

Relationship between childhood infections and measured intelligence

THOMAS McKEOWN AND R. G. RECORD

Department of Social Medicine, University of Birmingham

McKeown, T. and Record, R. G. (1976). *British Journal of Preventive and Social Medicine*, 30, 101-106. **Relationship between childhood infections and measured intelligence.** The possibility that some of the common childhood infections lead to unrecognized impairments of neurological function was examined in 43 820 Birmingham children whose intelligence was assessed in the 11-plus examination. Mean verbal reasoning scores were lower for children who had had measles or pertussis than for those who had had neither of these diseases. However, since attack rates and measured intelligence are related inversely to social class, the lower scores of children with measles and pertussis may be due to class differences which are not eliminated completely by standardization for maternal age and birth order. Mean scores were a little higher for children who had had rubella than for those who had not, and it is suggested that this difference may be due to more frequent reporting of the disease by the more intelligent mothers.

It is well known that most of the common infectious diseases of childhood may affect the central nervous system, and in serious cases may result in death or permanent disabilities such as mental defect. It has been more difficult to determine whether the diseases also lead to less serious impairments of neurological function, which either pass unnoticed or, if recognized are not seen to be related to the infections. This paper reports the results of an examination of this possibility in a large population of children, whose experience of infectious disease was recorded by health visitors and whose intelligence was assessed in the 11-plus examination.

The basic data were described previously (Record, McKeown, and Edwards, 1969). For the present investigation they comprise observations on all children born in Birmingham during the period 1 January 1950 to 31 August 1953, who took the 11-plus examination in Birmingham in the years 1961-64. During this period there were 69 891 total births, and 43 820 (63%) took the examination. The difference is accounted for mainly by those who had left Birmingham or died before the age of 11, or who did not take the examination because they were in private schools, in special schools for the handicapped, or although in ordinary

schools, had been assessed as 'borderline sub-normal'. There was also a small number of children who were judged ineducable.

Data recorded in respect of all Birmingham births included obstetric histories and observations on development and morbidity made by health visitors during the first five years of life. Specific inquiry was made about certain infectious diseases—measles, pertussis, rubella, mumps, and scarlet fever. Details of the 11-plus examination and the method of linkage with the birth record were outlined in earlier publications (Barker and Edwards, 1967; Record *et al.*, 1969).

At the outset it is clear that in examination of the relationship between infectious diseases and measured intelligence a correction must be made for the influence of maternal age and birth order. Attack rates of measles and other infections are highly correlated with these variables—they fall with increasing age and rise with increasing birth order (Table I). Mean verbal reasoning (VR) scores are also correlated, but inversely—they rise with increasing age and fall with increasing birth order (Table II). These relationships are of course determined largely by social and economic status; a distribution of births by maternal age and birth order is in effect a distribution by social class—poor

TABLE I
MEASLES ATTACK RATE (PER 100) ACCORDING TO BIRTH ORDER AND AGE OF MOTHER

No. of Previous Children	Maternal Age (years)							Total
	Under 20	20-24	25-29	30-34	35-39	40 and over	Not Stated	
0	45.4 (1363)	41.3 (6056)	38.2 (4367)	34.9 (1737)	32.6 (641)	32.2 (143)	— (35)	39.5 (14342)
1	65.3 (173)	60.0 (3106)	56.8 (4966)	50.5 (3031)	45.3 (1160)	38.7 (238)	— (33)	54.8 (12707)
2	— (15)	61.5 (974)	59.0 (2714)	50.6 (2377)	49.2 (1229)	38.6 (293)	— (21)	54.3 (7623)
3	— (1)	66.1 (254)	59.0 (1223)	54.9 (1425)	49.8 (881)	41.3 (269)	— (10)	54.7 (4063)
4	—	— (54)	59.3 (504)	57.1 (787)	49.7 (593)	45.3 (225)	—	54.3 (2163)
5 and over	—	— (13)	55.7 (305)	58.8 (837)	59.8 (1063)	51.5 (641)	—	57.2 (2859)
Not stated	— (1)	— (16)	— (5)	— (10)	— (1)	— (1)	— (29)	— (63)
Total	47.8 (1553)	49.5 (10473)	51.7 (14084)	49.7 (10204)	48.7 (5568)	43.9 (1810)	— (128)	49.8 (43820)

Numbers of children are shown in brackets. Attack rates are not given for cells containing fewer than 100 children

TABLE II
MEAN VR SCORES ACCORDING TO BIRTH ORDER AND AGE OF MOTHER

No. of Previous Children	Maternal Age (years)							Total
	Under 20	20-24	25-29	30-34	35-39	40 and over	Not Stated	
0	97.1	101.7	105.2	106.9	107.7	106.7	—	103.3
1	93.9	98.1	102.3	104.6	105.4	105.7	—	102.1
2	—	94.6	97.8	101.2	101.9	102.8	—	99.3
3	—	92.1	94.8	97.3	98.6	98.9	—	96.6
4	—	—	91.5	94.8	96.9	96.8	—	94.7
5 and over	—	—	88.8	90.4	92.7	93.4	—	91.8
Not stated	—	—	—	—	—	—	—	—
Total	96.7	99.6	101.0	101.3	100.5	98.8	—	100.5

Numbers of children are shown in Table I. Mean scores are not given for cells containing fewer than 100 children

TABLE III
PERCENTAGE DISTRIBUTION OF VR SCORES

Disease	No. of Children	VR Score							Mean VR Score	
		75 and under	76-85	86-95	96-105	106-115	116-125	Over 125	Crude	Standardized
Measles only	10236	5.5	12.6	22.7	26.4	20.1	9.5	3.3	99.46	99.88
Pertussis only	3875	4.4	11.3	21.2	25.9	22.3	11.0	3.8	100.88	100.55
Rubella only	976	3.8	9.8	17.6	28.1	20.7	14.1	5.8	102.76	101.86
Mumps only	710	4.6	10.4	20.3	25.2	23.7	11.1	4.6	101.50	101.60
Scarlet fever only	180	2.2	7.8	29.4	23.3	20.0	12.2	5.0	101.80	101.55
None of the above infections	8929	3.4	9.3	19.5	25.5	23.2	13.4	5.6	101.91	101.06

mothers have more children than the well-to-do and they are born at lower ages. It is therefore essential to correct so far as possible for the effects of the two variables. In the analysis which follows this has been done by simultaneous standardization.

The data were analysed in two ways: first, by examining the distributions of VR scores of all children who had had each infection (in this treatment those with measles, for example, include children who also had had other infections); and secondly, by examining distributions of VR scores of children who had had only one infection (in this treatment those with measles exclude children who had had other infections). The results were similar in the two cases, and as the second is the more direct treatment it has been used in Table III.

Since the reported frequency of neurological complications of the five diseases varies considerably, it will be desirable to discuss them separately.

MEASLES

Although the electroencephalogram shows abnormalities in a considerable proportion of patients with measles (over half in hospital cases examined by Gibbs *et al.*, 1959), encephalitis is only occasionally diagnosed—about one per thousand in a large representative British series reported by Miller (1964) and one in 700 in New York (Greenberg, Pellitteri, and Eisenstein, 1955). Hospital patients, of course, show a higher incidence of encephalitis; for example, Tidström (1968) found 14 per 1000 in a Copenhagen study. The mortality rate of measles encephalitis is about 10% and at least half the survivors recover completely. Permanent sequelae include paralysis, cerebellar ataxia, mental retardation, and behavioural changes. Ford (1973) estimated that about one-third show moderate reduction of intelligence and instability of mood, but Tidström (1968) reported that only eight of the 59 survivors in his series were mentally retarded.

There appears to have been only one large-scale attempt to investigate the total effect of measles on intellectual development (Douglas, 1964). Of the 5000 children in the national survey born during the first week of March 1946, 3797 were tested at the age of 11, by which time 87% had had measles. For children receiving normal education those who had had measles before the age of two years scored slightly lower, and those who had had measles after this age slightly higher, than those who had not had measles. Of the 68 children mentally unfit for education in ordinary schools, 71% had had measles. The proportion attacked before the age of two was similar to that shown by the school population. So far as they go, the results of this

survey did not indicate that measles affected subsequent mental development of children who had escaped the risk of encephalitis. The same conclusion was suggested by a small study of 132 children who had had measles; here there was no difference in IQ between those attacked before and those attacked after age two (Wilner, Cannon, and Brody, 1969).

The results of the present examination are as follows (see Table III):

Mean VR score (standardized)	
Children with no infection	101·06
Children with measles	99·88
	Difference
	$-1·18 \pm 0·22$

This result suggests that there was a significant difference in measured intelligence between children who had had, and those who had not had measles. However this finding must be interpreted with regard for other differences—particularly in social class distribution—between the two groups, and it will be more satisfactory to discuss it below when the results for the other infections have been presented.

PERTUSSIS

In contrast to the viral infections, pertussis does not produce a true encephalitis. Nevertheless nervous involvement, usually characterized by convulsions are not infrequent, especially in very young infants, and mortality may be high. In an extensive survey in a Brooklyn hospital cerebral symptoms were observed in nearly 1% of cases admitted and 40% of these patients died. Of those who survived, only half were found to be neurologically normal at follow-up (Litvak *et al.*, 1948). In a smaller study in Boston, four out of 10 children who had signs of encephalopathy in the course of whooping cough later showed evidence of permanent brain damage (Byers and Rizzo, 1950).

Retrospective investigations of mentally retarded children, not surprisingly, have given less consistent results. Among 1000 successive admissions to Washington State Institution for children with IQs of 70 or less, there were 20 in whom 'there appeared to be a definite causal relationship between whooping cough and the intellectual retardation which followed' (Levy and Perry, 1948). However, Berg (1961) considered that there were only two of 800 mentally retarded children seen at the Fountain Hospital, London, whose abnormality could be ascribed to this disease.

Our results (from Table III) for Birmingham children are as follows:

Mean VR scores (standardized)

Children with no infection	101·06
Children with pertussis	100·55
Difference	$-0·51 \pm 0·29$

RUBELLA

Encephalomyelitis is a rare but serious complication of rubella. It occurred in 14 patients during a large epidemic in Detroit in 1942 (an estimated incidence of one in 6000) and four died (Margolis, Wilson, and Top, 1943). Steen and Torp (1956) added one to the 88 cases (17 of them fatal) already reported in the literature. Permanent sequelae appear to be rare.

The Birmingham findings are:

Mean VR scores (standardized)

Children with no infection	101·06
Children with rubella	101·86
Difference	$+0·80 \pm 0·51$

MUMPS

A meningeal reaction is a common complication in mumps (23% affected in one survey) and is usually followed by complete recovery; encephalitis is rare. A follow-up in Florida of 16 children who had mumps meningitis and three who had meningoencephalitis provided no evidence of intellectual impairment (Levitt *et al.*, 1970).

The Birmingham findings are:

Mean VR scores (standardized)

Children with no infection	101·06
Children with mumps	101·60
Difference	$+0·54 \pm 0·58$

SCARLET FEVER

Scarlet fever, like pertussis, differs from the viral infections in not causing a true encephalitis, although the brain may be involved, either locally by extension from the middle ear, or generally in the septicaemic form of the disease. Both conditions are now extremely rare and there is no evidence that scarlet fever is followed by permanent brain damage.

Our results are as follows:

Mean VR scores (standardized)

Children with no infection	101·06
Children with scarlet fever	101·55
Difference	$+0·49 \pm 1·13$

DISCUSSION

The results exhibited above show that mean VR scores were lower for children who had had either measles or pertussis than for children who had had none of the diseases. But whether scores were lower *because* they had had measles and pertussis is another, and more complex, question.

At first sight it seems suggestive that the two of the five diseases which gave this positive finding are those occasionally associated with serious complications of the central nervous system—encephalitis in measles and less specific, but nevertheless severe, neurological complications in pertussis. However when interpreting this result, it must be remembered that the incidence of any disease whose distribution is related to social class is likely to show a correlation with a variable, such as measured intelligence, which is also associated with class.

We have attempted, so far as possible, to remove this source of correlation between disease and score by standardizing VR scores for maternal age and birth order. However, although these variables are correlated with social class, we cannot be confident that we have removed completely the effects of the association, and it is still possible that some class variation remains, for example, within the cells of Tables I and II. Since attack rates are higher and measured intelligence is lower in poor than in well-to-do families, it is possible that the difference between scores of children who had had and who had not had measles or pertussis is explained partly, or even wholly, in this way.

One way to explore this possibility a little further is to compare the distributions of VR scores of children with and without a history of a disease such as measles. If the difference between the means were attributable to unrecognized but substantial neurological effects on a small number of children, one might expect the score difference to appear mainly at the lower end of the distribution. The Figure shows that it is distributed evenly over the whole range, a finding consistent with the conclusion that the difference between means is due mainly to social class variation in attack rates and measured intelligence, rather than to the effect of measles and pertussis on the central nervous system.

A different explanation is needed for the slightly higher mean scores of children who had had rubella (scores of children who had had mumps and scarlet fever were about the same as for those who had had none of the infections). In the light of the conclusion concerning measles and pertussis it is tempting to think again of social class differences,

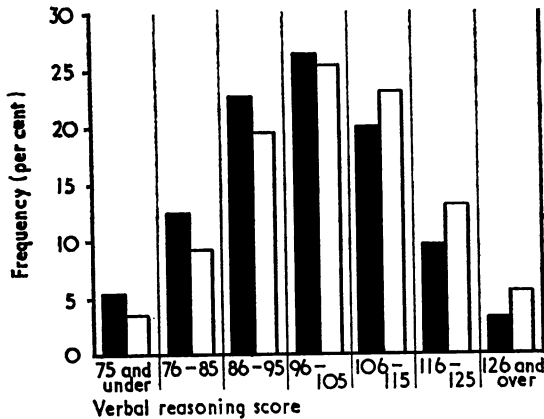


FIGURE Distribution of verbal reasoning scores of children who at the age of five years had had measles (black) compared with those who had not had measles, pertussis, rubella, mumps, or scarlet fever (white).

but these are unlikely to account for higher scores of infected than of not-infected children. The only explanation we can offer, with reservations, is that since the recording of rubella by health visitors was based largely on information provided by mothers, it is possible that the disease was more likely to be observed and reported by the more intelligent. If this is the case, it would not be surprising if their children's scores were a little higher than those of other groups, including children who had had no infectious disease.

Although this paper has been concerned mainly with examination of the possibility that some of the common infections led to unrecognized impairments of neurological function, data are available for the same population of children which show the attack rates from the diseases in mentally subnormal children. They are based on single children born in Birmingham during 1950-54, known to be alive

at the age of five years and ascertained as 'intellectually subnormal', that is to have an IQ below 75 (for further details see Barker, 1966).

There were 753 subnormal children. One had had whooping cough encephalopathy and another had had measles encephalitis and it is possible that these were the cause of the subnormality. In a further nine cases a history of encephalitis was obtained but since all these were treated in hospitals which do not knowingly admit infectious patients it seems unlikely that any were the result of measles or other specific infections. There were a further 135 children with abnormalities such as Down's disease (61 cases), microcephaly (24), or hydrocephalus (12) to which the subnormality was attributed. A history of infectious disease to the age of five years was recorded for 587 of the remaining 607 children. They were divided into three groups according to IQ and attack rates were calculated. As in the previous tables, the rates were standardized for maternal age and birth order—to the distribution of the 11-plus candidates who represent the general population of children.

The results are given in Table IV, and as in other published reports on the same problem, they are frankly inconclusive. In the case of the two common infections, measles and pertussis (numbers of children with the other three diseases were very small), attack rates were lowest for subnormal children with IQs of under 50, and increased with increasing IQ. Two explanations can be suggested for this trend: the most severely handicapped are less often in contact with other children; they are also in somewhat better social circumstances than those at the higher levels of subnormality. Comparison of attack rates from these diseases in subnormal and other children (shown in the last column of Table IV) are clearly inconclusive; the rates are lower for those with IQs of under 50 and higher for those with IQs of 65-74. But in

TABLE IV
ATTACK RATES (PER 100) FOR MENTALLY SUBNORMAL CHILDREN AND FOR CHILDREN WHO SAT THE 11-PLUS EXAMINATION

Disease	IQ of Mentally Subnormal Children			11-plus Candidates
	Under 50	50-64	65-74	
Measles	40.3	54.0	55.0	49.8
Pertussis	24.2	28.7	37.3	31.2
Rubella	8.7	6.1	9.1	9.6
Mumps	5.3	5.4	7.9	10.2
Scarlet fever	3.6	0.5	1.0	2.1
No. of children	118	178	291	43820

The rates for the mentally subnormal have been standardized to the same distribution by maternal age and birth order as the 11-plus candidates

both cases the results are undoubtedly affected both by social class selection (which is not eliminated completely by standardization), and by the relative isolation of the severely handicapped which has already been referred to.

Requests for reprints: R. G. Record, Department of Social Medicine, University of Birmingham.

REFERENCES

- BARKER, D. J. P. (1966). Low intelligence and obstetric complications. *Brit. J. prev. soc. Med.*, **20**, 15.
- and EDWARDS, J. H. (1967). Obstetric complications and school performance. *Brit. med. J.*, **3**, 695.
- BERG, J. M. (1961). Complications neurologiques de la coqueluche. *Wld Neurol.*, **2**, 56.
- BYERS, R. K. and RIZZO, N. D. (1950). A follow-up study of pertussis in infancy. *New Engl. J. Med.*, **242**, 887.
- DOUGLAS, J. W. B. (1964). Ability and adjustment of children who have had measles. *Brit. med. J.*, **2**, 1301.
- FORD, F. R. (1973). *Diseases of the Nervous System in Infancy, Childhood and Adolescence*, 6th ed. Thomas, Springfield, Illinois.
- GIBBS, F. A., GIBBS, E. L., CARPENTER, P. R., and SPIES, H. W. (1959). Electroencephalographic abnormality in 'uncomplicated' childhood diseases. *J. Amer. med. Ass.*, **171**, 1050.
- GREENBERG, M., PELLITTERI, O., and EISENSTEIN, D. T. (1955). Measles encephalitis. I. Prophylactic effect of gamma-globulin. *J. Pediat.*, **46**, 642.
- LEVITT, L. P., RICH, T. A., KINDE, S. W., LEWIS, A. L., GATES, E. H., and BOND, J. O. (1970). Central nervous system mumps. A review of 64 cases. *Neurology (Minneapolis)*, **20**, 829.
- LEVY, S. and PERRY, H. (1948). Pertussis as a cause of mental deficiency. *Amer. J. ment. Defic.*, **52**, 217.
- LITVAK, A. M., GIBEL, H., ROSENTHAL, S. E., and ROSENBLATT, P. (1948). Cerebral complications in pertussis. *J. Pediat.*, **32**, 357.
- MARGOLIS, F. J., WILSON, J. L., and TOP, F. H. (1943). Postrubella encephalomyelitis. Report of cases in Detroit and review of literature. *J. Pediat.*, **23**, 158.
- MILLER, D. L. (1964). Frequency of complications of measles, 1963. Report on a national inquiry by the Public Health Laboratory Service in collaboration with the Society of Medical Officers of Health. *Brit. med. J.*, **2**, 75.
- RECORD, R. G., MCKEOWN, T., and EDWARDS, J. H. (1969). The relation of measured intelligence to birth order and maternal age. *Ann. hum. Genet.*, **33**, 61.
- STEEN, E. and TORP, K. H. (1956). Encephalitis and thrombocytopenic purpura after rubella. *Arch. Dis. Childh.*, **31**, 470.
- TIDSTRØM, B. (1968). Complications in measles with special reference to encephalitis. *Acta med. scand.*, **184**, 411.
- WILNER, E., CANNON, J., and BRODY, J. A. (1969). Measles, minor neurological signs and intelligence. *Develop. Med. Child Neurol.*, **11**, 449.