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ORIGINAL ARTICLE

Seroepidemiology of pertussis among elementary school children in northern Taiwan



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Abstract *Background/Purpose:* Pertussis has been considered a vaccine-preventable "childhood disease", but a shift in age distribution has been reported worldwide. We conducted a seroepidemiological study in 2013 in Taiwan to elucidate the seroprevalence of pertussis among elementary school children.

Methods: With a multilevel randomized method, which included 14 variables (4 population variables, 4 socio-educational variables, and 6 medical facilities' variables), the 29 executive districts of New Taipei City, Taiwan, were categorized into five strata. From each stratum, the number of school children as well as the number of elementary schools were proportionally selected. Enzyme immunoassay was applied for pertussis immunoglobulin-G measurement.

Results: A total of 936 children from 14 schools were recruited. Most participants (98.89%) received at least three doses of acellular diphtheria-tetanus-pertussis vaccine. The overall seropositive rate for pertussis was 33.97%. The seropositive rate was highest for students in Grade 1 (49.36%) and then declined with time, except for Grade 6 students. Students from Grade 1 to Grade 4 had a significant higher seropositive rate (37.18% vs. 27.56%, $p = 0.002$) than those from Grade 5 to Grade 6, but a lower geometric mean titer (18.71 NovaTec Unit/mL vs. 20.04 NovaTec Unit/mL, $p = 0.20$). For the class grades, geometric mean titers were positively correlated with seroprevalence ($p < 0.005$).

Conclusion: Currently, almost one-third of elementary school children in Taiwan were seropositive for pertussis, a rate lower than expected. Seroprevalence declined with increasing class

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grades except for Grade 6. The current national immunization program may not provide adequate protection for children against pertussis.

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Introduction

Pertussis is a highly contagious acute respiratory tract disease caused by *Bordetella pertussis*, an exclusive human pathogen. Characterized by paroxysmal severe coughing spells, pertussis sometimes causes severe complications in infants and young children including pneumonia, seizure, encephalopathy, and even death.¹ Despite progress in vaccinations, pertussis remains one of the top 10 causes of death worldwide in childhood, accounting for 30,000,000–50,000,000 cases and nearly 300,000 deaths in children every year.² So far, breakthrough diseases in cycles were still observed every 3–5 years even in vaccinated populations.^{3,4}

In Taiwan, whole-cell diphtheria-tetanus-pertussis vaccines had been offered to children free of charge at 2 months, 4 months, 6 months, and 18 months of age since 1954, based on the national immunization program. The incidence of reported pertussis cases per year has declined significantly thereafter from 77 cases per million in 1955 to less than one case per million in 1970, and this low incidence was retained from 1971 to 1991 before an unexpected outbreak developed in 1992.⁵ Two types of acellular diphtheria-tetanus-pertussis (DTaP) vaccines from Kaket-suken (Chemo-Sero-Therapeutic Research Institute), Okubo, Kumamoto, Japan [DPT “KAKETSUKEN” SYRINGE consisting PtxS1B and filamentous hemagglutinin (FHA)] and SmithKline Beecham Biologicals (became GlaxoSmithKline Biologicals since 2000), Rixensart, Belgium (INFANRIX consisting of PtxS1B, FHA, and Prn1 from the Tohama strain) were licensed for use since 1996 and 1998, respectively, at the patient's own expense. The DTaP vaccine was later universally substituted by the diphtheria and tetanus toxoid with acellular pertussis, *Haemophilus influenzae* type b, and inactivated polio vaccine; INFANRIX-IPV + Hib consisting pertussis toxin (PT), FHA, and pertactin from GlaxoSmithKline Biologicals, Rixensart, Belgium, or PEDIACEL consisting PT, FHA, pertactin, and fimbrial agglutinogens 2 + 3 from Sanofi Pasteur, Toronto, Ontario, and included in the expanded program on immunization (EPI), since 2010. In addition, since March, 2009 the reduced dose tetanus, diphtheria, and acellular pertussis vaccine (Tdap; ADACEL consisting PT, FHA, pertactin, fimbrial agglutinogens 2 + 3 from Sanofi Pasteur, Toronto, Ontario) was introduced into EPI as a booster for children from 5 years of age to elementary school Grade 1.

Completion of at least three doses of acellular pertussis vaccine was thought to result in higher efficacy in preventing typical whooping cough and in preventing mild pertussis disease, compared with administration of one to two doses only.⁶ However, in children who completed five doses of pertussis vaccine, pertussis was still observed in older children, and the odds increased as the time since last

DTap increased, suggesting waning protection despite the five-dose-DTap schedule.⁷ An increase in yearly reported pertussis cases of children aged 5–9 years was observed in Taiwan recently, but both of their associated vaccination status and seroepidemiologic information were lacking.⁵ The purpose of this study was to establish the seroepidemiologic data of pertussis among children attending elementary schools in New Taipei City, Taiwan, which would be the pilot study of nationwide surveillance, and would be provided as a reference of the national immunization program in Taiwan.

Methods

Ethics statement

The study proposal was reviewed and approved by the Institutional Review Board of Chang Gung Memorial Hospital, Taoyuan, Taiwan in 2012. Informed consent in written form was obtained from all participants, as well as their guardians.

Study populations

A cross-sectional survey of anti-*B. pertussis* immunoglobulin (Ig)-G antibodies in the population of elementary school children in New Taipei City was conducted from September 2012 to June 2013. New Taipei City comprises 29 administrative districts and is the second largest special municipality in northern Taiwan. A total of 225,234 pupils resided in this city, which accounted for 16.5% of all primary school children in Taiwan in 2012. A multistage stratified method with probability proportional to size sampling was employed to obtain samples. The whole 29 administrative districts of New Taipei City were classified into five strata based on 14 variables, which included four demographic variables [population density (persons/km²), proportion of population older than 65 years, younger than 15 years, and younger than 6 years], four socio-educational variables (number of low-income households per 10,000 people, number of near-poor households per 10,000 people, proportion of agriculture population, proportion of population with college degree or above), and six medical facilities' variables (number of physicians per 10,000 people, number of nursing staffs per 10,000 people, number of nursing staffs in health centers per 10,000 people, number of medical personnel in health centers per 10,000 people, number of staffs in health centers per 10,000 people). Elementary schools in each stratum were selected with selection probability proportional to their size. One class was drawn from each grade in a sampled school, that is, six classes in total were drawn from each sampled school. In each selected school, the number of students in

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