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The severity of whooping cough in hospitalised children – is it declining?

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SUMMARY

Four hundred and sixty admissions for whooping cough to three hospitals between 1974–9 were reviewed. Many children had a long illness. More than half of them had severe or moderately severe coughing spasms and a quarter had pronounced feeding difficulties. The incidence of clinical pneumonia and convulsions was low and there were no deaths. The disease continues to be much more severe in infancy. There was some evidence that the disease declined in severity over the period studied. A number of factors including increased use of erythromycin may have contributed to this change.

INTRODUCTION

In recent years valuable information has been obtained about the efficacy (Church, 1979; Pollard, 1980; Grob, Crowder & Robbins, 1981; PHLS, 1982) and possible toxicity of whooping cough vaccine (Miller *et al.* 1981; Pollock & Morris, 1983). One of the crucial aspects of the controversy about the continuing need for whooping cough vaccination (Miller, Alderslade & Ross, 1982) is, however, the question of the current severity of the illness. The enormous variations in the course of whooping cough (Lapin, 1943) make severity difficult to assess and though there are several reports of the features and complications of the illness in the late 1970s, such reports may poorly reflect the impact of the disease on a child. Indeed, children may suffer a debilitating protracted illness without any of the conventional complications of the illness. Furthermore, there have been suggestions that the severity of the illness is declining, but apart from the reduced case-fatality in the last decade (DHSS, 1981), the evidence for such a decline is mostly anecdotal (Christie, 1980) and a recent study concluded that severity did not change in hospitalised children between 1974–5 and 1978–80 (Pollock, Miller & Lobb, 1984).

In view of these difficulties in assessing the severity of whooping cough and the uncertainty as to whether it is declining, we have reviewed the case-notes of children hospitalised between 1974 and 1979 to compare the severity in the two epidemics of 1974–5 and 1977–9.

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PATIENTS AND METHODS

The hospital notes of all children admitted between 1974 and 1979 with whooping cough to three adjacent South London hospitals were reviewed. The notes were identified from Hospital Activity Analysis (HAA) records (ICD codes 033, 033·0, 033·1, 033·9) and were selected for study on the basis of the following diagnostic criteria: (1) culture positive for *Bordetella pertussis*; or (2) typical paroxysmal cough with either a lymphocytosis or typical whoop or apnoeic attack(s) with spasms; or (3) typical cough for at least 2 weeks plus contact with a known case or vomiting or cyanosis associated with spasms. Information was extracted relating to the details of the admission, the illness (including aspects before admission and after discharge), investigations, treatment and prior vaccination.

With regard to the illness, the total duration of cough was estimated by adding the length of the pre-admission history, length of stay and length of persistence of cough after discharge, if known. Cough present at one clinic visit and not at the next was considered to have lasted until halfway between those clinic visits unless stated otherwise. The severity of cough was graded as severe, moderate or mild on the basis of medical and nursing notes. Feeding behaviour was graded according to the number of days for which nursing reports referred to poor feeding and the need for a nasogastric tube. The percentage weight lost from admission was estimated provided weight had been recorded at least every second day. The temperature, pulse and respiratory rate on admission and for three subsequent readings 12 hourly was recorded and the mean of the four readings used in analysis.

The severity of the illness in the two epidemics, defined as 1974–6 and 1977–9 was compared. In view of the differing age distribution between the two epidemics comparisons were made separately for infants and for those of 1 year or older. Analysis of covariance was used to compare admission temperature, pulse and respiration between epidemics whilst controlling for age. The prevalence of a particular item was normally taken to be the number of cases recorded as positive for that item related to the total number of cases, irrespective of the number with missing information. The proportions of cases with missing information about a particular item were compared between the two epidemics to assess whether recording habits had changed. The χ^2 test was used for comparison of categorical variables and the t-test for continuous variables.

RESULTS

HAA listed 474 admissions between 1974–79. Three of these were wrongly coded and 11 did not meet the diagnostic criteria; 272 (59%) of the remaining 460 cases were female and 250 (54%) were infants. Social classes 3 manual, 4 and 5 contributed 65% of cases. In the 60% for whom a contact history was recorded, 49% had a home contact with whooping cough and in 32% there was no obvious source.

The overall severity of the illness

The duration of the illness before admission was 2 weeks or less in 58%, 2–4 weeks in 32% and 4–10 weeks in 10%. Most admissions (60%) lasted 7 days or less

Table 1. *Number (and percentage) of children in each age group in relation to duration of stay in hospital*

	Stay in hospital (days)					
Children	0–3	4–7	8–14	15–21	22+	
< 1 yr age						
1974–6	12 (12)	21 (20)	23 (22)	22 (21)	25 (24)	Total $\chi^2 = 16{\cdot}5$, $P = 0{\cdot}002$
1977–9	29 (20)	37 (25)	49 (33)	16 (11)	16 (11)	χ^2 trend $= 12{\cdot}1$, $P = 0{\cdot}0005$
Total	41 (16)	58 (23)	72 (29)	38 (15)	41 (16)	
⩾ 1 yr age						
1974–6	21 (48)	13 (30)	7 (16)	2 (5)	1 (2)	Total $\chi^2 = 1{\cdot}8$, $P = 0{\cdot}6$
1977–9	91 (55)	51 (31)	17 (10)	5 (3)	2 (1)	χ^2 trend $= 1{\cdot}5$, $P = 0{\cdot}2$
Total	112 (53)	64 (31)	24 (11)	7 (3)	3 (1)	
Total	153 (33)	122 (27)	96 (21)	45 (10)	44 (10)	

Table 2. *Symptoms and signs before and during admission*

	Cases under 1 year (percent)			Cases 1 year or over (percent)			All cases 1974–9 (percent)
	1974–6 $n = 103$	1977–9 $n = 147$	Total $n = 250$	1974–6 $n = 44$	1977–9 $n = 166$	Total $n = 210$	Total $n = 460$
Before admission							
Cyanosis	52 (51)*	53 (36)	105 (42)	15 (34)	59 (36)	74 (35)	179 (39)
Apnoea	10 (10)	10 (7)	20 (8)	5 (11)	11 (7)	16 (8)	36 (8)
Whoop	31 (30)	50 (34)	81 (32)	15 (34)	74 (47)	89 (42)	170 (37)
Vomiting	60 (58)	102 (69)	162 (65)	33 (75)	128 (77)	161 (77)	323 (70)
Fever	6 (6)	15 (10)	21 (8)	6 (14)	22 (13)	28 (13)	49 (11)
During admission							
Cyanosis	40 (39)	48 (33)	88 (35)	3 (7)	18 (11)	21 (10)	109 (24)
Apnoea	13 (13)	14 (10)	27 (11)	1 (2)	6 (4)	7 (3)	34 (7)
Whoop	36 (35)**	75 (51)	111 (44)	18 (41)	79 (48)	97 (46)	208 (45)
Vomiting	63 (31)	85 (58)	148 (59)	23 (52)	92 (55)	115 (55)	263 (59)
+Fever > 38 °C	22 (41)*	17 (22)	37 (28)	4 (24)	13 (22)	17 (22)	56 (27)

* $P < 0{\cdot}05$; ** $P < 0{\cdot}01$; +Data as percentage of those for whom temperature charts available.

Table 3. *Comparison of cough severity between the two epidemics* (% n)

	Cases under 1 year (percent)			Cases 1 year or over (percent)			All cases 1974–9 (percent)
	1974–6 $n = 102$	1977–9 $n = 146$	Total $n = 248$	1974–6 $n = 44$	1977–9 $n = 160$	Total $n = 204$	Total $n = 452$
Severe	24 (24)	13 (9)	37 (15)	2 (5)	3 (2)	5 (3)	42 (9)
Moderate	57 (56)	82 (56)	139 (56)	17 (39)	72 (45)	89 (44)	228 (50)
Mild	21 (21)	51 (35)	72 (29)	25 (57)	85 (53)	110 (54)	182 (40)
	Total $\chi^2 = 12{\cdot}9$, $P = 0{\cdot}002$ χ^2 trend $= 12{\cdot}0$, $P = 0{\cdot}0005$			Total $\chi^2 = 1{\cdot}4$, $P = 0{\cdot}5$			

(Table 1), though 10% were in hospital for between 3 and 12 weeks. Though 87% had a cough (of varying severity) at discharge, only 40% were followed up. For all cases, at least 45% had an illness lasting 5–12 weeks and 9% 3 months or more. These figures under-estimate the true length of illness since in only 69 cases (15%) was the duration of the cough definitely known, of whom 65% had an illness lasting 5–12 weeks and 28% an illness lasting 3 months or more. Thirteen percent of all cases required re-admission within 1 month.

All cases had paroxysmal cough, and of the other symptoms and signs (Table 2), vomiting was commonest, reported in 70% before admission and 59% during admission. Overall, 59% were thought to have a severe or moderately severe cough (Table 3) and 27% had feeding difficulties. Weight charts were available for 262 patients (57%) and 50% of these showed weight loss (mean 4% of admission weight). Clinically detected pneumonia occurred in 4%, though consolidation on the chest radiograph was reported in 22%. Fits occurred in 2%, otitis media in 4%, other complications in 5% and coincidental illness (such as gastroenteritis and specific viral illnesses) in 14%. There were no clinically detected cases of atelectasis (though radiologically this was reported in 5%), no cases of encephalopathy and no deaths.

Compared with those aged 1 or older, infants tended to be admitted earlier ($P = 0{\cdot}002$) though 8% were ill for 4–10 weeks before admission. Infants had longer admissions ($P < 0{\cdot}0001$) and were more likely to have cyanosis ($P < 0{\cdot}0001$), apnoea ($P = 0{\cdot}002$), a fever of more than 38 °C ($P = 0{\cdot}03$) and a severe or moderately severe cough ($P < 0{\cdot}0001$). Infants had more feeding difficulties (37% *vs.* 16%, $P < 0{\cdot}001$) and required a nasogastric tube more often (13% *vs.* 1%, $P < 0{\cdot}001$) but did not suffer more complications than the older children and had fewer coincidental illnesses (11% *vs.* 18%, $P = 0{\cdot}04$). Four children required intensive care and three, all infants, were ventilated by hand for a short period, one of these three subsequently requiring mechanical ventilation for a period of 4 days. Intravenous fluids were given to eight (four infants).

Seventy-seven percent of cases had pernasal swabs reported and 29% of these were positive for *B. pertussis*. In the 72 cases from whom both pernasal swabs and virological studies were obtained, the proportions with positive virology did not differ significantly between those with and without a positive pernasal swab (22% *vs.* 25%). The mean white cell count was 18800/mm^3 and mean lymphocyte count 13300/mm^3 with no significant difference between infants and the rest. Very few children had been vaccinated against whooping cough and even in those hospitalised after infancy, only 9% were fully vaccinated (Table 4), with a highly significant difference between the proportions of children vaccinated against whooping cough as against diphtheria/tetanus.

Comparison of epidemics

The proportion of infants fell from 70 to 47% between the two epidemics (Table 5), whereas the age distribution of those aged 1 or more did not differ between epidemics. Comparisons were therefore made for these two age bands separately.

Between 1974–6 and 1977–9 there was an increase in the proportion of infants who had been breast fed (15% *vs.* 35%, $P = 0{\cdot}0004$) and a decline in the number

Table 4. *Vaccination against whooping cough and diphtheria/tetanus in cases hospitalised after infancy*

	Not vaccinated	Partially vaccinated	Fully vaccinated	Vaccination history known
Whooping cough	173 (86)	11 (5)	18 (9)	202
Diphtheria+Tetanus	34 (20)	36 (21)	104 (60)	174

Total $\chi^2 = 166$, χ^2 trend $= 155$ } $P < 0{\cdot}0001$.

Table 5. *Comparison of age of admission in the two epidemics*

	1974–6 (percent) $n = 147$	1977–9 (percent) $n = 313$
< 1 year	103 (70)	147 (47)
1–2 years	27 (18)	104 (33)
3–4 years	10 (7)	44 (14)
5+years	7 (5)	18 (6)

$\chi^2 = 22{\cdot}2$, $P = 0{\cdot}0001$

of siblings among those 1 year or more ($P = 0{\cdot}0004$), though there were no social class differences. There were no differences in the length of illness before admission between the epidemics. Although there was a lower incidence of cyanosis before admission in infants in 1977–9, the proportion of cases with missing information for this item differed between epidemics.

In infants in 1977–9, length of stay was significantly shorter and during admission there was both a highly significant trend to reduced cough severity and for those that did have a 'severe' cough, this lasted for fewer days. Infants were also less likely to have had a fever greater than 38 °C though more likely to have whooped. For those of 1 year or more there was a similar trend to less severe cough but this was not significant. There were no differences in feeding, weight loss or complications in either age group between the two epidemics. Controlling for age, the admission pulse was 4·2 beats per min lower in 1977–9 but admission temperature and respiratory rate were unchanged. The proportion of cases followed up was similar in the two epidemics (45 % *vs.* 37 %) and the total length of cough recorded did not differ, though this was not the true length of illness because of incomplete follow up in many cases.

There was a clear increase in the proportion of positive pernasal swabs in 1977–9 (18 % *vs.* 34 %, $P = 0{\cdot}002$) but no differences in the total leucocyte or the lymphocyte counts. The chest radiograph was more commonly reported to show consolidation in 1977–9 (18 % *vs.* 34 %, $P = 0{\cdot}002$). Amongst those aged 1 year or more, the proportion of those fully vaccinated against whooping cough fell significantly (21 % *vs.* 6 %, $P = 0{\cdot}002$) whilst for diphtheria/tetanus there was no significant change between epidemics (54 % *vs.* 61 %). Before admission 30 % of children had received ampicillin and 19 % penicillin with little difference between

epidemics. However, there were major differences in the proportion receiving erythromycin both before (3 % *vs.* 19 %, $P < 0{\cdot}0001$) and during admission (0 % *vs.* 47 %, $P < 0{\cdot}0001$) though for the pre-admission data the proportions of cases with missing information about drugs also changed significantly. During admission the use of ampicillin (57 % *vs.* 18 %, $P < 0{\cdot}001$) and sedatives apart from phenobarbitone (16 % *vs.* 5 %, $P < 0{\cdot}001$) fell significantly whilst salbutamol usage increased though still at low level (1 % *vs.* 9 %, $P = 0{\cdot}002$).

DISCUSSION

This study shows that whooping cough is still a substantial illness. Several previous studies have tried to grade the severity of whooping cough (Miller & Fletcher, 1976; Melchior & Jessen, 1976; Robinson *et al.* 1981). Robinson *et al.* (1981) included an assessment of a child's distress during a coughing spasm but, in general, scales of severity have given an inadequate picture of the severity of the illness. Such scales tend to be weighted by the presence of complications, in spite of the fact that a child may be extremely ill without any of the conventional complications of the illness. In the present study, we have thus looked at the various indicators of severity separately.

The illness lasted less than 2 months, between 2 and 3 months, and more than 3 months in about one third of cases respectively, supporting the DHSS (1981) estimate of 10–12 weeks. Despite the relatively small proportion of cases for whom the length of illness was known, our estimate is still more realistic than those from previous hospital surveys, in which time to discharge has been taken as the length of illness (Bennett, 1973; Walker *et al.* 1981). The incidence of cyanosis (24 %) and of apnoea (7 %) during admission compare with previous estimates of 13–36 % and 5–13 % respectively (Miller & Fletcher, 1976; McKendrick, Gully & Geddes, 1980; Robinson *et al.* 1981; Walker *et al.* 1981). The incidences of whoop (45 %) and vomiting (59 %) are generally lower than previous estimates of 68–89 % (Walker *et al.* 1981; McKendrick, Gully & Geddes, 1980) and 41–82 % (Miller & Fletcher, 1976; Robinson *et al.* 1981; Walker *et al.* 1981) respectively, and there are two possible explanations for this. First, some studies have used whoop as a major diagnostic criterion (McKendrick, Gully & Geddes, 1980; Walker *et al.* 1981). Secondly, in about one third of our cases relevant information was missing and since previous studies make no comment on this aspect of retrospective analysis, comparison becomes difficult. Of the other clinical features, fever, not usually considered prominent (Court, Jackson & Knox, 1953; Olson, 1975), was not uncommon with over a quarter recording a fever higher than 38 °C.

The assessment of cough severity, though subjective and only previously used in the MRC antibiotic trials (MRC, 1953), is probably an important measure of the distress caused by the spasms, and nearly two thirds had a severe or moderately severe cough. Miller & Fletcher (1976) clearly felt that the main factors determining the severity of the illness were the severity of cough and vomiting rather than complications which, as defined in the present study, were relatively infrequent. While the assessment of feeding behaviour was also subjective the need for a nasogastric tube in 13 % of infants probably provided more objective evidence of severity. Loss of weight was found in only 50 % confirming, along with a previous

report of weight loss in a minority (RCGP, 1981), that weight loss is less common than might be supposed. The study also confirms the continuing greater severity of whooping cough in infants compared with older children (Christie, 1980; RCGP, 1981); they had longer admissions and were significantly more likely to have had cyanosis, apnoeic attacks, a severe cough and feeding difficulties. Fewer infants had coincidental illnesses suggesting that they were more likely to be admitted solely because of the severity of their whooping cough.

How representative were these hospitalised children? In two studies in 1974–5, 10% of notified cases (Miller & Fletcher, 1976) and 22% of a much smaller study (Vesselinova-Jenkins *et al.* 1978) were admitted while in several studies in 1977–9 only 3% or less of cases overall were admitted (Grob, Crowder & Robbins, 1981; RCGP, 1981; Pollock, Miller & Lobb, 1984) and 12–15% of infants (RCGP, 1981; Pollock, Miller & Lobb, 1984). The present cases thus probably form a small proportion of the total cases of whooping cough in the general population and may not be representative. Nevertheless, whooping cough in the community is not always less severe than that seen in hospital and there are no available comparative data. Children may often be admitted for social reasons (Wynne & Hull, 1977) and admissions for whooping cough are more frequent with lower social class (RCGP, 1981; Pollock, Miller & Lobb, 1984). In the present study, it was not possible to define retrospectively the exact reasons for admission but those admitted after infancy were of lower social class than those admitted in infancy, implying that in the later age group the severity of the illness was of less importance in determining admission.

Our study provides some of the first evidence to suggest a decline in the severity of whooping cough. In particular, infants had shorter admissions, reduced fever, reduced cough severity and length of severe cough and slightly slower pulse rate on admission in 1977–9 compared with 1974–6. There are, however, alternative explanations for these findings. Multiple comparisons might have led to some significant differences (though only whoop was increased in 1977–9) and shorter admissions and less severe cough might be due to increased medical and nursing familiarity with the disease by 1977–9. An increased proportion of mild cases might have been admitted in the second epidemic though this is not supported by the available data on admission rates discussed above. It seems unlikely that these factors are sufficient to account for our findings. Pollock, Miller & Lobb (1984), however, who also reported a decreased length of stay, concluded that there was no change in the severity of the illness in hospitalised children over a similar period. Their study was based on notified cases and since these are known to be only a proportion of the true numbers with whooping cough (Miller, Jacombs & Pollock, 1980; Jenkinson, 1983) it is possible that an incomplete picture was obtained. The difference between the two studies probably lies however in our use of certain indicators of severity such as cough severity, additional to the customary recording of features and complications for which we too found no differences between the two epidemics.

Previous evidence for a decline in severity of whooping cough has been anecdotal (Islur, Anglin & Middleton, 1975; Christie, 1980; DHSS, 1981), apart from the fall in case-fatality in the 1970s (DHSS, 1981) and an apparent decrease in chest

infections and otitis media in Glasgow in the same period (Walker *et al.* 1981). No single observer has systematically studied the severity of whooping cough over more than about a decade and in only one study have assessments been made over a longer period in the same institution (Jernelius, 1958). The problems caused by attempts to compare assessments of severity in different studies are illustrated by the conclusion of Robinson *et al.* (1981) that fewer (9%) were 'more seriously ill' in 1977–8 than the 50% reported by Miller & Fletcher (1976) for 1974–5. However, the latter authors classed cases with cyanosis as severe (Miller & Fletcher, 1976) while the former clearly did not since 16% of their cases were cyanosed (Robinson *et al.* 1981).

There has been debate as to whether the impression of declining severity mentioned above might be due to improved nursing care (Trollfors, 1979), increased expertise in paediatric intensive care (Harris, Bush & Lewis, 1979) or a shift in age distribution to older children in 1977–9 as seen in the present study and in others (DHSS, 1981; Walker *et al.* 1981; Robinson *et al.* 1981), though this latter factor cannot be involved in the present study since comparisons were made within age groups. Improving socio-economic conditions have been invoked both in the steep fall in case fatality in the first half of this century (Emerson, 1939; Mortimer & Jones, 1979) and in the more recent decline in incidence (Bassili & Stewart, 1976). However, though mortality is certainly much higher in developing countries in present times (Cvjetanovic, Grab & Vemura, 1978; Walsh & Warren, 1979) there is little evidence available to suggest that the illness is otherwise more severe in these countries (Voorhoeve *et al.* 1978). Alternatively, it is possible that *B. pertussis* has become less virulent with the change to serotype 1, 3 (Preston, 1963) which might be associated with less severe disease (Demina *et al.* 1973).

Perhaps the most important factor that might be involved in a real decline in severity, particularly over the relatively short period of this study, is antibiotic usage. The effect of widespread community use of antibiotics is difficult to evaluate (Linnemann, 1979) but in the present study there was a striking increase in erythromycin usage both before and during admission in the second epidemic, this latter finding also being seen by Pollock, Miller & Lobb, (1984). An early study showed a reduction in severity with antibiotics given early in the illness (MRC, 1953). Erythromycin itself is known to clear the nasopharynx of organisms promptly (Baraff, Wilkins & Wehrle, 1978) and there have been more anecdotal recent suggestions of reduced severity and complications with the drug (Islur *et al.* 1975; Barrie, 1982). Two specific studies of erythromycin in the treatment of whooping cough have however shown no benefit (Bass *et al.* 1969; Baraff, Wilkins & Wehrle, 1978), though both studies were relatively small and used poor indicators of severity. In the absence of convincing evidence about erythromycin it is therefore possible that the wide use of the drug may have reduced severity.

Finally, the use of salbutamol, which has been suggested to have a beneficial effect on whoop and the number of spasms (Pavesio & Ponzone, 1977; Peltola & Michelsson, 1982) also increased between epidemics though still remaining at a relatively low level.

In conclusion, the present study shows that whooping cough may still be a long illness with considerable impact on the child, particularly in infancy. Further work,

to be presented shortly, will examine the effect of the illness on the child's subsequent behaviour and the impact on the family. In addition, the data suggests that whooping cough as seen in hospitalised children in 1977–9 may have been less severe than in 1974–6 and a number of factors, in particular erythromycin usage, may have contributed to this change.

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