The Re-Emergence of Pertussis in Israel

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Abstract

Background: Pertussis is the only vaccine-preventable disease that has re-emerged in Israel. The reported crude incidence of the disease increased 16-fold since 1998.

Objectives: To describe the epidemiology of pertussis and explain the substantial increase in reported pertussis incidence in Israel in recent years.

Methods: Crude and specific pertussis incidence by age, patient immunization status, hospitalization rate, and national immunization coverage rate were calculated from information provided by the public health offices of the Ministry of Health.

Results: The reported crude incidence of pertussis increased from 1–2/100,000 in 1994–98 to 23/100,000 in 2004. The trend was observed in all age groups, being most prominent in infants under age 1 year and in children aged 5–14. The incidence of pertussis was substantially higher in unvaccinated and partly vaccinated compared to fully vaccinated persons. Fifteen percent of notified cases were hospitalized, but in infants under age 1 year the hospitalization rate was 50%. National pertussis immunization coverage by age 2 years was stable during the last 10 years.

Conclusions: There are several possible explanations for the re-emergence of pertussis in Israel. The most plausible reason seems to be the waning of vaccine-induced immunity in face of infrequent natural exposure to the infectious agent and lack of a pertussis vaccine booster dose after age 1.

Pertussis is an endemic worldwide disease that affects about 40 million people annually [1]. Susceptibility in unvaccinated individuals is universal. The disease is common in young children, but also occurs in adolescents and adults despite prior disease or active immunization [2-4]. The introduction of pertussis vaccine to the routine immunization program in Israel in 1957 resulted in a 100-fold decline in pertussis incidence in the 1960s and 1970s. For 40 years pertussis containment was satisfactory, with a stable 1–2/100,000 annual incidence rate and outbreaks of modest magnitude every 3–4 years.

Since 1999, pertussis seems to have re-emerged in Israel, showing a consistent increase in reported annual incidence. Similar trends were reported in the last 10 years in many countries with high immunization coverage rates, including the United States, Canada, the Netherlands and France [5-8]. Although immunization coverage with killed whole-cell pertussis vaccine was high and stable during the past 10 years, both the medical community and the public demanded the change to acellular pertussis vaccine. This pressure influenced the Israel Ministry of Health to introduce the acellular pertussis vaccine in 2002 with the hope of increasing pertussis immunization compliance still further. In this report, we assess and analyze pertussis morbidity in Israel and suggest possible explanations for its resurgence.

Methods

Pertussis has been notifiable in Israel since the early 1950s. Practitioners are required to notify all new cases to the local public health office. The 15 public health offices and the Army Health Branch (since 2004) report new cases to the Department of Epidemiology of the Ministry of Health on a weekly basis. Each notification includes: age, gender, nationality, address, date of disease onset, laboratory method of pertussis diagnosis, and the number of pertussis vaccine doses received by the patient in the past.

Any clinical case reported by a physician is considered to be pertussis, and no laboratory confirmation is required for the case to be included in Health Ministry statistics. In fact, serologic or polymerase chain reaction confirmation is sought in most cases in various government, hospital and community laboratories. These laboratory methods are not standardized nationally, and the Ministry of Health has not issued laboratory criteria for confirmation of pertussis diagnosis. Nevertheless, we will indicate the proportion of pertussis cases notified in recent years for which laboratory support was provided.

Public health office epidemiologic nurses investigate each reported case and obtain demographic information as well as information on the immunization status of the patient and his/her family from available immunization records. National immunization coverage is calculated every year by the public health offices and submitted to the Department of Epidemiology, which prepares an annual national summary. The calculation is based on a representative sample of children born in each health district and registered in the public Mother and Child Health Services.

Results

National incidence

In the 1950s, before the introduction of pertussis vaccine, about 10,000 cases of pertussis were reported annually to the Ministry of Health. In the early 1960s, following the implementation of routine pertussis immunization, the annual incidence declined to a few hundred cases per year, and for about four decades remained at 1–2 per 100,000, punctuated by small outbreaks every 3–4 years. The reported crude incidence of the disease started to increase in 1999 and reached 23 per 100,000 in 2004 (Figure 1).
Increased pertussis incidence was observed in all age groups in 1999–2004; it rose from 11 per 100,000 in 1998 to 116 per 100,000 in infants under age 1 year; from 2 to 23 per 100,000 in 1–4 year olds; from 1.9 to 60 per 100,000 in children aged 5–9; 4.2 to 74 per 100,000 in youngsters 10–14; and 0.6 to 14 per 100,000 in persons aged 15–44 [Figure 2].

Although during 1999–2004, the highest age-specific incidence rate occurred in infants under age 1 year, the most prominent rise in incidence, about 30-fold, was observed in children 5–9 years of age.

**Pertussis incidence by vaccination status**

The estimated incidence in unvaccinated and partly vaccinated children aged 1–15 years old in 2000–2004 was considerably higher than in fully vaccinated children (four doses). The highest ratio of incidence in unvaccinated and partly vaccinated children compared with those vaccinated, about 8:1, was in children aged 1–4 years [Figure 3].

**Pertussis diagnosis supported by the laboratory**

Table 1 shows the proportion of notified cases of pertussis supported by laboratory methods. This proportion has remained stable and high (85–93%) throughout the period of pertussis re-emergence.

**Hospitalization rate**

Fifteen percent of pertussis cases in the years 2000–2004 were hospitalized. The hospitalization rate was inversely related to age: about 50% of infants and only 2–3% of adolescents and adults were treated in hospitals, reflecting the variable severity of the disease in the different age groups.

**Deaths attributed to pertussis**

There were 16 deaths attributed to pertussis during 1970–2004, three of them in the last 4 years. All deaths were in young unvaccinated babies.

**Immunization coverage rate**

No changes in annual immunization coverage in 2 year old children were observed during the last decade and the rate remained stable: 92–93% of 2 year olds had received four doses of pertussis vaccine, and 94–95% had received three doses.

**Discussion**

The incidence of pertussis in Israel increased from a few cases reported each year in the 1970s and 1980s to over 1600 cases in 2004, despite excellent immunization coverage. Even though there were small year-to-year variations in immunization coverage in each district, there was no consistent pattern of changes of pertussis incidence corresponding to immunization coverage.

The highest incidence occurred in infants, the lowest in 1–4 year olds, and the most striking increases in incidence were in children aged 5–9 years. Cases from the military sector were
The case definition for reported pertussis in Israel is clinical pertussis as diagnosed by a physician, with or without laboratory confirmation. The incidence of pertussis started to rise in 1999, when a study was conducted in the Haifa district to seek pertussis cases among children with prolonged cough. Moreover, in the same year a new computerized reporting network was introduced by the Ministry of Health to simplify and improve reporting. These two parallel changes could explain partially the increased reported pertussis incidence since 1999. Nevertheless, as we have shown, the proportion of notified cases of pertussis supported by laboratory methods, particularly PCR, has been stable over the past 5 years and it is unlikely to have influenced the continued rise in reported incidence since 1999.

- Non-specific case definition: The case definition for reported pertussis in Israel is clinical pertussis as diagnosed by a physician, with or without laboratory confirmation. The advantage of this case definition is its low specificity in comparison with the more specific but less sensitive case definitions used by the U.S. Centers for Disease Control and the World Health Organization [10,11]. The disadvantage of this case definition is its low specificity in comparison with the more specific but less sensitive case definitions used by the U.S. Centers for Disease Control and the World Health Organization [10,11].

- Increasing physician awareness and improved notification: The incidence of pertussis started to rise in 1999, when a study was conducted in the Haifa district to seek pertussis cases among children with prolonged cough. Moreover, in the same year a new computerized reporting network was introduced by the Ministry of Health to simplify and improve reporting. These two parallel changes could explain partially the temporal rise of reported pertussis in 1999–2000, but not the continued rise in incidence in 2003–2004.

- Availability of highly sensitive laboratory methods: Although the clinical picture is officially sufficient for case reporting, most clinicians are reluctant to notify pertussis without laboratory support, either by PCR, where it is available, or single-point serology. These methods have relatively high sensitivity for pertussis diagnosis and their use might have artificially increased the reported incidence of pertussis [12].

### Achieving better pertussis control in Israel

Today, most developed countries, in accordance with the Global Pertussis Initiative, have five or even six dose schedules for pertussis immunization, and a number of them prescribe a booster dose in the adolescent years [18-21].

In Israel, beginning in 2006, a fifth dose of pertussis vaccine was introduced for the first time among 7 year old schoolchildren. The plan is to continue to monitor the pattern of pertussis occurrence in the coming years, as successive cohorts of 7 year olds receive the fifth dose, to observe whether the additional dose has the intended effect of diminishing pertussis incidence in older schoolchildren as well as in their infant siblings. The data will be used to determine the need for changing the timing of the additional dose or for adding a sixth dose of pertussis vaccine.

### Conclusions

There appear to be several reasons for the re-emergence of pertussis in Israel, of which the most feasible is the waning of vaccine-induced immunity in an environment of infrequent exposure to the infectious agent and the lack of additional doses of pertussis vaccine after age 1 year. Increased physician awareness and reporting and the availability of more sensitive diagnostic aids may also have contributed to the rise in incidence. The next step towards re-establishing pertussis containment in Israel must be a second booster dose of pertussis vaccine for schoolchildren to minimize disease risk in adolescents and adults and to interrupt the spread of pertussis from older children and young adults to small babies.

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Genetic link to obesity?

Obesity is thought to be partly heritable, but the genes responsible are difficult to identify, probably because they are numerous and each exerts only a small effect. Herbert and team scanned the genomes of a group of well-characterized patients with markers for over 86,000 genetic polymorphisms. One of the markers was associated with an index of obesity, the body mass index. In follow-up studies of five completely independent groups of people that included adults and children, the association was present in four of the groups. The polymorphism is located upstream of a gene involved in global fat metabolism and could potentially affect its function.

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