Epidemiologie 1-010 27.1.2010 11:38 Str. 25
proLékaře.cz | 9.11.2026

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A Steady Rise in Incidence of Pertussis Since Nineties in the Czech Republic

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Summary

Study objective: The objective was to analyze the incidence and trends of pertussis in the Czech Republic, particularly by age groups. An important part of the analysis was the immunization coverage.
Materials and methods: The incidence data were obtained from the following information sources: archives of the National Institute of Public Health for the period up to 1964, archives of the Institute of Health Information and Statistics for 1965-1981, Communicable Disease Information System for 1982-1992 and Communicable Disease Notification System EPIDAT for 1992-2008. The mortality data were obtained, apart from the aforementioned sources, also from the literature. The case definition was based on that provided by the Bulletin of the Ministry of Health and the EC Directive. Cases were notified in accordance with the guidelines of the respective information systems and the principles of pertussis surveillance laid down by the regulations. An epidemiological investigation form was filled in for each case of pertussis, indicating the type of laboratory analysis. The methods used for laboratory diagnosis of pertussis were culture, serology and a PCR assay.
Results: An upward trend in notified cases of pertussis has been observed since the 1990s. The highest annual number of cases (767) in the last 42 years was notified in 2008 (7.3/100,000 population). In 1988-2008, most (93.1 %) cases were notified in patients aged 0-19 years. During this period the peak moved from the youngest and preschool age groups toward younger and older school age children (the highest age-specific incidence of pertussis, i.e. 79.8/100,000, was observed in 10 - 14 - olds. In 2008, a 3.4 fold rise in pertussis cases was observed in 15 - 19 - year - olds as compared with the rates in the last six years. More cases were also notified in the age groups of potential parents and grandparents. In the 0 - year - old children, the incidence of pertussis was decreasing since the 1950s (3 804.9/100,000 in 1956) to remain under 10.0/100,000 between 1974 and 1999. It showed a continuing upward trend from 3.8/100,000 in 1987 to 26.7/100,000 in 2008, even with three deaths notified, after 35 years, in 2005, 2007 and 2009.
Conclusion: Despite the high immunization coverage with pertussis vaccine (>97 %), the pertussis incidence is rising in the Czech Republic. An upward trend in pertussis cases has been observed since 1993, peaking in 2008. More than 75 % of pertussis cases were notified in patients who had been vaccinated with 5 doses of pertussis vaccine before infection. During the period 1988-2008, the highest age-specific incidence, i.e. 79.8/100,000, was observed in 10-14-year-olds. After 35 years, three deaths from pertussis were notified in 2005, 2007 and 2009. All three fatal cases occurred in unvaccinated children under one year of age. The focus needs to be on active surveillance of pertussis and quality improvement of all its parts.

Key words: Whooping cough – pertussis - incidence - immunization – surveillance.

Souhrn

Fabiánová K., Beneš Č., Kříž B.: Stálý nárůst incidence pertuse v České republice od 90. let

Cíl práce: Cílem práce bylo analyzovat výskyt a vývoj onemocnění pertusí v České republice, zejména s ohledem na jednotlivé věkové skupiny. Důležitou součástí rozboru byla rovněž analýza proočkovanosti.
Metodika: Údaje o nemocnosti byly získány z následujících informačních systémů: do roku 1964 z archivu SZÚ, v letech 1965 - 1981 z Ústavu zdravotnických informací v Praze, v letech 1982 - 1992 z Informačního systému přenosných onemocnění (ISPO) a v letech 1992 - 2008 z informačního systému přenosných onemocnění EPIDAT. Údaje o úmrtnosti byly kromě uvedených zdrojů získány i z literatury. Pro definici případu onemocnění byla použita definice případu z Věstníku MZ a podle direktivy EC. Pro hlášení případů v předchozím období byly použity platné směrnice příslušných informačních systémů a zásady surveillance pertuse zakotvené legislativními pokyny. V listu epidemiologického šetření každého případu pertuse se dokladoval způsob laboratorního vyšetření. Laboratorní diagnóza onemocnění byla prováděna kultivačním, sérologickým a PCR vyšetřením.

Epidemiologie 1-010 27.1.2010 11:38 Str. 26
proLékaře.cz | 9.11.2026

Výsledky: Počty hlášených případů pertuse mají od devadesátých let minulého stoketí vzestupný trend. Nejvíce případů (767) za posledních 42 let bylo registrováno v roce 2008 (incidence 7.3/100,000 obyvatel). Většina případů z celé populace za období 1988 - 2008 je hlášena z kategorie 0 - 19 let - 93.1 % případů. Nemocnost se ve sledovaném období postupně přesunula ze skupiny nejmenších a předškolních dětí do skupiny mladších a starších školních dětí (nejvyšší specifická nemocnost podle věku za období 1987 - 2008 byla zaznamenána u 10 - 14 letých dětí 79.8/100,000). V roce 2008 narostl 3,4 krát oproti posledním šesti letům rovněž počet nemocných ve skupině 15 - 19 let. Nárůst nemocnosti je rovněž registrován ve skupinách potencionálních "rodičů" a "prarodičů". Incidence ve skupině 0letých dětí klesala od padesátých let minulého století (3 804.9/100,00 v roce 1956) a v letech 1974 až 1999 se udržovala pod hranicí 10.0/100,000. Ve sledovaném období začala postupně narůstat; v roce 1987 3.8/100,000, v roce 2008 26.7/100,000, a dokonce byla v této věkové skupině zaznamenána po 35 letech postupně 3 úmrtí; v roce 2005, 2007 a 2009.

Závěr: Přes vysokou proočkovanost pertusovou vakcínou (>97%) se incidence onemocnění v ČR zvyšuje. Od roku 1993 je pozorován vzestupný trend incidence onemocnění se zatím nejvyšším výskytem v roce 2008 (7.3/100,000 obyvatel). Přes 75 % registrovaných nemocných mělo před onemocněním kompletní očkování tj. 5 dávek. Nejvyšší specifická nemocnost podle věku za období 1988 - 2008 byla zaznamenána u 10 - 14 letých dětí 79.8/100,000. Po 35 letech byla zaznamenána postupně 3 úmrtí v souvislosti s pertusí; v roce 2005, 2007 a 2009. Ve všech třech případech se jednalo o dosud neočkované děti do jednoho roku života. Je nezbytné zaměřit se na důsledně prováděnou aktivní surveillance pertuse a zlepšit kvalitu surveillance ve všech jejích částech.

Klíčová slova: černý kašel – pertuse – incidence – imunizace – surveillance.

Introduction

Before the vaccination was introduced, pertussis together with diphtheria and measles had been among the most dangerous childhood infections. According to the oldest data from 1890, the whooping cough case fatality rate was 65.7/100,000 in the Czech Lands [14].

The highest pertussis incidence rate was recorded in 1956 – 520.5/100,000. After the vaccination against pertussis was included in the compulsory childhood immunization schedule in the Czech Republic in 1958, the annual numbers of reported cases of whooping cough were rapidly declining from the initial 30,000-50,000 to 5-48 in the second half of the 1970s through 1992, but never reached zero. Since 1993, an upward trend in whooping cough cases has been observed in all age groups, similarly to other developed countries. The highest pertussis incidence rates were repeatedly found in 10-14-year olds. In 2008 the highest number of pertussis cases was notified since 1966.

Materials and methods

A descriptive analysis was performed of the data from the following information sources: archives of the National Institute of Public Health for the period up to 1964, archives of the Institute of Health Information and Statistics for 1965-1981, Communicable Disease Information System for 1982-1992 and Communicable Disease Notification System EPIDAT for 1992-2008. For comparison, older data was also processed, when available.

The mortality data were obtained, apart from the aforementioned sources, also from the literature.

The pertussis case definition was based on the case definition for infectious disease notification in accordance with the Bulletin of the Ministry of Health of the Czech Republic, Chapter 13, of December 2002, where a clinical case of pertussis is defined as follows: „cough persisting for at least 2 weeks associated with one or more of the following symptoms: whooping cough seizures, whooping cough or vomiting following a cough seizure without any other evident cause".

The cases of pertussis laboratory confirmed by serology, culture or a PCR assay, as well as cases diagnosed based on the clinical picture and/or establishment of epidemiological linkage are notified to the EPIDAT system.

The notification of pertussis cases before December 2002 was performed in accordance with the guidelines of the respective information systems and the surveillance programme, with the classification of suspected and confirmed cases of pertussis that relied on the regulations then in force. For each case of pertussis, an epidemiological investigation form was completed where the type of laboratory confirmation was indicated (culture or serology).

Results

Incidence rates by age group and sex

The incidence rates in the 1980s varied in the range of 0.1-0.3/100,000

An upward trend in the incidence of pertussis in the Czech Republic has been observed since the 1990s, with a peak of 7.3 cases /100,000 population (767 cases) in 2008, the highest rate in the last 42 years (Figure 1).

Most pertussis cases in 1988-2008, i.e. 93.1 % of all cases, were diagnosed in patients aged 0-19 years. The peak rate moved from the youngest and preschool age groups toward younger and

Epidemiologie 1-010 27.1.2010 11:38 Str. 27
proLékaře.cz | 9.11.2026

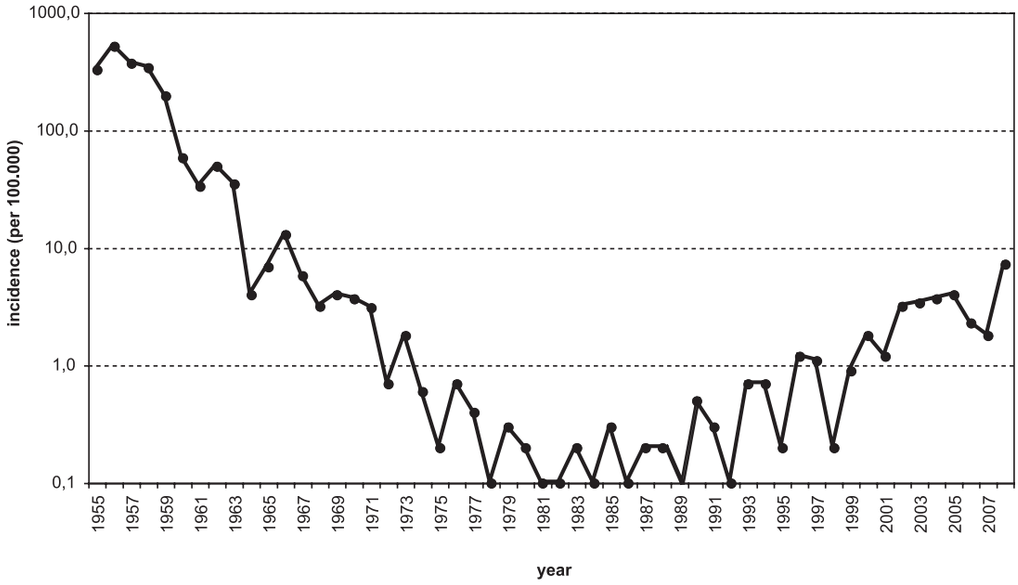


Figure 1: Pertussis, Czech Republic, notified cases, 1955-2008

Tab. 1. Pertussis, incidence by age group 0-24 years, 1988-2008

ROK	0	1-4	5-9	10-14	15-19	20-24
1988	4,6	1,3	0,1	0,8	0,0	0,0
1989	2,3	0,4	0,0	0,0	0,0	0,0
1990	1,6	2,1	2,6	1,9	0,0	0,0
1991	4,7	1,6	1,0	1,0	0,3	0,0
1992	1,6	0,4	0,3	0,4	0,0	0,0
1993	7,5	3,7	2,0	2,3	0,8	0,4
1994	9,7	4,6	1,8	3,2	0,6	0,0
1995	0,0	0,4	0,3	1,7	0,3	0,1
1996	7,3	4,0	5,1	7,6	0,9	0,0
1997	5,5	3,0	4,7	7,7	1,0	0,1
1998	1,1	1,8	1,1	0,8	0,5	0,0
1999	7,8	4,0	4,1	4,6	2,0	0,0
2000	15,6	9,1	6,6	11,3	2,9	0,1
2001	4,5	5,6	4,9	8,2	2,2	0,0
2002	9,7	12,9	15,3	22,0	6,6	0,1
2003	18,2	10,6	11,5	28,0	5,3	0,5
2004	9,6	9,7	20,2	27,4	5,3	0,5
2005	13,3	6,2	18,7	33,4	7,2	0,7
2006	10,7	1,1	10,3	20,7	6,3	0
2007	15,1	0,5	7,3	14,4	6,1	0,3
2008	26,7	6,4	22,6	79,8	21,8	0,8

older school age children. The highest increase in pertussis cases occurred in 10-14-year-olds and increasing incidence is also reported in the following age groups: 5-9 years, 15-19 years and 0 years (Table 1).

In 2008, a 3.4 fold rise in pertussis cases was observed in 15-19-year-olds in comparison with the data reported over the last six years.

The incidence of pertussis in 0-year-olds was declining since the 1950s (3 804.9/100,000 in 1956) and remained below 10.0/100,000 in 1974 through 1999. During the study period, the

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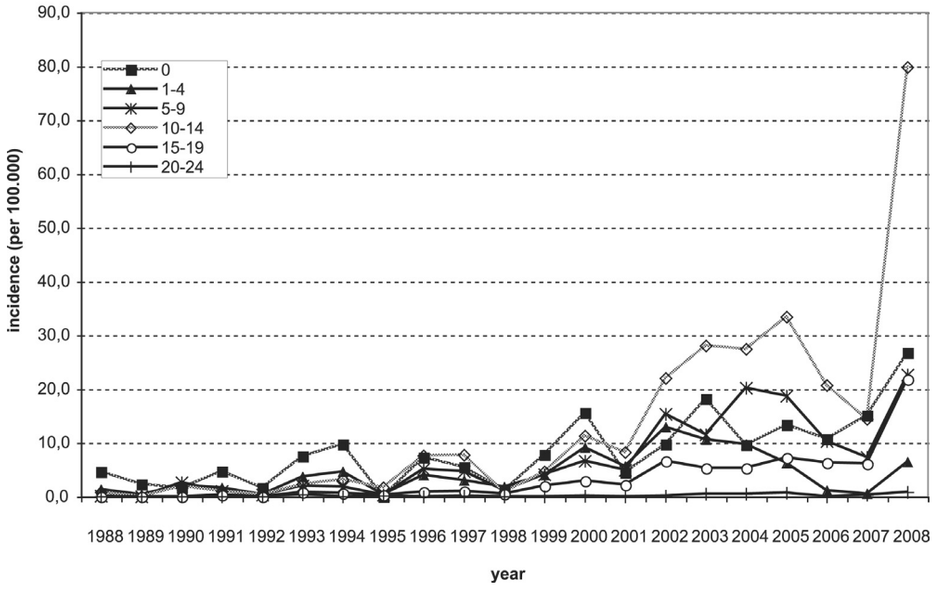


Figure 2: Pertussis, Czech Republic, incidence by age groups (0-24 years), 1987-2008

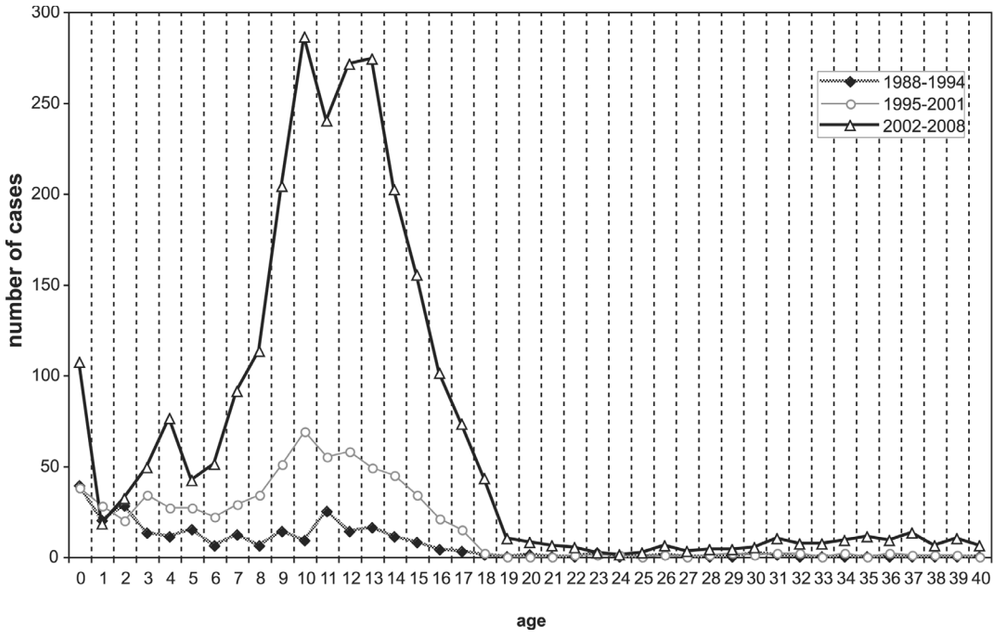


Figure 3: Pertussis, Czech Republic, by age 0-40 years, 1988-2008

incidence rate was fluctuating in four years periods from 4.6/100,000 in 1987 to 26.7/100,000 in 2008 and after 35 years, three deaths were reported in this age group in 2005, 2007 and 2009. (Figure 2)

The age of the 0 – 40 years old cases is analyzed in more detail way in three periods 1988-1994, 1995-2001, 2002-2008.

The low numbers of cases was reported in 1988-1994, with the exception of the first three years of life. In 1995-2001, increased numbers of pertussis cases were reported, peaking in the tenth year of life. A sharp rise in pertussis cases was observed in 2001-2008, peaking in the 10th to 13th year of life.

Higher numbers of pertussis cases are also observed in the groups of potential parents and grandparents. (Fig. 3)

During the period in question specific incidence in females was higher than in males. MxF ratio 1:1.29

Epidemiologie 1-010 27.1.2010 11:38 Str. 29
proLékaře.cz | 9.11.2026

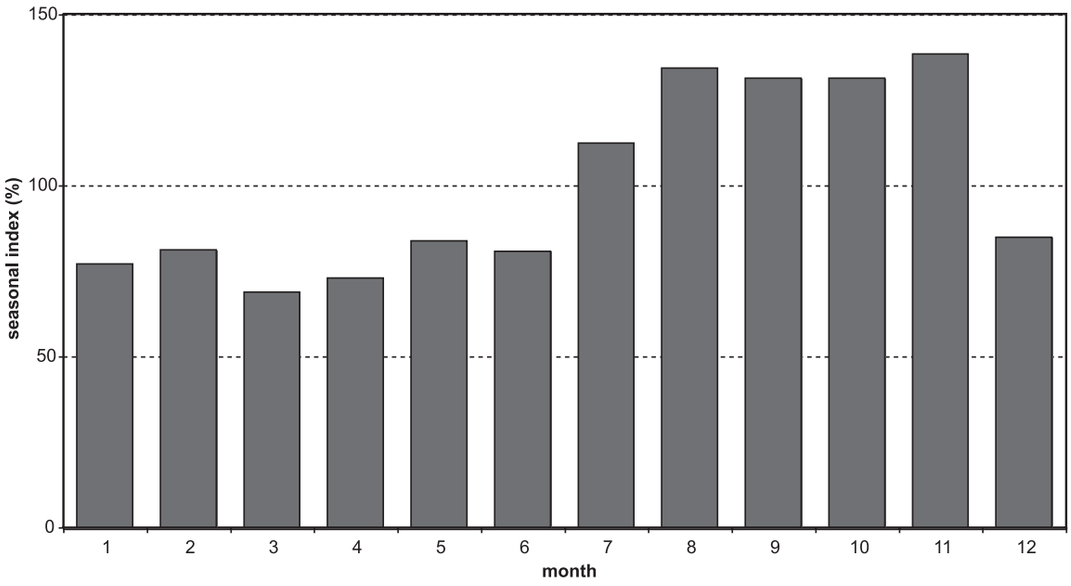


Figure 4: Pertussis, Czech Republic, seasonal trend, 1993-2008

Pertussis cases by calendar month and seasonal index

From the rates of pertussis cases by calendar month in 1993-2008 it follows that the disease is less common in the first half of the year, from January to June, while more pertussis cases are reported from July to November. (Fig. 4)

Imported cases

In 1998-2008, 18 imported pertussis cases were reported: 17 cases were diagnosed in Czech travellers and 1 case in a foreigner, 10 were females and 8 males, 16 of them under 18 years of age, 1 person aged 34 years and 1 person aged 53 years. Sixteen cases were imported from European countries (3 cases from Croatia, 2 cases from Italy, 2 cases from each Greece, Spain and Slovakia and 1 case from each Russia, Hungary, Germany, Austria and Yugoslavia) and one case from each Tunisia and Ecuador.

Deaths

After 35 years, three deaths of pertussis were reported in 2005, 2007 and 2009. All three cases occurred in unvaccinated children under one year of age (a 1-month-old boy, 4-month-old girl, 2-month-old girl). The epidemiological investigation resulted in laboratory confirmation of the source of infection in the family in two cases (older siblings, parent) and the suspected source of infection in the third case, based on the epidemiological investigation and case history, were family members (parent, older siblings).

Vaccination and contraindications

Routine immunization against pertussis in the Czech Republic started in 1958. It consisted of three basic doses followed by two booster doses [8,10].

Based on the WHO data, pertussis vaccination coverage in the Czech Republic has been above 97 % since 1991 [26].

In this study, vaccination data were analyzed for the period 1998-2008. Overall, 3074 pertussis cases were notified to the EPIDAT system during the study period.

Analysis of the EPIDAT data showed that 90.1 % of patients with pertussis had been vaccinated against pertussis (2771 subjects, with the data on individual doses missing for 71 of them). Altogether 9.2 % (282) of subjects were not vaccinated and no record on vaccination against pertussis was found for 0.7 % (23) of subjects. Nevertheless, the indication „vaccinated: YES“ in the records does not mean that the patient received all five doses of pertussis vaccine or the respective age-specific number of doses as required in accordance with the immunization schedule 2008. Full immunization with five or more doses of pertussis vaccine was reported in 75.3 % (2317) of pertussis cases for the study period 1998-2008.

In the age group of 10-14 years that showed the highest incidence of pertussis in the study period,

Epidemiologie 1-010 27.1.2010 11:38 Str. 30
proLékaře.cz | 9.11.2026

1434 (46.6 %) cases were notified. In total, 91.3 % (1310) of patients from this age group received all five doses of pertussis vaccine. A higher number of doses, i.e. 6 or 7, were recorded in 8 and 1 patient, respectively.

In older age groups, the numbers of fully immunized subjects decreased, since the population vaccinated at the very beginning of the compulsory immunization programme was 49-50 years old.

Laboratory detection

Most pertussis (99 %) cases notified in 1988-2008 were laboratory confirmed. Most study cases were diagnosed serologicaly, others had been confirmed by culture or on the basis of clinical symptoms and epidemiological data (school and family outbreaks).

Discussion

As the data analyzed in this article originated from different time periods and different notification systems, not all categories of data are available for the entire study period and the available data often are not comparable since varying with the changes made to the notification systems and with the methods used for their collection, and their evaluation is therefore feasible with difficulty.

Despite high pertussis vaccination coverage, the pertussis incidence in the Czech Republic is increasing. The upward trend has been observed since 1993. One of the reasons can be social and political changes after 1989 that made it possible for the population to travel freely to other countries, including those with low vaccination coverage and high incidence of pertussis.

The peak pertussis season moved from the typical influenza period to summer and autumn months. Children and adolescents probably get infected during their holiday activities, e.g. summer camps, typically in close contact with others, and return to school with infection. The disease can spread further through family contacts (parents, grandparents, etc.) to the youngest children who are the most vulnerable [5,11,25,].

Routine vaccination against pertussis in the Czech Republic started in 1958. A trivaccine with a whole cell pertussis component produced in Czechoslovakia (with the composition being adjusted to cover *B. pertussis* strains circulating among the population) was used for vaccination. Even in earlier years, selected collectives of children were immunized with pertussis monovaccines from the UK, Switzerland and France, that showed low efficacy, on the one hand, due to their quality varying from batch to batch, and on the other hand, to poor adherence to the immunization schedule indicated by the manufacturer and unsystematic immunization policy [2].

From the Report of the Ministry of Health of the Czech Republic to the WHO/UNICEF, i.e. the World Health Communicable Disease Annual Reporting Form 2008, it follows that the DTP4 coverage is high – 99.4 %. Nevertheless, the pertussis incidence among the Czech population is increasing, showing noticeable 3-4-year cycles suggestive of *B. pertussis* circulation among the population. It is highly probable that opening up the borders after 1989 could have been associated with the emergence of antigenically different *B. pertussis* strains imported from other countries. Another question is whether *B. pertussis* could adapt to the vaccine. In the Netherlands, the reduction in genotypic diversity in the 1960s-1980s associated with the expansion of *B. pertussis* strains antigenically different from the vaccine strains suggested polymorphism of pertussis toxin and pertactin [20]. Therefore, it is possible that the antigenic components used in the vaccine do not correspond with those of *B. pertussis* strains that circulate in the Czech population. According to the pertussis incidence in the Czech Republic by age the immunity induced by vaccination against pertussis does not last, as increase in pertussis cases is observed as early as three years after the last dose of vaccine. Data on the immune status by age group could throw more light on the phenomenon, but more serological surveys should be needed.

Since 1994, several changes have been progressively made to the immunization schedule and different types of vaccine have been used (switch from the DTP vaccine – trivaccine - to DTP-Hib vaccine – tetravaccine - as of January 1, 2001, introduction of an acellular pertussis vaccine in 2003 and the use of a hexavaccine including an acellular pertussis component since January 1, 2007).

Analysis of pertussis cases by age from birth to 40 years of age in three 7-year intervals revealed a low number of cases in 1988-1994, with the exception of the first three years of age, and confirmed the good quality of the then used Czechoslovak vaccine.

Since 1993, increase in pertussis cases has been observed in all age groups with a shift to older age groups as reported particularly in 2008. The upward trend in pertussis cases in the study period also suggests low immunogenicity of

Epidemiologie 1-010 27.1.2010 11:38 Str. 31
proLékaře.cz | 9.11.2026

foreign vaccines already being used in these years as confirmed by the results of serological surveys conducted in 1996 and 2001 [21,22].

The numbers of pertussis cases in the three 7-year periods declined concordantly until 19 years of age and only isolated cases were reported at older age. It can be assumed that changing a children's general practitioner for an adult's general practitioner is associated with a changed attitude towards the cough in both the physician and the patient. Pertussis has long been considered an exclusive childhood disease that is vaccine preventable and cannot occur in adults.

Vaccination against pertussis does not provide lifelong protection from the disease. The youngest still unvaccinated children are the most vulnerable. At older age and in a vaccinated population, pertussis has a less severe course, but with persistent annoying cough. Therefore, it is essential to maintain the high immunization coverage, to administer the vaccine at the prescribed dosage intervals and age and not to underestimate cough, particularly in the families with newborns or infants.

Pertussis cases in the Czech Republic, similarly to other countries in the world, have been underreported. Based on the literature data, the reported cases are only the tip of the iceberg, about 1-30 % of all actual cases. The remaining unreported cases are patients with a mild course who do not present to physicians, unrecognised or misdiagnosed cases, etc. [4,6,13].

Since these cases are a source of infection for the population in general and pose the highest risk to the youngest still unvaccinated or incompletely vaccinated children, pertussis needs early diagnosis and adequate treatment [1,12,15].

The case definitions formulated by the EU Commission [19] that are also binding on the Czech Republic require the laboratory criteria to be met to confirm the diagnosis of pertussis.

The number of cultures carried out in the study patients is very low (another problem is posed by the fact that the detection of *B. pertussis* decreases with the length of the disease since many patients with cough delay to present to the physician or are only sampled for *B. pertussis* culture after the institution of antibiotic therapy. Nevertheless, the studies of persistent cough revealed *B. pertussis* to be the causative agent in 13-20 % of adolescents and adults [3] and therefore, pertussis screening needs to be encouraged.

It is also important to remind the need for an early, targeted and adequately performed screening for *B. pertussis* in patients with pertussis-like cough. In view of the high susceptibility of *B. pertussis* to the environment, the good sampling technique and subsequent transport to the laboratory are of utmost importance for the culture of the agent. The patient should be sampled for culture before the institution of antibiotic therapy (even a single dose of an antibiotic can inhibit the growth of *Bordetella*). A fasting sample is preferably collected in the morning or possibly not less than 3 hours after a meal. The screened patient should not eat, drink, smoke or clean his/her teeth prior to the sampling. The highest detection is obtained at the catarrhal stage and in the first two weeks of the paroxysmal stage. As some studies have reported the detection of *B. pertussis* even at one week after the antibiotic therapy ended, *B. pertussis* culture should not be neglected (it is taken into account in Regulation No. 473/2008 of the Ministry of Health of the Czech Republic as follows: „A child after a laboratory confirmed disease caused by *B. pertussis* or *B. parapertussis* can only join the collective after having tested culture negative on day 4 or 5 after the therapy had ended").

As far as we know, PCR assays have been used for the detection of *B. pertussis* in some laboratories, but the number of the performed PCR tests cannot be determined from the EPIDAT data.

The mortality analysis in the former Czechoslovakia showed a significant reduction in the pertussis death rates after 1953 in children under one year of age due to chloramphenicol therapy. In 1957, before the start of the routine vaccination, the death rate in these children was still 45.0/100,000. After the vaccination was introduced, this rate dramatically decreased. In 1962, the death rate in children under one year of age was 0.14/100,000 only. The overall mortality rate decreased from 6.9 /100,000 in 1949 to 0.02 in 1962. In children above one year of age, no death was reported from 1966 to 1970 when one death from pertussis was confirmed [16,23].

In 2008, 75 (9.8 %) patients with pertussis were admitted to hospital, 20 of them in an infectious disease ward and 55 in another health care setting, based on the EPIDAT data. In the youngest age group under one year of age, i.e. in the most vulnerable children, 25 (78 %) of 32 pertussis cases required hospitalization. Among the 10-14-year olds with the highest pertussis incidence rate, 21 (5.5 %) patients of the total of 380 pertussis cases were hospitalised [7].

Laboratory diagnosis as a pivotal tool of the epidemiological surveillance programme is used for the monitoring of pertussis in the Czech Republic. It proved helpful in elucidating many controversial issues such as the efficacy of active

Epidemiologie 1-010 27.1.2010 11:38 Str. 32
proLékaře.cz | 9.11.2026

immunization against pertussis, tracing an ineffective vaccine, etc., and in confirming the importance of the surveillance for the identification of the factors that play a role in the spread of infection [24].

The concept of surveillance presented by Professor Raška in the 1960s has become a generally recognized comprehensive method for the monitoring, control and prevention of infectious diseases [9,17,18].

Conclusion

Despite high pertussis vaccine coverage (>97 %), the incidence of the disease is increasing. Since 1993, an upward trend in pertussis cases has been observed, peaking in 2008 (7.3/100,000 population). More than 75 % of cases were notified in patients fully vaccinated with five doses of pertussis vaccine. The highest age-specific incidence in 1987-2008 was observed in 10-14-year-olds. After 35 years, 3 deaths of pertussis were reported in 2005, 2007 and 2009. All three cases occurred in unvaccinated children under one year of age.

The focus needs to be on systematic active surveillance of pertussis and quality improvement of all its parts.

It is also necessary to improve the collaboration with the NRL for Pertussis and Diphtheria of the National Institute of Public Health in Prague and to refer *B. pertussis* isolates to the NRL for the confirmation of the diagnosis and further identification of strains helpful in the study of epidemiological links between strains and antigenic coverage of the vaccine with reference to the circulating strains.

The upward trend in pertussis incidence in 10-14-year-olds brought about an amendment to Regulation No. 537/2006 of the Ministry of Health of the Czech Republic on immunization against infectious diseases. Regulation No. 65/2009 of the Ministry of Health of the Czech Republic that came into force on March 12, 2009 lays down that the existing pertussis immunization shall be extended to include 6 doses of pertussis vaccine, with the sixth one to be administered "at the age between 10 and 11 years".

In view of increasing trend of pertussis incidence in 10-14-year-olds (see Figure 3), the vaccination schedule should be changed again. Sixth "booster" dose should be administered in 9th year of life. Vaccination of adults, especially parents, grandparents and other persons caring of the youngest still unvaccinated children should be considered.

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