นิพนธ์ต้นฉบับ

Evidence of pertussis vaccine efficacy from pertussis outbreaks in Nakhonratchasima, Thailand.

Pipat Luksamijarulkul* Thirapong Thiramanus**
Somchai Phirapakorn*** Pairatana Gunakasem*

Luksamijarulkul P, Thiramanus T, Phirapakorn S, Gunakasem P. Evidence of pertussis vaccine efficacy from pertussis outbreaks in Nakhonratchasima, Thailand. Chula Med J 1988 Mar; 32(3): 225-231

Between June 1983 and June 1984, unusual outbreaks of pertussis occurred in 5 sub-districts of Buayai District, Nakhonratchasima Provice. There were 47 primary cases under the age of fifteen and 127 household contacts under the age of twenty. A survey of 127 household contacts showed that 26 contacts became ill with non-specific symptoms of upper respiratory tract infection within 5 to 28 days after the date of onset of the primary cases and the serological test for recent pertussis infection was positive. The overall secondary attack rate was 20.5%. The relationship between the attack rates and the ages of secondary cases exhibited a negative correlation. The attack rates in contacts with and without complete basic DTP vaccination were 11.1% and 21.2% respectively. Comparing contacts 20 years old or younger who had received 3 or more doses of DTP and those with no DTP vaccination, the efficacy of pertussis vaccine in DTP was estimated at 47.6%. However, the vaccine efficacy increased from 47.6% in the contacts under 20 years of age to 81.3% in the contacts below 5 years of age.

Reprint requests : Luksamijarulkul P. Department of Microbiology, Faculty of Public Health, Mahidol University, Khet Praya Thai, Bangkok 10400, Thailand.
Received for publication. January 27, 1987.

* Department of Microbiology, Faculty of Public Health, Mahidol University.
** Department of Epidemiology, Faculty of Public Health, Khonkaen University.
*** Division of Epidemiology, Ministry of Public Health.

พิพัฒน์ ลักษมีจรัลกุล, ถิระพงษ์ ถิระมนัส, สมชาย พีระปกรณ์, ไพยรัตน์ คุณะเกษม. ประสิทธิผลของวัคซีนป้องกันโรคไอกรน จากการระบาดของโรคไอกรนในจังหวัดนครราชสีมา, ประเทศไทย. จุฬาลงกรณ์เวชสาร 2531 มีนาคม; 32(3) : 225-231

ระหว่างเดือนมิถุนายน พ.ศ. 2526 ถึงเดือนมิถุนายน พ.ศ. 2527 เกิดการระบาดของโรคไอกรนใน 5 ตำบล ของอำเภอบัวใหญ่ จังหวัดนครราชสีมา พบผู้ป่วยปฐมภูมิ 47 รายที่มีอายุต่ำกว่า 15 ปี และผู้สัมผัสโรคในครัวเรือน 127 ราย ที่มีอายุต่ำกว่า 20 ปี จากการศึกษาผู้สัมผัสโรคทั้ง 127 ราย พบผู้ป่วยทุติยภูมิ 26 รายที่ให้ผลบวกทางน้ำเหลืองวิทยา แสดงการติดเชื้อโรคไอกรนจากการระบาดครั้งนี้ อัตราป่วยระลอกสองของทุกกลุ่มอายุเท่ากับร้อยละ 20.5 อัตราป่วยระลอกสองจะลดลงเมื่ออายุผู้ป่วยสูงขึ้น อัตราป่วยระลอกสองของผู้สัมผัสโรคที่มีประวัติเคยได้รับวัคซีน ดีทีพี ครบ 3 ครั้ง หรือมากกว่า และผู้สัมผัสโรคที่มีประวัติไม่เคยได้รับวัคซีนดีทีพีเท่ากับ ร้อยละ 11.1 และร้อยละ 21.2 ตามลำดับ ดังนั้นเมื่อประเมินประสิทธิผลของวัคซีนป้องกันโรคไอกรนในวัคซีนดีทีพี จากการระบาดของโรคครั้งนี้เท่ากับร้อยละ 47.6 อย่างไรก็ตามประสิทธิผลของวัคซีนจะสูงขึ้นเป็นร้อยละ 81.3 ในกลุ่มผู้สัมผัสโรคที่มีอายุต่ำกว่า 5 ปี

Pertussis is one of the acute respiratory tract infections in infants and young children.[1] In Thailand, as in many developing countries, pertussis presents a major health problem. The trend of this disease showed fluctuations with an increased morbidity rate during 1975-1983.[2] However, its real incidence may be higher or lower than that reported. The disease is sometimes difficult to diagnose clinically because the whoop is only present in 20% of cases of paroxysmal coughing[3] Older children with pertussis have often been diagnosed as having an upper respiratory tract infection or a persistent bronchitis.[4] On the other hand, some viral infections, such as respiratory syncytial virus, cytomegalovirus and adenovirus can play a role in causing pertussis-like disease.[5] In recent years, there were several outbreaks in certain provinces of Thailand including Nakhonratchasima, Chiangrai, Nan and Phayao,[6,7,8,9] when children with completed basic DTP vaccination were reported to be ill with pertussis.[9,10] The failure may be due to many factors. Firstly, the coverage of pertussis vaccination infants and young children is inadequate to produce herd immunity. Secondly, the antibody level after three doses of DTP vaccine may not be high enough to protect against the disease and the booster doses in older children are often missed. Lastly, the strains of Bordetella pertussis used for vaccine production may not be broad enough to combat pertussis in the community, so that the efficacy of the pertussis vaccine to protect against the local strains causing the disease, may be doubtful.

During the period of June 1983 to June 1984. the unusual, high case incidence outbreaks of pertussis occurred in several areas of Buayai District, Nakhonratchasima Province, which afforded an opportunity to estimate the efficacy of pertussis vaccine in DTP.

Materials and Methods.

The epidemiological surveillance of pertussis was set up at Nakhonratchasima during the period of June 1983 to June 1984. During this period the pertussis outbreaks occurred in 5 subdistricts of Buayai District. A mobile team was formed to investigate and study the epidemiology of the disease immediately. The efficacy of pertussis vaccine was also estimated.

Case definitions

Laboratory-defined case : An individual with nasopharyngeal swabbing that was positive for B. pertussis by culture and/or individual with a four-fold rising titers or greater, between the first and the second sera by micro-agglutination test. The patient could be either symptomatic or asymptomatic.

Clinical case or pertussis-like case : A patient who developed a prolonged cough ($\geq$ 2 weeks) and was under 15 years of age.

Primary case : The first symptomatic case of pertussis, either clinically or laboratory-defined, occurring in a household.

Co-primary case : A case with an onset within one to four days of the primary case in the same household.

Secondary case : A household contact under the age of twenty who developed a non-specific symptom of upper respiratory tract infection within 5 to 28 days after the onset of the primary case and showed positive serological test for the recent pertussis infection ($\geq$ 4-fold rising titers between the first and the second sera by micro-agglutination test).

Individual case study.

Patients with prolonged coughing ($\geq$ 2 weeks) were selected for nasopharyngeal swab and capillary blood test to confirm B. pertussis infection. Medical and social histories were investigated individually.

Household contacts survey

The mobile team was encouraged to complete a more extensive investigation of secondary spread in households with primary cases. The report form consisted of a roster of household members on age, sex, DTP vaccination status of those under the age of twenty, the date of the primary case onset and of any secondary case onset. All household contacts under the age of twenty had capillary blood tests at least twice to confirm the recent pertussis infection. The first blood test made at the date of the first interview and the second was about 3-4 weeks after.

Calculation of the secondary attack rate

$$\text{Secondary attack rate} = \frac{\text{Number of secondary cases}}{\text{Number of all household contacts under the age of twenty}} \times 100\%$$

Laboratory methods

B. pertussis isolation was performed on Bordet-Gengou medium with 15-20% sheep blood. Suspicious colonies were picked up for gram staining and identification by slide agglutination test with a standard anti-pertussis serum provided by the Division of Biological Standards NIH, Bethesda, Maryland, USA.

The sera of patients and household contacts were tested for antibody titers against B. pertussis strain 134+165 (Standard strains, Phase I) by the micro-agglutination test after Manclark and Meade.[11] The standard anti-pertussis serum provided by the Division of Biological Standards NIH, Bethesda, Maryland, USA and the normal rabbit serum obtained from the Biological Products Division, the Government Pharmaceutical Organization, Ministry of Public Health were used as positive and negative control sera in the test. The criteria of diagnosis for the recent pertussis infection was a four-fold rising titer of greater, between the first and the second sera.

Statistical method. Confidence interval was based on the Miettinen approximation.[12]

Results

In the course of investigation, of the 47 primary cases there were 28 cases (59.6%) identified positive by culture and/or serological test for B.pertussis infection (Table 1). The highest percentage of positivity was reported in the group of age 1-4 years (68.8%). Nine of the 28 laboratory-defined cases were positive for B.pertussis isolation. The sex ratio (Male : Female) of the laboratory-defined cases was 1:1.3

Table 1 The primary cases and laboratory-defined cases in each age group from the investigation.

Age group (years)	Number of primary cases	Laboratory-defined cases	
		Number	% in each age group
under 1	1	0	0
1 - 4	16	11 (1)*	68.8
5 - 9	26	16 (8)*	61.5
10 - 14	4	1	25.0
Total	47	28 (9)*	59.6

( )* Number of patients positive for *B. pertussis* isolation
Male : Female of laboratory-defined cases = 1 : 1.3

A household contacts survey of 47 primary cases found 127 contacts under the age of twenty. Twenty-six of the household contacts became ill with non-specific symptoms of upper respiratory tract infection within 5 to 28 days after the date of onset of the primary cases and showed positive serological test for B. pertussis infection. The overall secondary attack rate was 20.5% (Table 2). The attack rate decreased from 50.0% in the under 1 year age group to 8.6% in the 15-20 years age group.

Table 2 The secondary attack rates by age in the household contacts.

Age group (years)	Household contacts		Secondary attack rate by age (%)
	No. of contacts	No. of positive serology	
under 1	4	2	50.0
1 - 4	32	10	31.3
5 - 9	28	8	28.6
10 - 14	28	3	10.7
15 - 20	35	3	8.6
Total	127	26	20.5

In Table 3, the secondary attack rate in household contacts was examined by ages and the history of DTP vacination. The attack rates in contacts who had received 3 doses of DTP vaccine or more and in those who had no DTP vaccination were 11.1% and 21.2% respectively. The vaccine efficacy was estimated by the following formula :

$$\text{Vaccine efficacy} = \frac{\text{Attack rate among unvaccinated - attack rate among vaccinated}}{\text{Attack rate among unvaccinated}} \times 100\%$$

Comparing the contacts 20 years of age and younger who had received complete DTP vaccination (⩾ 3 doses of DTP) and those without, the efficacy of pertussis vaccine in DTP was estimated to be 47.6% (95% confidence, limits 45.9 to 50.7%)

Table 3 Pertussis secondary attack rates in 127 household contacts by age and DTP vaccination status

Age group (years)		DTP vaccination status				Total
		⩾ 3 doses	1-2 doses	None	Unknown	
under 1	total	1	2	1	0	4
	ill	0	1	1	0	2
	AR (%)	0	50.0	100.0	-	50.0
1 - 4	total	7	17	8	0	32
	ill	1	4	5	0	10
	AR (%)	14.3	23.5	62.5	-	31.3
5 - 9	total	1	10	16	1	28
	ill	0	1	6	1	8
	AR (%)	0	10.0	37.5	100.0	28.6
10 - 14	total	0	1	26	1	28
	ill	0	0	3	0	3
	AR (%)	-	0	11.5	0	10.7
15 - 20	total	0	0	34	1	35
	ill	0	0	3	0	3
	AR (%)	-	-	8.8	0	8.6
Total	total	9	30	85	3	127
	ill	1	6	18	1	26
	AR* (%)	11.1	20.0	21.2	33.3	20.5

* Secondary attack rate

$$\text{Vaccine efficacy (overall)} = \left(\frac{21.2 - 11.1}{21.2}\right) \times 100\% = 47.6\%$$

95% Confidence limits 45.9 to 50.7%

However, the efficacy of the vaccine increased from 47.6% in the contacts under 20 years of age to 81.3% in the contacts under 5 years of age (Table 4)

Table 4 Pertussis vaccine efficacies in contacts under 10 years of age.

Age group		DTP vaccination status		
		⩾ 3 doses	1 - 2 doses	None
under 5 years	total	8	19	9
	ill	1	5	6
	AR (%)	12.5	26.3	66.7
	Vaccine efficacy		81.3%	
under 10 years	total	9	29	25
	ill	1	6	12
	AR (%)	11.1	20.7	48.0
	Vaccine efficacy		76.9%	

Discussion

This pertussis outbreak investigation afforded an opportunity to study some epidemiological aspects and to estimate the efficacy of pertussis vaccine in DTP.

Pertussis is transmitted directly by droplets from coughing or sneezing.[13] The most infectious period is the early part of the disease prior to the development of a paroxysmal cough.[4] Older children and adults whose immunity-acquired naturally or by immunization-may have faded, may be ill with atypical pertussis or an upper respiratory tract infection.[4,14] These unrecognized patients may transmit pertussis infection to others or even to young infants before immunization.[14] The spread of the infection may be followed from patient to patient, and from household to household.[4,13] The secondary attack rate in susceptible persons may be as high as 70%.[15] However, the attack rate in children who had partial immunity was lower than that in susceptible children. In this study, the overall secondary attack rate was only 20.5%, but 50% in those under one year of age.

The efficacy of pertussis vaccine has been questioned recently by Stewart, who alleged minimal benefit and significant risk from the use of the vaccine.[16] Recent community-wide studies have shown conflicting estimates of efficacy; two showed high efficacies (85% and 84%) and one showed essentially no efficacy.[17,18,19] However, those studies had relatively few laboratory-defined cases and were not based on comparison of secondary attack rates in households. Estimates based on secondary attack rates may be more reliable because the exposure can be assumed to be more uniform. Broome, et al (1981) investigated an epidemic in Atlanta and studied the secondary attack rates in households to estimate the efficacy of pertussis vaccine.[20] They found a vaccine efficacy, among household contacts of 63%. In this study, we found an efficacy of 47.6% in contacts under 20 years of age and 81.3% in contacts under 5 years of age. The differences in the degree of efficacy of the vaccine may have been affected by many factors including the study design, the age of contacts, the criteria of diagnosis, the coverage of vaccine in the studied community, and the different serotypes of the B. pertussis prevalent in the community from those in the vaccine. However, there were a substantial number of cases among the vaccinated, suggesting that there is still a need for a continued assessment and improvement of the vaccine.

Acknowledgements.

Acknowledgement is greatefully expressed to the health staffs of local health offices and Buayai Community Hospital for data and specimens collection. Appreciation is also extended to Assistant Professor Dechavudh Nityasuddhi for calculating the confidence interval.

References

1. Olson LC. Pertussis. Medicine (Baltimore) 1975 Nov; 54 (6) : 427-469
2. Division of Epidemiology, Ministry of Public Health. Epidemiological Surveillance Reports Bangkok, Thailand 1975-1983.
3. Wilson AT, Henderson IR, Moore EJH, Heywood SN. Whooping-cough : Difficulties in diagnosis and ineffectiveness of immunization. Br Med J 1965 Sep; II (5462) : 623-626
4. Linnemann CC, Partin JC, Perlstein PH, Englender GS. Pertussis : persistent problems. J Pediatr 1974 Oct; 85 (4) : 589-591
5. Sturdy PM, Court SD, Gardner PS. Viruses and whooping cough. Lancet 1971 Oct 30; 2 (7731) : 978-979
6. Luksamijarulkul P, Gunakasem P, Phirapakorn S, Songkasuwan P. The outbreak investigation of pertussis in Nakhonratchasima Province, Thailand. J Public Health 1985 Mar; 15 (3) : 187-197
7. Luksamijarulkul P, Chayaniyothin T, Makprathan C. Pertussis outbreak in Chiangrai Province: Laboratory result. J Public Health 1986 Jan; 16 (1) : 1-10
8. Luksamijarulkul P, Chayaniyothin T. Pertussis outbreak in Nan Province 1984. Mahidol Univesity Annual Research Abstracts and Bibliography of Non-Formal Publications, 1985; 12:232
9. Luksamijarulkul P, Pinyowiwat W, Tamsathienchai K. Whooping cough outbreak in Phayoa, Thailand 1985. Ramathibodi Med J 1986 Jan; 9 (1) : 35-38
10. Limpakarnjanarat K, Preuksakorn S, Surapat N. The study of pertussis in Chiang-Mai University Hospital between 1981-1982. Chiangmai Med Bull 1983 Jan; 22 (1) : 15-23
11. Manclark CR, Meade BE. Serological response to Bordetella pertussis. In : Rose NR, Friedman H. 2 nd ed. Manual of Clinical Immunology, Washington DC : American Society for Microbiology, 1980. 496-499
12. Miettinen O. Estimability and estimation in casereferent studies. Am J Epidemiol 1976 Feb; 103 (2) : 226-235
13. Kendrick PL. Can whooping cough be eradicated? J Infect Dis 1975 Dec; 132 (6) : 707-712
14. Nelson JD. The changing epidemiology of pertussis in young infants : The role of adults as reservoirs of infection. Am J Dis Child 1978 Apr; 132 (4) : 371-373
15. Immunization Practices Advisory Committee, Centers for Disease Control. Diphtheria, tetanus, and pertussis : guidelines for vaccine prophylaxis and other preventive measures. Ann Intern Med 1981 Dec; 95 (6) : 723-728
16. Stewart GT. Vaccination against whooping cough: Efficacy versus risks. Lancet 1977 Jan 29; 1 (8005) : 234-237
17. Church MA. Evidence of whooping-cough-vaccine efficacy from the 1978 whooping-cough epidemic in Hertfordshire. Lancet 1979 Jul 28; 2 (8135) : 188-190
18. Jenkinson D. Outbreak of whooping cough in general practice. Br Med J 1978 Aug 19; 2 (6136) : 577-578
19. Ditchburn RK. Whooping cough after stopping pertussis immunization. Br Med J 1979 Jun 16; 1 (6178) : 1601-1603
20. Broome CV, Preblud SR, Bruner B, McGowan JE, Hayes PS, Harris PP. Epidemiology of pertusis, Atlanta, 1977. J Pediatr 1981 Mar; 98 (3) : 362-367