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Risk Assessment: Pertussis Outbreak Situation in Japan

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Japan Institute for Health Security
National Institute of Infectious Diseases

Department of Bacteriology II
Center for Public Health Action in Applied Epidemiology
Field Epidemiology Training Program
Infectious Disease Epidemiology Research Group
Center for Emergency Preparedness and Response

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Overview

Pertussis, also called whooping cough, is mainly caused by *Bordetella pertussis* and is a highly contagious acute respiratory tract infection characterized by spasmodic coughing attacks. It can become severe in

infants (especially newborns and young infants). It is classified as a Category V Infectious Diseases that requires complete notification in the National Epidemiological Surveillance of Infectious Disease as defined by the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (the Infectious Diseases Control Law). Reported numbers of pertussis has decreased worldwide from 2020 to 2022 due to the strengthening of infection control measures against respiratory infections caused by the novel coronavirus disease (COVID-19) epidemic. As measures were relaxed, epidemics of Pertussis have been reported worldwide from 2023 onwards. A similar trend has been observed in Japan, where the number of reported cases has decreased significantly since 2020, then increased since 2024. In addition, reports of *B. pertussis* strains resistant to macrolide antibiotics, which are used as first-line drugs, have been rising in East Asia since around 2008 and have also been reported in Japan in 2024.
In the future, the number of reports of pertussis and resistant strains may increase both domestically and overseas. Therefore, it is necessary to continue to monitor the domestic incidence and detection of macrolide-resistant strains closely. It is also recommended that people be thoroughly vaccinated with pertussis antigen-containing vaccines as part of their routine immunizations under the Immunization Act and that people who are suspected to have whooping cough seek medical attention and take preventive measures.

About pertussis

Pertussis is an acute respiratory tract infection characterized by convulsive attacks (paroxysmal coughing) caused by the gram-negative bacteria *Bordetella pertussis*. The mechanism of its pathogenesis has not been elucidated. *B. parapertussis* can also be a cause, but only pertussis caused by *B. pertussis* is subject to notification under the Infectious Diseases Control Law.

The infection route of *B. pertussis* is through droplet infection from secretions from the nasopharynx and respiratory tract and through contact, and it is known to be highly contagious. The incubation period is usually around 7 to 10 days, and the clinical course begins with cold

symptoms and cough becomes severe in a catarrhal phase, next in a paroxysmal phase typical coughing and breathing sounds are observed, and then leads to a recovery phase. In infants (especially newborns and early infancy), the disease can become severe during the paroxysmal phase, leading to complications such as pneumonia, encephalopathy, and in rare cases, death. In adults with pertussis, coughing persists for an extended period, but typical paroxysmal coughing is rarely seen.

Vaccination with pertussis-containing combination vaccines (DPT; Diphtheria, Pertussis, and Tetanus, DPT-IPV, DPT-IPV-Hib) are effective for preventing pertussis, and the penta vaccine will mainly be used from 2024 onwards. In Japan, the first round of pertussis routine immunization is given three times between 2 and 7 months of age, usually with an interval of at least 20 days to 56 days. In addition, as an additional round of regular vaccinations, one dose is given at least 6 months after the first round, usually with an interval of at least 6 months to 18 months (four times in a total).

Macrolide antibiotics are used as the first-line drug for treatment.

Pertussis current situation

Current global situation

Since public health measures against COVID-19 were relaxed, outbreaks of respiratory infections, such as influenza and respiratory syncytial virus infection, and infectious diseases transmitted by droplets and airborne, such as measles, have been increasingly reported in countries around the world, including Japan. Similarly, pertussis outbreaks have been reported in Europe, the United States, and Asia since 2023. Still, many countries do not conduct surveillance using unified diagnostic criteria, making it difficult to grasp the situation of global epidemic.

Among the territories reporting pertussis outbreaks, the European Union (EU) /European Economic Area (EEA) reported over 25,000 pertussis cases in 2023 and over 32,000 cases between January and March 2024 (ECDC, 2024).

In the United States, the number of cases reported in 2024 was 35,435 as of Dec 28 (week 52), more than five times higher than the same period in 2023 and higher than in 2019 before the COVID-19 pandemic (CDC,

2025).

In China, more than 41,000 pertussis cases were reported in 2023, and cases have increased since the beginning of 2024, with a total of more than 59,000 cases reported between January and March 2024 and an additional 97,000 cases reported in May (China CDC, 2024). During this 2024 outbreak, the number of infected children aged 3 to 6 and 6 to 16 in China has been reported to be increasing (Hu Y, 2024). In addition, it has been reported that 832 (87%) of the 960 pertussis cases reported in 2024 in the Jeju Special Self-Governing Province of South Korea were students, and the proportion of those who had received appropriate routine immunization was 66.8% (Park D, 2025) and that the proportion of children aged 5 to 14 years old was high among the pertussis cases reported in South Korea in 2024 (Lee J. 2025). It has been pointed out that in last year's outbreak in East Asia, the age group of infected people has shifted to older children compared to previous years. In response to this situation, Chinese Center for Disease Control and Prevention decided to change from the DT (diphtheria and tetanus) vaccine to the DPT vaccine for 6-year-olds in the routine immunization program (China CDC, 2024).

Current situation in Japan

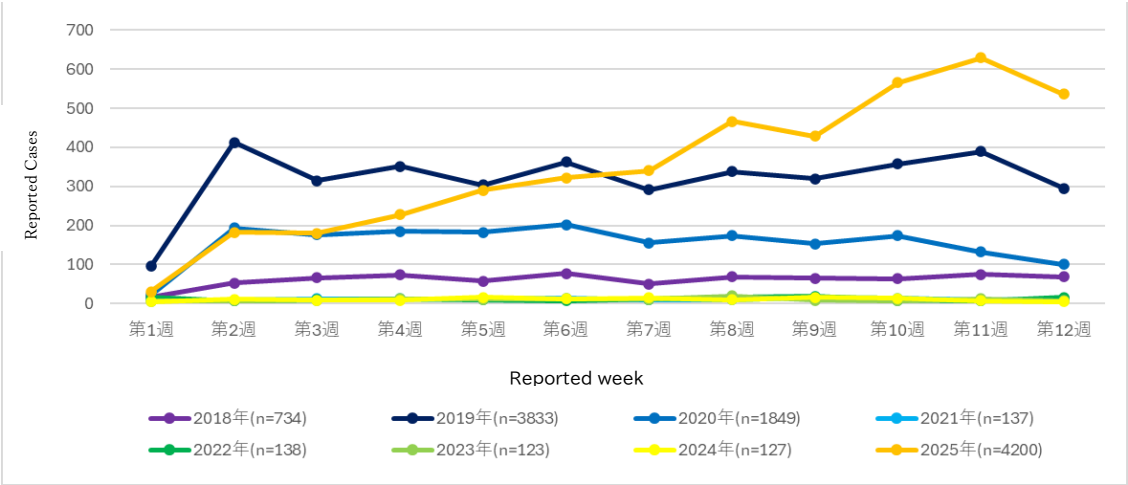
Until 2017, pertussis was a category V infectious diseases subject to regular notification by pediatric sentinel sites under the Infectious Diseases Control Law. Still, as of Jan 1, 2018, it was changed to a category V infectious disease subject to mandatory notification that all doctors must report.

The reporting criteria for pertussis as a notifiable disease that requires complete notification are as follows: when pertussis is suspected as a result of the examination of individuals with clinical characteristics of pertussis (such as a characteristic cough), and a diagnosis of pertussis is made through any of the following laboratory tests: "detection of the pathogen by isolation and identification," "detection of the pathogen's genes using nucleic acid amplification methods (PCR/LAMP/others)," "detection of pathogen antigens using immunochromatography (added to the reporting criteria on Jun 3, 2021)," or "antibody detection (positive

antibody conversion or significant increase in antibody titer in paired serum, or high antibody titer in a single serum)," or "clinical determination (individuals who contacted with a laboratory-confirmed case)" (MHLW, 2025).

The number of annual reports was 12,117 in 2018 and 16,850 in 2019, but it significantly decreased with 2,794 in 2020, 704 in 2021, and 494 in 2022 compared with previous years. In 2023, there were 1,000 cases, which was about twice as many as in 2022, but it was still at a low level (about 94% decrease from 2019) (Japan Institute for Health Security, 2025). Since then, there has been an increasing trend in 2024 and 2025, with 4,200 cases as of the 12th week of diagnosis in 2025. This is the highest number of cases in the same period (12th week) since 2018, when the disease became a notifiable disease with mandatory reporting (Figure 1), and has already exceeded the annual number of reports in 2024, which was 4,054 cases.

Figure 1: Number of pertussis cases notified by week of diagnosis in weeks 1-12 (2018-2025)



Confirmed cases of pertussis reported to the Infectious Disease Surveillance System (provisional figures as of Apr 3, 2025)

In 2018, the testing and diagnosis methods for the notified cases were pathogen gene detection by nucleic acid amplification method and diagnosis by high single serum antibody titer, which accounted for

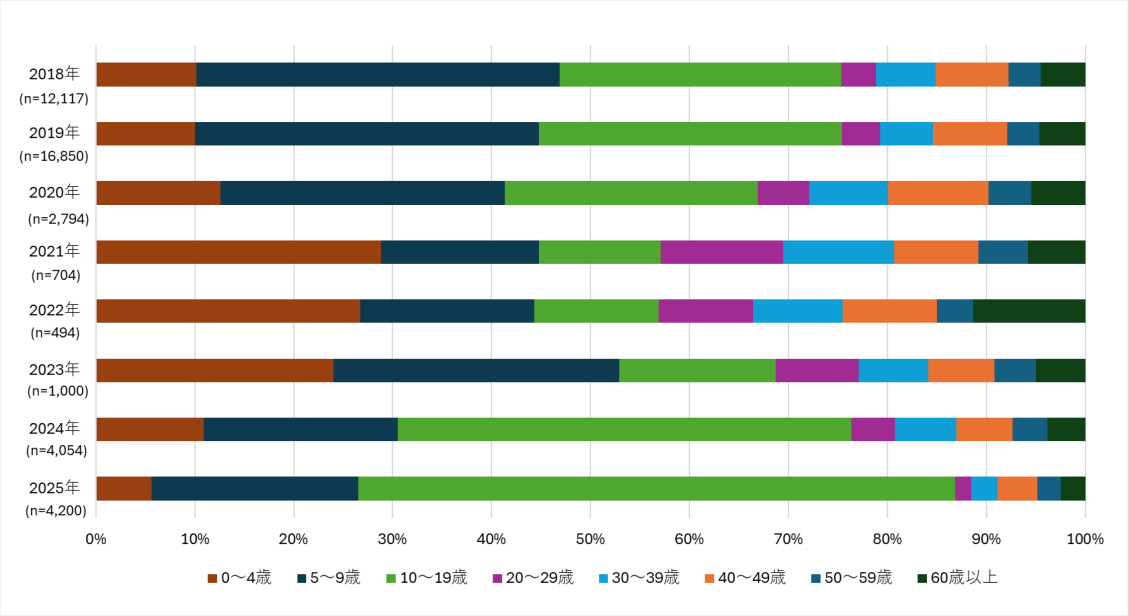
approximately half of the cases. However, since the detection of pathogen antigens by immunochromatography was added as a method for reporting in 2021, the analysis results up to 2023 showed that detection of pathogen antigens by immunochromatography and diagnosis by high single serum antibody titer increased, accounting for approximately half of the cases (National Institute of Infectious Diseases, 2025). In the most recent data of 2025 (out of 4,200 cases as of the 12th week), isolation and identification accounted for 1.3% (56 cases), gene detection (PCR method/LAMP method/others) for 59.1% (2,481 cases), immunochromatography for 10% (420 cases), antibody detection for 27.4% (1,149 cases), and clinical determination for 2.2% (94 cases).

Figure 2 shows the age distribution of notified cases for each year from 2018 to 2025. From 2021 to 2023, the proportion of 0–4-year-olds increased significantly compared to the previous year, accounting for approximately 25% of the total. On the other hand, in 2024 and 2025, the number of 10–19-year-olds increased significantly compared to the previous year, accounting for approximately 50% of the total, and the proportion of 0-4-year-olds decreased. In 2025, as of the 12th week of diagnosis, the largest age group was 10–19-year-olds at 60.3% (2,532 cases), followed by 5-9-year-olds at 21.0% (880 cases).

The cumulative number of reports from weeks 1 to 12 and the age distribution of the reported cases are shown in Figure 3. In 2025, compared to the same period from 2019 to 2024, the proportion of 10–19-year-olds increased significantly, while the proportion of 20 years or older decreased.

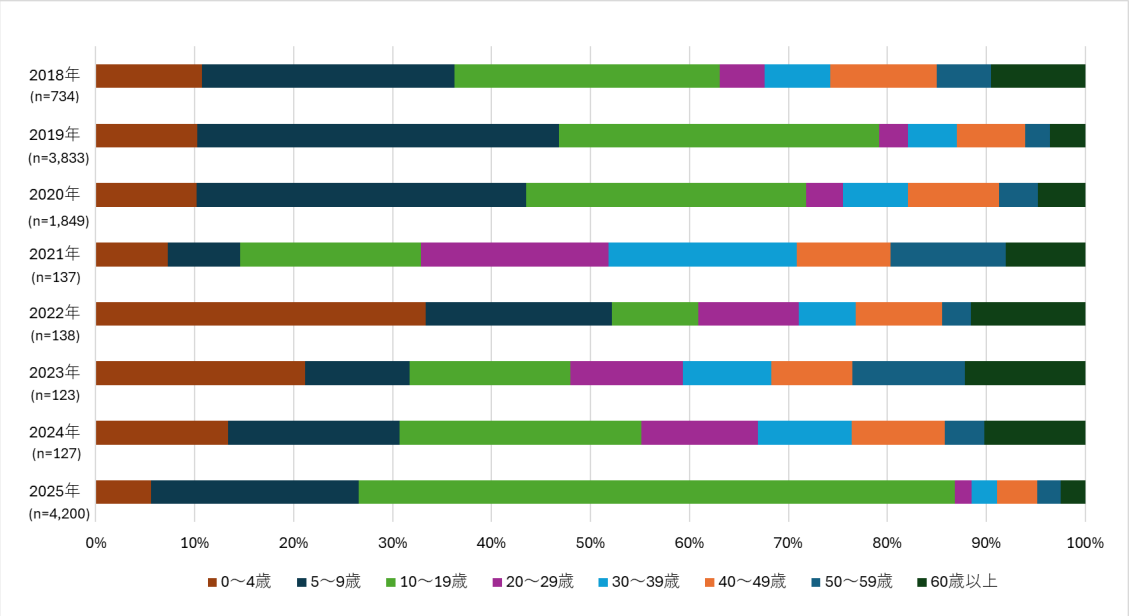
In 2024 and 2025, there have been reports of cases clustering in the same area, and of possible infections in schools, etc. (Yamagata pref., 2025、Okinawa pref., 2025, Shimane pref. Infectious Disease Information Center, 2025, Ueda et al., 2025).

Figure 2: Age distribution of notified cases by year of diagnosis (2018 to 2025) (up to week 12 of 2025)



Confirmed cases of pertussis reported to the Infectious Diseases Surveillance System (provisional figures as of Apr 3, 2025)

Figure 3: Age distribution of notified cases in weeks 1 to 12 (2018 to 2025) (up to week 12 for 2025)



Confirmed cases of pertussis reported to the Infectious Diseases Surveillance System (provisional figures as of Apr 3, 2025)

Bacteriological findings of *Bordetella pertussis*

Current situation and trends of drug resistance *Bordetella pertussis*

The first-choice drugs for the treatment of pertussis are macrolide antibiotics, including erythromycin, clarithromycin, and azithromycin. However, there is problems that Macrolide-resistant *B. pertussis* (MRBP) has appeared and spread in many countries, particularly in China in recent years. The only known resistance mechanism in *B. pertussis* is the A2047G point mutation in the 23S rRNA gene (Ivanska L, 2022). Macrolide antibiotics target domain V of 23S rRNA, which constitutes the 50S subunit of the bacterial ribosome, and inhibit protein synthesis, but when this gene mutation occurs, the affinity of the drug to the ribosome decreases. The *B. pertussis* genome contains three copies of the 23S rRNA gene, and it is known that if even one of these copies undergoes a gene mutation, the bacteria will become highly resistant to macrolide antibiotics (Bartkus JM, 2003).

MRBP was first isolated from a 2-month-old boy in Arizona, USA in 1994, but has only occurred sporadically in other countries except China (Lewis K, 1995, Korgenski EK, 1997, Lee B, 2000, Wilson KE, 2002, Cassiday PK, 2008, Guillot S, 2012). Only a few strains of MRBP were detected in China until around 2008, but their distribution has expanded rapidly since then, and MRBP is now endemic in mainland China (Yang Y, 2015, Feng Y, 2021). Furthermore, there has been an explosive increase in reports of pertussis patients since the latter half of 2023, and it has been shown that most cases are MRBP (Yahong H, 2024, Fu P, 2024).

In Japan, one case each of MRBP strain was clinically isolated in Osaka Prefecture and Tokyo Metropolis, respectively in 2018 (Yamaguchi T, 2020; Koide K, 2022a; Koide K, 2022b). However, due to the COVID-19 epidemic, the number of pertussis patients in Japan decreased, and no MRBP detections were reported for about five years. However, when the number of reported patients began to increase in 2024, MRBPs were reported one after another (Taniguchi, 2025; Araki, 2025; Ueda, 2025). In some areas, epidemics consisting only of macrolide-susceptible *B. pertussis* (MSBP) have been observed, but most of the current pertussis epidemics in Japan are mixed epidemics of MRBP and MSBP. As of April 2025, reports of MRBP detection have been received from nine prefectures.

For the treatment of MRBP infections in which macrolide antibiotics are ineffective, the use of trimethoprim-sulfamethoxazole (SMZ-TMP) is recommended as an alternative drug (Mi YM, 2024). In addition, drug susceptibility testing using Etest has confirmed susceptibility to minocycline and quinolone antibiotics, so these drugs may be an option for patients who cannot use ST combination antibiotics. However, a drug susceptibility survey of clinical isolates of *B. pertussis* from 2004 to 2006 has already found several strains derived from children that are resistant to quinolones due to the A87G mutation in the *gyrA gene* (Ohtsuka M, 2009). Therefore, quinolone antibiotics should be cautiously used to prevent the acquisition of resistance. In addition, although *B. pertussis* has a natural resistance to some β - lactam antibiotics such as cephalexin, small-scale clinical trials in China have suggested that piperacillin-tazobactam and cefoperazone-tazobactam are effective in treating pediatric MRBP infections (Hua CZ, Mi YM, 2021). However, there is not enough data to prove the clinical effectiveness of any drug, including ST combination drugs, against MRBP infections, so it is essential to accumulate treatment results in Japan in the future.

Bacteriological characteristics of epidemic strains of *Bordetella pertussis*

The world's major pertussis epidemic strains are broadly divided into the *ptxP1* and *ptxP3 lineages* based on genetic polymorphisms in the promoter region (*ptxP*) of the pertussis toxin gene and have shifted from the ptxP1 lineage to the ptxP3 lineage over time. Furthermore, the domestic pertussis epidemic strains have been analyzed by multiple-locus variable-number tandem repeat analysis (MLVA), the production of major antigens (pertussis toxin PT, Classification based on filamentous hemagglutinin (FHA), pertactin (PRN), and fimbriae (Fim2 or Fim3) has revealed that the characteristics differ before and after the COVID-19 pandemic. Before the COVID-19 pandemic (before 2019), Fim3-producing strains belonging to MLVA type (MT)27 of the *ptxP3* lineage were predominant, but the proportion of Fim2-producing strains belonging to MT28 of the same *ptxP3* lineage has increased among strains isolated since 2024 after the COVID-19 pandemic. In addition,

some MT28-MRBP strains have been identified as lacking Prn production. Regarding the drug susceptibility of strains isolated since 2024, MT27 strains were susceptible to macrolide antibiotics, whereas all MT28 strains to date have shown high resistance.

Several reports have pointed out the possibility that MRBP in Japan may have originated from outside the country. Two MRBP strains isolated in 2018 were both classified as *ptxP1* -MT195, and whole genome analysis showed that they were closely related to the Chinese MRBP epidemic strains at the time (Koide K, 2024). Furthermore, the two strains have significant differences in genome structure, suggesting that they were brought into Japan from China via different routes. Meanwhile, the main MRBP since 2024 has been classified as *ptxP3* -MT28. These are the identical genotypes as the MRBP strains that have been rapidly increasing in Shanghai, China, since 2020 (Fu P, 2023), and it is speculated that they entered and spread through Chinese visitors to Japan after the COVID-19 pandemic. In addition, the MT107-MRBP strain, which suggests a connection to Vietnam, has also been detected in Japan, and the possibility of an influx of MRBP originating from a country other than China has been pointed out (Komatsu, 2025). Currently, the movement of people around the world is increasing, and it is expected that MRBP will enter Japan through various routes and continue to mutate, expanding its distribution further in the future.

Risk assessment and response

- Pertussis is a respiratory infection mainly caused by *B. pertussis*. Due to the spread of COVID-19 and the resulting strengthening of infection control measures, the number of reported cases has been decreasing worldwide. Still, since the relaxation of infection control measures against COVID-19, the number of reported cases has been increasing overseas since 2023 and in Japan since 2024. In addition, it has been reported that the center of the epidemic in China and South Korea in 2024 was school-age children, and the number of reported cases in Japan has also increased, so there is a possibility that the number of reported cases in Japan will increase in the future, mainly among children of school age and older.

- MRBPs have been reported mainly in East Asia, and MRBPs originating from Asian countries have also been reported in Japan. In addition, since resistance to drugs other than macrolide antibiotics has been reported, it is necessary to continue bacteriological and epidemiological analysis to understand the future trends of drug resistance in *B. pertussis*.

- Regarding pertussis countermeasures, particularly from the perspective of preventing severe diseases, it is essential that infants who reach the age for routine vaccination are promptly vaccinated with a pertussis antigen-containing vaccine. The National Epidemiological Surveillance of Vaccine-Preventable Disease has shown that antibody possession rates are maintained among infants at high risk of developing severe symptoms, so it is necessary to continue to implement routine immunizations in accordance with the Vaccination Act thoroughly. In situations where pertussis is prevalent in a region, it is helpful for people over the age of elementary, junior high, and high school students, including adults, to keep in mind the possibility of pertussis when they have persistent cough for a long time and to visit a medical institution and take preventive measures, especially in the vicinity of infants and pregnant women.

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