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Pertussis Epidemic in Lower-Grade Schoolchildren Without Preschool Vaccination Boosters

We investigated the characteristics of patients with pertussis who did not receive preschool vaccination boosters. Fifteen patients with laboratory-confirmed pertussis and 29 pertussis-negative patients were compared. All pertussis-positive patients, but only 17% of pertussis-negative patients, were elementary school age and older. There is a need to study the utility of routine preschool pertussis vaccine booster in Japan.

Keywords: DPT, Immunization, LAMP, Seroprevalence.

The pertussis vaccine is effective in preventing *Bordetella pertussis* infection and death, and the risk is high in young infants who do not receive the vaccine [1]. *B. pertussis* infection in siblings is considered a common route of transmission to young infants [2]. Currently, three brands of DPT-IPV (acellular pertussis, diphtheria and tetanus toxoids, and inactivated polio combined) are used in Japan. All contain pertussis toxin and filamentous hemagglutinin (6-23.5 and 23.5-51.5 µg/0.5 mL, respectively), and one contains additional pertactin and fimbriae (5 and 1 µg/0.5 mL, respectively) [3]. Children receive a total of four doses of DPT-IPV: three primary doses at the ages of 3, 4, and 5 months, and one booster dose at 18 to 23 months as a national routine vaccination. In 2018, vaccine coverage for the four doses was 95.0%, 95.7%, 96.2%, and 96.2%, respectively [4]. The preschool pertussis vaccination booster is used in some Asian countries like India, but not in Japan [5]; even though Japan has one of the highest primary pertussis vaccination rates in the world [6]. We, herein present data from an outbreak of pertussis, which occurred mainly in lower-grade school children without preschool vaccination boosters.

A retrospective chart-based study was conducted on patients who visited the Saiwai Pediatric Clinic, Tokyo, Japan, with persistent cough. Patients were examined by board-

certified pediatricians for suspected pertussis and received a laboratory diagnosis between August and September, 2018. In accordance with the Pediatric Respiratory Infection Practice Guidelines in Japan [7], diagnostic tests for pertussis were defined as positive by either nasal swab loop-mediated isothermal amplification (LAMP) or anti-pertussis IgM/IgA in sera. The positive and negative predictive rates of LAMP are 100% and 97%, respectively (Loopamp Pertussis Detecting Reagents D; Eiken Chemical Corporation). The sensitivity of anti-pertussis IgM and IgA are 29-56% and 25-44%, respectively and the specificities are 93% and 99%, respectively (Novagnost *Bordetella pertussis* IgM/IgA; Siemens Healthcare Diagnostics KK). The patient background (sex, age, and vaccination history), and diagnosis method were collected.

Statistical analyses included a bar graph review and Fisher exact test of age-distribution comparisons. We used SPSS Statistics 25 (IBM Corp.) and BellCurve for Excel for Windows (Social Survey Research Information Co. Ltd.) software programs.

Of the 44 patients (age distribution: 0-21 years, median: 6 years), data of 15 patients who were diagnosed with laboratory-confirmed pertussis (age: 7-21 years, median: 8 years) and 29 patients who were pertussis-negative (age: 0-11 years, median: 5 years) were compared. All patients ($n=15$) who were pertussis-positive but only 17% ($n=7$) of patients who were pertussis-negative were elementary school age and older ($P<0.001$) (Fig. 1). All 16 preschool children were negative. Excluding serodiagnosis cases (3 positive cases, 1 negative case), a significant difference in age distribution ($P<0.001$) was also observed. When a 2×2 table was prepared with 7 years of age as the cut-off value, the sensitivity, specificity, positive predictive rate, and negative predictive rates were 100%, 83%, 75%, and 100%, respectively.

None of the 44 patients had a history of preschool vaccination booster at around 5 years of age. Of 15 children who were positive, 14 patients had received four routine vaccinations and the booster history was uncertain in 1 patient. Of 29 children who were negative, 26 patients had received four routine vacci-

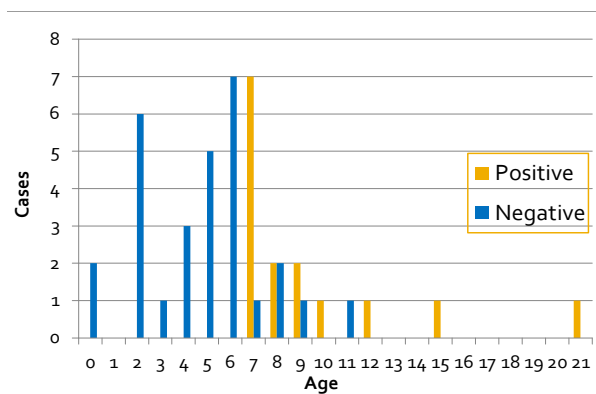


Fig. 1 Pertussis test results and age distribution.

nations, but two patients who were a few months old were vaccinated 0 and 2 times, and the booster history was uncertain in another patient.

The absence of pertussis in preschool children and the presence of pertussis in lower-grade schoolchildren suggest the need of additional preschool vaccinations. It has been reported that the prevalence of anti-pertussis toxin titer in individuals aged 4 to 7 years declines to 26-38% even among regular vaccines [8]. During our research period, the Japanese Society of Pediatrics began to recommend that preschool children aged 5 to 6 years receive a DPT vaccination, but this is on a voluntary basis [9].

This report covers a limited number of cases in a single institution, and the question remains of whether the data on sensitivity and specificity for pertussis at age 7 years or older can be generalized. However, the all-Japanese pertussis cases reported indicate that over 60% of cases are between the ages of 6 and 15 years, peaking at the age of 7 years [10], which is consistent with the age distribution reported herein.

We experienced a pertussis epidemic in elementary school-age children, all of whom had been immunized with at least three doses of primary DPT-IPV immunization. We believe that popularizing the preschool pertussis vaccination is important in order to eliminate the infection source for young infants. Consideration should be given to routine preschool pertussis vaccination boosters in Japan if larger community-based studies confirm our findings.

Ethics approval: Keio University School of Medicine Ethical Committee, Tokyo, Japan; No. 20190205, dated December 26, 2019.

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