

Seroepidemiology of Pertussis in the Adult Population of Singapore

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Abstract

Introduction: Pertussis is a highly communicable, vaccine-preventable respiratory disease and a frequent but often underestimated cause of prolonged cough illness in adults. Protection after childhood vaccination is minimal after 10 years without boosting. The need for adult booster depends on the national epidemiology. **Materials and Methods:** We did a seroepidemiological survey amongst the adult population (aged 18 to 45 years) of Singapore. None had received pertussis booster vaccine in the preceding 10 years. We measured IgG antibodies to pertussis whole cell antigen. **Results:** Two hundred and seventy subjects with the median age of 30 years were enrolled. We found positive IgG antibody levels in 97% of the population. Seropositivity was not associated with age, gender or race. **Conclusion:** The seroprevalence in adults was much higher than the previously documented seroprevalence of around 50% in the adolescent age group in Singapore. The increase is most likely due to natural infection with *B. pertussis*. Pertussis booster vaccine for adolescents/young adults in Singapore would be indicated.

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Key words: Acellular pertussis vaccine, Adolescent pertussis seroprevalence, Pertussis booster vaccine, Pertussis seroepidemiology, Whooping cough

Introduction

Pertussis is a highly communicable, vaccine-preventable respiratory disease and is a frequent but often underestimated cause of prolonged cough illness in adults.¹ Whereas in children pertussis is characterised by paroxysmal cough, whooping cough and post-tussive vomiting, in adults the disease is often atypical, sometimes manifested only by a protracted, non-distinctive cough.² High attack rates of pertussis have been observed among adults in the setting of community outbreaks of pertussis, even in highly immunised populations, and this is thought to reflect waning of the immunity from childhood vaccination.³ About a quarter of prolonged cough illnesses in adults is due to pertussis.^{1,2,4} The incidence of adult pertussis has been estimated to be 200 to 500 per 100,000 persons years, similar to the incidence of peptic ulcer disease.⁵⁻⁸ Adults are often also the source of infection for young children.⁹ The morbidity in adults is mainly associated with prolonged cough, with the average duration being 44 days.¹ Complications increase with age. Rare complications are hemoptysis, otitis media, pneumonia, urinary incontinence, rib fractures, pneumothorax, cough syncope, seizures, and loss of consciousness triggered by coughing episodes.¹⁰ In one study amongst elderly patients with pertussis, 4 out of 75

died from intracranial bleeding.¹¹ The economic burden of pertussis in adults is substantial and therefore broader use of adult booster vaccination would be justified.^{6,12}

Pertussis vaccines have been in routine paediatric use for >50 years and have dramatically decreased the incidence and complications of whooping cough in children,^{13,14} but protection is thought to be minimal after 10 years without boosting.^{15,16} Because of concerns about the reactogenicity of whole-cell pertussis vaccines in older children and adults, no booster vaccinations were recommended. Acellular pertussis (aP) vaccines have now been evaluated in adolescents and adults and confer safe and effective protection against pertussis.^{8,17,18} The vaccine protection was estimated to be 92%.⁸ However, universal adult booster vaccination against pertussis remains controversial.¹⁹ The recent recommendations from the International Consensus Group on Pertussis Immunisation state that public health policy makers should target pertussis booster to adult risk groups.¹⁵ Vaccination of adolescents has been recommended in France, Germany and Canada.^{15,20} In March 2006, the American Academy of Pediatrics published their recommendations for pertussis booster to adolescents in the US.¹⁷

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Recommendations for adolescent or adult booster against pertussis depend on the national epidemiology. We did a seroepidemiological study on pertussis seroprevalence in adults in Singapore.

Materials and Methods

We conducted a cross-sectional seroepidemiological study in Singapore over 2 days in August 2002. Blood was drawn from asymptomatic volunteers comprising visitors and staff to a large public hospital. We targeted a sample size of 100 per age group (18 to 25 years, 26 to 35 years and 36 to 45 years). Age, gender, race, and nationality were recorded.

IgG antibodies to pertussis whole cell antigen (containing pertussis toxin and filamentous haemagglutinin) were measured and results interpreted according to the instructions by the manufacturer (IBL Immuno-Biological Laboratories, Hamburg, Germany), as qualitative results (negative, borderline and positive) as well as absolute IgG antibody levels. Logistic regression models were used to identify risk factors associated with acquisition of pertussis. Data analysis was carried out in Stata (V7.0) and all statistical tests were conducted at the 5% level of significance.

The study was approved by the Ethics Committee, Tan Tock Seng Hospital, Singapore. All subjects gave written informed consent.

Results

We enrolled 270 subjects (92 for the 18 to 25 years age group, 89 for the 26 to 35 years age group and 89 for the 36 to 45 years age group), of whom 178 (66%) were female and the median age was 30 years (range, 18 to 45). Of the 270, 227 (84%) were Singaporean, 20 (7%) permanent residents and 23 (9%) foreigners working in Singapore (all of whom originated from South East Asian countries). The racial distribution was as follows: 141(52%) Chinese, 61(23%) Indians, 48 (18%) Malays and the remainder were of other races. Nine (4%) were healthcare workers from Tan Tock Seng Hospital. None of the subjects had received pertussis booster in the past 5 years. All were asymptomatic at the time of blood taking.

Of these 270 subjects, 261 (97%) had a positive pertussis serology, with 96% in the 18 to 25 years old cohort, 99% in the 26 to 35 years old cohort and 96% in the 36 to 45 years old cohort. There were 5 subjects with negative and 4 with borderline pertussis antibodies. For the purpose of univariate analysis, we grouped the negative and borderline results together as negative.

The prevalence of positive pertussis serology was 97% for both genders (89 out of 92 males, 172 out of 178 females). The prevalence was similar for the 3 races (97% for Chinese, 96% for Malays and 98% for Indians). For the

227 subjects with Singaporean nationality, 220 (97%) were pertussis positive, compared with 41/43 (95%) Asian foreigners. In the univariate analysis, neither age, gender, race nor nationality was found to be statistically associated with pertussis serology positivity.

The mean (SD) for pertussis antibodies was 44.2 (SD 35.0) and the median was 32.1 (range, 3.2 to 210.7). Using regression models, age, gender, race and nationality were not associated with antibody levels.

Discussion

We documented a 97% seroprevalence of pertussis antibodies in the adult population in Singapore between the ages of 18 and 45 years, which was independent of age (within this age range), gender, race and nationality. This is consistent with high seroprevalence rates above 80% in adults reported from various other countries.^{21,22} Pertussis vaccination was introduced into the national childhood vaccination programme in Singapore in 1957.²³ As all subjects were born after 1957, it can be assumed that a large proportion of Singaporean subjects were vaccinated during childhood. None of the subjects received an adult booster. Given the fact that vaccine antibodies begin to wane 4 years after the last dose,¹⁰ together with the fact that immunity to pertussis vaccine decreases to 0% to 20% over a 10-year interval,⁶ it can be concluded that our documented high pertussis seroprevalence in adults is due to natural infection with *Bordetella pertussis*. No differences were seen in pertussis seroprevalence between those vaccinated in childhood and those not vaccinated (born after 1957 versus before 1957) in a study in older Singaporeans (median age 48).²⁴ The limitation of this study is that we did not conduct a population based randomised study, and therefore a recruitment bias is possible. However, this bias is likely to be small as our large hospital attracts visitors and staff from all over Singapore.

In previous serological studies in Singapore, the pertussis seropositivity rate was 51% in the 10 to 14 years age group, and 50% in the 15 to 19 years age group; all had received childhood pertussis vaccination.²⁵ These seroprevalence rates in the adolescent age group in Singapore are in keeping with those from other countries.^{16,26} The increment of seroprevalence between the adolescent and adult age group is assumed to be due to natural pertussis infection. The consistently high levels of seroprevalence in the 18 to 45 years old cohort would suggest that the increment in seroprevalence most likely occurs as a result of natural pertussis infection between adolescence and early adulthood. This would be consistent with previous studies showing a high incidence of pertussis infections in adolescents, which is increasing in countries with good childhood vaccination coverage.^{4,8,16,27-29} In a population-based prospective study among persons aged 10 to 49 years

with pertussis cough illness, adolescents (10 to 19 years) accounted for 41% of all cases, adults aged 20 to 29 years for 7%, adults aged 30 to 39 years for 17% and adults aged 40 to 49 years for 28%.⁷

In summary, our data from Singapore are in accordance with other reports that *B. pertussis* is a problem amongst adolescents and adults.^{2,9,20} Despite universal immunisation of children with multiple doses of paediatric diphtheria and tetanus toxoids and acellular or whole cell pertussis vaccine, pertussis remains endemic with a steady increase in the number of reported cases in adolescents and adults.^{1,8} Our data support other published reports that adolescents are at high risk of acquiring pertussis, at a time when vaccine-induced immunity has waned.^{8,17} Acellular pertussis (aP) vaccines confer safe and effective protection against pertussis in adolescents and adults.^{8,18} An evaluation of strategies for use of aP vaccine in adolescents and adults have shown that a booster vaccine is cost-effective, particularly if the acellular pertussis vaccine is given as a combination Tdap vaccine (Tetanus, adult diphtheria, acellular pertussis).⁶ Tdap products for boosting adolescents were licensed in 2005 in the US¹⁷ and also in Singapore. In March 2006, the American Academy of Pediatrics published their recommendation that adolescents 11 to 18 years of age should receive a single dose of Tdap instead of tetanus and diphtheria toxoids vaccine for booster immunisation.¹⁷ Our data would suggest that this strategy should be considered for Singapore. However, further research is needed to determine the incidence of pertussis, morbidity and complications in adolescents and adults in Singapore and to evaluate the cost-effectiveness of such a strategy.

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