

## Natural course of 500 consecutive cases of whooping cough: a general practice population study

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### Abstract

**Objective**—To describe the natural course of whooping cough.

**Design**—Observational study of a general practice population.

**Setting**—Discrete semirural East Midlands practice of 11 500 patients.

**Subjects**—500 consecutive cases of whooping cough diagnosed clinically during 1977-92.

**Main outcome measures**—Incidence of vomiting, whooping, apnoea, admission to hospital, and complications; duration and frequency of paroxysms. Pattern of spread.

**Results**—The incidence in the practice population was 4347/100 000 population compared with a notification rate for England and Wales of 717/100 000. Most cases were relatively mild. 284 patients vomited after paroxysms, 242 whooped, and 57 had apnoea. Duration and frequency of paroxysms varied widely. Female and unimmunised patients suffered more severe disease. *Bordetella* was isolated from fewer immunised patients (24/96 v 63/122 unimmunised). Infection was usually spread through contacts with someone with clinical whooping cough. Five patients developed pneumonia, three of whom had been immunised. Three patients required hospital admission.

**Conclusions**—Most cases of whooping cough are relatively mild. Such cases are difficult to diagnose without a high index of suspicion because doctors are unlikely to hear the characteristic cough, which may be the only symptom. Parents can be reassured that a serious outcome is unlikely. Adults also get whooping cough, especially from their children, and get the same symptoms as children. The difficulty of early diagnosis and probability of missed cases reinforces the need to keep the incidence low through immunisation in order to protect infants, who are the most vulnerable.

### Introduction

Whooping cough is caused by infection with *Bordetella pertussis* or, more rarely, *Bordetella parapertussis*. It is a highly infectious disease with a broad spectrum of clinical severity ranging from a trivial cough, through the classic picture of vomiting, whooping, and apnoea with paroxysmal coughing, to pneumonia, encephalopathy, and death.<sup>1</sup>

Publicity given to the more severe consequences of whooping cough has created a widely held perception that the disease is always severe, debilitating, and dangerous. Such a perception helps to encourage immunisation, but if untrue it degrades diagnostic accuracy, produces inaccurate epidemiological data, and hinders the wise management of those with the disease or at risk of it.

I studied every case of whooping cough since 1977

that I could discover in the practice in which I work. This paper describes the natural course of the disease in this general practice population.

### Patients and methods

The patients studied were registered with a stable, semirural, four doctor practice with around 11 500 patients, most of whom are in social classes II and III. The study started in 1977 at the start of a large outbreak of whooping cough in the practice<sup>2</sup> and nationally, and all cases since then have been studied. Many were detected at routine consultations, and inquiries were then made about possible sources of infection. Sources of infection were followed up by me or a health visitor by examination of case notes and talking to teachers and parents. I questioned and examined most of the 500 patients at least once, the remainder being seen by a health visitor or partner. Patients were thereafter examined according to clinical need and followed up, often by telephone, until the condition was no longer troublesome or had cleared.

Clinical diagnosis was based on a history of three weeks of coughing characteristic of the disease—that is, choking fits with the patient attempting to expel every bit of air from the lungs and going red or blue in the face. I also included patients with less than three weeks of paroxysms but strong alternative evidence such as a positive *bordetella* culture or a family member with clear symptomatic whooping cough.

Information recorded included vomiting, whooping, apnoea, maximum number of paroxysms in 24 hours, known contacts, culture results, immunisation, attendance at school or play group, complications, drug treatment, age, date of onset, age and immunisation status of siblings, and whether siblings were affected. Duration was recorded as accurately as possible in a disease with no clear end point. Parnasal swabs were taken whenever possible. They were often not taken, however, as the procedure is unpleasant and rendered useless by some antibiotics.

The  $\chi^2$  test was used to analyse categorical data and the *t* test for parametric data.

### Results

The nature and duration of the cough alone was sufficiently distinctive for diagnosis in about 95% of cases. At about two weeks into the illness the cough was almost exclusively paroxysmal, with no coughing between episodes of severe paroxysm. Frequency of paroxysms varied from every 15 minutes to 12 hours. The diagnosis could be suspected at an earlier stage if other symptoms such as vomiting, whooping, and apnoea were present and there was a known source of infection, but sore throat, catarrhal symptoms (present in only about a third of patients), and sticky sputum were unhelpful.

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The disease seemed to have three phases. In the first phase, which lasted 3 to 14 days, an unremarkable dry cough became paroxysmal. The second phase was characterised by paroxysms, in which the patient made repeated expiratory coughing efforts without pausing for inspiration, so that each successive burst became shorter as the breath available diminished until there was no more. The face went red and the body went tense, then often was still for a variable time, with occasional cyanosis. This was followed by a sudden inspiration, sometimes strident: the whoop. Several such cycles usually occurred together and lasted minutes, sometimes ending with or including vomiting. Patients able to describe the apnoea sensation said it felt as if they had "forgotten how to breathe." This phase lasted at least two weeks. In the third phase the paroxysms gradually became less frequent.

The infrequency of paroxysms even in the severe phase (mean 13.5 a day) meant that a doctor was unlikely to hear one. Most parents had no idea what a whoop was but recognised it when it was imitated. Six adults recalled having whooping cough in childhood, and one 3 year old in the study got it again at 13.

Many children had only three or four paroxysms a day, mostly at night. Their parents had not suspected whooping cough, and there were probably other cases which remained undetected. There were 24 patients whose paroxysms lasted less than three weeks but were considered to have clinical pertussis. Sixteen of these had positive swab cultures. The remainder had convincing symptoms for under three weeks and close contact with the disease.

#### DISTRIBUTION AND SYMPTOMS

Five hundred cases of whooping cough were diagnosed between 1977 and 1992, with almost half occurring in the first three years. Table I shows the number of cases, annual incidence in the practice, and the notification rates in England and Wales. The ratio of practice incidence to the notification rate for the years 1977-92 was about 6 to 1 (4347 per 100 000 to 717 per 100 000).

Table II shows the age and sex distribution of the cases. The peak incidence was in 3 year olds, but there was another small peak in those in their 30s. Of the 500, 219 (44%) were male and 281 (56%) female. Of 50 adults affected, 16 (32%) were men and 34 (68%) women.

The duration of paroxysmal coughing was recorded in 351 cases. Mean duration was 51.7 days (range 2 to 164; 95% confidence interval 46 to 57). The duration correlated indirectly with age ( $r = -0.11$ ,  $P = 0.04$ ; 95% confidence interval  $-0.006$  to  $-0.21$ ) and directly with the number of paroxysms a day (170 patients,  $r = 0.27$ ,  $P = 0.0004$ ;  $0.12$  to  $0.40$ ). The number of paroxysms a day was known for 186 patients and ranged from 2 to 100 (mean 13.5; 95% confidence interval 11.5-15.4).

A total of 284 (57%) patients vomited after some paroxysms, 242 (49%) whooped at some stage, and 57 (11%) stopped breathing long enough to cause anxiety or go blue; 51 of those who stopped breathing also whooped. The pattern in adults was similar to that overall, with 22 (44%) vomiting, 23 (50%) whooping, and 6 (12%) developing cyanosis. Compared with males, females vomited more (174 (62%) v 112 (51%),  $P = 0.02$ ), whooped more (149 (53%) v 96 (44%),  $P = 0.05$ ) and had more frequent paroxysms (data on 186;  $15.1/\text{day}$  v  $11.5/\text{day}$ ,  $P = 0.04$ ; 95% confidence interval for difference  $0.2$  to  $6.9$ ).

One hundred and eighty two of the patients had been immunised, 277 had not, and no immunisation data were available for 41. Those who had been immunised experienced fewer symptoms: 89 (49%) v 179 (65%) vomited ( $P = 0.001$ ), 70 (39%) v 155 (56%) whooped ( $P = 0.0002$ ), and 14 (8%) v 41 (15%) had apnoea

( $P = 0.02$ ). The mean duration was 55 days in unimmunised patients and 49 days in immunised patients (data on 351;  $P = 0.05$ ; 95% confidence interval  $-0.17$  to  $12.4$ ). The mean number of paroxysms a day was 15 in unimmunised patients and 11 in immunised patients (data on 186;  $P = 0.02$ ; 95% confidence interval  $0.7$  to  $7.5$ ).

Culture information was obtained for 239 patients. One hundred were positive for *B pertussis* and two for *B parapertussis* (43%). The immunisation status was known for 218 of the 239 patients: 63 of 122 unimmunised patients had positive cultures (52%) compared with 24 of 96 (25%) immunised ( $\chi^2 = 15.9$ ,  $df = 1$ ;  $P = 0.0001$ ).

The pattern of spread was usually traceable from case to case in the early stages of an outbreak. Schools were the main centres of clustering. The figure shows the probable pattern of spread at the start of an outbreak in 1985. Thirty adults acquired infection from their children.

Systematic upset was uncommon and usually confined to infants or toddlers, in whom feeding would precipitate a paroxysm. The greatest distress was often suffered by parents who, when dealing with a child with severe paroxysms, experienced weeks of sleepless nights.

Five children developed pneumonia but all fully recovered. Four of these children were aged 5-7 and three were immunised. The fifth child was 5 weeks old and presented with pneumonia. Swabs subsequently grew *B pertussis*. She required hospital admission. Two other children were admitted to hospital, one after a two minute apnoea attack and another with poor home circumstances. Otitis media was seen but not specifically recorded. I did not see a subconjunctival haemorrhage caused by whooping cough or any similar traumatic phenomenon.

Although many asthmatic patients got whooping cough, it did not seem to exacerbate asthma. Indeed, during and after whooping cough asthma was less troublesome and often remained so for many months.

#### Discussion

This study gives a general practice perspective of the natural course of whooping cough at a time when the consequences of a fall and rise in immunisation became clear. It has the advantage of being by a single observer in a stable and discrete practice, although it was too small to measure rare events such as convulsions and death. The overall impression was of a disease much less severe than suggested by textbook descriptions or parents' fears.

#### OTHER STUDIES

Most population based studies of whooping cough have relied on notified cases either exclusively or as a basis for further case finding, and they show widely differing results. Vesselinova-Jenkins *et al* found that 8.3% developed pneumonia, 7% had convulsions, and 22% were admitted to hospital.<sup>3</sup> A study based on notified cases in a similar area found a much lower rate of complications and a hospital admission rate of 2.8%,<sup>4</sup> while another study of 8000 notified cases showed a hospital admission rate of 10%.<sup>5</sup> Grob *et al* looked at cases diagnosed clinically by 68 general practitioners and found a pattern similar to that in this study, observing, "The classical picture of whooping cough as typified by a moderately ill child with paroxysmal cough and characteristic whoop was not often encountered."<sup>6</sup>

The range of severity in this study, from two paroxysms a day to a critically ill 5 week old baby with pneumonia, is consistent with standard accounts of this disease,<sup>1</sup> but the relatively mild course of most

TABLE I—No of cases and annual incidence of whooping cough in Keyworth and national incidence figures

	Keyworth		England and Wales
	No of cases	Cases/100 000	(cases/100 000)
1977	163	1417	35
1978	59	513	134
1979	13	113	62
1980	3	43	42
1981	40	347	39
1982	22	191	132
1983	3	26	38
1984	0	0	11
1985	55	473	44
1986	40	347	72
1987	40	347	30
1988	1	8	10
1989	17	147	22
1990	30	260	30
1991	8	69	10
1992	4	34	4.6

TABLE II—Incidence of whooping cough by age and sex, 1977-92

Age (years)	Males	Females	Total
0	8	7	15
1	15	20	35
2	22	21	43
3	28	58	86
4	31	28	59
5	27	26	53
6	24	27	51
7	16	14	30
8	10	7	17
9	5	16	21
10	3	10	13
11	7	3	10
12	1	1	2
13	0	5	5
14	1	2	3
15	2	1	3
16	2	0	2
17	1	1	2
18	0	0	0
19	0	0	0
20-	3	6	9
30-	6	17	23
40-	6	8	14
50-	1	1	2
>60	0	2	2



cases with a mean of 13.5 paroxysms a day, half of patients never whooping, and less than 1% with significant complications is not. The differences are probably due to the fact that case finding was by consulting room diagnosis, and possibly that most patients came from higher social classes.

#### IDENTIFYING WHOOPING COUGH

The only reliable distinguishing characteristic of whooping cough was the exclusively paroxysmal cough. This, however, was rarely observed by a doctor, so the initial diagnosis was usually made on history alone and could be easily missed without a high index of suspicion. Staff sometimes heard the characteristic cough in the waiting room and diagnosed it. Similarly, experienced parents pointed out the possible diagnosis to other parents.

If my practice was typical, the incidence of whooping cough was about six times greater than the national notification rate during the study period. This suggests that most cases of whooping cough that occur are either not notified or not recognised, other previous work indicates that cases are probably not being notified.<sup>7</sup>

#### DISTRIBUTION

The disease was most common in 3 year olds, with a small peak in those in their 30s. This reflected the age of parents of children with whooping cough. Most were surprised when told they also had it, believing it to be a childhood condition. Six adults had a childhood history of the disease.

The duration of coughing illustrates the variability of the condition. The mean duration was 52 days, but the range was 2 to 164. The duration of coughing correlated with decreasing age in line with the disease being more serious in the young. The duration of illness correlated with the frequency of paroxysms, although duration of coughing, frequency, vomiting, or whooping did not seem related to severity in individual cases. On the other hand, apnoea and the duration of individual paroxysms did. In many of the most distressing cases the patient had infrequent severe paroxysms whereas in some of the least distressing paroxysms were frequent but short.

The sex ratio of patients is consistent with previous findings that females are more susceptible, and in adults twice as many females were affected, possibly reflecting more contact with children. Adults displayed similar symptoms to children, although a different clinical picture has been reported by some.<sup>18</sup> Females also had more vomiting, whooping, and paroxysms.

#### PROTECTING THE VULNERABLE

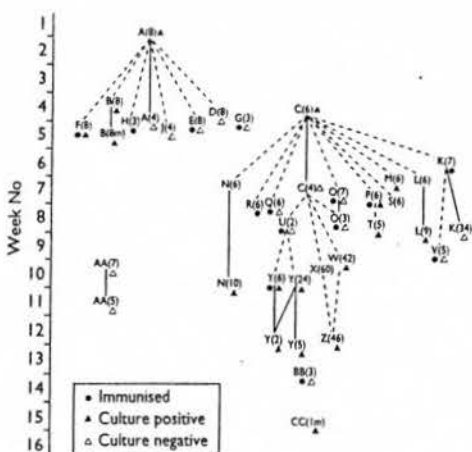
The effects of immunisation on prevention in this population have been reported,<sup>9\*</sup> but if prevention fails this study confirms that the disease is less severe in those who have been immunised. Isolation of bordetella was also less common in immunised patients, suggesting that immunised children are less infectious.

#### Key messages

- Whooping cough is widely thought of as a serious disease
- In this study of 500 cases, most were mild and half the patients did not whoop
- An exclusively paroxysmal cough is the most reliable diagnostic indicator
- Low frequency of such coughs means that the diagnosis may be missed without a high index of suspicion
- Herd immunity must be maintained by immunisation programmes in order to protect those too young to be immunised

This finding provides evidence that herd immunity plays a part in the efficacy of pertussis vaccine.

Plotting routes of spread from case to case is a helpful way of strengthening clinical diagnosis.<sup>10</sup> The example shown in the figure demonstrates the highly infectious nature of the disease, with two patients probably infecting many others. The unconnected cases suggest the existence of subclinical or missed cases.



Connections between all cases of whooping cough occurring between July and October 1985. Lines show presumed routes of transmission; solid for family contact, broken for other. Each family is represented by a letter (A to Z) then two letters (AA, BB, etc) and ages in brackets

Most of the adults and parents did not think that they or their children were particularly ill. They did not suspect whooping cough, and often took considerable persuading of the diagnosis. Many cases were detected while searching for the source of another patient's infection. Those identified in this way often said that they would never have considered going to a doctor since, although the cough was severe, it was infrequent. These cases would normally have been overlooked.

If whooping cough is commonly a mild disease and likely to be missed, what are the implications for clinical practice? If whooping cough were perceived as a less severe disease it might have an adverse effect on immunisation uptake. Since early diagnosis is difficult, and neither isolation nor treatment with antibiotics is sufficiently effective, it is important to emphasise the vaccine's major role in maintaining herd immunity.

Information for professionals and the public should give a more balanced view of the natural course of whooping cough, recognising the high prevalence of mild cases as well as the continued seriousness for infants.<sup>11</sup> Parents of children with the disease or in contact with it should be reassured that serious illness with complications is unlikely, but education should ensure that parents understand that a high immunisation rate is the only practical means of reducing damage and deaths in those too young to be immunised.

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