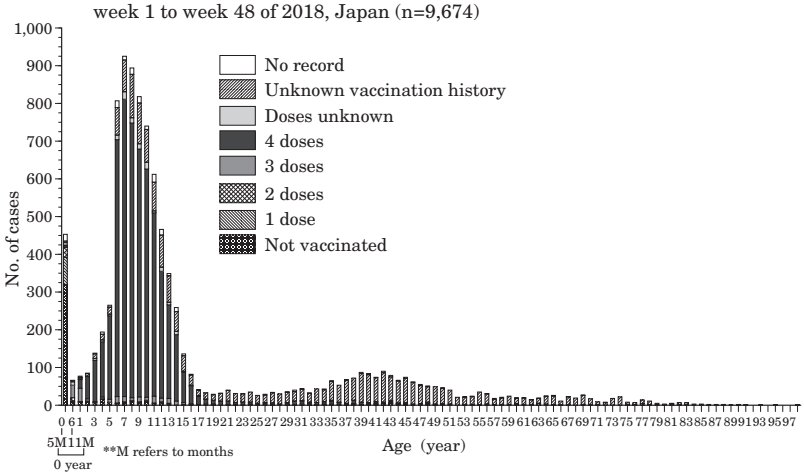
The median age of notified cases since January 2018 was 10 years (range 0-98), and 5-9 year-olds were the most numerous, accounting for 38%, followed by 10-14 year-olds (25%). Approximately six percent of the cases were less than one year of age (Fig. 3). When assessed by age group, there was a predominance of cases among elementary and junior high school students aged 6-13 years (Fig. 4). There were 453 cases in those less than six months of age, an age group considered to have the highest risk for severe outcomes (see pp. 4 & 5 of this issue). In addition, the existence of pertussis patients among the adult population became clear, which was not apparent from the hitherto pediatric sentinel system (Fig. 3 & Fig. 4, see pp. 4 & 13 of this issue).

Figure 3. Proportion of notified pertussis cases* by age group, week 1 to week 48 of 2018, Japan (n=9,674)



*Restricted to cases that meet the definition described in the pertussis reporting guideline
https://www.niid.go.jp/niid/ja/id/610-disease-based/ha/pertussis/idsc/7994-pertussis-guideline-180425.html
(National Epidemiological Surveillance of Infectious Diseases: as of 5 December 2018)

Figure 4. Number of notified pertussis cases* by age and immunization status, week 1 to week 48 of 2018, Japan (n=9,674)



*Restricted to cases that meet the definition described in the pertussis reporting guideline
https://www.niid.go.jp/niid/ja/id/610-disease-based/ha/pertussis/idsc/7994-pertussis-guideline-180425.html
(National Epidemiological Surveillance of Infectious Diseases: as of 5 December 2018)

All 47 prefectures notified pertussis cases. The prefecture with the most notifications was Tokyo Metropolis (2,074 cases), followed by Osaka (855 cases), Kanagawa (594 cases), Saitama (549 cases), and Hyogo (456 cases) prefectures. The highest pertussis notification rate during the period (per 100,000 persons) by prefecture was in Kagawa (47 cases), followed by Miyazaki (25 cases), Kochi (23 cases), and Saga (16 cases) (population data as of October 1, 2016 from the Statistics Bureau of the Ministry of Internal Affairs and Communications).

Among the notified pertussis cases with vaccination history information, 58% (5,577/9,674 cases) had four doses of a pertussis-containing vaccine. Among cases in those under 20 years of age, 73% (5,435/7,471 cases) had four doses, and restricted to those aged 5 to 15 years, 80% (4,926/6,135 cases) had four doses, indicating that the majority of the pediatric cases had been vaccinated (Fig. 4).

Outbreaks: In 2007, Japan experienced large-scale pertussis outbreaks in universities with more than 200 persons suspected to have been infected, indicating the high transmissibility of pertussis in situations where individuals share an enclosed space for a prolonged period of time (IASR 29: 70-71, 2008). Recently, several pertussis outbreaks originating from primary and junior high schools that led to an increased occurrence of pertussis in the local community (IASR 36: 142-143, 2015, IASR 38: 25-26 & 26-28, 2017) and outbreaks in urban areas (see pp. 7 & 10 of this issue) have been reported.

Seroprevalence in the Japanese population: According to the latest results from the 2013 National Epidemiological Surveillance of Vaccine-Preventable Diseases (NESVPD) seroprevalence survey, the proportion positive for anti-pertussis toxin (PT) IgG antibody reached 90% among those 6-11 months of age. However, antibody-positivity decreased with age, and reached the lowest level of 26-29% among 5-6 year-olds. Thereafter, antibody-positivity increased with age (IASR 38: 31-33, 2017).

Pathogenic agents of pertussis and molecular epidemiology: Pertussis-like symptoms are also caused by other *Bordetella* species such as *Bordetella parapertussis* and *Bordetella holmesii*. However, only few such infections have been reported in Japan. In 2018, regional epidemics were reported from Niigata Prefecture and Tokyo Metropolis, and all bacteria isolated from the Niigata epidemic were *B. pertussis* of the same genotype, MT27c (see p. 6 of this issue). However, in the Tokyo epidemic, both *B. parapertussis* and *B. pertussis* were isolated, and two different *B. pertussis* genotypes, MT27a and MT36, were detected (see p. 7 of this issue). Furthermore, recently in Japan, genotype MT27, a strain circulating in Europe and the US, is increasing (see p. 3 of this issue).

Conclusion: Due to the start of all-case notifications for pertussis since January 1, 2018, more detailed epidemiological information, such as the number of cases among those less than six months of age and among adults, clinical symptoms of the patients, and vaccination history, has become available. The accumulation of more accurate epidemiologic information for pertussis will enable early detection and early response of outbreaks, and is expected to contribute to effective pertussis prevention and countermeasures.

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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