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Paediatric surveillance of pertussis in the Netherlands in 1998

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Abstract

Objective. To gain insight into the severity of pertussis in hospitalised cases.
Methods. In 1998, hospitalisation data were collected through paediatric surveillance.
Results. From 115 hospitalisation admissions collected, 55% of the patients were younger than 3 months of age and not vaccinated; 12% were 3-5 months of age and of these, 50% were incompletely vaccinated; 33% were 6 months and older and of these, 61% were vaccinated. Fourty-six percent of the patients were diagnosed as having pertussis, confirmed by a positive culture or PCR, and 44% by positive serology. Three unvaccinated cases less than three months old died. Cyanosis, apnoea, administration of oxygen, artifical respiration and bradycardia were more frequently reported for unvaccinated cases compared to vaccinated cases and the hospitalisation time was longer (median 10 days vs. 4.5 days). Although complications were not often reported for vaccinated cases, the only case with encephalopathy was vaccinated and 17% of vaccinated cases had pneumonia.
Conclusion. The lower number of reported cases in 1998 seems to reflect the lower pertussis incidence that was also observed in routine surveillance of notifications and cases with positive serology. Like in 1997 pertussis was most severe and complications were more frequently reported in young unvaccinated infants less than three months of age. However, also typical and severe pertussis cases occurred among vaccinated individuals. Active monthly paediatric surveillance is useful to verify trends in routine surveillance; interpretation of the routine sources is hampered by changes in the notification law and decentralisation of serology.

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Samenvatting

Introductie. In 1997 werd pediatrische surveillance gestart naar aanleiding van de kinkhoest epidemie in 1996-97. Kinkhoest was het meest ernstig onder zuigelingen te jong voor vaccinatie. Echter, uit de pediatrische surveillance en een studie onder aangegeven patienten bleek dat ook onder gevaccineerden typische kinkhoest voor kwam. We concludeerden dat de relatief grote kinkhoest toename in 1996-97 onder gevaccineerden waargenomen in routine surveillance voornamelijk typisch verlopende kinkhoest betrof. Dit rapport beschrijft de resultaten van de pediatrische surveillance in 1998.
Methoden. Ziekenhuisopnamen ten gevolge van kinkhoest onder kinderen jonger dan 15 jaar werden maandelijks gerapporteerd via het Nederlands Signalerings-Centrum Kindergeneeskunde (NSCK). Met behulp van een vragenlijst werden gegevens verzameld over symptomatologie, vaccinatiestatus en laboratorium diagnostiek. Na informed consent werd de vaccinatie status geverifieerd bij de Provinciale Entadministratie.
Resultaten. In 1998 werden 144 ziekenhuisopnamen wegen kinkhoest gerapporteerd. Vragenlijstgegevens werden voor 115 patiënten (80%) verkregen. Het dekkingspercentage van de NSCK meldingen op grond van ziekenhuisopnamen geregistreerd in de landelijke medische registratie werd geschat op 47%, terwijl de dekking 37% bedroeg op grond van meldingen met vragenlijstgegevens. Zowel de leeftijd- en geslachtsverdeling als de mediane opnameduur was vergelijkbaar met de nationale registratie. Vijfenvijftig procent van de patiënten was jonger dan 3 maanden en te jong voor vaccinatie; 12% was 3 tot 5 maanden oud (7% ongevaccineerd; 50% incompleet gevaccineerd; 7% compleet gevaccineerd, 36% onbekend); 33% was tenminste 6 maanden (5% ongevaccineerd; 61% compleet gevaccineerd, 34% onbekend). Bij 90% van de patiënten werd de klinische diagnose met laboratorium diagnostiek bevestigd met behulp van kweek en/of PCR (46%) of serologisch (44%). Drie patiënten overleden. Zij waren jonger dan 3 maanden en ongevaccineerd. De mediane opname duur was hoger voor ongevaccineerden versus gevaccineerden (10 versus 4,5 dagen). Cyanose, apneu en zuurstoftoediening werd vaker gerapporteerd voor ongevaccineerde patiënten. De enkele patiënten met bradycardie of kunstmatige beademing waren ongevaccineerd. Zowel voor gevaccineerden als ongevaccineerden werd vaak paroxysmaal hoesten en overgeven gerapporteerd. Hoewel complicaties niet frequent werden gemeld voor gevaccineerden, was de enige patiënt met encephalopathie gevaccineerd. Ook had 17% van de gevaccineerde patiënten longontsteking.
Discussie. In 1998 was het aantal meldingen lager (n=144) dan in 1997 (n=204). Omdat de dekkingsgraad van het systeem niet lager werd, lijkt dit de lagere kinkhoest incidentie in 1998 ten opzichte van 1997 te reflecteren, die ook in de routine surveillance van aangiften en positieve serologie werd waargenomen. Evenals in 1997 was kinkhoest het meest ernstig en kwamen complicaties het frequentst voor bij ongevaccineerde zuigelingen jonger dan 3 maanden. Echter, typische en ernstige kinkhoestklachten kwamen ook voor onder gevaccineerden. Pediatrische surveillance wordt gebruikt om trends uit routine surveillance te verifiëren; interpretatie van routine surveillance wordt bemoeilijkt door de nieuwe aangifte-wet en decentralisatie van serologie.

Summary

Introduction. Paediatric monthly surveillance started in 1997 in response to the pertussis epidemic in 1996-1997, showed that pertussis was most severe among infants too young to be vaccinated (i.e. less than three months). Both the pediatric surveillance and an study among notified cases in 1997 showed that also among vaccinated children typical pertussis occurred. We concluded that the relatively large increase in pertussis observed among vaccinated children in routine surveillance in 1996-1997 primarily consisted of cases with typical disease. This report gives results of hospitalisations reported through the paediatric system in 1998.
Methods. Pertussis hospitalisations among children less than 15 years were reported monthly through the Dutch Paediatric Surveillance Centre (NSCK). Questionnaire data on symptomatology, vaccination status and laboratory diagnosis was collected. After informed consent the vaccination status was verified at the Provincial Vaccination Administration.
Results. In 1998, 144 hospital admissions due to pertussis were reported. For 115 (80%) questionnaire information was available. While the overall coverage of this paediatric surveillance estimated from the national registration of hospital admissions was 47%, the coverage of reports with questionnaire data amounted to 37%. The age and gender distribution and time of hospitalisation were similar to those in the national registration. Fifty-five percent of the cases was less than three months and too young to be vaccinated; 12% was 3-5 months of age (7% unvaccinated, 50% incompletely vaccinated, 7% completely vaccinated, 36% unknown); 33% was at least 6 months of age (5% unvaccinated, 61% vaccinated, 34% unknown). In 90% the clinical diagnosis was laboratory confirmed either by culture and/or PCR (46%) or serology (44%). Three cases died. They were less than three months old and unvaccinated. The median time of hospitalisation was longer among unvaccinated cases compared to vaccinated cases (10 versus 4.5 days). Cyanosis, apnoea and administration of oxygen were more frequently reported for unvaccinated cases. The few cases with bradycardia or artificial respiration all involved unvaccinated cases. Both for vaccinated and unvaccinated cases paroxysmal coughing and vomiting were frequently reported. Complications were not often reported for vaccinated cases. However, the only case with encephalopathy was vaccinated and 17% of vaccinated cases had pneumonia.
Discussion. In 1998, the number of reports was lower (n=144) compared to 1997 (n=204). Since the coverage of the system did not decrease, this seems to reflect the lower incidence of pertussis in 1998 compared to 1997 which was also observed in routine surveillance of notifications and cases with positive serology. Like in 1997 pertussis was most severe and complications were more frequently reported for unvaccinated young infants less than three months of age. However, also typical and severe pertussis cases occurred among vaccinated individuals. Active monthly paediatric surveillance is useful to verify trends in routine surveillance; interpretation of the routine sources is hampered by changes in the notification law and decentralisation of serology.

1 Introduction

According to surveillance data from notifications, serology data and hospital admissions a resurgence of pertussis was observed in the Netherlands in 1996 despite high vaccination coverage (1,2). While the average annual incidence according to notifications amounted to 2.3 per 100.000 in the period 1989 to 1995, the incidence increased to 27.3 per 100,000 in 1996. Most cases occurred among vaccinated children aged 1-9 years resulting in a lower estimation of vaccine efficacy as calculated retrospectively from notification data (1,2). A decline of estimated vaccine efficacy had already begun in 1994 and 1995 (1,2). Surveillance data in 1997 to 1998 showed that de incidence of pertussis decreased, but that the incidence was probably still higher than before the epidemic in 1996 (3). Furthermore, recent data of 1999 show an increase in pertussis incidence.

The constant ratio of hospital admissions and notifications and of hospital admissions and cases with positive two-point serology among infants less than one year of age, was taken to indicate that the virulence of the circulating strains had not change (2). However, in older age groups the number of hospital admissions had increased much less than the number of notifications and positive serology in that age group (2). This suggested a surplus of cases that was less severe. The re-emergence was found to be associated with the expansion of strains, which are antigenically distinct from vaccine strains (4). Therefore we believed it was possible that the decline of vaccine efficacy since 1994 and the increased incidence of pertussis since 1996 are related to antigenic changes of B. pertussis over time leading to a relative mismatch between vaccine-induced immunity and presently circulating strains. Possibly the properties of the Dutch vaccine has resulted in a greater vulnerability of the vaccinated Dutch population to antigenic changes in B. pertussis (2).

However, surveillance data did not provide direct insight into the severity of pertussis for vaccinated versus unvaccinated cases. Therefore, we started in 1997 with active (monthly) surveillance through paediatricians of children admitted to the hospital due to pertussis (5). Information on symptoms, diagnostics and vaccination status was obtained. Furthermore, in that year additional information was collected from notifications similar to the information collected in the paediatric surveillance. Since only a few unvaccinated cases were more than 6 months of age, we could not study the independent effect of vaccination and age. These results showed that pertussis was most severe among unvaccinated infants less than three months of age. However, also among vaccinated children typical pertussis symptoms occurred, although severe complications were seldom reported (5). Thus, the relatively large increase among vaccinated children concerned mostly typical cases and was not due to solely mild atypical cases.

The active paediatric surveillance was continued because of the epidemiological situation of pertussis and the importance to remain informed on the severity of disease among infants (5).

Protection of these very young children who are most vulnerable to complications and death through pertussis is the main reason for introduction of pertussis vaccination. Furthermore, the paediatric surveillance can be used to verify trends observed in notification data which are much more sensitive to changes in case definition for notification, availability and interpretation of laboratory tests, notification rate and diagnostic practice. The trend in hospital admissions likely reflects the real incidence of severe pertussis.
In this report the results of paediatric surveillance of pertussis hospitalisations is given for children admitted in 1998.

2 Methods

In 1998, active surveillance of pertussis hospitalisations in paediatric practice through the Netherlands Paediatric Surveillance Centre (Nederlands Signalerings-Centrum Kindergeneeskunde (NSCK)), that was started in 1997, was continued. The formation of the NSCK was an initiative of the Netherlands Paediatric Association (NVK) and is co-ordinated by TNO Prevention and Health (Dr. RA Hirasing). Monthly, a number of rare disorders are reported and in 1997 91% of all practising paediatricians participate (6). All practising physicians receive a card on which the disorders are listed. They are asked to tick off every disorder that they observed in a patient for the first time (new case) during the last month and to state the patients initials and date of birth. If they do not see any of the disorders listed, they have to tick off 'no observation'. In either way, the card has to be sent back to the NSCK. The pertussis cases reported to the NSCK have to meet the following case-definition: *hospital admission due to suspicion of pertussis*. Positive reactions are passed by the NSCK to the pertussis investigators, who subsequently start additional data collection through a questionnaire. In this manner, further information on clinical, diagnostic and vaccination status is obtained (Figure 1). If the paediatrician does not respond within 3 to 4 weeks, he or she is reminded by telephone to return the questionnaire. For analyses only cases that were admitted to the hospital in 1998 were included.

Case definition NSCK: hospital admissions due to suspicion of pertussis

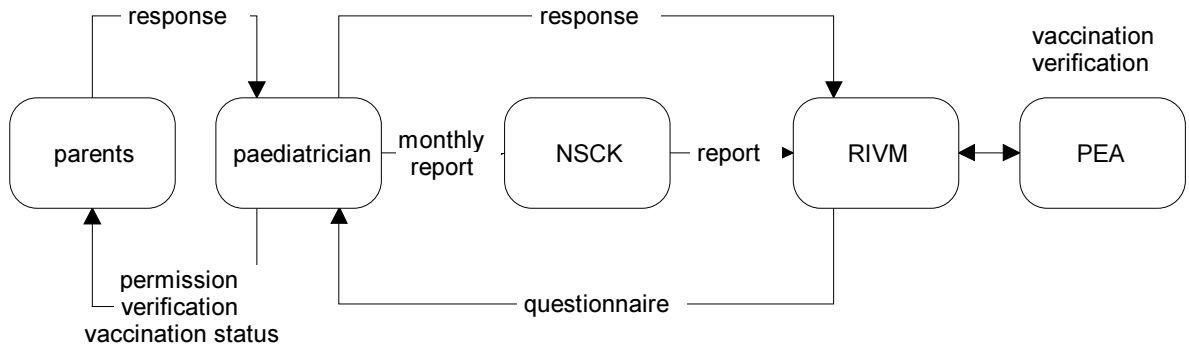

Figure 1. Scheme of the NSCK surveillance system

2.1 Verification and definition of the vaccination status

To collect complete data about the vaccination status, the paediatrician asked the parents of the patient for permission to verify the vaccination status at the Provincial Vaccination Administrations (PEA). In 1997, in addition to information from the Provincial Vaccination Administration information on vaccination status was obtained from the Child Health Centre and/or Municipal Health Services. Comparison of the vaccination status obtained from these

sources showed that information on vaccination status from the Provincial Vaccination Administrations was most easily obtained and was reliable for those patients vaccinated before onset of pertussis symptoms (5). Therefore, in 1998 only information was obtained on vaccination status from the Provincial Vaccination Administration.

Vaccinations administered after the first day of illness were not included to determine the patient's vaccination status. For analysis a patient was considered to be unvaccinated in case: 1) no informed consent was obtained from the parents to obtain information at the Provincial Vaccination Administration but the pediatrician mentioned the reason why the pertussis case was not vaccinated; 2) the patient was younger than 3 months of age; 3) all vaccines administered did not include the pertussis component according to the record from the PEA. A patient was classified as incompletely vaccinated when records from the PEA were available showing 1 or 2 doses with a pertussis component. The classification vaccinated was used for patients who received 3 or 4 doses of the pertussis vaccine according to the record from the PEA. In all other cases a patient was classified as unknown, i.e. no informed consent was given by the parents to obtain information from the PEA and the patient was at least 3 months of age.

Vaccination status	
unvaccinated	no informed consent to obtain information from PEA but reason given by paediatrician for being unvaccinated or younger than 3 months of age or no pertussis component in vaccine according to information from PEA
incompletely vaccinated	1 or 2 doses according to the PEA
vaccinated	3 or 4 doses according to the PEA
unknown	no information available from PEA because no informed consent was given

All data collected were entered twice using Epi Info (version 6.04) by two investigators. Differences were checked and corrected. For analysis all data were converted to SAS-data using DBMS-copy. The analyses were performed using the Statistical Package SAS (version 6.12). Differences in proportions were tested by χ^2-test or Fisher exact test (expected cell number < 5). A p-value of 0.05 was used as significance level.

2.2 National hospital admission data

Information about all hospital admissions with a primary or secondary diagnosis of pertussis (International Classification of Diseases Ninth revision, Clinical Modification code: 0330-0339) in 1998 was provided by the Foundation Information Centre for Health Care (SIG). For 1998 the SIG included only those hospitalisations with day of discharge in 1998. Information on age at date of admission, gender and primary or secondary diagnosis was available. The data were retrieved as an ASCI-file and converted to SAS-data using DBMS-copy. The analyses were performed using the Statistical Package SAS (version 6.12). The age and

gender distribution and the median time of hospitalisation were compared with these distributions and median time in the active paediatric surveillance. The coverage of the active paediatric surveillance was calculated by dividing the number of reports in the paediatric surveillance by the total number of hospital admissions registered by the Foundation Information Centre for Health Care.

3 Results

3.1 Response of the paediatric surveillance

Table 1 shows that 14 of the 158 cases reported in 1998 were either duplicates or false reports. The response on the questionnaire for the remaining 144 cases amounted to 80%. Slightly more males than females were reported.

Table 1. NSCK reports of pertussis in 1998

Reports	Number (%)
Total reports	**158**
Duplicates	9
False report (no pertussis/no hospital admission)	5
Remaining reports	**144**
No questionnaire returned	29
Questionnaire returned	115
Gender (n=115)	
Male	61
Female	54

3.2 National hospital admission data and coverage paediatric surveillance

The national registration of hospital admissions showed that 308 patients younger than 15 years were admitted to the hospital due to pertussis. The coverage of the active monthly surveillance amounted to 47% for all reports (144/308) and 37% (115/308) for reports with questionnaire data.

The age and gender distribution among the NSCK cases and the SIG cases were similar (Figure 2 and Table 2). For comparison, age was calculated by the time between the date of birth and the date of hospital discharge. The median time of hospitalisation amounted to 6 and 7 days according to SIG cases and NSCK cases, respectively.

Table 2. Characteristics of cases reported by the SIG in 1998

Characteristics	Number (%)
total number of hospital admissions < 15 years of age*	308 (100%)
gender	
male	157 (51%)
female	151 (49%)
diagnosis	
primary	274 (89%)
secondary	34 (11%)
median number of days of hospital admission (range)	6 (0-353)

* 12 hospital admissions >= 15 years of age were excluded

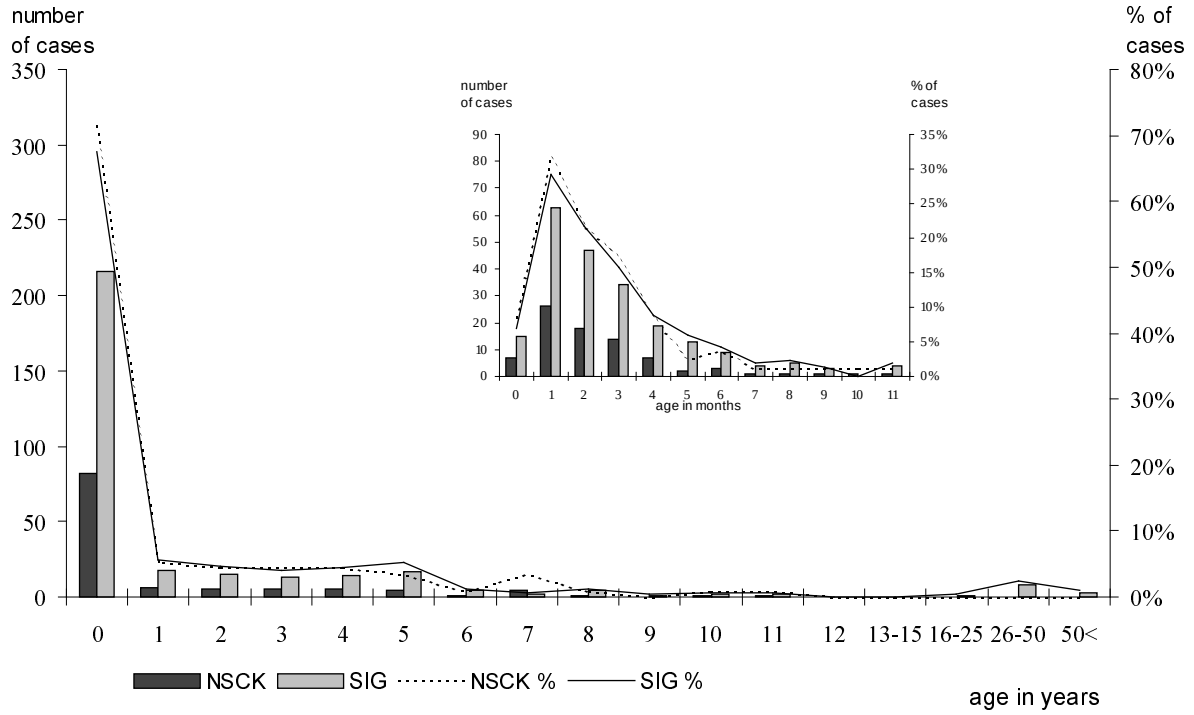

Figure 2. Age distribution of pertussis cases reported by the NSCK (n=144) compared with cases reported by the SIG (n=308)

3.3 Vaccination status of the cases in the paediatric surveillance

Table 3 presents the vaccination status of the NSCK cases according to the vaccination records of the PEA and the paediatricians. Fifty-seven percent of the cases were unvaccinated, mainly because they were too young to be vaccinated. Seven percent received 1 or 2 doses, while 21% received 3 or 4 doses. In 16% of the cases no information about the vaccination status could be obtained.

Table 3. Vaccination status of pertussis cases; NSCK 1998

Vaccination status	Number (%)
Not vaccinated	66 (57%)
1 dose	3 (3%)
2 doses	4 (4%)
3 doses	6 (5%)
4 doses	18 (16%)
unknown	18 (16%)
total	115 (100%)

Figure 3 shows the distribution of cases according to vaccination status and age. In contrast with Figure 2, age was calculated by the time between the date of birth and the date of onset of disease. The vaccination status was classified as described in paragraph 2.1. Most cases (71%) were less than one year of age. Fifty-five percent was less than three months of age and were too young to be vaccinated. Cases aged 3 to 5 months were mostly incompletely vaccinated, while most cases above 6 months of age received 3 to 4 doses or the vaccination status was unknown.

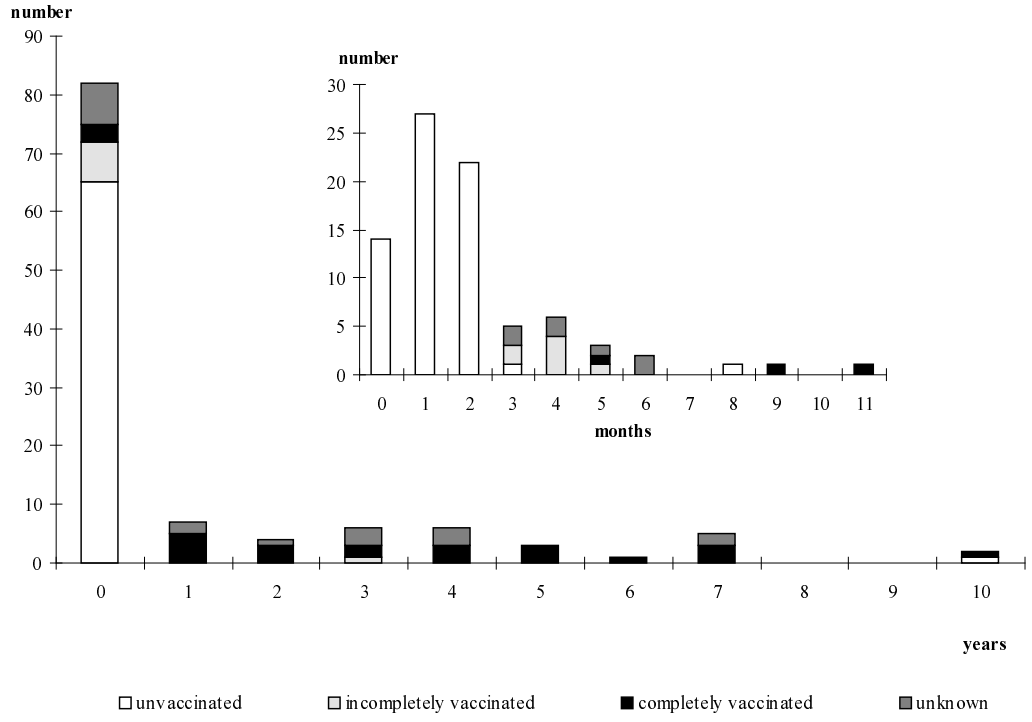

Figure 3 Pertussis cases according to vaccination status and age (age at onset of disease); NSCK 1998

Table 4 shows the number children according to age and vaccination status. Almost all children less than 6 months of age are unvaccinated or incompletely vaccinated. As a result children with unknown vaccination status the proportion of vaccinated children might be higher than the proportion given in table 4.

Table 4. Proportion vaccinated of NSCK pertussis cases in different age groups

Age	Total	Vaccinated	Unvaccinated or incompletely vac.	Unknown	Proportion vaccinated
0-5 months	77	1	71	5	1%
6-11 months	5	2	1	2	40%
1-4 years	22	13	0	9	36%
5-9 years	9	7	0	2	78%
10 years	2	1	1	0	50%

3.4 Diagnosis of the paediatric surveillance cases

Table 5 shows the results of the laboratory diagnosis. For those cases who were laboratory confirmed (90%) about half were microbiologically confirmed with PCR/culture and half by positive serology.

Table 5. Laboratory method in hierarchical order[*] resulting in confirmation of pertussis diagnosis in NSCK cases

Result of laboratory diagnosis	Number (%)
positive culture and/or PCR	53 (46%)
positive two-point serology[**]	30 (26%)
positive one-point serology[**]	21 (18%)
other[***]	11 (10%)
total	115 (100%)

[*] the method of diagnosis was scored according to the following hierarchy: positive culture and/or PCR, positive two-point serology, positive one-point serology, other result

[**] PCR and culture not done, negative or missing

[***] PCR and culture and serological method not done, negative or unknown

3.5 Symptoms, complications and duration of the paediatric surveillance cases

The median age of unvaccinated children and incompletely vaccinated children was lower (one month and four months) than for vaccinated children (44 months). Both for unvaccinated and incompletely children the delay between first day of illness and hospitalisation was shorter than for vaccinated children. The median time of hospitalisation was twice as high for unvaccinated children compared to both vaccinated and incompletely vaccinated children.

Table 6. Time characteristics (median (range)) of hospitalisation of pertussis cases according to vaccination status; NSCK 1998

Characteristics	Unvaccinated N=66*	incompletely vac. n=7*	Vaccinated n=24*	Unknown n=18*	Total n=115*
Age (months)	1 (0 - 126)	4 (3 - 5)	44 (5 - 131)	24.5 (3 - 95)	2 (0-131)
Days between onset of Illness and hospitalisation	8 (0 -52)	6 (2-53)	18 (1 - 71)	13 (4 - 67)	13 (0-71)
Weeks coughing before hospitalisation	2 (1 - 7)	1 (1 - 6)	3 (1 - 8)	2 (0 - 8)	2 (0 - 8)
Days hospitalisation	10 (1 - 106)	5 (4 - 10)	4.5 (1 - 14)	6 (1 - 23)	7 (0-106)

* the total number of cases varies due to excluded cases with missing values

In Table 7 the symptoms reported for the pertussis cases are presented stratified by vaccination status. Irrespectively of vaccination status almost all cases reported coughing. No clear differences were seen between vaccinated and unvaccinated cases with respect to the frequency of reporting aspecific cough and paroxysmal coughing. Cyanosis, apnoea, administration of oxygen were statistically significantly more frequently reported for unvaccinated cases compared to vaccinated cases. For other symptoms no statistically significantly differences were observed. However, pneumonia, wheezing breathing and vomiting were slightly more often reported for vaccinated cases. Bradycardia and artificial respiration were seldom reported but all involved unvaccinated cases.

Table 7. Reported symptoms of pertussis in NSCK pertussis cases according to vaccination status

Symptoms	Unvaccinated n=66* (%)	Incompletely vac. n=7* (%)	Vaccinated n=24* (%)	Unknown n=18* (%)	Total n=115* (%)
Coughing	63 (96)	7 (100)	23 (96)	18 (100)	111 (97)
Aspecific coughing	13 (20)	1 (14)	5 (21)	2 (11)	21 (19)
Paroxysmal coughing	45 (69)	6 (86)	16(67)	11 (61)	78 (68)
Vomiting	37 (57)	3 (43)	17 (71)	9 (50)	66 (58)
Cyanosis***	42 (65)	6 (86)	7 (29)	8 (44)	63 (55)
Phlegm	23 (36)	3 (43)	6 (25)	6 (33)	38 (34)
Wheezy breathing	9 (14)	4 (57)	8 (33)	3 (17)	21 (21)
Apnoea***	18 (28)	2 (28.5)	0 (0)	1 (6)	21 (18)
Pneumonia	6 (9)	1 (14)	4 (17)	2 (11)	13 (11)
Collapse after coughing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Artificial respiration	7 (11)	0 (0)	0 (0)	0 (0)	7 (6)
Administration of oxygen***	34 (52)	0 (0)	1 (4)	4 (24)	39 (35)
Convulsions	1 (2)	0 (0)	0 (0)	0 (0)	1 (1)
Bradycardia	2 (3)	0 (0)	0 (0)	0 (0)	2 (2)
Encephalopathy	0 (0)	0 (0)	1 (4)	0 (0)	1 (1)
Other symptoms**	5 (8)	0 (0)	2 (8)	4 (22)	11 (10)
Fever	16 (25)	0 (0%)	8 (35)	4 (24)	28 (25)
Med. highest temp.(range)	38.4 (38 - 28.7)	--	39 (38 - 39.9)	39.8 (38.5 - 39.8)	8.5 (38 - 39.9)

* the total number of cases varies due to excluded cases with missing values for some symptoms

** other symptoms: no appetite, weight loss, groaning, be stifled, atomize, RSV infection, panic, peribronchitis, petechiae, drop in saturation

*** χ^2 or Fisher exact test for differences in proportions for vaccinated and unvaccinated cases $p < 0.05$

Since vaccination status was highly associated with age, i.e. almost all unvaccinated cases were less than three months of age, while all vaccinated cases were at least 6 months of age, the effect of age could only be studied stratified by vaccination status (Figures 4 and 5). For unvaccinated cases the age groups that could be distinguished were 0, 1 and 2 months. Only three vaccinated cases were 6 to 11 months of age. Therefore in that stratum, only 1-4-year-olds could be compared with those aged 5-12-year-olds.

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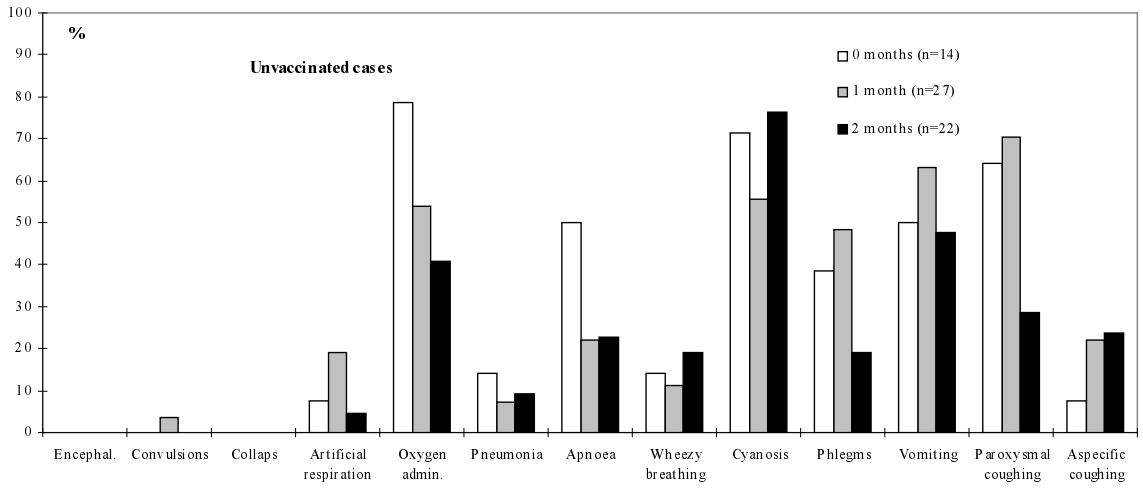

Figure 4. Relative distribution of symptoms in each age group in unvaccinated NSCK cases

Within the unvacccinated cases only for oxygen administration and phlegms a statistically significant difference was observed, i.e. unvaccinated cases aged one month reported more frequently phlegms than those aged two months and unvaccinated cases less than one month more often received oxygen than those aged one or two months. Although not statistically significant aspecific cough was less frequently reported by unvaccinated cases younger than one month and apnoea more frequently.

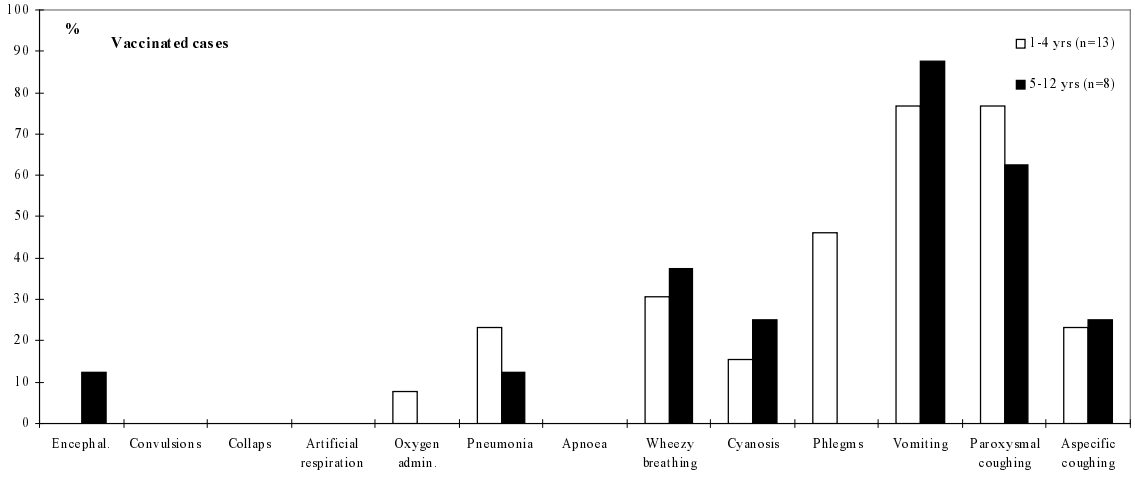

Figure 5. Relative distribution of symptoms in each age group in vaccinated NSCK cases

Phlegms were only reported for vaccinated 1-4-year-olds (46 %) and not for older vaccinated cases. For the other symptoms no age effect was observed.

3.6 Underling disorders and risk factors of the paediatric surveillance cases

As shown in Table 8 underlying respiratory disorders were most often reported for vaccinated children and included COPD, asthma and bronchitis (including bronchial hyperactivity and bronchospasm).

Table 8. Reported underlying respiratory disorders in NSCK pertussis cases according to vaccination status

Respiratory disorders	Unvaccinated n=66	Incompletely vac. n=7	Vaccinated n=24	Unknown n=18	Total n=115
COPD/asthma/bronchitis	0 (0%)	0 (0%)	12 (50%)	2 (12%)	14 (12%)
bronchopulmonal dysplasia	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
cricoid stenosis	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
immotile cilia	0 (0%)	0 (0%)	0 (0%)	1 (6%)	1 (1%)

Table 9 shows the condition at discharge of the cases. The three pertussis cases that died were all unvaccinated infants (boys, 0, 1, 2 months of age). A large part of the cases were still coughing at discharge.

Table 9. Reported condition at discharge from hospital in NSCK pertussis cases according to vaccination status

Condition at discharge	Unvaccinated n=66*	Incompletely vac. n=7*	Vaccinated n=24*	Unknown n=18*	Total n=115*
recovered	22 (33)	2 (29)	7 (29)	4 (22)	35 (30)
coughing	35 (53)	5 (71)	16 (67)	13 (72)	69 (60)
other symptoms besides coughing	6 (9)	0 (0)	1 (4)	1 (6)	8 (7)
died	3 (5)	0 (0)	0 (0)	0 (0)	3 (3)

* the total number of cases varies due to excluded cases with missing values for some symptoms

4 Discussion

In 1998, the second year of active monthly paediatric surveillance of pertussis, the number of reports was lower (n=144) compared to the previous year (n=204). Since the coverage of the system did not decrease (see below), this seems to reflect the lower incidence of pertussis in 1998 compared to 1997 which was also observed for notifications and cases with positive serology (3).
Like in 1997 pertussis was most severe and complications were more frequently reported for unvaccinated young infants less than three months of age. However, as was also reported in 1997, hospitalisation also occurred for vaccinated children. The slightly lower proportion of infants aged 3 to 11 months and higher proportion of infants aged 0 to 2 months in 1998 compared to 1997, might reflect a beneficial effect of the slightly higher content of pertussis toxin in the Dutch whole cell vaccine since November 1997.

4.1 Coverage of the paediatric surveillance

The coverage of the paediatric surveillance in 1998 according to the national registration of hospital admissions amounted to 47% for all reports compared to 43% in 1997. However, the somewhat higher coverage was nullified when the number of reports with questionnaire data was taken into account (37.3% in 1998 and 37.5% in 1997). This resulted from a decrease in response on the questionnaire for all reports from 88% in 1997 to 80% in 1998.
Despite this coverage, the reported cases were probably representative for all hospitalised cases less than 15 years; the age and gender distribution as well as the time of hospitalisation was similar for the paediatric surveillance and national hospital registration.

4.2 Laboratory diagnosis, vaccination status, age and clinical findings

The clinical diagnosis of pertussis was laboratory confirmed for 90% of the reported hospitalised cases in 1998 compared to 96% in 1997. This lower percentage was caused by a lower proportion of cases with positive culture or PCR (46%) compared to 1997 (53%). While the proportion of cases with positive two point serology was slightly higher (26% versus 23%) and the proportion of cases with positive one point serology was slightly lower (18% versus 21%) in 1998 compared to 1997.

Most hospitalisations occurred among children less than one year, particularly among infants less than three months, i.e. too young to be vaccinated. Twenty percent of the hospitalised children were 1 to 4 years of age and 10% was 5 to 10 years of age. For children at least 1 year of age the age distribution for 1997 was similar with this distribution in 1998; for all age groups a lower number of cases were reported compared to 1997. However, for infants less than one year of age the proportion of cases aged less than three months was higher (77% versus 59%), while the proportion of cases aged 3 to 11 months was lower in 1998 compared to 1997 (23% versus 41%). One of the possible explanations is that this might reflect a beneficial effect of the slightly higher content of pertussis toxin in the whole cell vaccine

since November 1997. For those children too young to be vaccinated no (or hardly any) effect is expected from this change. However, for those children who are (incompletely) vaccinated this change might have resulted in a somewhat lower incidence of hospitalised cases. This might also explain the somewhat higher median aged for vaccinated children compared to 1997 (44 months versus 19 months). However, it should be stressed that since the only way to study this reliably on a short term would have been a controlled trail, this indirect manner of studying this effect of the change in the vaccine must be interpreted very cautiously. Other unknown effects can not be ruled out. Therefore, longer follow-up and more data have to be available for a more reliable evaluation of this effect.

Since almost all unvaccinated children were less than three months of age and almost all vaccinated children were at least 1 year of age, the effect of vaccination status and age age could not be distinguished. This was also the case in 1997.
Among unvaccinated children pertussis was more severe and more often complications were observed than for vaccinated children: the three cases who died were all unvaccinated infants (0, 1 and 2 months old), the median time of hospitalisation was longer (10 days versus 4.5 days), cyanosis, apnoea and administration of oxygen were statistically significantly more frequently reported for unvaccinated compared to vaccinated cases, and although seldom reported, bradycardia and artificial respiration all involved unvaccinated cases.
Within unvaccinated cases symptoms were stratified by the age groups 0, 1 and 2 month. Phlegms, administration of oxygen and to a lesser extent apnoea were less frequently reported for cases aged two months while aspecific cough was slightly more often reported.
Comparison with other paediatric studies is difficult because of differences in case definition and study methods. However, the frequency of reported symptoms (such as vomiting, apnoea, pneumonia) found in our study were not remarkably different from two paediatric studies in France and Canada (7,8). Like in our study most hospitalised cases were less than one year of age and consisted mainly of unvaccinated infants less than three months old. The age distribution reflects both the selection of patients (paediatric cases) and high vaccination coverage. Thus even in well-vaccinated populations, pertussis remains an important cause of morbidity in young infants.

No remarkable differences were seen for the frequency of reported symptoms nor for the reported underlying disorders for cases reported in 1998 compared to 1997. Among vaccinated children frequently COPD, asthma or bronchitis was reported as underlying disorder. However, as reported in 1997, age-specific rates are needed (i.e. vaccinated children are older than unvaccinated children). Perhaps individuals with a respiratory disorder might be more easily acquire pertussis or have more severe symptoms.

4.3 Future developments and conclusive remarks

The paediatric surveillance was continued in 1999 and will be continued in the coming years. Despite incomplete coverage, it provides insight into the occurrence of severe pertussis in the

Netherlands. Important information on vaccination status, symptomatology and severity of pertussis is collected. Furthermore, it provides information on hospitalized cases in a shorter time than the national registration of hospital admissions (once a year).

Because possibly antigenic changes of *B. pertussis* play a role in the increased incidence since 1996, it might be worthwhile to consider collection of strains of patients reported in the paediatric surveillance for molecular epidemiological research (9). Information on serotype and genotype might be useful to study the association between serotype or genotype and severity of disease.

This active monthly paediatric surveillance will more frequently be used to verify trends observed in the routine sources, since the interpretation of our routine surveillance of notifications and laboratory data (serology and isolates of *Bordetella pertussis*) is hampered by various factors. The factors that hamper the interpretation of routine surveillance data include: (1) The change in case definition in April 1997. Since then also pertussis cases confirmed by positive one point serology should be notified. The criteria of interpretation of one-point serology have recently have been defined (10). The result of this change in case definition is that the proportion of cases with positive one point serology among the notifications has increased. Therefore, differences in the level of notifications between various years are difficult to interpret. (2) Decentralisation of serology. The National Institute of Public Health and the Environment was the only laboratory that performed pertussis serology till 1998. Therefore these data could be used as a national surveillance source. However, the number of other laboratories that perform pertussis serology is increasing, such that coverage of the serological surveillance according to data from our institute is decreasing to an unknown amount.
Hospital admissions are probably less sensitive to changes in the factors described. While only once a year information is obtained from the national registration of hospital admissions, with the monthly paediatric surveillance trends could be verified in an earlier stage.

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Appendix 1 abbreviations

CBS	Centraal Bureau voor Statistiek / Central Statistics Netherlands
COPD	Chronic Obstructive Pulmonary Disease
NSCK	Nederlands Signalerings-Centrum Kindergeneeskunde/ Netherlands Paediatric Surveillance Centre
PCR	Polymerase Chain Reaction
PEA	Provinciale Entadministratie / Provincial Vaccination Administration
SAS	Statistical Analysis Computer Program
SIG	Stichting Informatiecentrum Gezondheidszorg / Foundation Information Centre for Health Care
TNO	Nederlandse Organisatie voor Toegepast-Natuurwetenschappelijk Onderzoek / Netherlands Organisation for Applied Scientific Research

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