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Epidemiology of Pertussis in Taiwan, 1993-1998, and Its Control Measures

Introduction

Taiwan began to offer children DPT (diphtheria, pertussis and tetanus combined) vaccines in 1954, and the whole-cell pertussis vaccine in early 1955. The number of reported pertussis cases subsequently decreased yearly from 691 in 1955 to only a few in 1970. This low incidence remained throughout the period between 1971 and 1991 until a sudden increase of 226 cases occurred in an outbreak in 1992. Then, the Epidemiology Meeting of the Department of Health formulated a set of standards for the reporting and classification of pertussis cases; and at the same time, it was decided that in addition to the isolation of *Bordetella pertussis* by laboratory testing, a confirmed case must also meet the criteria determined by epidemiological surveys to remedy any likely deficit in the sensitivity of laboratory testing.

Due to poor reporting in the past, any epidemiological cycles of pertussis in Taiwan were not properly recorded. In the US, even in groups of high immunization coverage, the infection has a cycle of every two to five years[(1)]. Though vaccines have changed several aspects of pertussis infection, they have

not been able to alter its epidemiological intervals. Vaccines may have an impact on the occurrence of infection, but they have little effect on the transmission of *Bordetella pertussis* in human beings[2]. In 1993, the most serious outbreak of pertussis in twenty years occurred in the US. This outbreak caused people to suspect that the whole-cell vaccines had become less effective after decades of use. Studies have shown that vaccines are protective temporarily. Adults and adolescents with mild symptoms are the major sources of infection; they transmit the disease to infants and young children who then experience serious infection. The present report will focus on the epidemiological characteristics of pertussis infection in Taiwan in 1993-1998, and also measures for the prevention and control of the infection.

Pertussis Infections in Europe and the USA

1.The Epidemiology

Reporting of pertussis in the US began in 1922. In 1938, the number of cases reported reached the highest peak of 260,000. The whole-cell vaccines were approved for marketing in 1949. In 1976 the number of reported cases decreased the lowest number of 1,010. In the last ten years, the average number of cases reported each year was 2,900, with 5-6 deaths[3]. Incidence increased in the years 1983, 1986, 1990, and 1993, and to 6,467 cases in 1996. In the period between 1992 and 1994, 15,286 cases were reported. From the 13,615 cases with more comprehensive information for analysis, it was found[4] that 41% of the cases were under one year of age, 20% in the 1-4 year age group, 11% in the 5-9 year age group, and 28% over ten years of age. Of the cases under one year of age, 81% were younger than six months. The average rate of hospitalization was 33.6%. Fatality was 0.2%. Of the 23 cases who died in

1992-1993, 11 (47.8%) were younger than two months, and 18 (78.2%) younger than six months. In 1993-1995 in Germany, the PCR method was used to analyze the nasopharyngeal discharge of cases of sudden infant death to find 18% (9/51) of them positive for *Bordetella pertussis*, suggesting some association between pertussis and sudden infant deaths. The number of pertussis deaths may also have been underestimated[5].

Vaccines are protective for a maximum of 12 years[6]. They also reduce the risk of natural infection. In the US for instance, the number of susceptible adults was estimated to be 5 million in the 70's, 20 million in the 80's, increasing to 70 million in the 90's[7]. Data of the US CDC also indicates that the age of cases is rising[8]. In 1979, 15.1% of all cases were over 10 years of age; it was 19.8% in the 80's, and 28% in 1992-1993.

The Serological method has been used by some to study the prevalence of pertussis among adults. Nennig et al.[9], by using immunoflurorescence method to measure the concentration of IgG antibody induced by pertussis toxin in 153 adults in San Francisco who had been coughing for more than two weeks, found a prevalence rate of 12.4%, and an incidence of 176 persons per 100,000 population per year. Cromer et al.[10], in a study of 156 adolescents with different definitions of serum-positive, estimated their infection rate to be 1.2-8.2% per year. In the five-year follow-up, none, however, had been diagnosed as pertussis. Deville et at.[11], in a six-year follow-up study of 51 medical personnel on their concentrations of IgG and IgA antibodies against four toxin antigens (PT, FHA, PRN, and fimbriae 2), found that more than 90% of them demonstrated significant increases in concentration against at least one of the antigens; 55% of them had had second infections; and 21% had repeated infections. Cherry et al.[12] studied the IgG and IgA antibody concentrations of German and American youths. As IgA antibody is primarily a product of infection, and no difference between immunized Americans and

non-immunized Germans was noted, the indication is that infection was fairly common among youths of both countries. Many studies have shown that chronic coughing in adolescents and adults is induced by pertussis. As these symptoms may be atypical, they are unrecognized and are likely to be incorrectly or incompletely treated. They then transmit the infection to family members, particularly to infants and young children not yet fully immunized. Long et al.[13] in their follow-up study of index cases in family transmission, found that the infection was, in most cases, passed on from the older members of the family to the younger ones. Deen et al.[14], in their study of 40 index cases and 255 family members, found that very often the first infected person was older than the index case. 90% of the index cases were four years younger. Only 32% of the index cases were infected together with others in the first wave of infection. A study in the US[15] found 23 pertussis deaths in 16 families. In 13 (81%) families, family members had coughing previously. 46% of the cases in which death resulted were infected by adults.

2.Immunization and its Value

The major problem with the use of the whole-cell vaccines is the general and local adverse reactions. Acetaminophen can be used to treat local pain or fever. The incidence of reactions such as cerebral disorders is about 0-10.5 cases per million population[16]. During epidemics of Pertussis, the immunization schedule can be shortened to begin at four weeks after birth, with completion of the basic immunization in four weeks[17]. Four doses should be given as soon as possible. Children younger than seven years who have not been immunized in the last three years should be given a booster. Children with a previous history of infection, regardless of either positive or positive-associated reactions, do not need a further booster[16]. Infection rate is as high as 100% in groups with close contact[18]. Immunized individuals could also be infected, although symptoms are milder. The effect of the whole-cell

vaccines is 80%[19]. Vaccines are protective for 2-3 years, and the effect declines year by year thereafter. Immunity disappears after 10-12 years. However adults and adolescents who have had complete childhood basic immunization may still be infected and transmit the infection to infants and young children. A pertussis outbreak occurred in Cincinnati City in 1993[20], regardless of the fact that 74% of children between seven months and 12 years had completed the basic immunization with whole-cell vaccines. Vaccines did not seem entirely protective against the infection.

When Japan, the United Kingdom and Sweden terminated the use of the whole-cell vaccines because of their adverse reactions, outbreaks occurred soon after. DTaP has PT, FHA, PRN and fimbrial antigens as its components. One vaccine contains at least one component. Assessments of 13 acellular and two whole-cell vaccines were made in the US in 1991-1992[21,22] revealed that the DTaP vaccines had fewer reactions and milder symptoms. The two whole-cell vaccines made by two different manufacturers produced different antibody titers. Clinically, the relationship between vaccine protection and the levels of antibody titer is not clear. Some large-scale efficacy tests of vaccines in Sweden and Italy[23] showed that the whole-cell vaccines produced more reactions, and that the chances of the DTaP vaccines producing reactions were similar to diphtheria and tetanus toxoid vaccines. Vaccines of different components have different vaccination effects, immunization schedules, definitions of cases, and different methods of manufacturing antigens[24]. When replacing the whole-cell vaccines with the DTaP vaccines, the following issues should be considered[25]:

1. Types and dosages of antigens: what antigen components and dosage are safer and more effective?
2. Different vaccines have different decline time of immunity (the

relationship between the titer of antibody and the protection of vaccine is still not clear). A good vaccine should offer not only protection against disease, but also protection against bacterial multiplication and infection.

3. Are acellular pertussis vaccines protective against parapertussis? Will there be parapertussis outbreaks if vaccines with pertussis toxin component only are used?

4. When DTaP vaccines are used for basic immunization, in boosters, what is the mechanism that causes them to produce more local reactions than the whole-cell vaccines?

5. When various vaccines are used together with DTaP, more studies are needed to make clear if there will be any interference with the production of antibodies and immunity.

6. From economical and practical points of view, will the new DTaP be less expensive, and easier to manufacture in sufficient amount to supply the whole world?

Although many studies have recommended giving adults booster immunization, the issue whether it is more cost-effective to develop a more effective DTaP basic immunization is still under debate[26].

3.Clinical Diagnosis

In the early stage of pertussis infection, major symptoms result from of mucosal inflammation of the upper respiratory tract infection such as rhinitis, nasal discharge, coughing, and possibly mild fever. Although the condition is not serious, communicability is the highest at this stage. This

stage lasts for 1-2 weeks , then proceeds to the most serious stage of paroxysms characterized by continuous and spastic coughing. Coughing disrupts inspiration, and after paroxysms of coughing, there often are noisy inspiratory sounds, and even vomiting. Patients then enter the recovery stage two weeks later with diminishing symptoms. Paroxysms may continue because of a simultaneous viral infection. Disease process may continue for eight weeks in young unimmunized children .

In laboratory diagnosis, symptoms of pertussis during the catarrhal stage are not easy to differentiate from symptoms of bronchitis or influenza. Pneumonia caused by pulmonary tuberculosis bacilli, adenovirus and chlamydial bacteria can also induce continuous coughing. Adenovirus and respiratory syncytial virus infections can also induce pertussis-like manifestations such as paroxysms and lymphocytosis[27].

Sporadic cases may often be overlooked due to the absence of typical inspiratory whoop. Laboratory and radiological data are not diagnostic. Continuous coughing is the common expression of adolescents and adults. The WBC can be normal, though the number can be as high as 20,000-50,000, mostly lymphocytes. In young children, whooping or increase of lymphocytes may not necessarily occur.

Early diagnosis is essential to effective epidemiological management. Clinical diagnostic definition of a case is one with symptoms of upper respiratory tract infection and paroxysms of coughing, or acute unexplainable coughing for more than 14 days. At time of epidemics, clinical characteristics can be used for diagnosis. Sensitivity of clinical diagnosis is as high as 84%, and its accuracy, 63%[28].

The definition of a clinical case decided in Taiwan in 1992 is one who has coughing for more than two weeks without any specific reasons, and with one of the following three conditions:

1. paroxysms of coughing
2. inspiratory whoop
3. post-tussive vomiting.

4.Specimen Collection and Laboratory Diagnosis

Culture

The golden rule of the diagnosis of pertussis is the isolation of the pathogenic agent from respiratory tract secretions. Though specificity of the laboratory procedures is high, their sensitivity depends on the conditions of culturing. Sensitivity is affected by the following factors[29]: 1.Methods of specimen collection: NPAs are better than nasopharyngeal swabs[30]. Physicians, however, are not familiar with this technique. Some suggest more swabs for several days. This is not practical. 2. Transportation and culture media for multiplication: should not be exposed to cold air; Regan-Lowe transportation medium should be used for transportation and bacteria multiplication. 3. Time and conditions of transportation: the shorter time, the better. 4. Facilities, transportation, and culture media for multiplication. 5. Selection of culture media and test reagents for the selection of bacteria species. 6. Time and conditions of culturing. For details, please refer to "Pertussis in Taiwan, 1995"[31], and Manual of Standard Laboratory Operations for Disease Control developed by the former National Institute of Preventive Medicine[32]. Experience in culturing is also an important factor. Factors facilitating the isolation of bacteria: Isolation is easier shortly before and after the incubation period, during the catarrhal stage, and at the early stage of paroxysms[30]. However, pertussis infection is rarely suspected at this stage. Thus culturing as a tool of diagnosis is limited. The sensitivity of culturing at two weeks after infection is 80%; it goes down to 14% at four weeks; and to 0 at five weeks[33]. Isolation in

older people is more difficult. In Germany, the culture positive rate for adults was 3%[34]. Use of effective antibiotics such as macrolides, co-trimoxazole, tetracycline, but not penicillin and ampicillin, makes isolation difficult. Isolation is more difficult in cases with more complete doses of immunization.

DFA (Direct Fluorescein-Conjugated Antibody)

During periods of pertussis epidemics, DFA can offer more rapid preliminary diagnosis with a higher prediction rate of positive reactions. The major defects of the method are low sensitivity and higher false-positive rate. Skills and experience of laboratory technicians, and the quality of laboratories facilities all have an impact on the reading of laboratory findings. DFA, therefore, should not be used alone for diagnosis. The monoclonal antibody recently developed can precisely detect the presence of *Bordetella pertussis*, with a sensitivity of 65.1%, and an accuracy rate of 99.6%[35]. This reagent has been adopted by several countries. In the long run, DFA will be replaced by the more sensitive polymerase chain reaction.

PCR (Polymerase Chain Reaction)

PCR procedures have been studied by many. Different procedures such as the selection of target genes, enlargement of the probe, detection systems such as ethidium bromide staining, and some methodological limitations, demonstrate different sensitivity. Likely reasons for false-positive reactions are specimens being contaminated by the DNA of the bacteria of similar gene sequence; contamination in laboratory by other pertussis bacteria or other *Bordetella* species; or cross-contamination of residual specimens. Likely reasons for false-negative reactions are insufficient amount of bacteria from nasopharynx; test conducted during either the early or late stage of the infection; poor collection resulting in insufficient amount of bacteria; bacterial inhibitors in specimens; loss or damage of bacteria or DNA in the process of storage or laboratory testing; techniques of laboratory testing; detection system of low sensitivity; and genetic change

or mutation of strains different from the sample. The major reason, however, is that specimens contain inhibiting substances to polymerase[36] such as hemoglobin, phenol-benzene and others. Although not all factors can be controlled, the internal control of specimens is helpful to the reading of PCR findings[37].

The sensitivity of identification by PCR is significantly better than culturing. It is, however, difficult to decide whether a PCR(+) and culture(-) case is positive. More PCR testing, DFA testing, or serological methods are needed. Cases of PCR(+) and culture(-) can only be decided positive when they meet the WHO clinical diagnostic standards[38] . PCR(+) and culture(-) cases occur more often at the late stage of infection, and in immunized cases, cases previously treated with antibiotics, or close contacts of culture positive cases[39].

Analysis of PCR data of clinical specimens from two highly immunized countries, Finland and Switzerland, showed[40] that of the 1,904 specimens from Finland, 447 (23%) were positive. Of the 829 specimens tested by PCR and culture methods simultaneously, only seven were culture positive but PCR negative. The positive rate of PCR was associated with the number of colonies grown on the culture media simultaneously cultured. Of the 1,830 specimens in Switzerland tested by PCR alone, 683 were positive. Of the 868 cases in the control group, 29 were PCR false-positives. None of the three methods, PCR, culture, and immunoflurorescence, can detect all infected cases. However, the testing time for PCR is 2.5 hours to 1-2 days, and is faster than the 3-7 days of culturing. Edelman et al.[41] compared the identification rates of PCR and culture methods after the use of erythromycin to find that after four days of erythromycin use, 56% of the patients were culture-positive, and 89% of them, PCR-positive. After seven days, the percentages went down to 0% and 56% respectively. Data from

Finland and Switzerland using PCR as the diagnostic tool showed[42] that the infection rate of children 1-6 years was higher in Switzerland and Finland. One likely reason was, that in Finland one booster dose was given to children at age two years. Sensitivity of laboratory testing declines with the age of patients, a fact probably associated with the development of the immunity system of patients. Data from Finland showed that PCR was more effective in detecting cases without symptoms in children under seven years. In older children and adults, PCR was more effective in detecting cases with symptoms.

Serology

There are still some doubts about serological testing, primarily because the natural immunological history of pertussis is not clear. Sensitivity of serological testing can be higher than that of the culture method; some studies even demonstrated a rate as high as 87%[43]. This high sensitivity can be achieved only with sera of both acute and convalescence stages and matching of three different Ig antibodies (A, G, M) with two antigens. A single testing does not yield sufficient sensitivity and accuracy, because no reliable standard can be established for serum values, and the three different anti-pertussis immunoglobulins each has a different half-life. They react to both immunization and natural infection, and therefore, it is almost impossible to tell whether the antibodies in a single specimen come from either immunization or natural infection[44]. The use of erythromycin does not seem to significantly interfere with the production of antibodies[38].

Cattaneo et al.[45], in a study of the sera of 585 persons aged 1 through 65 years in 1996, noticed two antibody peaks in pertussis, one at ages 4-6 at the time of booster immunization; and another at ages 13-17, suggesting infection during the adolescent period. A study in France[46] of 360 completely immunized children aged 0.5 month through 158 months

showed that their PT, PRN and agglutinogen antibodies went down first and up again, though anti-FHA continued to exist, suggesting that silent infections were fairly common in France. The possibility of infection increased six years after the last dose of immunization. Seroepidemiology is a method commonly used in the investigation of large-scale epidemics and the efficacy of vaccines, and is an important method in the study of adolescents and adults with symptoms.

In the next ten years in developing countries, bacterial isolation will still be the cost-effective and practical alternative. In developed countries, however, following the collection of specimens at different stages of the disease process, different methods will be used for the laboratory testing of pertussis (Table 1). PCR is effective in detecting cases of pertussis and parapertussis, in particular, cases with mild symptoms, previous immunization, and the use of antibiotics.

5.The Risk Factors

An outbreak of pertussis occurred in Chicago in 1993. The average age of patients was eight months. By case-control method[47] to study the risk factors, it was noted that mothers of adolescents and young children and mothers with coughing for more than seven days during the incubation period of sick children were the major risk factor of infant infection. Biellik et al., in a study of the differences in risk factors between household and community pertussis infections[48], noticed that families with children of 2-18 years were the risk factor for household infection; and that outdoor exposure was the major predictive factor of community infection, in particular among adolescents. Factors associated with secondary transmission was the prophylactic use of erythromycin and the timing of use. In 1992, Sprauer et al. investigated the secondary transmission of pertussis in households with the early use of erythromycin[49]. They found that early

administration of erythromycin to cases and contacts was effective in the prevention of secondary transmission. Dodhia et al. reviewed studies on the use of erythromycin for the prevention of secondary transmission[50]. They noticed that the effect was moderate, and was close to the use of high-quality whole-cell vaccines. Erythromycin produces three side effects, nausea, vomiting, and abdominal pain. In highly immunized countries, erythromycin is used on close contacts, particularly on infants not immunized or partially immunized, and adults in close contact with sick children.

Epidemiological Characteristics of Pertussis in Taiwan, 1993-1998

Sources of Data

1. Annual Report of Communicable Diseases in the Taiwan Area, National Quarantine Service, 1993-1998
2. Health and Vital Statistics, Department of Health
3. Questionnaires of 150 confirmed pertussis cases, 1996-1998

Method of Analysis

Dbase was used for the establishment of databases; Epi-inf 6 and Microsoft Excel were used in data analysis.

Results

1. Number of Confirmed and Reported Cases per Year, from 1993-1998

In the period between 1993 and 1998, there were 7, 6, 26, 15, 101, and 34 confirmed cases (Figure 1), and 63, 51, 86, 146, 477, and 283 reported cases each year. Most of them were household infections. In 1997 for instance, there were 23 household infections involving 61 cases. Three were of small-scale community infections in two primary schools and one hospital involving 20 patients, all reported by the National Taiwan University Hospital. 20 were sporadic cases.

2. Sex Distribution

Of confirmed cases, 88 were males and 101 females, giving a male-female ratio of 0.87 to 1.

3. Age Distribution

Ages of confirmed cases ranged from 20 days to 70 years: 61 cases (32.3%) under one year, 23 (12.2%) in the 1-4 year group, 47 (24.9%) in the 5-9 year group, 9 (4.8%) in the 10-19 year group, 9 (4.8%) in the 20-29 year group, 28 (14.8%) in the 30-39 year group, 6 (3.2%) in the 40-49 year group, 2 (1.1%) in the 50-59 year group, and 4 (2.1%) of 60 years and above (Figure 2).

4. Trends in Age Distribution

In the six years between 1993 and 1998, the proportions of confirmed cases under one year of age to total confirmed cases of the year were respectively 57.1, 83.3, 30.8, 66.7, 22.8, and 32.4%. The proportions of confirmed cases older than 10 years to total confirmed cases of the year were respectively 0, 0, 30.7, 20.0, 33.7, and 38.2% (Figure 3). Of the 1,106 reported cases, the proportions of cases under one year of age by year were respectively 58.7, 76.5, 66.3, 67.3, 33.3, and 45.9%. The proportions of cases older than 10 years to total reported cases of the year were respectively 0, 2.0, 15.1, 12.3, 28.3, and 20.1%. The ages of cases seemed to have moved upward.

5. Month of Onset

Of the 189 confirmed cases in 1993-1998, most cases occurred in the months between April and September (Figure 4). Summer is the major season of infection. Long-lasting coughing after summer can be an indicator of pertussis infection.

6. Geographic Distribution

Of the 189 confirmed cases in 1993-1998, 77 (40.7%) were in Taipei County, 58 (30.7%) in Taipei City, 19 (10.1%) in Changhua County, 10 (5.3%) in Taichung County, 5 (2.6%) in Taichung City, 4 (2.1%) in Hsinchu County, 4 (2.1%) in Yunlin County, 2 (1.6%) in Taitung County, 2 (1.6%) in Taoyuan County, 1 (0.5%) in Nantou County, 1 (0.5%) in Hsinchu City, 1 (0.5%) in Kaohsiung City, and 1 (0.5%) in Penghu County. Geographically, of all counties and cities south to Yunlin County, only Kaohsiung City and Penghu County had just one case each in 1996. Confirmed cases in the southern counties and cities in the six years accounted for only 1% of the total confirmed cases. Confirmed cases in both Taipei City and Taipei County accounted for 71% of all. For the incidence per 100,000 population in all counties and cities, please refer to Table 2.

7. Immunization Records

From the immunization records of the 150 cases of 1996-1998, it was found that of those younger than two months, 7 cases (4.7%) had not been immunized. Of the 26 cases (17.3%) between 2-3 months of age, 16 had not been immunized, and 10 had had only one dose. Of the four cases (2.73%) between 4-5 months of age, one had not been immunized, two had had only one dose, and one had had two doses. Of the 12 cases (8.0%) between 1-17 months of age, four had not been immunized, one had had only one dose, three had had two doses, and four had had three doses. Of the 13 cases (8.7%) between 18 months and four years, one had not been immunized, one had had three doses, and 11 had had four doses. Of the 37 cases (24.7%) between 5-9 years, one had not been immunized, three had had three doses, and 33 (22%) had had four doses. Of those in the 10-19 year group, nine (6%) had had complete immunization. Of all 150 cases, 63 (41%) had had four doses. Of them, 53 (35%) were younger than 20 years (Table 3).

8. Attack Rate by Age

In 1997 for instance, the attack rate was the highest in the age group under one year; then, in age groups 5-9 years and 1-4 years. The attack rates were lower in age groups 10-19 years and 40 years and above (Table 4).

9. Distribution of Symptoms

Of the 150 cases in 1996-1998 for them questionnaire surveys were conducted, 98.0% had coughing, 76.0% had paroxysms of coughing, 39.3% had whooping, 28.0% had cyanosis, 40.0% had vomiting, and 22.6% had asphyxia.

Discussion

1. There were more pertussis cases in 1997 than the 15 cases in 1996; and the number of reported cases was also the highest, increasing from 146 in the previous year to 477. A few counties (Yunlin, Kinmen and Matsu) did not report cases. In the greater Taipei area (Taipei City and County), a total of 339 cases (71%) was reported. 82 of them were positive, giving a positive rate of 24%. In other counties and cities, a total of 138 cases were reported; of them, 19 were positive, giving a positive rate of 13.7%. The positive rate in the greater Taipei area was significantly different from that of other counties and cities ($p<0.05$). In the southern counties and cities in the six years, only 91 cases were reported. Of them, two were positive. According to the incidence of reported cases, geographically, Taipei County and City were the high infection areas.
2. Various medical centers, with different degrees of development in pertussis laboratory techniques, reported cases with a large discrepancy. Many factors are associated with laboratory testing, cases of pertussis are often underestimated. When patients demonstrate chronic and typical symptoms, or coughing for more than two weeks, blood specimens can be collected for WBC counting or serum antibody test. The findings,

however, are for information only. Though culturing is the rule of laboratory diagnosis, collection of nasopharyngeal swabs and preparation of special culture media, and the cost and time required for testing are some technical problems, and are a burden to hospitals and patients. Therefore, if the sensitivity of PCR is close to that of nasopharyngeal and pharyngeal swabs, PCR testing by using pharyngeal swabs seems to be the most useful method of diagnosis. Medical centers have brought in PCR techniques. Early diagnosis and reporting of pertussis cases are still the most important means of disease prevention and control.

3. The effect of vaccines is another issue. Before 1993, vaccines were procured by the Provincial and municipal health departments separately. Vaccines procured in 1989-1992 by various administrations were different. People could have their immunization at different places at different times for the total four doses. Chances are they would be immunized with vaccines of different brands. Immunization records of the 150 confirmed cases in 1996-1998 showed that 41% of them had completed the four doses. The protection of vaccines is estimated to last for 12 years. Of those under 20 years who had had four doses, 35%, or one-third, who were supposed to be still under the protection of the vaccines, had been infected. On the other hand, from the prespective of immunization and seriousness of disease process, in 1997 for instance, of the 21 hospitalized cases, only one had had the complete immunization series , suggesting that immunization was still effective in the control of symptoms.
4. The odds ratio of attack rate for children under one year of age was the highest; and attack rates in general for children under nine years of age were higher. There were two peaks in the age distribution of cases; one was young children in age groups under nine years, and the other, their

caretakers in the 30-39 age group. The ages of patients seemed to have moved upward, and the number of cases older than 10 years increased year by year; while the proportion of cases under one year of age declined. How to prevent adults from bringing home pathogenic agents to infect young children without immunity is one major aspect of the control measures.

5. Vaccines and the use of antibiotics in Taiwan have resulted in many pertussis infections with unrecognized symptoms. Only partially immunized young children show typical symptoms, and will be reported by medical care personnel as suspected pertussis cases. Sero-epidemiological investigations will reveal the infection status by age groups. The National Taiwan University Hospital brought in DTaP vaccines, and measured the basic serum values of the whole-cell vaccines in 1991[51]. However, no sero-epidemiological data were available for adolescents and adults. And yet, they are the major target groups for disease prevention and control. Serological studies are therefore recommended. If it is proved that children of school ages 5-9 years are low in immunity, they should be given one booster of DTaP to improve their immunity.

Management and Control at Time of Epidemics

1. Appropriate management at the time of epidemics includes complete immunization of susceptible young children, development of vigilance to the infection, early identification of cases and management of patients and contacts, and prompt reporting to health authorities.
2. Administer erythromycin for 14 days. Pertussis bacteria can be eliminated after five days of erythromycin use. However, 10% of patients without 14 days of erythromycin use may develop symptoms again.

3. Supportive treatment: Patients younger than one year with paroxysms, dyspnea, and cyanosis, must be placed in hospital care with antibiotics and supportive treatment such as oxygen administration, intravenous fluids, total intravenous alimentation, and nasal suctioning. Studies have shown that Salbutamol will reduce the frequency and duration of paroxysms.
4. Hospitalized patients must be isolated for at least five days until the antibiotic treatment is completed.
5. The use of erythromycin in suspected cases has been proved to be effective in the prevention of secondary transmission. Prophylactic medication by erythromycin can reduce secondary attack from 35% to 4%. In one study, the attack rate was reduced from 75% to 16% two weeks after prophylactic medication. Each household contact, regardless of his/her age and immunization status, should be given prophylactic medication for 14 days.
6. Children with symptoms must be isolated. They are allowed to return to school only after five days of medication or the disappearance of symptoms.
7. During epidemics, treatment and prophylactic medication should begin before the culture reports are available.
8. Cases of occupational exposure should be given antibiotics soon after exposure for 14 days. Cases with symptoms should be ordered to rest and placed on antibiotic treatment for at least five days.
9. All close contacts should be given prophylactic medication.

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Table1 Laboratory Diagnosis of Pertussis

Patients	Laboratory Methods Used[a]				
	1-2weeks		3-4weeks		＞4weeks
	not treated	treated[b]	not treated	treated[b]	not treated of treated
Infants not immunized	PCR, culture, DFA[c]	PCR, DFA	Culture (PCR)	Serology[d] (PCR)	Serology
Young children not immunized	PCR, culture, DFA	PCR, DFA	PCR, serology (culture)	Serology (PCR)	Serology
Infants and young children immunized	PCR, culture, DFA	PCR, DFA	PCR, serology (culture)	Serology (PCR)	Serology
Adolescents and adults	PCR, culture, DFA	PCR, DFA	PCR, serology (culture)	Serology (PCR)	Serology

[a] When many methods were used for one item, the first method was more adequate. Sensitivity of methods in parentheses declined in the nest stages of disease process.
[b] Less than one week of treatment with adequate antibiotics
[c] DFA used with either culture or PCR
[d] Newborns many not produce specific IgA antibodies.

Table2 Incidence per 100,000 Population by County and City

County/City	1998	1997	1996	1995	1994	1993
Taipei Co.	0.37	1.20	0.21	0.28	0.13	0.13
Taipei C.	0.30	1.60		0.26		0.04
Taitung Co.		0.79			0.39	
Taoyuan Co.		0.13				0.07
Changhua Co.	0.38	0.18	0.08	0.47		
Taichung Co.	0.20	0.42			0.08	
Kaohsiung C.			0.07			
Hsinchu Co.			0.74	0.25		
Nantou Co.		0.29				
Hsinchu C.		0.29				
Yunlin Co.	0.53					
Taichung C.			0.24	0.36		
Ilan Co.						0.22
Hualien Co.	0.28					
Penghu Co.			1.10			

Note：No Confirmed cases of pertussis had been reported from Keeling City, Miaoli County, Tainan City and County, Kaohsiung County, Pingtung County, Kinmen and Matsu in the six year period.

Table 3 Immunization Records by Age

Age	Dose Recommended	Immunization Record						Total
		0	1	2	3	4	unknown	
Under 2 months	0	7						7
2-3months	1	16	10					26
4-5months	2	1	2	1				4
6-17months	3	4	1	3	4			12
18months-4 years	4	1			1	11		13
5-9 years	4	1			3	33		37
10-19 years	4	0				9		9
20-29 years	4	1				5	3	9
30-39 years	4	2				5	14	21
40-49 years	0	3					3	6
50-59 years	0	2				0		2
60 years and above	0	4						4
Total		42	13	4	8	63	20	150

Source: Annual Report of Communicable Disease in the Taiwan Area, National Quarantine Service, 1996-1998

Note: DPT combined vaccines were bought into Taiwan for use in 1954. Persons of 45 years and above would have not been immunized with DPT

Table 4 Age-Specific Attack Rates of Pertussis, Taiwan, 1997

Age	No. of Cases (%)	1997 Mid-year Population	Age-Specific Attack Rate (1/100,000)	Relative Odds Ratio
<1 year	23 (23.0%)	300,000	7.67	35.46*
1-4 years	16 (16.0%)	1,280,000	1.25	5.78*
5-9 years	28 (28.0%)	1,600,000	1.75	8.09*
10-19 years	3 (3.0%)	3,760,000	0.08	0.37
20-29 years	8 (8.0%)	3,700,000	0.22	參考值 (reference)
30-39 years	17 (17.0%)	3,820,000	0.46	2.06
>=40 years	6 (6.0%)	7,140,000	0.08	0.39
Total	101 (100.0%)	21,600,000	0.47	1.88

*P<0.05 by χ^2 test