Reading attainment and physical development after whooping cough

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SUMMARY Anthropometric measurements were made on 360 primary school children with a history of whooping cough and on 711 controls. Altogether 245 (68%) cases and 469 (66%) controls had taken tests of reading attainment and a smaller number had taken tests of intelligence. No significant differences were found between cases and controls in any of the anthropometric measurements nor in reading age or intelligence quotient after controlling for social class and parental smoking. Whooping cough is, in general, unlikely to cause subsequent deficiency in physical or mental development.

During an attack of whooping cough, cyanosis during paroxysms of coughing is common and is sometimes accompanied by episodes of apnoea, particularly in infancy.^{1–4} The pathology of the now rare whooping cough encephalopathy is that of severe vascular damage with anoxic changes,^{1,5,6} but the long-term effects of cerebral hypoxia on the survivors of the illness are unknown. Previous studies, mainly conducted in the prevaccination era, have suggested an association between a history of whooping cough and mental deficiency^{7–10} or behavioural disturbance.^{10,11} The only modern study found that a small, uncontrolled group of children hospitalised for whooping cough was more likely to be rated intellectually abnormal at age 5.¹² Neither is it known whether whooping cough, which may be a protracted illness with persistent vomiting and weight loss,^{1–4} has any effect on physical development.

The resurgence of whooping cough in recent years⁴ and the risks-benefits debate over vaccination¹³ make these questions of current concern. We have thus studied indices of school performance and the physical development of children with a history of whooping cough compared with a control group.

Methods

The sampling methods for obtaining cases and controls and our criteria for a diagnosis of whooping cough have been previously presented in detail.¹⁴ Briefly, children of primary school age with a history

of whooping cough were identified from three sources: hospital records, notifications, and screening of school classes. The hospital records of admissions in our study area for whooping cough between 1970 and 1979 were reviewed (total 641). Children of primary school age were selected if the following diagnostic criteria for the disease were satisfied: (1) culture positive for *Bordetella pertussis*; or (2) typical paroxysmal cough with either a lymphocytosis or typical whoop or apnoeic attack(s) after coughing spasms; or (3) a typical cough for at least two weeks plus contact with a known case or vomiting or cyanosis associated with spasms. We tried to contact the parents of 286 cases thus selected, and 160 (56%) responded. Following exclusions (living outside the study area) 138 cases remained (the "hospital" group). The parents of 532 children notified as having whooping cough between 1970 and 1979 in two boroughs were sent a screening questionnaire based on our diagnostic criteria, and 413 (78%) responded. In a third borough, the area health authority contacted 550 parents, and 185 (34%) responded. Of a total of 598 children, 154 were excluded (outside study area or failed diagnostic criteria) and 444 were left for study ("notified" group).

These hospital and notified cases attended 192 schools. Schools were selected which contained cases who had been hospitalised or who had had whooping cough in infancy, or at least three notified cases, leaving a manageable total of 128 schools. A respiratory questionnaire was sent to the parents of all children in the same school class as each of the

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cases, and 80% of 7337 parents replied. This questionnaire provided information about a history of whooping cough, past and present respiratory symptoms, social class, parental smoking, family size, and hospital admissions. Parental replies identified another group of children with past whooping cough, and if parental responses to the screening questionnaire met our diagnostic criteria, these children formed a third group of cases ("parental" group). Eighteen further cases who had been hospitalised were also identified and added to the hospital group. At some schools there were too many notified and parental cases for our resources, and children with whooping cough at older ages were excluded. A total of 360 cases was examined; 148/156 (95%) of the hospital group, 135/444 (30%) of the notified group and 77/150 (51%) of the parental group. Comparisons of the illness severity (from the screening questionnaire) were made between those studied and those not studied in the notified and parental groups.

From those children whose parents reported no history of whooping cough, two children in the same school class and of the same sex were randomly selected as controls (total 711) for each index case. All children were examined at school by one of us (IDAJ) who was "blind" to their whooping cough status. Weight was measured to 0.1 kg with portable field-survey scales (CMS Weighing Equipment Ltd) and height to 0.001 m with a portable stadiometer (Holtain Ltd). Skinfold thicknesses at four sites (biceps, triceps, subscapular and anterior superior iliac spine) were measured on the left side to 0.1 mm (Harpenden Skinfold Calipers), together with arm circumference to 1 mm in accordance with standard recommendations.¹⁵ Fat-free mass was derived from the skinfold thicknesses using the equation for boys and girls.¹⁶ Skinfold thicknesses were transformed using the equation: $\text{skinfold transform (ST)} = 100 \log_{10} (\text{skinfold reading in } 0.1 \text{ mm} - 18)$.¹⁷ A further measurement of lean body mass, the muscle and bone component of the arm (MB area) was derived from the equation: $\text{MB area} = 1/4 \pi [\text{arm circumference} - \pi/2 (\text{triceps} + \text{biceps skinfold})]^2$.¹⁸ Ethnic group was classified as Caucasian, African, Indian, Oriental or other.

Details of performance on reading tests and intelligence tests undertaken at age 7 or 8 years were obtained from the schools. In one borough we also obtained the results of a 19 point teacher-completed checklist designed to assess the child in the areas of (i) speech and communication, (ii) perceptual, motor, emotional, and social development, and (iii) response to learning situations (personal communication, Croydon Education Department).

The χ^2 test was used to analyse categorical variables and the t test for comparisons of continuous variables. Reading age was expressed as a percentage of chronological age at the time of testing (RA%). Stepwise regression of RA% on social class, parental smoking, family size, and number of hospital admissions identified social class and parental smoking as significant independent variables. Subsequently an analysis of covariance was performed to control RA% for the effects of social class and parental smoking using an equation of the form $\text{RA\%} = a + b_0 \times \text{social class} + b_1 \times \text{parental smoking} + b_2 \times \text{WC}$, where WC is a dummy variable taking the value 0 (control) or 1 (case). Approval was obtained from relevant ethical committees, and parents gave signed consent for their child to be examined.

Results

Most cases had had whooping cough between 1974 and 1976 (36%) or between 1977 and 1979 (46%), the others between 1968 and 1973 (17%). One hundred and two cases (28%) had had their illness in infancy, 78 (22%) at 1–2 years, 141 (39%) at 3–4 years, and 39 (11%) at 5 years or more. Seventy-four (50%) of the hospital group had had whooping cough in infancy compared with six (4%) of the notified group. Of those hospitalised, apnoea was recorded in 8%, cyanosis in 27%, and fits in 4%, but there were no cases of encephalopathy. The cases studied were currently aged 5 to 13 years, and 2 to 13 years had elapsed since their illness.

With respect to the severity of their illness (cases) and social factors at the time of study (cases and controls), neither cases nor controls differed from the remainder of the populations from which they were selected. When compared with controls, there was a slightly higher proportion of Caucasian cases overall (93% v 90%, $p < 0.05$). Hospital cases were more likely than their controls to have siblings aged 5–14 (78% v 63%, $p < 0.001$), parents who smoked (74% v 62%, $p < 0.01$), and to be of manual social class (64% v 54%, $p < 0.05$). There were no relevant differences between cases and controls in the notified or parental groups.

Mean values of age, height, weight, arm circumference, skinfold transforms, fat-free mass, and muscle and bone area did not differ significantly between cases and controls in any group, though the hospital cases had consistently smaller anthropometric indices compared with their controls (table 1).

All boroughs in the study area routinely gave tests of reading attainment to children of age 7 or 8 years, and data were available for all children of this age or

Table 1 Age and anthropometry (means and standard deviations)[†]

	Hospital		Notified		Parental		All	
	Cases n=148	Controls n=292	Cases n=135	Controls n=268	Cases n=77	Controls n=151	Cases n=360	Controls n=711
Age (years)	8.0 (1.8)	8.1 (1.7)	8.3 (1.7)	8.4 (1.8)	8.4 (1.8)	8.4 (1.8)	8.2 (1.7)	8.3 (1.8)
Height (cm)	125.8(10.8)	127.3(11.1)	128.5(10.5)	129.1(10.7)	129.5(12.0)	129.3(11.0)	127.6(11.0)	128.4(11.0)
Weight (kg)	25.6 (6.9)	26.4 (6.5)	27.1 (7.3)	27.6 (7.3)	27.0 (6.4)	27.2 (6.6)	26.4 (7.0)	27.0 (6.8)
Arm circumference (cm)	19.0 (2.2)	19.3 (2.1)	19.6 (2.4)	19.7 (2.4)	19.5 (1.6)	19.4 (2.1)	19.3 (2.2)	19.4 (2.2)
Biceps ST	160.0(23.4)	164.2(21.2)	166.2(24.2)	163.0(25.8)	164.0(22.2)	159.6(26.7)	163.2(23.6)	162.8(24.2)
Triceps ST	191.9(17.2)	194.7(15.7)	194.9(19.6)	193.9(17.7)	196.1(14.2)	192.9(17.6)	193.9(17.6)	194.0(16.9)
Subscapular ST	160.5(20.9)	161.9(19.9)	162.0(22.3)	161.4(21.8)	161.1(16.6)	160.8(21.8)	161.2(20.6)	161.4(21.0)
Asis* ST	167.4(26.4)	169.2(25.5)	169.6(29.2)	170.4(28.6)	169.8(23.7)	167.5(28.8)	168.8(26.9)	169.3(27.4)
Fat-free mass (kg)	20.4 (4.8)	20.9 (5.0)	21.4 (4.8)	21.8 (5.0)	21.5 (5.0)	21.7 (4.7)	21.0 (4.9)	21.4 (4.9)
Muscle and bone area (cm ²)	21.5 (4.3)	21.8 (4.4)	22.2 (4.5)	22.8 (5.0)	22.1 (3.7)	22.1 (4.0)	21.9 (4.3)	22.2 (4.6)

*Anterior superior iliac spine.

[†]No comparisons show significant differences (*t* tests).

older apart from the occasional child who had been absent at the time of testing or who had moved into the area at a later date. Some children aged under 7 years had also taken reading tests, but this information was incomplete and was not used. Different boroughs used different reading tests; the most common was the Young's Group Reading Test (228 subjects) followed by the Salford Sentence Test (192) and the Neale Analysis of Reading Ability (162). Comparisons between cases and controls were performed for these three tests separately. Other tests used were the Burt (89), Schonell (75), Holborn (39), Daniels and Diack (8), and others (18). Many of these latter tests had been performed by only small numbers, and the results were further analysed after combining the RA% achieved by each child irrespective of the test used. Some children had taken more than one test, but in these instances a Young's test had always been taken, and the Young RA% was the index selected for analysis.

No significant differences between cases and controls were found in RA% for any of the three main reading tests, the Young, Salford or Neale, though for the Young's test there was a consistently lower score for cases (table 2). When results from all tests were combined, the hospital cases had a significantly lower RA% than their controls (102.7 v 108.0, $p<0.01$). However, both social class and parental smoking had highly significant ($p<0.0001$) effects on RA% (table 3) with mean RA% progressively declining with lower social class and with increasing parental smoking. Information on both social class and parental smoking was available for 93% of all cases and controls. For these subjects, analysis of covariance showed that, when the data were controlled for social class and parental smoking, there were no significant differences in RA% (all tests combined) between cases and controls in any group, all 95% confidence limits embracing zero (table 4).

Table 2 RA% for Young, Salford, and Neale reading tests and all tests combined (means and standard deviations): Raw reading ages and chronological ages presented only for Young test

	Hospital		Notified		Parental		All	
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Young	n=20	n=34	n=43	n=80	n=17	n=34	n=80	n=148
RA	7.5 (1.5)	7.7 (1.4)	7.7 (1.1)	8.0 (1.2)	8.2 (1.1)	8.0 (1.0)	7.8 (1.2)	8.0 (1.2)
CA	7.7 (0.9)	7.8 (0.9)	7.8 (0.8)	7.8 (0.7)	7.9 (0.9)	7.7 (0.9)	7.8 (0.8)	7.9 (0.8)
RA%	96.9(11.5)	98.8(14.1)	98.8(12.5)	102.5(13.4)	103.3(11.7)	103.8(14.1)	99.3(12.1)	102.0(13.8)
Salford	n=19	n=38	n=26	n=54	n=19	n=36	n=64	n=128
RA%	106.6(11.6)	111.5(14.5)	113.9(13.1)	113.1(16.1)	114.5(16.2)	109.5(14.6)	111.9(13.9)	111.4(15.2)
Neale	n=18	n=31	n=33	n=57	n=8	n=15	n=59	n=103
RA%	109.2 (8.6)	107.4 (9.7)	107.6(10.6)	108.8(13.7)	101.6(14.5)	107.2(10.2)	107.3(10.7)	108.1(12.0)
All tests combined	n=95	n=179	n=95	n=182	n=55	n=108	n=245	n=469
RA%	102.7(15.4)**	108.0(16.7)	106.1(14.1)	107.2(15.5)	109.6(17.8)	106.1(15.5)	105.6(15.7)	107.3(16.0)
IQ	n=18	n=36	n=31	n=55	n=17	n=36	n=66	n=127
	99.7(15.3)	104.4(17.4)	109.3(10.2)	110.5(14.3)	106.4(15.4)	108.7(10.1)	105.9(13.5)	108.3(14.4)

** $p<0.01$.

Table 3 Effect of social class and parental smoking on RA% (for all tests combined)

	n	Mean RA%	SD
Social class*			
I	44	113.9	15.1
II	141	112.5	15.2
III NM	117	110.0	15.3
III M	269	104.3	14.6
IV	70	101.6	19.4
V	24	99.3	12.1
Parental smoking*			
Neither	271	110.7	15.2
One	280	105.6	16.2
Both	164	101.9	14.6

*Analysis of variance $p < 0.0001$.

Within the hospital group, cases hospitalised in infancy ($n=56$) had a lower RA% (all tests) than their controls ($n=108$) [$103.8 \nu 108.3$, $p=NS$], as did those hospitalised between the age of 1 and 4 years ($n=33$) compared with their controls ($n=61$) [$101.2 \nu 107.8$, $p < 0.05$]. After controlling for social class and parental smoking, the differences in RA% between cases and controls in these two subsets were not significant; that for cases hospitalised in infancy being -1.5% (95% confidence limits -7.0% to $+4.0\%$) and that for those hospitalised between 1 and 4 years being -5.5% (95% confidence limits -12.5% to $+1.6\%$). Of hospitalised cases who had documented cyanosis or apnoea during their admission and for whom reading age data were available (23 cases), the RA% for all tests combined was lower, but not significantly, than in 45 controls after controlling for parental smoking and social class (difference $= -3.2\%$; 95% confidence limits -10.5% to $+4.1\%$).

Intelligence testing was routinely performed in one borough only, using the Young's non-readers test. Altogether 193 children had performed this test, and the IQ derived from this test was consistently lower, though not significantly so, in all the main groups of cases (table 2). The largest difference was between hospital cases and their controls, the discrepancy being larger, though again not significant, for those hospitalised in infancy ($n=9$) compared with their controls ($n=19$) [$100.1 \nu 106.1$, $p=NS$]. Again, after controlling for social class and parental smoking, the difference between cases and controls in IQ was not significant in any of the main groups (table 4). The number of cases hospitalised in infancy

who had taken an IQ test was too small to permit further analysis; 19-point teacher checklist scores were available for 59 cases and 105 controls. No significant differences were seen in these scores between any group of cases and controls.

Discussion

The possibility of long-term cerebral sequelae after whooping cough is raised, firstly, because apnoeic attacks, cyanosis, fits, and encephalopathy may occur during the acute illness and, secondly, by the findings of previous studies. Apnoea, usually after a spasm, has been noted in between 5 and 9% in series of hospitalised patients,^{3 19 20} and cyanosis is seen in 16 to 36%,^{3 19-22} though these figures are likely to be underestimates, and both features occur with greater frequency and severity in infancy.¹ Though convulsions have occurred in 7% of hospitalised children in an individual series,²³ overall in eight studies of admissions for whooping cough in the 1970s, the incidence of convulsions was 97/3290 (2.9%).^{3 19 22 23-27} In these same studies, encephalopathy occurred in only 4/3290 (0.1%). In community studies, the incidence of fits has varied widely from 0.05% to 7% with only two instances of encephalopathy in 10 499 cases (0.02%).^{2 19 28 29} The incidence of apnoea, cyanosis, fits, and encephalopathy in the present study is thus similar to that in previous studies. The pathogenesis of the fits and encephalopathy is still unclear and may be secondary to ischaemia and anoxia⁵ or pertussis toxin,^{30 31} though hyponatraemia³² or hypoglycaemia³³ may play a role.

In former times, survivors of whooping cough encephalopathy frequently had obvious neurological defects such as paralysis, deafness, or blindness.^{1 34-36} Relatively few modern studies report any follow-up, but those by contrast have found no apparent short-term sequelae after convulsions alone^{22 23 25} or encephalopathy^{19 25} apart from one death.² In the two follow-up studies of long-term sequelae, Byers and Rizzo⁷ found six children with severe intellectual difficulties which they ascribed to whooping cough out of only 39 followed up, while White *et al*⁸ found reduced IQ in black children who had had whooping cough compared with black controls. Several early retrospective analyses suggested a relation between the illness and subsequent mental deficiency^{9 10} or

Table 4 Differences and 95% confidence limits in RA% (all tests combined) and IQ between cases and controls after controlling for social class and parental smoking

	Hospital	Notified	Parental	All
RA%	-3.2 (-7.3 to +1.0)	-1.6 (-5.2 to +2.0)	+3.7 (-8.6 to +1.8)	-0.9 (-3.4 to +1.5)
IQ	-4.1 (-12.9 to +4.8)	-1.1 (-6.7 to +4.6)	-4.3 (-11.5 to +2.9)	-2.6 (-6.7 to +1.4)

behaviour disturbance,^{10 11} though this was later disputed.³⁷ Unfortunately, all these studies had serious methodological flaws. Controls were inadequate or even absent, and authors often relied heavily on retrospective ascertainment of a history of whooping cough. Importantly, the children in these studies had their illness over 30 years ago, many in the pre-antibiotic era and when the illness was probably more severe.^{1 26 38} Modern authors continue to refer to neurological and developmental retardation after whooping cough,³⁹ but the only recent evidence comes from a cohort study which found that 40 children, born in 1970, who had been hospitalised with whooping cough were later three times more likely to be rated as intellectually abnormal than expected from their social class distribution, though few further details are given.¹² Persisting behavioural disturbance at two months after the illness has also recently been found.⁴⁰

The present study shows no significant differences in reading age or IQ at age 7 or 8 years in those with a history of whooping cough compared with controls. This conclusion applies irrespective of whether the cases were hospitalised and, for reading age, irrespective of the age at hospitalisation or the occurrence of apnoea or cyanosis during admission. The design of the study, methods of selection of cases and controls, and reliability of the ascertainment of the diagnosis of whooping cough have been discussed in detail elsewhere.¹⁴ In brief, both cases and controls were representative of the populations from which they were drawn, and the reliability of the diagnosis of whooping cough was likely to be high though clearly greater in hospitalised children whose case-records were all reviewed.

We acknowledge that the results of reading and intelligence tests performed in school by teachers are unlikely to be precise indicators of a child's mental development. In addition, IQ data were available for only a small number of subjects in the important group of children hospitalised in infancy, and the group with cyanosis or apnoea was likewise small. The data were gathered during a study of lung function after whooping cough,¹⁴ and our resources did not permit formal psychological testing. Nevertheless it is likely that analysis of reading ages would show large differences between cases and controls should they exist. The tests were free of any bias associated with the study since they had been performed independently and at a different time as part of the routine assessment of children in particular boroughs. We attempted to reduce the variability of the tests by restricting analysis to tests carried out on 7 and 8 year old children only. The reading ages showed the same relation to social class, parental smoking, and family size that others have

shown,⁴¹ though for both reading age and IQ only social class and parental smoking remained significant in the stepwise regression.

The results are reassuring in that no significant effect of whooping cough was shown, though our study is unable to exclude an effect of whooping cough on small groups of children, in particular those with fits or encephalopathy during the illness. Furthermore, in some subgroups only small numbers of subjects were available for analysis of certain reading tests (eg, the Neale test), and conclusions from these analyses must therefore be regarded with caution. We suggest that more detailed psychological testing should now be carried out to investigate the possibility of more subtle differences than those likely to be detected by analysis of reading age and IQ.

There have been no previous studies of long-term physical development after a specific childhood illness. A reduction in attained height in later childhood is known to be independently associated, with social class, family size, number of smokers in the home, smoking in pregnancy, and parental height⁴¹⁻⁴⁵ and with a history of asthma.^{46 47} Detailed anthropometric testing in the present study showed no significant differences between any group of cases and controls. The hospitalised cases were, however, slightly smaller on all measured indices but this was also the group with significantly lower social class, larger families, and more parental smoking than controls, and important data such as parental height were not available to enable further analysis of these differences.

We conclude that whooping cough in recent times is unlikely to be important in causing disturbance of reading attainment or physical development in later childhood.

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