Pertussis: epidemiology and control*

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Pertussis is a common, highly infectious, respiratory disease that predominantly affects children. As many as 60 million cases with more than half a million deaths occur annually. The highest incidence rates are observed in developing countries where immunization coverage is low. Accurate diagnosis under field conditions is hampered by current laboratory methods. The control of pertussis is accomplished largely through immunization and improvement of socioeconomic conditions. Although the adsorbed DPT vaccine is associated with some side-effects, its benefits outweigh the risks when the vaccine sequelae are compared to the morbidity and mortality caused by the natural disease. Surveillance of pertussis and outbreak investigations provide valuable information about the disease and the effectiveness of ongoing immunization programmes.

Pertussis (whooping cough) is a common childhood disease, which typically is responsible for exhausting paroxysms of coughing over several weeks. There is no effective treatment.

WHO estimates that the total number of cases of pertussis is 60 million annually, and that the disease is responsible for half a million to one million deaths per annum. The following annual incidence rates were reported for 1982: 2–2000 per 100 000 in the WHO African Region; less than 1–590 per 100 000 in the Western Pacific Region; and 0.25–85 per 100 000 in the European Region. Reliable statistics on the incidence rates are not available, since in many countries the disease is not notifiable. In developing countries the great majority of cases are not likely to be reported either because of deficiencies in the reporting system or because the patient does not come into contact with the health services; even in England and Wales it has been estimated that only 10–20% of all cases are reported (I). Furthermore, the disease may go unrecognized by health staff. Nevertheless, inter- and intraregional differences may to some extent reflect immunization coverage.

The epidemiology of pertussis is unusual in that infants are susceptible from birth. Infections producing the disease in mild form may go unrecognized and are common, particularly among immunized children and adults. At present, no satisfactory methods are available to monitor immunity to pertussis, although the development of new serological techniques holds promise for the future. Over the last 30 years routine immunization of infants has been accompanied by a dramatic decrease in the incidence of pertussis in countries where high vaccine coverage rates have been maintained.

THE DISEASE

Pertussis is an acute, highly communicable disease in man, predominantly affecting children, and is
caused by *Bordetella pertussis*. The disease varies clinically from severe illness with frequent coughing paroxysms followed by an inspiratory whoop to very mild cases that may be mistaken for a cold; the latter form occurs mostly in adults. In young infants the disease may not be recognized because the paroxysms of coughing may be followed by choking rather than a whoop. Other patients may present with pneumonia accompanied by an atypical cough (2).

The incubation period for whooping cough is usually 7–10 days and the clinical illness has two distinct stages. The catarrhal phase, lasting up to two weeks, is characterized by low-grade fever, coryza, and a mild intermittent cough. The cough gradually intensifies and becomes paroxysmal. The second stage is characterized by these spasms of coughing and is called the spasmotic or paroxysmal phase. The racking cough of this phase lasts 4–6 weeks and may continue even longer (hence the name "the one-hundred-day cough", used in several countries).

During the paroxysmal phase, thick mucus forms in the airways of the lung, and mucus plugs often cause atelectasis and subsegmental collapse. While pneumonia is not uncommon (20% in some hospital series), long-term pulmonary problems are rare (3, 4).

Infants, especially, may sustain apnoea and hypoxaemia during coughing spells. Neurological complications of pertussis range from fine tremors occurring simultaneously with coughing to generalized seizures. It is generally agreed that major neurological problems are observed in less than 5% of patients with pertussis. The incidence of encephalopathy in one large series of 6000 hospitalized children was 1% (5).

The disease is probably only transmitted by droplet infection, i.e., by direct contact with organisms coughed up by an infected person, and is generally more prevalent among those living under crowded conditions. A patient remains infectious from 2 weeks to 3 months after the onset of the catarrhal stage. Subclinical reinfections do occur, although their frequency is not known with certainty. One attack of clinical pertussis is usually sufficient to provide immunity against a second, clinically manifest infection later in life.

**Diagnosis**

In areas where the population is familiar with the symptoms of pertussis, the mother of the child often makes a presumptive diagnosis. Frequently, health staff have to make their diagnosis based on the case history reported by the mother because the typical paroxysms may not occur during the examination.

Laboratory tests for the diagnosis of pertussis, should they be available, often give results that are equivocal. Culture techniques have, under optimum conditions, indicated isolation rates of 40–60% from clinically typical cases. A specimen for culture of *B. pertussis* is best obtained by pernasal swab. In contrast, the technique involving cough plates, though still used, produces few positive cultures. A low yield of *B. pertussis* is isolated using transport media. Inoculation of Bordet-Gengou plates in the field is, however, rarely practical. Direct analysis of nasopharyngeal smears using a fluorescent antibody test can be used as an additional method of demonstrating the presence of *B. pertussis*. The test is relatively easy to carry out, and smears can be collected and stored for later examination; however, the sensitivity and specificity of the test have not yet been fully defined.

Almost all antibody studies are based on the detection of agglutinins in serum. In general, immunization usually elicits a satisfactory agglutinating antibody response, whereas infection with the natural disease often does not. For pertussis, agglutinating antibodies may be absent in up to 40% of culture-proven cases of the disease when paired sera are compared at an interval of 2 months (6). The frequency of false positives may be reduced by absorbing the sera before testing (7).

A total white-blood-cell count and a differential lymphocyte count can be of assistance in confirming the clinical diagnosis, and white-blood-cell counts of > 30 000 with ≥ 60% lymphocytes strongly support a clinical diagnosis of pertussis.

**EPIDEMIOLOGY**

**Incidence rates**

In Europe, depending on country, the annual incidence rate ranges from 0.25 to 85 per 100 000 population. On the whole, increases in vaccine coverage rates correlate with a decrease in incidence of the disease.

A population-based, longitudinal study in Mackos, Kenya, involving active pertussis surveillance, initially by fortnightly and subsequently by monthly domestic visits, was performed over 7 years and indicated an annual incidence rate of 16 per 1000 children under 15 years of age (8, 9). Immunization coverage in the study area was low. An investigation in the Guatemalan village of Santa Maria Cauqué showed an attack rate of 19% for children ≤ 14 years (10). Because pertussis had not occurred in the study area for 10 years, the pool of susceptibles was very large. When the attack rate is adjusted, the annual average incidence is 19 per 1000 children under 15 years of age—a value quite similar to that in the Kenyan study.
Many early reports have commented on the ubiquity of pertussis in the pre-vaccine era (11-13). WHO has estimated that in countries without an immunization programme 80% of surviving newborns will acquire pertussis in the first 5 years of life (17). Approximately half of these cases will be of the classical type.

**Mortality**

Reported fatality rates for hospitalized cases range from 0.05% in England and Wales to almost 14% in Uganda (14). Mortality is inordinately frequent in children below the age of 1 year (12), being particularly so during the first few months of life (13).

The above-mentioned study in Kenya revealed a case fatality rate of 1.2% among children younger than 15 years of age, while among infants the rate was 3.2% (6). In the Santa Maria Cauqué study 15% of cases died, the deaths among girls being twice as frequent as among boys (10). It is interesting to note that the highest mortality (44% of all deaths) occurred in the second year of life.

**Epidemic pattern**

In England and Wales pertussis occurs in epidemic waves with a period of 3–4 years. This pattern has been remarkably constant over the years, in spite of considerable fluctuations in vaccine coverage, and this may be because the total number of susceptibles was not affected by immunization (11). In Machakos, Kenya, a pattern of increased incidence with a 3-year period was observed.

**Age and sex distribution**

Unlike most infectious diseases, pertussis can develop soon after birth (14, 15). Passive immunity through transfer of maternal antibodies is uncommon because most women of child-bearing age lack demonstrable levels of antibodies; however, infants who do have maternal antibodies at the time of immunization exhibit a reduced antibody response (16, 17). A history of clinical pertussis in the mother and/or of her having received pertussis vaccine in infancy or early childhood does not correlate with the presence or level of antibodies in the serum of the newborn infant (18).

The medium age of pertussis cases in developing countries is generally lower than that in the pre-immunization era in Europe and North America. Analysis of collated data from outpatient clinics in 17 developing countries indicated that the median age of cases ranged from 1.4 to 2.7 years (19). In contrast, the median age of cases in the Machakos study was 3.5 years, and, of the 953 cases recorded, 69% were children under 5 years of age: 17% were infants (i.e., less than 1 year of age); and 14% were children of 3–4 years of age. Although fewer in number, 3–4-year olds had a higher attack rate than infants. In the USA, where only young infants are not protected by immunization, the highest incidence rates of cases reported between 1979 and 1981 were among children of less than 1 year of age (20). Recent studies of outbreaks of pertussis reveal that a large proportion of infections occur in older children and adults (21, 22); many of these are atypical cases. All studies report a higher attack rate among girls than boys.

**Secondary attack rates**

In the early fifties, during a British vaccine trial, an 87% secondary attack rate was found among non-immunized household contacts under 5 years of age (23). During a pertussis outbreak in Atlanta, GA, USA, the secondary attack rate among household contacts ranged from 89% among non-immunized infants to 8% among adults older than 20 years of age of unknown immunization status (24). Similar secondary attack rates were found in the USA by the Pertussis Sporadic Case Reports Surveillance System (20) and also by a study in Finland (22).

**Asymptomatic infection**

True asymptomatic pertussis infections are probably rare. If monitored carefully for the occurrence of symptoms, most culture-positive contacts of pertussis cases will develop an illness similar to an ordinary upper respiratory tract infection (25). Chronic carriers do not exist (26). There is increasing evidence that adults (often with the disease in mild form) are the most common source of infection of young, non-immunized infants in populations with good immunization coverage (15).

**Pertussis and malnutrition**

Weight loss following pertussis has been reported (10, 19); however, in a study in Kenya no significant difference was found between the upper arm circumference of cases and matched controls 3 months, 1 year, and 2 years after the disease (6). Furthermore, no relationship has been established between pre-existing malnutrition and severity of pertussis. Indeed, the case fatality rate is highest in pre-weaned children, an age when weight gain is usually satisfactory.

**Role of Bordetella parapertussis and adenovirus**

*Bordetella parapertussis* has a major self-specific antigen and a minor antigen in common with
B. pertussis. This gives rise to a degree of cross-agglutination with B. pertussis, but not to cross-immunity. In short-term studies B. parapertussis has been detected in up to 20–30% of all Bordetella isolations; however, in long-term studies the level is usually less than 5% (27). One explanation for this might be that high isolation rates of B. parapertussis coincide with epidemics caused by this microorganism. B. parapertussis infections are probably as equally widespread as those of B. pertussis, but only a small proportion of them are clinically recognized. Asymptomatic parapertussis infections are common.

On the basis of observations over an 11-year period prior to the introduction of routine immunization in Denmark, the incidence of infection caused by B. pertussis was more than 20 times higher than that associated with B. parapertussis. After introduction of routine immunization, both pertussis and parapertussis epidemics decreased in magnitude (27). B. pertussis, but not B. parapertussis, has been recovered from family members of two seriously ill patients from whom B. parapertussis was isolated (28). These observations suggest that parapertussis and pertussis do not constitute two distinct infections but may both be caused by B. pertussis and that B. parapertussis may represent a non-toxigenic strain of B. pertussis (29). On the other hand, in laboratory examinations the two organisms have different characteristics.

Regular DPT vaccine to which has been added killed B. parapertussis organisms is highly effective in preventing infection with B. parapertussis (30); however, it appears that such infections do not constitute a major threat to the control of clinical pertussis by immunization. Many reports of a pertussis-like syndrome associated with adenovirus have appeared (31-33). In some instances, adenovirus, but not B. pertussis, has been isolated from children with clinically diagnosed pertussis (31). Other studies of clinical “pertussis” indicate that the recovery rate of adenovirus was no greater from patients who were culture-negative for B. pertussis than from those who were culture-positive. This suggests that adenovirus is not a major causative agent of pertussis (25), and that outbreaks of the disease should be assumed to be caused by B. pertussis until proven otherwise.

CONTROL OF PERTUSSIS

In industrial countries incidence rates of pertussis, like those of many other infectious diseases, have gradually decreased since the early part of the twentieth century, presumably largely because of greatly improved socioeconomic conditions (34). However, there is little doubt that the rate of reduction of morbidity, and particularly of mortality, from pertussis has increased considerably since the introduction of pertussis immunization (35). In recent years, however, public concern and conflicting views within the medical profession have raised the question in some developed countries as to whether the benefits of pertussis immunization outweigh its risks (36, 37). This led to reduced vaccine acceptance or official discontinuation of routine pertussis immunization in countries such as Japan, Sweden, and the United Kingdom, followed by an upsurge in pertussis incidence. Official policy in most industrial countries continues to recommend routine pertussis immunization of all infants, because the weight of scientific evidence still favours this practice (37-39). The argument in favour of routine pertussis immunization is even more cogent in developing nations, where the disease is common and morbidity and mortality rates are high.

The vaccine

Controlled trials in the 1940s in the USA (40, 41) and the United Kingdom (23, 42, 43) have left little doubt about the efficacy of a variety of pertussis vaccines. Recent studies of intrafamilial spread of secondary cases of pertussis among immunized and non-immunized contacts indicate a vaccine efficacy of 62–80% (20, 44).

Adsorbed DPT vaccine is now used in most countries, but both the number of killed B. pertussis organisms in the vaccine—usually between 10×10⁶ and 16×10⁹ per dose—and production methods vary, leading to vaccines of different potencies. The situation is complicated by the fact that the mouse protection test used to determine the protective capacity of the vaccine is unsatisfactory (45).

The presence of high titres of agglutinins (>1/320) in human serum is usually considered to indicate immunity to pertussis, although the relation between immunity and agglutinating antibody titres is not unequivocal (46). One reason for this may be that for a positive result in the agglutinating antibody test it is sufficient that any one of the three major agglutinin types be present in serum (45). The absence of agglutinating antibodies does not exclude protection; indeed, these antibodies are frequently absent after a bout of the natural disease, which, of course, confers definite and prolonged immunity in most cases.

The duration of immunity after immunization is not clear, but vaccinees who develop pertussis tend to experience a milder form of the illness (47). In general, the greater the number of doses of vaccine received by an individual the milder are the disease’s signs and symptoms (24). It has been observed that even one dose of pertussis vaccine gives some protection against a fatal outcome (19). The existence of persistent immunity in populations immunized
against pertussis depends on the occurrence of subclinical or mild infections (25).

The occurrence of fever and mild local reactions related to the pertussis component of DPT vaccine are common. The estimated risk of severe neurological illness attributable to DPT is 1 in 170,000 administered doses, while that for permanent neurological sequelae is 1 in 470,000 doses.4

**Immunization schedules**

**Age at time of immunization.** Because young infants are at risk of contracting a severe form of pertussis, their early immunization is important. Interference by maternal antibodies with the infant's antibody response to the vaccine is of no significance because these are usually absent. Unfortunately, if pertussis immunization is started within 24 hours of birth and is followed by 2 doses at monthly intervals the agglutinating antibody response produced is not adequate (48). Nevertheless, it has been reported that adequate protection is afforded when the primary series of vaccine is given at 1, 6, and 12 weeks after birth, followed by a booster at 1 year of age, but details of the trial were not given (49). In a study in Nigeria (50), pertussis incidence over a 2-year follow-up period after three doses of DPT administered at monthly intervals starting at birth was similar to the incidence in a group of children who received the first dose at 1 month of age. The youngest children included in the original trials of pertussis vaccine in the USA (40, 41) were 2 months of age, while a study in New Orleans (51) suggested that administration of the first dose between 1 and 2 months of age, followed by two doses at monthly intervals was also effective.

The presence of high protective antibody titres in 29 mothers and newborn infants has been reported after immunization of the mother during the sixth or seventh month of pregnancy (52). Serious general adverse reactions did not occur, but local reactions were common and at times very painful. The protective effect for the young infant and the safety of antenatal immunization for both mother and child need to be investigated further.

Currently, depending on the country, the age at which a child is given the first dose of DPT vaccine varies from 5 weeks to 6 months. For countries with a high incidence of pertussis, WHO recommends that immunization should start at 6 weeks of age and that the schedule involve three doses spaced at 4-week intervals (53). The administration of a booster dose at school entry, i.e., at 6 years of age, is not universally accepted. There is no evidence, however, that the adverse effects caused by pertussis vaccine are more serious in adults than in children. In one study, 436 adults were vaccinated, because of an outbreak of pertussis among hospital staff (54). Agglutinating antibody response was satisfactory in 77% of vaccinees, and no serious general reaction occurred, although local reactions were common (52, 54).

**Spacing and number of doses.** The usual DPT immunization schedule consists of a primary series of three doses, at least 4 weeks apart, a booster dose 1 year later, and, in some countries a second booster dose at school entry. Delaying the third dose of the primary series until 4–5 months after the second produces a higher mean antibody response but postpones the development of a high degree of protection (55).

For developing countries a primary series of two rather than three vaccine doses would simplify immunization schedules by reducing the number of contacts of the child with the health services. In the original trials of pertussis vaccine in the USA, two doses of an alum-precipitated vaccine containing $10 \times 10^9$ B. pertussis organisms per dose at 4-week intervals were found to be highly effective in a 2–3-year follow-up study (40, 41). A primary series of two widely spaced doses of DPT (more than 2 months apart) stimulates an agglutinin response comparable to the three-dose routine schedule (17, 56), but agglutinating antibody titres were lower after two doses of DPT at 2-month intervals than after three doses at 1-month intervals (57). In a study in Machakos, Kenya, a rather rapid decrease in the number of agglutinating antibodies was found after a period of 2 years and this was more pronounced after two DPT doses at an interval of 6 months than after three doses at an interval of 3 months (8). In Machakos, serotypes 1, 2, 3 and 1, 2, 3, 4 preclude (58).

Since factor 2 is the most potent immunogen, protection against serotype 1, 3, 4 is somewhat uncertain without the third dose of vaccine (59). There was no significant difference in the incidence of pertussis in Machakos over a 4-year follow-up study involving two or three doses of a high potency vaccine. The trend that emerged, however, suggested that the three-dose schedule provided greater protection (8). A 74% reduction in attack rates was observed among the trial children relative to that among controls of the same age. Vaccine efficacy was estimated to be 58% in New Zealand, where a schedule providing two doses at 3 and 5 months of age has been in operation since 1971 (60). In an investigation of an outbreak of pertussis in North Sulawesi, Indonesia, where the recommended full course of DPT consists of two doses given between 3 and 14 months of age separated by an interval of at least 3 months, vaccine efficacy

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was estimated to be 87% (47). A study in East Java showed that two doses of DPT vaccine administered 3 months apart produced a better agglutinating antibody response than two doses at an interval of 6 weeks.\(^b\) The available literature suggests that a two-dose schedule might be considered if there is limited access to health services; however, the major limitation for infants of such a schedule is the long period of risk without adequate protection between doses. Unless the interval can be shortened to 4 weeks, wide use of this schedule is not advisable in endemic areas.

It might be expected that high vaccine coverage would provide herd immunity and reduce the risk of disease among infants who have not yet been immunized. However, pertussis vaccine is more effective in protecting against disease than against infection (11, 24), and even in countries where vaccine coverage is excellent, transmission of pertussis continues. The concept of herd immunity is further weakened by evidence that immunized adults in developed nations are the most common source of pertussis infections in neonates and children (15).

**Effects of malnutrition and infection on the immune response to vaccines**

Data on the effect of malnutrition and infections on the immune response to vaccines have been reviewed recently (62, 63); however, little information is available on the response of malnourished children to DPT vaccine. Although the immune reactions of malnourished children are impaired, there is no evidence that the response to DPT vaccine is inadequate, and, in general, malnutrition is considered an indication rather than a contraindication for immunization. Contraindications have been extensively reviewed and it was concluded that low-grade fever, mild respiratory infection, or diarrhoea should not be considered a contraindication to immunization (63).

**SURVEILLANCE**

**Routine reporting**

In many countries pertussis is not a notifiable disease, but even where it is, the completeness of reporting varies and is often not known. However, notification rates may at least reflect trends in disease incidence. In England and Wales the age-specific notification rates and consultation rates for pertussis in a limited number of general practices correlate well with the isolation rates of *B. pertussis* from laboratory analysis of samples from suspects. Completeness of reporting can be evaluated by comparing the actual number of reported cases with the estimated number of probable cases, calculated by multiplying the number of newborns by a crude incidence of 0.3 (300/1000). When calculated in this way, the number of cases must be corrected for the number of fully and partially immune children who are at reduced risk. Such estimates are more valuable in gauging long-term trends since no account of cyclic pertussis activity is included in the calculation. As previously noted, the unfortunate reality is that information on pertussis incidence, even in countries where it is a notifiable disease, is poor, and some reasons for this, together with suggested solutions, are shown in Table 1.

**Sentinel disease surveillance**

Sentinel systems have been extensively described and are probably the most efficient method of obtaining data for monitoring and evaluation, particularly since the routine system of disease reporting in many countries is deficient.\(^c\) Retrospective analysis of hospital records to calculate the proportion of all paediatric hospitalizations and of all known deaths from pertussis may provide useful data on disease trends, although records should be interpreted with caution, as shown for measles in the Machakos study (64). It may also be useful to

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\(^c\) Dondero, T. *EPI target disease surveillance and disease reduction targets*, unpublished WHO document EPI/GEN/84/6.

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**Table 1. Some problems encountered in obtaining accurate information about incidence of pertussis, together with some solutions**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Proposed solution</th>
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<tr>
<td>Sick children not brought to attention of health facilities</td>
<td>Consider introduction of lay reporting networks</td>
</tr>
<tr>
<td>Providers do not report illness</td>
<td>Provide incentives, feedback, and support</td>
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<tr>
<td>Providers report but diagnosis is incorrect</td>
<td>Provide in-service training and disease-identification criteria</td>
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<tr>
<td>Information systems inefficient, data lost, data not used after collection, or no local use made of reports</td>
<td>Simplify reporting requirements, reduce number of reportable diseases. Encourage local data analysis and rapid transmission. Consider sentinel systems for early case detection. Provide incentives for good reporting.</td>
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compare the number of reported cases of pertussis within a district with those of measles. In the absence of major differences in immunization coverage for the two diseases, similar trends can be expected for both. Also, incidence rates may be compared with those obtained from other districts.

Active surveillance

The active search for cases of pertussis has occasionally been carried out as part of prospective, population-based studies. Approaches of this type yield data of relatively high reliability but are expensive and require extensive supervision, and both these factors limit the size of the study population. The high resource requirements also make population-based studies difficult to repeat.

Large-scale culture of nasopharyngeal samples from healthy children is not a realistic method of active surveillance. In one such study, only five positive pertussis cultures were found among 1102 swabs taken from healthy babies, preschool-age children, and family and neighbourhood contacts of all ages in New Orleans at a time when pertussis was epidemic (26). The five positive cultures came from persons with mild upper respiratory symptoms or persons who developed a cough soon afterwards.

Cross-sectional morbidity and mortality surveys

Cross-sectional surveys are considerably easier to carry out than prospective studies. Surveys of this type are performed to obtain information on age-specific attack rates, vaccine efficacy, case fatality rates, and, in some instances, secondary attack rates; however, they require a sizeable investment of manpower and organizational effort. The reliability of such studies depends on the ability of the mother to recognize pertussis and to report it to the investigator, and this is liable to vary from one area to another.

It is not purposeful to carry out cross-sectional surveys of morbidity from pertussis without also having the means to estimate their reliability. In this respect attention is drawn to a study in Kenya involving 830 mothers whose children had been diagnosed as having pertussis 6–12 months previously (6). Most (94%) confirmed that their child had suffered from pertussis, but half of the mothers gave a different account of the duration and nature of the symptoms, while 6% denied that their child had had pertussis. No conclusions can be drawn from this small study about the reliability of the mothers’ accounts, particularly because mothers whose children had not been diagnosed as having pertussis were not included. Nevertheless, in the absence of reliability measurements, cross-sectional studies of morbidity should use a short recall period, not exceeding 6 months.

Serological tools for disease confirmation. In recent years an enzyme-linked immunosorbent assay (ELISA) technique that is more sensitive than agglutination tests has been developed for the determination of B. pertussis-specific IgA, IgG, and IgM antibodies in serum. The technique uses either whole or fractionated antigen (65–67), fimbrial haemagglutinin (FHA), and lymphocytosis promoting factor (LPF) (17, 68). High IgA antibody levels appear to be the result of infection rather than immunization, but further evaluation of the ELISA test for diagnostic purposes requires prospective serological studies. The determination by ELISA of secretory IgA antibodies in nasal secretions may also be of value in the detection of recent pertussis infections (69). If further studies confirm the epidemiological value of determining pertussis IgA antibodies in serum and nasal secretions, the ELISA test will be a powerful tool for disease investigation, especially if it can be used under field conditions.

Outbreak investigations

Outbreak investigations are of considerable potential value since, if well planned, they provide age-specific attack rates, case fatality rates, the rate of secondary cases, and vaccine efficacy data. Before any such studies are undertaken, however, the diagnosis of pertussis must be verified. Only then should an outbreak investigation be launched. Guidelines for carrying out an outbreak investigation have recently been developed by WHO, and the remainder of this section provides an overview of the procedures for carrying out such an investigation of a pertussis outbreak.

Planning

The quality and value of an outbreak investigation depend substantially on the thoroughness of the planning. A well-planned investigation will yield information that will contribute to the improvement of immunization services. The planning process should involve all available resource persons, especially those involved in collecting data and in their analysis. If previous investigations have been carried out, the individuals involved and their reports should be consulted. Resource documents on population and geography should also be obtained. Finally, a written case definition should be agreed upon and

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Strassburg, M. A. Guidelines for the investigation and control of outbreaks of EPI target diseases, unpublished WHO document EPI/GEN/84/7.
distributed to everyone involved in the investigation. For this purpose, standard case definitions have been prepared by WHO. The following steps in planning are important:

— The target information sought from the field work should be carefully outlined. Often this includes the name, address, age, sex, and immunization status of all cases. Data on the date of onset of illness, exposure history, deaths, and secondary cases may all need to be collected. After completion of this step, questionnaires should be drawn up, field-tested, and an investigation timetable planned.

— If laboratory information is to form part of the field study, the logistics of testing and the selection of tests should be discussed with laboratory personnel. Limitations on personnel and finance need to be considered as the scope of the investigation progresses.

— An important step in the planning process is the involvement and notification of politicians and medical practitioners in the outbreak area because they can provide substantial help in the field work.

Conducting the investigation

One individual should be responsible for supervising the investigation, and each day’s results must be reviewed and discussed with team members. Sick children encountered in the field work should be attended to with respect and kindness, and children who are severely ill ought to be referred to appropriate clinical facilities.

Outbreak control

A single dose of pertussis vaccine given to susceptibles provides little protection against infection. Hence, it is unlikely that immunization will play an important role in outbreak control. A course of erythromycin (50 mg/kg/day in four divided doses) from the beginning of the catarrhal stage to the paroxysmal stage usually renders children non-infectious. Erythromycin may also be effective in preventing illness among contacts (70). Nevertheless, cases of pertussis have been reported in children given prophylaxis, although no controlled trials have been carried out (71).

Analysis

Data collected from field work should be analysed to provide an epidemic curve, the age and sex distribution of cases, the severity of the illness, case fatality rates, attack rates (by age, sex and immunization status), and the geographical distribution of cases (to identify clusters). Vaccine efficacy can be determined by calculating the attack rate among immunized and non-immunized children. Secondary attack rates in households are also worth determining, and for this purpose a definition of a secondary case should be included at the planning stage. Once the investigation is completed, the data should be compiled into a report containing conclusions and recommendations. This in turn should be forwarded to the local health and administrative authorities, followed by a meeting between the investigators and the public health officials, which will help in follow-up.

NEW DEVELOPMENTS IN IMMUNIZATION

In recent years there have been various new approaches to pertussis immunization. Oral administration of a whole-cell vaccine (containing $10^9$ organisms) to newborns and young infants produces low titres of agglutinins in serum and higher titres in saliva, indicating local immunity (72). Small-scale trials suggest that aerosol pertussis vaccine imparts immunity by producing respiratory IgA antibodies (73). Such a vaccine might be particularly useful, should a rapid response be needed; however, further studies as to its usefulness in the control of pertussis need to be carried out.

A component vaccine against pertussis has been used in Japan on a large scale since 1981 (74). This vaccine contains purified fimbrial haemagglutinin (FHA) and lymphocytosis-promoting factor (LPF), and, after detoxification with formalin, is mixed with diphtheria and tetanus toxoids and adsorbed on aluminium hydroxide. In a non-randomized trial the pertussis secondary attack rate in households was 11% among children immunized with the component vaccine, 14% among those who received conventional whole-cell pertussis vaccine, and 83% among non-immunized children. Good anti-FHA, anti-LPF, and agglutinating antibody responses were produced by either vaccine, but side-effects were less with the component preparation. The efficacy of the component vaccine among children younger than 6 months of age could not be established in the trial because this age group was underrepresented. It is not yet known whether the component vaccine contains all three major serotypes of B. pertussis. This is of importance since lack of type 3 antigen may result in vaccine failure on the long term (74).

The Japanese acellular vaccine has been rigorously tested in several laboratories in Europe and the USA as part of a WHO Collaborative Study. The vaccine

* Provisional guidelines for the diagnosis and classification of EPI target diseases for primary health care, surveillance and special studies, unpublished WHO document EPI/GEN/83/4.

† OVENSTEIN, W. A. ET AL. Field evaluation of vaccine efficacy, unpublished WHO document EPI/GEN/84/10.
meets all the toxicity criteria required of current whole-cell vaccines but failed the standard intracerebral-challenge, mouse-protection test. Work is in progress to formulate detailed recommendations for methods of evaluating candidate acellular vaccines in the laboratory, and clinical trials should be designed to further evaluate the safety and efficacy of such vaccines (61).

RéSUMÉ
COQUELUCHE: ÉPIDÉMIOLOGIE ET LUTTE

Selon des estimations de l'OMS, le nombre total de cas de coqueluche est de 60 millions par an. Cette maladie entraîne chaque année la mort de 500 000 à 1 million de personnes. La coqueluche est difficile à diagnostiquer car les quintes typiques surviennent rarement au cours de l'examen. Le diagnostic repose donc sur les renseignements fournis par la mère. Les infections qui provoquent les formes bénignes de la maladie peuvent passer inaperçues et sont fréquentes, notamment chez les enfants et les adultes vaccinés; leur rôle dans la transmission de la maladie n'est toutefois pas clair.

L'épidémiologie de la coqueluche est inhabituelle en ce sens que les nourrissons y sont sensibles dès la naissance. Dans les pays en développement, où la couverture vaccinale est faible, l'âge médian au moment de l'infection est de 1,4 à 3,5 ans. Lors d'une étude longitudinale portant sur l'ensemble de la population, à Machakos, au Kenya, où la couverture vaccinale est faible, on a trouvé que 17% des cas étaient survenus chez des enfants de moins d'un an. Aux Etats-Unis d'Amérique, où seuls les très jeunes bébés ne sont pas protégés par la vaccination, les taux d'incidence des cas notifiés sont de loin les plus élevés pour une maladie infantile, et le taux d'atteinte secondaire chez les enfants de moins de cinq ans avoisine 80%.

Bien que l'incidence de la coqueluche dans les pays industrialisés ait diminué, en grande partie grâce à l'amélioration des conditions socio-économiques, il fait peu de doute que la baisse de morbidité et de mortalité observée est surtout due à l'introduction de la vaccination systématique de tous les enfants. La plupart des vaccins anticoquelucheux actuellement utilisés sont efficaces; toutefois, leur efficacité ne dépasse généralement pas 80% après administration des trois doses, et la durée de l'immunité n'est pas bien définie. Il n'en reste pas moins que les sujets vaccinés, même s'ils contractent la maladie, n'en présenteront qu'une forme atténuée.

Dans plusieurs pays de haut niveau socio-économique, l'administration systématique du vaccin anticoquelucheux est controversée en raison du risque faible mais incontestable associé à la vaccination. Toutefois, la plupart des pays industrialisés continuent de recommander la vaccination anticoquelucheuse systématique de tous les enfants. Dans les pays en développement, où la mortalité et la morbidité coqueluchées sont élevées, l'intérêt de la vaccination systématique l'emporte largement. On s'efforce actuelle-ment de mettre au point un nouveau vaccin "sous-unité" d'efficacité convenable mais qui n'aurait pas les effets indésirables associés aux vaccins actuels à germes entiers. De plus, des données fiables semblent indiquer que deux doses plus espacées d'un vaccin à forte activité pourraient, dans certains cas, remplacer l'administration en trois doses. Rien ne montre qu'une immunité collective, même avec une couverture vaccinale très importante, puisse diminuer le risque de maladie chez les enfants non vaccinés. Il n'a pas non plus été démontré que la malnutrition et les infections font obstacle à la réponse immunitaire au vaccin anticoquelucheux; ces états sont plutôt considérés comme des indications que comme des contre-indications à la vaccination.

Les systèmes de notification de la coqueluche sont très insuffisants, et cela dans le monde entier, soit parce que le malade ne passe pas par les services officiels de santé soit parce que, même s'il le fait, la maladie n'est pas correctement diagnostiquée. Il arrive aussi souvent que les agents de santé omettent de notifier la maladie ou que la notification ne soit pas convenablement transmise au sein du système de soins de santé. Dans de nombreux pays, l'établissement d'un système efficace de surveillance systématique peut relever de l'utopie, aussi envisagera-t-on de déléguer le travail de surveillance à un système "sentinelle". Au niveau du village, l'agent de santé communautaire peut être capable d'effectuer une surveillance active dans le cadre du système de soins de santé primaires. Il est utile de procéder à des enquêtes transversales de morbidité et de mortalité afin d'évaluer les programmes de vaccination et de faciliter l'étude des flambées. Toutefois, comme ces enquêtes reposent sur les renseignements fournis par la mère, la fiabilité de telles enquêtes ne peut être évaluée.

Il est utile d'étudier les flambées car elles fournissent des renseignements sur les taux d'atteinte selon l'âge, l'efficacité du vaccin, les taux de léthalité et peut-être les taux d'atteinte secondaire. Ces études exigent toutefois un investissement considérable en main-d'œuvre et en travail d'organisation et doivent être soigneusement planifiées, exécutées, analysées et rapportées pour présenter un quelconque intérêt. Les efforts de lutte contre la coqueluche doivent être axés sur la vaccination systématique de la population-cible. Lorsqu'une flambée se déclare, il est en effet difficile d'endiguer la maladie.

REFERENCES


40. Bell, J. A. Pertussis prophylaxis with two doses of alum-precipitated vaccine, Public health reports, 56: 1535–1546 (1941).


57. BHANDORI, B. Seroconversion following primary immunization with DPT vaccine: 2 versus 3 doses. Indian pediatrics, 18: 41 (1981)


