Whooping cough—a study of severity in hospital cases

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SUMMARY In an attempt to determine the clinical severity and prognosis of children admitted to hospital with whooping cough, 127 patients were studied prospectively during a 12-month period. Clinical and laboratory criteria were used and the impression gained was that most cases were mild, although 3 children were dangerously ill and at least 30% had symptoms lasting 2 months or longer. There were no deaths, and no permanent sequelae were noted. The mean age of patients was higher than in other series, which might have accounted for the fairly low severity. Although there was some evidence of a decline in severity and mortality, whooping cough is still an unpleasant and protracted illness.

During 1977 and 1978 the largest epidemic of whooping cough for 20 years was experienced in the UK. It occurred at a time of controversy concerning whooping-cough vaccine. Doubts about the efficacy and safety of the vaccine were set against a belief that the disease itself posed less of a threat than it had in the past. The notified case fatality ratio of 0.18/1000 in 1978¹ was lower by a factor of 4 than is generally the case, and anecdotal evidence suggested that the whooping cough was milder and more difficult to diagnose. In an attempt to evaluate the up-to-date clinical picture of the more severe forms of whooping cough, a prospective study was made of all patients admitted to the Regional Infectious Diseases Unit at Monsall Hospital, Manchester during a 12-month period.

Method

Monsall Hospital provides a regional infectious disease service for the North-western Region. Its catchment area for the more common infections, including whooping cough, extends to about half of greater Manchester which has a population of about 2½ million. As far as could be ascertained, about half the number of children with whooping cough admitted to hospital in greater Manchester during the 12-month period had been admitted to Monsall Hospital. Patients were included in the study if they had been referred to the hospital because of whooping cough, or if a diagnosis of whooping cough had been made after admission. Patients remained in the study unless a senior clinician decided, on clinical grounds, that the diagnosis was

not whooping cough. This appears to have provided an adequate criterion for study even though some degree of bias might have been expected. A standard clinical history was taken in each case. This included details of family size and rank, other cases of whooping cough in the family, vaccination history, and any treatment with antibiotics before admission. After the clinical examination the severity was assessed using criteria described below. Chest radiographs were taken as soon after admission as possible and a differential white blood cell count was made on the day of admission. Parnasal swabs were taken on admission and on the next 2 days and examined for *Bordetella pertussis*. Throat swabs were taken at the same time for viral studies. Two sera were obtained for pertussis serology, the first on admission and the second on discharge or after 2 weeks, whichever was earlier. During the stay in hospital the severity of illness was recorded every 12 hours. The grading used (described in detail below) appeared to be consistent with other more objective findings. Cyanotic attacks and convulsions were recorded, and an electroencephalogram was carried out on the only child in the series who suffered from convulsions. All patients were given a follow-up appointment 2 months after discharge and at that consultation an assessment of the clinical improvement and current status was made.

Results

From 1 October 1977 to 30 September 1978, 127 cases of whooping cough were studied. This represented 4.5% of the cases notified for the catchment

Table 1 Age and sex of 127 children with whooping cough

Age	Boys	Girls	Total
	No (%)	No (%)	No (%)
< 3 months	5 (8)	13 (19)	18 (14)
3-5 months	5 (8)	5 (7)	10 (8)
6-11 months	10 (17)	10 (15)	20 (16)
1-2 years	23 (39)	25 (37)	48 (38)
3-4 years	14 (24)	10 (15)	24 (19)
> 5 years	2 (3)	5 (7)	7 (5)

area of the hospital. A further 20 cases were excluded on clinical grounds. Parnasal swabs were taken from all these 20 patients but *B. pertussis* was not isolated from any. The ages of the children and the sex distribution are shown in Table 1.

Preadmission details.

Family size and history

It is said that whooping cough is more common in larger families.² The mean number of children in the affected households was 2.3, marginally greater than the national average. Sixteen affected children came from families with 4 or more children. Of the 91 patients from households with more than 1 child, 75 (83%) were the youngest in the household. In only 10 cases was the child who was admitted to hospital the oldest in the household.

The reasons for admission to hospital are often complex, and the presence of two cases of whooping cough in one household may well lead to one of them being admitted, whether or not the clinical condition of the child fully justifies such action. Of the 91 households mentioned above there were 40 (48%) in which at least 1 other child was suffering from whooping cough.

Vaccination status

Information about vaccination was obtained from the parents and from the records kept by the Area Health Authorities. The information from the parents was more complete, although the accuracy of neither source could be relied on completely, except in younger children where a firm decision against pertussis vaccine had often been made and was remembered. Both sets of data are given in Table 2 for comparison. The first column (0 doses) includes 35 children who were too young to have started courses of vaccine. Seven of the 127 children had probably received full courses of vaccine.

Antibiotics before admission

Details of any treatment with antibiotics were obtained from the parent or referring doctor, or

Table 2 Pertussis vaccination status

Information source	Doses given				Not known
	0	1	2	3	
Parents	115	1	4	7	—
Area Health Authority	92	5	1	2	27

from both. Ninety-three (73%) of the 127 children had been receiving antibiotics (generally erythromycin, penicillin, or ampicillin) for the whooping cough for at least 3 days.

Clinical history.

Nature of cough

All the patients in the series gave a history of cough. Ninety-seven (76%) of the 127 had recognisably spasmodic coughs. Two children had spasmodic sneezing.

Duration of cough and vomiting

The duration of cough, which in some cases was the stated reason for admission, is shown in Table 3. Thirty-seven per cent of the patients had coughed for at least 3 weeks and one child apparently had had symptoms for 10 weeks before admission. There was no significant correlation between the duration of cough before admission and size of family, one factor that might have been expected to predispose to early admission.

Vomiting was associated with the cough in 89 (70%) cases. Vomiting appeared to develop some time after the onset of the cough. Table 4 shows the duration of vomiting before admission.

Clinical examination. Only 20 (16%) of the children in the series had any abnormal clinical findings in the respiratory system. Nine had local signs that

Table 3 Duration of cough before admission

	Days									
	1-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41+	
No of patients (%)	14 (11)	37 (29)	28 (22)	1 (0.8)	30 (24)	12 (9)	4 (3)	0 (0)	1 (0.8)	

Table 4 Duration of vomiting before admission

	Days							
	0	1-5	6-10	11-15	16-20	21-25	26-30	31-35
No of patients (%)	38 (30)	29 (23)	26 (20)	15 (12)	1 (0.8)	12 (9)	4 (3)	2 (2)

suggested consolidation; a transient pleural rub was found in one child, and scattered rales or rhonchi were present in 11 children. A severity grading was used which took into account clinical and radiographic findings: grade 1, requiring symptomatic treatment only; grade 2, requiring specific treatment for complications; grade 3, requiring treatment for life threatening cardiorespiratory conditions. Three children were classed as grade 3: one had extensive pulmonary collapse with heart failure resulting from a bronchial plug, and the others had severe bronchopneumonia. Eight children required treatment for less severe bronchopneumonia or bronchitis, and the remaining 116 required symptomatic treatment only. Six of the 11 children classified as grades 2 or 3 were under 1-year old and 4 of them were under 3 months. This represents 12.5% and 22% respectively of the total children in these age groups.

Laboratory findings.

Bacteriology

Three pernasal swabs were taken from each child. *B. pertussis* was isolated from at least one swab in 72 (57%) cases.

Virology

Viruses were isolated from the nasopharynx of 25 (19.7%) children. The virus types were as follows: adenovirus (n=12), parainfluenza 3 (n=6), respiratory syncytial virus (n=2), rhinovirus (n=2), *Herpes simplex* (n=3), mumps virus (n=2). Two children had dual infections (1 had mumps plus adenovirus, and 1 had mumps plus *Herpes simplex*). Of these 25 children, 11 (44%) were also positive for *B. pertussis*.

White cell count

The total white cell count is of less diagnostic significance than the total lymphocyte count. The

distribution is shown in Table 5. The mean lymphocyte count in *B. pertussis*-positive children was $15.1 \times 10^9/l$ compared with $9.9 \times 10^9/l$ in those from whom *B. pertussis* was not isolated. The difference in these distributions is highly significant ($P = <0.0005$), supporting the accepted belief that a high lymphocyte count is often associated with recoverable *B. pertussis* in cases of whooping cough.³

Chest radiography

In only 3 cases were major radiographic changes found. These were pulmonary collapse (in 1 patient) and severe bronchopneumonic consolidation (in 2 patients). In 26 cases there were less important abnormalities, ranging from minor consolidation to hilar lymph node enlargement.

Serology

Indirect haemagglutination and complement fixation tests for pertussis were performed on paired sera from 50 children. The rises in titre are shown in Table 6.

Clinical severity during stay in hospital. At the end of each day and night nursing shift, an assessment was made by the nursing staff of the clinical condition of each child with whooping cough. This was graded as follows:

- 0 = No cough, child quite well.
- 1 = Child coughs but is not distressed, does not vomit or become cyanosed; eats, sleeps, and plays normally.
- 2 = Child coughs and vomits. No cyanosis. Eats and sleeps well except during coughing bouts.
- 3 = Child coughs and vomits, or has cyanotic episodes. Severely distressed. Eating and sleeping greatly disturbed.

The nursing staff agreed that this was a workable grading and that it represented the clinical progress satisfactorily. The Figure shows the severity grading of the *B. pertussis*-positive and negative groups on admission and of those remaining on days 3, 7, 10, 14, and 21. The percentage of patients remaining at each interval who were *B. pertussis*-positive rose

Table 5 Lymphocyte count

<i>B. pertussis</i>	Lymphocyte count ($\times 10^9/l$)					
	0-4	5-9	10-14	15-19	20-24	25+
Positive	0	24	19	12	7	10
Negative	7	21	21	5	1	—

Table 6 Serology results on 50 cases. Rises in indirect haemagglutination (IHA) and complement fixation test (CFT) titres according to whether the children were *B. pertussis*-positive or negative

<i>B. pertussis</i>	< ×4		×4		×8		×16		×32		×64	
	IHA	CFT	IHA	CFT	IHA	CFT	IHA	CFT	IHA	CFT	IHA	CFT
Positive	17	19	3	3	2	1	—	2	2	—	1	—
Negative	20	23	2	—	2	2	—	—	1	—	—	—

Figure 7 Clinical severity of cases during stay in hospital.

Table 7 Cyanotic attacks

No of attacks	Age groups					
	<3	3-5	6-11 months	1-2	3-4	>5 years
1-20	7	2	2	4	—	1
21-50	3	—	—	—	—	—
>50	—	—	—	—	1	—
Total	10	2	2	4	1	1
(% of total in age groups)	(55)	(20)	(10)	(8)	(4)	(14)

steadily from 56% on day 3 to 88% on day 21. As was to be expected there was a shift from grade 3 towards grade 1 as time progressed, but even by day 21 there was one child in each of grades 2 and 3.

Cyanotic attacks. The feature of whooping cough often most distressing to children and parents is the cyanotic attack. Twenty children were observed to have cyanotic attacks. Although these occurred across the age range they were more common in the youngest children. The distribution by age is shown in Table 7.

Convulsions. One 19-month-old child developed epileptiform fits during her stay in hospital. An electroencephalogram showed no focal abnormality,

and although her convulsions persisted after her discharge, her condition was normal within 12 months.

Duration of stay and outcome. The mean duration of stay in hospital was 12 days. The mean for the *B. pertussis*-positive group was 14.2 days, that for the negative group 9.8 days. Forty-two (33%) of all patients were in hospital for at least 2 weeks. There were no deaths.

Follow-up. Only 57 patients returned for follow-up 2 months after discharge. One child, already mentioned, had neurological sequelae. A further 37, 29% of the original series, were still coughing, particularly at night. No clinical or radiological evidence was found of long-term respiratory sequelae.

Discussion

The diagnosis of whooping cough was made primarily on clinical grounds and the cases varied in severity. However, those from whom *B. pertussis* was isolated tended to be more ill. Although there was no difference in the duration of symptoms before admission, the *B. pertussis*-negative group had a shorter symptomatic period which is reflected in the rate of clinical improvement after admission. This may indicate the presence within this group of milder infections which had cleared spontaneously or it may be a result of treatment with antibiotics before admission. This view may be supported by the serology results which show no significant difference in the distribution of titres between the *B. pertussis*-positive and negative groups. It must be said however, that 14 children with proved *B. pertussis* infections showed insignificant rises to both tests which casts some doubt on the diagnostic value of such tests. It is interesting to note that 32% of those patients from whom *B. pertussis* was isolated had had symptoms for 3 weeks or longer, which goes against the common belief that the organism is difficult to recover except in the early stages of the infection.⁴

Of the 93 children who had been given antibiotics, 50 were found to be *B. pertussis*-positive on admission. Although 24 of them had been given ampicillin or penicillin, neither of which would be expected to achieve clearance of the nasopharynx, 13 children were known to have received courses of erythromycin or co-trimoxazole, both of which are known to be effective for this purpose.^{5,6} This may have significance in relation to the value of these antibiotics in the management of cases at home.

A further group within the *B. pertussis*-negative group may be those whose symptoms were caused by organisms other than *B. pertussis*. No other significant bacterial pathogens were found but a number of different viruses was isolated. Eleven of the 25 children with virus infections were also *B. pertussis*-positive. Of the 14 who were *B. pertussis*-negative, 12 had spasmodic coughs and 2 had spasmodic sneezing. There was no significant clinical difference between the children with or without viral infections and it is difficult to conclude that these viruses had much relevance to the clinical presentation or course.

The age distribution of children in this series shows a significant shift from children under 6 months into the 1- to 2-year age group compared with the series of children in hospital reported by Miller and Fletcher,⁷ and our experience in the previous 10 years. This may in part explain the fairly low severity of the illness in our study, but of those 11 children deemed to be more severely ill on admission, only 4 (36%) were under age 6 months. This compares with 93% in Miller and Fletcher's series. Furthermore, only 1 of the 3 critically ill children in our series was less than 12-months old.

No conclusions about the efficacy of pertussis vaccine can be drawn from the data presented in this series.

Although there were no deaths in the series, and all but a few of the children suffered a fairly mild illness, two points should be made. Firstly, all these children underwent admission to hospital, which is in itself undesirable, and secondly, the illness was protracted in most cases. At least 29% of the patients had symptoms for longer than 2 months, and while there was no evidence of long-term damage, an illness of this duration represents a stress to the children and their families.

There is evidence that the severity of whooping cough has declined and the death rate, at least in this last epidemic, shows a sharp fall from the expected figure. However, whooping cough remains a cause of protracted illness in younger children and since 5% may require to be admitted to hospital, it should not be considered as a past problem.

We record with regret that Dr Alastair Ironside died on 24 August 1980.

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