Pertussis outbreak detected by active surveillance in Cyprus in 2003

M Theodoridou[1], A Hadjipanagis[2], N Persianis[2], S Makri[3], C Hadjichristodoulou (xhatzi@med.uth.gr)[3]

1. First Department of Paediatrics, Agia Sofia Children's Hospital, University of Athens, Athens, Greece
2. Greece-Cyprus Paediatric Surveillance Unit, Nicosia, Cyprus
3. Department of Hygiene and Epidemiology, Faculty of Medicine, University of Thessaly, Larissa, Greece

Pertussis is a disease of substantial public health importance that still lacks an efficient surveillance system. It has been a notifiable disease in Cyprus since 1930, and has had an incidence rate of 1 per 100,000 persons during the last 10 years. In 2001, the Greece-Cyprus Paediatric Surveillance Unit (GCPSU) was established with the aim of active surveillance for rare paediatric diseases, including weekly data reporting, zero reporting, and obligatory laboratory tests. From November 2002, pertussis has been included in the active surveillance scheme of GCPSU, resulting in a very early detection of an outbreak in June 2003 that led to immediate and successful action.

Introduction

Although the introduction of childhood pertussis immunisation programmes has significantly reduced the occurrence of the disease in children, waning vaccine-induced immunity permits it to affect adolescents and adults, who in turn, transmit the disease to unimmunised or incompletely immunized infants [1,2]. In most developed countries, the incidence rate of pertussis is relatively low, but outbreaks are occurring every 3-5 years, and it is during those outbreaks that most adult cases are reported [1]. In almost all the countries where outbreaks have occurred, difficulties in implementing an efficient surveillance system for pertussis have been recognised. Different countries operate diverse vaccination and surveillance strategies [2,3]. In most European countries, a five-dose vaccination schedule is applied, and the passive notification surveillance system is used. In some countries, laboratory reporting is used as a supplementary surveillance system, while in others it is the only one [4,5]. In every passive surveillance system, an important issue is that the clinical diagnosis alone may not be specific and the laboratory confirmation is not always performed or standardised. Moreover, there is often a clear lack of awareness regarding loss of immunity and occurrence of the disease in adolescents and adults. The ongoing resurgence of pertussis in both developing and developed countries raises the demand for a more efficient surveillance system. The Global Pertussis Initiative [6,7,8,9] is an example of the international medical community's efforts to address this problem.

The GCPSU has been a member of the International Network of Paediatric Surveillance Units (INOPSU) [10] since 2002. The unit conducts active surveillance on rare paediatric diseases and common "target" communicable diseases, in order to evoke prompt public health actions. In Cyprus, there are 150,000 children aged 0-15 years. Eighty percent of these children are provided with a combined acellular diphtheria-tetanus vaccine by the private medical sector and 20 percent receive the whole cell vaccine by the public sector. The pertussis (DTPa) vaccine has been included in the childhood immunisation schedule at ages of 2, 4, 6, and 18 months and at 4-6 years of age since 1996. The coverage for pertussis vaccination of children aged 16-29 months (including DTP1, DTP2, and DTP3) in Cyprus has risen from 48% in 1980 to 97.7% in 1997 and 97.8% in 2003 (Cyprus Ministry of Health) [11]. These coverage rates are comparable to the rates of most developed countries or even higher [2,3]. Pertussis has been a notifiable disease in Cyprus since 1930. Individual data concerning every pertussis patient were mandatorily notified to the Ministry of Health with a delay of sometimes more than a month. Between 1995 and 2002, an average of less than seven pertussis cases per year were reported by the notification system, representing an incidence rate of 1 per 100,000 persons per year. Ninety percent of reported cases occurred in children less than one year of age. This report presents a pertussis outbreak detected and managed by active surveillance (GCPSU) in Cyprus.

Methods

The GCPSU surveillance system consists of all 196 paediatricians working in Cyprus, who voluntarily cooperate by reporting morbidity data. The GCPSU's goal is to support enhanced early detection, quantification, and localization of paediatric diseases of public health concern, on a national level. Real-time reporting is almost impossible, but collecting and analysing ambulatory clinical diagnoses, confirming them with reliable laboratory data and forwarding them for collection and analysis on a weekly basis through GCPSU is feasible, as shown below.

In November 2002, pertussis was included in the GCPSU surveillance scheme. It was considered a rare disease because of low incidence and high vaccination coverage of the population. The initiation of active pertussis surveillance was accompanied by an informative campaign of paediatricians to increase their awareness about the clinical and laboratory diagnosis of pertussis. Paediatricians ere encouraged to report "suspected" pertussis cases of any age, or provide a zero report on a weekly basis. There was a weekly deadline for the report, and physicians were contacted and reminded by telephone if the deadline was ignored. Every suspected case was initially reported, including information regarding sex, age and place of residence. If the case was laboratory-confirmed later, a detailed questionnaire was used to collect additional information on the vaccination status and about the possible source of infection.

For surveillance purposes, a patient that presented with a coughing illness lasting more than 14 days with either paroxysms of cough, inspiratory 'whoop', or post-tussive vomiting, without other apparent cause, was defined as a "suspected" pertussis case and had to be reported. Every suspected case had to be laboratory-confirmed by detection of *Bordetella pertussis*-specific IgA. All laboratory tests were carried out at the same reference laboratory in order to ensure consistency and reliability of the result. During the 2003 pertussis outbreak, case investigations were conducted to identify possible sources of infection among the household contacts.

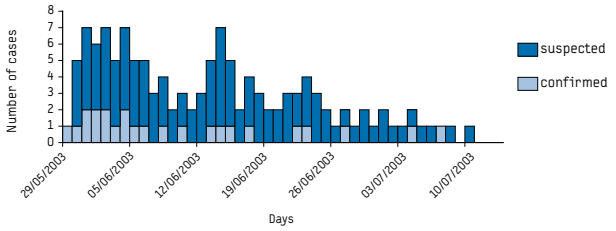
Results

Outbreak detection

During the period between June and early July 2003, the GCPSU recorded 128 "suspected" pertussis cases, 24 of which were confirmed by the detection of positive *Bordetella pertussis*-specific IgA, while the rest were negative. As shown in the epidemic curve (Figure 1), the ratio of the confirmed versus suspected cases was higher during the first days of the outbreak. This could be due to the fact that after the outbreak was registered and was known, paediatricians were more sensitised and did not follow the case definition for the suspected cases exactly, thereby reporting cases not fulfilling the criteria of the suspected cases.

FIGURE 1

Epidemic curve, pertussis outbreak in Cyprus, 2003 (n=128)



A total of 71 of the suspected pertussis cases presented in Ammohostos (17 of these confirmed), 31 in Larnaka (six confirmed), 17 in Nicosia (one confirmed) and nine suspected pertussis cases (none confirmed) in other areas of Cyprus (Figure 2). The estimated incidence rate of confirmed cases in the most affected area (Ammohostos) was 44.3 per 100,000. The sex distribution of suspected cases was similar to that of confirmed cases while a higher percentage of suspected cases (20%) were younger than 10 years. No major complications were reported; one case was hospitalised, for three days. In the following paragraph, further information for laboratory-confirmed cases is given.

Laboratory-confirmed cases

Three out of the 24 confirmed cases were identified during the case investigation process among close contacts. The majority of

FIGURE 2

Age distribution of confirmed pertussis cases, outbreak in Cyprus 2003 (n=24)

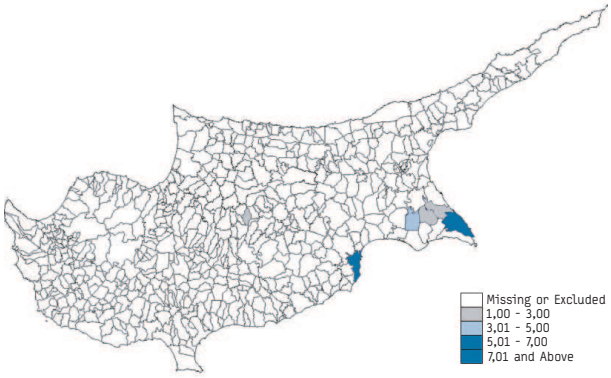
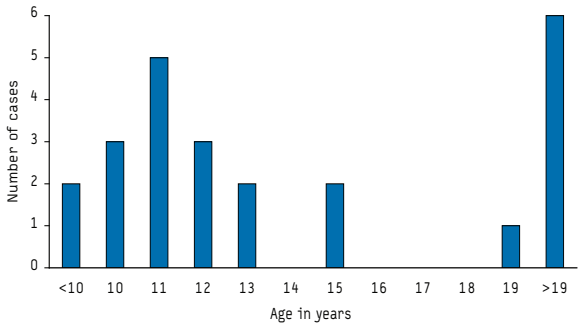


FIGURE 3

Age distribution of confirmed pertussis cases, outbreak in Cyprus 2003 (n=24)



cases were older than 10 years, two of 24 laboratory-confirmed cases were younger than 10 years, whereas 16 cases were between 10 and 20 years, and six cases were older than 20 years (Figure 3).

Most cases in the outbreak had previously been vaccinated for pertussis. Thirteen of the confirmed cases had received five vaccination doses and were correctly vaccinated. Six of the cases had received three to four doses, two cases one to two doses, and three cases were unvaccinated. The interval between the cases' last immunisation and the onset of disease was also estimated. Nine of the affected patients had received their last immunisation over 11 years previously, five cases eight to 11 years previously, nine cases four to seven years previously, and only one of the cases had received the last immunisation less than four year previously.

Control measures

The GCPSU, in close collaboration with District Public Health authorities, managed to control the outbreak by timely application of the appropriate control measures. As soon as the outbreak was registered, it was decided to vaccinate all close contacts (family members, schoolmates, friends etc) of cases who were considered not to be fully protected by the immunisation doses they had received so far. The following individuals were given a booster dose immediately:

- Children younger than seven years old who had received less than three vaccination doses,
- Children who had received their third vaccination dose more than six months ago, and
- Children who had received their fourth vaccination dose more than three years ago.

Moreover, preventive chemoprophylaxis using erythromycin (40-50 mg/kg per day for two weeks) was administered to those close contacts who were potentially susceptible. None of these developed pertussis. Finally, cases and their close contact persons were informed about the nature of the disease and the ways of transmission. It took approximately one month to control the outbreak.

Discussion

In 2003, a pertussis outbreak with 24 laboratory-confirmed cases among 128 clinically suspected cases was reported through active surveillance (GCPSU) in Cyprus. It took one week for the

GCPSU to register the beginning of the outbreak and to start applying control measures, whereas more than a month would normally be required for the mandatory notification system of the Ministry of Health. By that time and with the implementation of corrective actions by the GCPSU in collaboration with the District Public Health authorities, the outbreak was already almost over. By investigating this outbreak, we had the opportunity to assess the epidemiological patterns of pertussis in Cyprus and document the usefulness of an active surveillance system.

We cannot exclude that some of the suspected cases with negative serological tests were actually "true" pertussis cases, or vice-versa, since the IgA test has a satisfactory sensitivity and lower specificity due to cross-reactions. Culture (high specificity) and PCR with both high specificity and sensitivity were only available as part of a research protocol but not on a routine basis. As the aim of our project was to sensitise paediatricians in pertussis diagnosis, it was decided to use the test that would be routinely available to them after the end of the project, i.e. the IgA test, despite its limitations mentioned above. Moreover, the usual ratio of confirmed versus suspected cases was not known at that time of the outbreak since the GCPSU started operating in 2001 and pertussis was included in its surveillance scheme only in 2002. This ratio can now be calculated by using data from the syndromic surveillance of the Ministry of Health.

Pertussis is still a significant cause of morbidity globally, with a shift of the age distribution of reported cases to adolescence and adults as reported by notification systems of most developed countries [12]. This shift in age distribution was also detected during the outbreak in Cyprus in 2003. The age distribution of confirmed cases (most of the cases >10 years old) was similar to other investigated outbreaks in highly vaccinated populations, while in poorly vaccinated populations most of the cases were in children less than 10 years old [13,14]. Waning immunity in fully immunised individuals (54.1% in this study) or incomplete immunisation (45.9% in this study) are considered responsible for the documented shift in age distribution of pertussis cases in many studies.

Continuous improvement of immunisation (for example adolescence immunisation) and other preventive actions are being discussed and gradually applied worldwide, but considering the nature of the disease and the insufficient registration monitoring of epidemiological information on pertussis, it is clear that the introduction of a more functionally active surveillance system is also required. Reporting individual data on a weekly basis to a central data collecting unit and performing laboratory tests in reliable standardised laboratories proved to be very efficient in this outbreak. Even more effective was the decision to involve every possible primary or institutional paediatrician in the detection and registration of pertussis, by contacting and informing them systematically. Cyprus is a small island with around 150,000 children and a relatively small number of paediatricians (196). Thus, it is easy to motivate the paediatricians to report individual data immediately. In countries with larger populations, the involvement of only a geographically representative sample of paediatricians would be more appropriate.

The immediate implementation of corrective actions, which was only possible because of the early detection, made it possible to restrict the outbreak within very tight limits. One of the drawbacks of the GCPSU surveillance scheme for this specific disease was the fact that the system could not cover the adult cases and take into consideration the epidemiological patterns of pertussis in recent years This was one of the reasons why the Cyprus Ministry of Health decided to include pertussis in the syndromic surveillance system in which General Practitioners are included. The GCPSU is still functioning, but pertussis is no longer included in the diseases under surveillance. The aim of a paediatric surveillance unit is to initiate surveillance activities for rare diseases for a fixed time period and with specific objectives. Thus, the diseases under surveillance are changing. The objectives of pertussis surveillance were achieved by showing that the epidemiological patterns of pertussis documented worldwide are the same in Cyprus. Moreover, it was a useful experience to promote the initiation of syndromic surveillance in the Ministry of Health.

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