The effectiveness of pertussis immunization during a pertussis outbreak in Choiseul Province, Solomon Islands

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Abstract

In 1992, a pertussis outbreak among children <13 years old was investigated in Choseul Province, Solomon Islands. The purpose of this outbreak investigation was to determine if Diphtheria-Pertussis-Tetanus immunization (DPT) was protecting children from pertussis, and whether the effectiveness of DPT immunization differed by the age of the child. Pertussis cases were defined clinically, and the number of DPT doses received by each child was obtained from home health cards.

During the outbreak, 22% (52/237) of children aged one to 12 years old in seven villages were attacked. Overall, 19% (30/158) of the immunized and 28% (22/79) of the unimmunized were ill for a vaccine efficacy of 32% (p=0.12). The pertussis attack rates were lower in younger than older children. Among children 1 to 4 years old, the pertussis attack rate was 5% (4/85), and 32% (48/152) for 5 to 12 years old. There was some indication that vaccine efficacy differed by age of the child. For children aged 1 to 4 years, vaccine efficacy was 46% and 2% for 5 to 12 years old. Vaccine efficacy based on secondary attack rates was 53% for all children, with 100% protection for children 1 to 4 years old, and 10% for 5 to 12 years old.

These results, suggest that the higher pertussis attack rate in older than younger children may be associated with a reduced vaccine efficacy in the older age group. From these limited results it may be necessary to consider booster doses of pertussis vaccine to prevent this disease in older children.

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Introduction

In November 1991, provincial nursing staff reported an outbreak of pertussis in Choiseul, an island province with a population of 18,000 people mainly living in more than 300 coastal villages in the Solomon Islands. In December 1991, staff of the Maternal and Child Health Unit, Ministry of Health and Medical Services, visited Choiseul to investigate the outbreak. The conclusion of the initial investigation was that children aged 5 years and over were more likely than younger children to be reported ill with pertussis. The results also suggested that many children were not protected from pertussis by three doses of DPT which contained a whole cell pertussis component. In early January 1992, a detailed follow-up study was completed in Choiseul that allowed us to estimate the effectiveness of the pertussis immunization program in the area of the outbreak. The purpose of this investigation was to determine:

i) the effectiveness of DPT immunization in protecting children less than thirteen years of age from pertussis, and
ii) if the effectiveness of DPT program differed by age (1 to 4 years of age vs. 5 to 12 years of age).

Methods

This was an outbreak investigation of pertussis carried out in Choiseul Province, Solomon Islands. All residents regardless of age were surveyed in any village in which at least one person was identified as having the symptoms of pertussis. Villages with a case of pertussis were located by investigators from surveillance data at the Ministry of Health, from the previous site visit and during the current research.

Case definition. Laboratory facilities are not available in the Solomon Islands for isolation of *Bordetella pertussis*. Thus, a case of pertussis was defined clinically as any child over the age of 1 year reported by parents to have had the following symptoms over the last six months: cough for at least two

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weeks, nasal discharge, and cough spasms followed by the characteristic whoop of pertussis. Severity of the disease was not assessed. To reduce misclassification bias, children less than 1 year of age were excluded from the study because infants in the Solomon Islands suffer from a high incidence of respiratory disease that could be confused with pertussis. In addition, infants with pertussis do not necessarily have the characteristic "whoop" of disease[1].

Data collection. All households in a village were visited and all persons regardless of age and clinical status were surveyed for demographic information, clinical symptoms, and immunization history. The guardians of all children less than 13 years of age were asked to present home health cards to confirm their childrens' immunization status. Children with three recorded doses of DPT listed on their home health card were considered fully immunized, while children who received no doses of DPT, or did not have a home health card were considered unimmunized. Children with one or two doses of DPT were considered partially immunized, but included in the unimmunized group for analysis. Data were collected by a registered nurse and trained public health worker under the supervision of an epidemiologist. Structured and pretested survey instruments were used to collect data.

Data analysis. Data were analyzed using attack rates, relative risks with 95% confidence intervals, and percent vaccine efficacy. To increase the probability of exposure to a pertussis case when estimating vaccine efficacy, household secondary attack rates were also calculated. Children less than 13 years of age with the first clinically defined case of pertussis in the household were classified as the primary case. Co-primary cases, defined as cases that occurred within 14 days of each other, were excluded in the secondary attack rate analysis.

Vaccine efficacy for both the overall attack rates and secondary attack rates were calculated as follows:

$$\textit{Percent Vaccine Efficacy} = \frac{(ARU - ARV)}{ARU} \times 100$$

where ARU is the attack rate in the unvaccinated and ARV is the attack rate in the vaccinated[2]. Statistical significance was calculated using the chi-square test or Fisher's exact test when the expected value in a cell was less than five. Statistical significance was set at $p<0.05$ and was two tailed for all analyses.

Results

There were 52 cases of pertussis among children one to 12 years of age in seven villages. The outbreak began in August 1991, peaked by November and, after a total of six months, ended in January of 1992. There were 258 children less than 13 years of age in the villages. The proportion of children less than one year old, one to four years old, and 5 to 12 years old was 8% (n=21), 33% (n=85), 59% (n=152), respectively. Female children were 47% of the surveyed population. The pertussis attack rate was 22% (52/237) for children one to 12 years of age (see Table 1). There was no difference in the attack rate by sex. The age specific attack rates were 32% (48/152) in five to 12 year old children and 5% (4/85) among one to four year old children for a relative risk of 6.7 (95% CI: 2.5-18.0, $p<0.0001$). There were no fatalities attributed to pertussis.

Other frequently reported clinical symptoms among cases, besides those included in the case definition, were vomiting after cough, apnea after cough, and puffy eyes. Less often reported were subconjunctival bleeding, fever, and nose bleed after cough. The median lengths of time for which patients reported cough with whoop was 60 days (interquartile range: 32-74 days).

Seventy-three (31%) of children did not have an immunization record (child health card) and the proportion without a card increased with age ([11/85] 13% in the 1-4 year age group and [62/152] 41% in the 5-12 year age group). For all 237 children, 158 (67%) were fully immunized with three doses of DPT. The remaining 79 (33%) children received two doses (n=5) or no doses (n=74) of DPT. Children one to five years old showed a higher coverage with DPT than those more than five years old (84% vs. 58%).

Among all village children, 19% (30/158) of fully immunized children compared to 28% (22/79) of unimmunized children reported having symptoms of pertussis. The overall vaccine efficacy was 32% (see Table 1.) Among children who were one to five years of age, 4% (3/72) of the immunized compared to 8% (1/13) of the unimmunized children had symptoms for a vaccine efficacy of 46%. For older children aged five to 12 years, 31.3% (27/86) of the immunized and 31.8% (21/66) of the unimmunized had symptoms for a vaccine efficacy of 2%.

For secondary attack rates, 13% (9/69) had symptoms after being exposed to a clinically defined primary case of pertussis. Table 2. The attack rate was higher in children five to 12 years old (20%) than in children one to four years old (4%, $p=0.07$). Ten percent (5/50) of the immunized children compared to 21% (4/19) of the unimmunized became ill for an overall vaccine efficacy of 52%. Among children one to four years old, there were no cases (0%) among 24 immunized children and a single case among five (20%) unimmunized children. Among children five to 12 years old, 19% (5/26) of immunized children and 21% (4/19) of unimmunized children reported being ill for a vaccine efficacy of 10%.

Table 1. Overall attack rates, relative risks and vaccine efficacy (3 vs. 0 doses), by age

Variables		Doses	Cases	Total	Attack rates (%)	Relative risk		Vaccine efficiency %
						Point estimate	95% confidence interval	
Gender	Male		28	126	22.2	1	0.6 - 1.7 p=0.91	n/a
	Female		24	111	21.6			
Age (in years)	5 - 12		48	152	31.6	6.7	2.5 - 18.0 p=<0.0001	n/a
	1 - 4		4	85	4.7			
DPT doses (by age)	1 - 4	3	3	72	4.2	0.5	0.06 - 4.8 p=0.58	45.5
		0	1	13	7.7			
	5 - 12	3	27	86	31.3	1	0.6 - 1.6 p=0.96	1.6
		0	21	66	31.8			
	1 - 12	3	30	158	19	0.7	0.4 - 1.1 p=0.12	31.7
		0	22	79	27.8			

Discussion

The outbreak in Choiseul followed a typical epidemic curve, increasing up to three months, then decreasing, and ending after six months. The overall attack rate was high with more than one in five children symptomatic. There were no gender differences detected in rates of disease implying that biological or behavioral differences between children by gender did not influence these rates. There was, however, a marked difference in attack rates between one to four year olds and five to 12 year olds. These differences were statistically significant. The higher attack rate in five to 12 year olds is thought to indicate that the younger children were protected by immunization, while older children were not.

When examining vaccine efficacy, we could not find a statistically significant effect from DPT immunization either overall or when examining efficacy among younger or older children separately. It was apparent, however, that there was insufficient power to detect a difference given the small sample size. Still, there was a suggestion that the vaccine was more efficacious in the one to four year olds (45%) than in the five to 12 year olds (2%).

The secondary attack rates were also calculated to increase the probability that children were exposed to disease when calculating vaccine efficacy. Among children aged one to four years, none of 24 children immunized with three doses of DPT were ill with clinically defined pertussis. One out of

Table 2. Secondary attack rates, relative risks and vaccine efficacy (3 vs. 0 doses), by age

Variables		Doses	Cases	Total	Attack rates (%)	Relative risk		Vaccine efficiency %
						Point estimate	95% confidence interval	
Gender	Male		5	39	12.8	1	0.3 - 3.3 p=1.0	n/a
	Female		4	30	13.3			
Age (in years)	5 - 12		8	40	20	5.7	0.8 - 43.9 p=0.07	n/a
	1 - 4		1	29	3.5			
DPT doses (by age)	1 - 4	3	0	24	0	-	undefined p=0.17	100
		0	1	5	20			
	5 - 12	3	5	26	19.2	0.9	0.3 - 3.2 p=1.0	10.3
		0	3	14	21.4			
	1 - 12	3	5	50	10	0.5	0.1 - 1.6 p=0.25	52.5
		0	4	19	21.1			

five unimmunized children developed disease. These differences were not statistically significant. It was encouraging that all 24 immunized children remained protected despite intra-household exposure.

The higher attack rate among older children suggests waning active immunity from pertussis immunization. This lack of protection from pertussis immunization in older children is consistent with epidemiological findings elsewhere which suggest that the efficacy of pertussis vaccine is high only for a limited time and falls gradually with time after immunization[3,4,5,6,7]. In a longitudinal study in the UK, for example, vaccine efficacy was 100%, 84%, 52%, and 46% for children one, four, five and seven years of age, respectively[8].

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Alternatives to waning immunity as explanations for the increased attack rates in older children are that vaccine heat stableness, vaccine immunogenicity, or the quality of immunization services have significantly improved for the younger age group. It was not possible for the regional vaccine distributors to provide details of vaccine type or manufacturers for the period 1980 to 1991, leaving changes in vaccine type as an explanation for improved efficacy an open question. There have been, however, extensive inputs into the immunization program in Solomon Islands since 1989, including provision of new refrigerators and training of nurses in cold chain management and administration of vaccines. In particular, from 1989 vaccines were discarded with greater alacrity after cold chain failures than in earlier years. Regardless of these changes, a provincial survey in Choiseul in 1994 found continuing problems with the cold chain, including unreliability of temperature control, and uncertainty about storage requirements for killed and live vaccines[9]. Given the continuing problems with cold chain maintenance, we suggest that waning immunity is a more plausible explanation of increased pertussis attack rates in older children.

The results of this study should be considered cautiously. A limitation to this study was the use of a clinical definition of disease without laboratory confirmation of infection, a research situation common in smaller developing countries. Using a clinical case definition may have resulted in classifying other respiratory infections as pertussis, or mistakenly classifying mild forms of pertussis as non-cases. Recalling symptoms from an episode that occurred several weeks before may have further increased the difficulty of classifying individuals. However, the distinctive 'whoop' of pertussis and the presence of other clinical symptoms reported among cases (length of illness, vomit after cough, apnea after cough, subconjunctival bleeding) tend to support our conclusion that these episodes were pertussis. In addition, we attempted to improve the sensitivity and specificity of this definition by excluding infants, in whom the characteristic whoop of pertussis may not be present and who suffer from a high rate of other respiratory infections.

A second limitation was the ascertainment of immunization status through use of home-based, child health records. As these children get older, their health cards are more likely to be lost. If older, immunized children were misclassified as unimmunized, then the protection afforded by pertussis vaccine may have decreased the attack rates in the unimmunized group, thus decreasing estimated vaccine efficacy. Still, when we confined our analysis to those only with health records, the overall vaccine efficacy was still only 43%. For children without health cards, we also tried to validate their immunization status during the study interview through a series of vaccine history questions. We found, however, that 100% of guardians reported their children to be fully immunized with DPT even when home health records showed that no doses had been given. Possibly, guardians confused therapeutic injections as immunization with DPT.

This study was also limited to villages with at least one episode of pertussis. It is possible that other villages with better vaccine storage, handling, and coverage were exposed to disease, but did not have pertussis cases. Thus, the overall efficaciousness of DPT immunization for pertussis may have been higher than our estimates. Still, it was necessary to limit this study to villages with at least one case of pertussis since the presence of a case increased the probability that children in that village were exposed to *B. pertussis*. Finally, this study had small sample sizes for several statistical comparisons. Small sample size may hinder the ability to detect a difference between groups, if one exists.

Implications for immunization program and policy. It would be difficult to argue for a change in the immunization policy on the basis of this small study alone. However, the consensus of evidence from elsewhere and supported by this study is that, unlike immunity provided by live vaccines such as measles, immunity derived through immunization with a killed whole cell vaccine is neither permanent nor protective against infection with *B. pertussis* per se. Pertussis vaccine appears to protect to a greater extent against disease than infection, to protect against high levels of challenge, and to decrease in protective efficacy with time, i.e., provides relative rather than absolute protection[10].

In Solomon Islands, the immunization schedule relies on a primary series of DPT given at two, four and six months of age. Booster doses of DPT are not given, but additional doses of polio and tetanus toxoid vaccines are given at school entry (6–8 years of age). In five countries in the Western Pacific Region, a DPT booster dose is given at school entry as a fourth dose. Booster doses at 12 to 24 months of age are also common in 42% of countries in the region. The importance of booster doses may lie in maintaining immunity in older children and reducing transmission to younger children by vaccinated individuals[4]. The most important consideration for control of pertussis still remains to complete the primary series of immunizations as early as possible and achieve the highest possible coverage.

Duration of immunity following pertussis immunization is still an open issue. An additional dose of DPT administered one year after completing a primary series prolongs the duration of immunity and maintains immunity against pertussis in older children[3]. Before Solomon Islands considers the use of additional doses of DPT vaccine, the cost benefit of vaccine and the potential effect of such doses on the epidemiology of pertussis and especially the age distribution of the disease needs to be considered (one would expect a continuing shift in cases to older age groups). Additional resources would be required and the likely availability of resources must be considered, particularly since Pacific countries now have to pay for their own vaccines. To be effective at the population level, additional doses would need to achieve high coverage and this is not certain since school entry is often delayed in rural areas to eight or nine years of age and only 60–70% of children attend primary school. Giving booster doses at an earlier age would probably result in higher coverage and, although there is a clear booster effect, the duration is not certain[11]. If duration of protective efficacy is similar to a primary series, then a booster given at 24 months would have low efficacy by six or seven years of age and thus may not greatly reduce transmission.

Pertussis vaccine is usually not given to persons seven years or older since the disease is milder and reactions are alleged to be increased in older children and adults, but this has not been substantiated by available data[1]. Given that DPT vaccine is already part of the school immunization schedule in many countries and is only fractionally more expensive, a case could be made to replace TT in the present schedule with a fourth dose of DPT at minimal cost. However the possibility of neurological sequelae of the vaccine, although rare, has caused considerable controversy, leading to declining coverage in developed countries, and even withdrawal of the vaccine from the immunization schedule. These factors have to be balanced against the perceived benefit to the population of booster doses for older children.

Conclusions

We identified an outbreak of a disease that strongly resembled pertussis in Choiseul Province, Solomon Islands. When examining the effectiveness of three doses of DPT, we found that children aged 5–12 years were more likely to have clinically defined pertussis than children aged 1–4 years and among older children there was little sign of any protective efficacy from DPT. Immunization in children in the 1–4 year age group may be effective, against intra-household exposure, but the small number of unimmunized children in the investigation limited the possibility of drawing firm conclusions about actual vaccine efficacy which must await future investigations of larger outbreaks.

We recommend that health care providers and those involved in disease surveillance are made aware of the widely reported declining immunity in older children. We suggest that the question of booster doses of DPT be carefully reviewed by Ministries of Health and WHO, in particular for evidence of possible negative effects of the vaccine in older children and on immunization programs due to the extra resources required for booster doses. These effects must be balanced against the possible epidemiological benefits of reducing transmission to infants by children whose immunity has waned and who remain an important potential source of transmission.

Doubts about vaccine efficacy in older children should not deflect attention from the importance of monitoring immunization coverage, vaccine efficacy, logistical issues, incorrect storage and improper administration of vaccines, plus pertussis morbidity.

Doubts about vaccine efficacy in older children should not deflect attention from the importance of monitoring immunization coverage, vaccine efficacy, logistical issues, incorrect storage and improper administration of vaccines, plus pertussis morbidity. The paramount consideration is to complete the primary series of immunization by six months of age and to achieve the highest possible coverage in order to provide maximally available protection of infants in whom the disease is most serious. Future research, including serological examination, and careful review would be advisable before any changes to vaccine strategy and policy are made.

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Through effective governance, Pacific island countries can overcome constraints to community-based development which include: inadequate political and administrative support, lack of income distribution policies and/or mechanisms, defective plans and project designs, deficient service delivery to marginalized groups and remote communities, insensitivity of project interventions to culture, lack of functional monitoring systems and poor coordination of programmes and projects.

Suva Declaration on Sustainable Development in the Pacific, 1994