Studies in Mental Handicap

II: Some Obstetric Factors of Possible Aetiological Significance

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A previous paper (Drillien, Jameson, and Wilkinson, 1966b) described a group of 406 mentally handicapped children, comprising all those with IQ test scores below 70, born in the years 1950–56, who were themselves resident in Edinburgh and/or whose mothers were resident in Edinburgh in 1962–64. Details were given of prevalence and distribution by clinical type and severity of defect.

In this paper some data are presented relating to obstetric factors which appear to be of significance in the aetiology of mental handicap in this group. The following factors are considered: maternal reproductive history; complications of pregnancy, labour, and delivery; birthweight; intrauterine growth and gestation period.

Children with recognizable conditions other than mongolism (Clinical Types 6A and 6B in Part I) have been omitted because of the small numbers of cases of individual conditions, as have 6 children whose mental and neurological defects were attributed to kernikterus. The remaining 367 children have been divided by clinical condition into the categories shown in Table I. In 24* cases there was good evidence that mental handicap (together with neurological defects in all but one case) was postnatal in origin, and obstetric factors would not be expected to have any aetiological significance. Equally, complications of late pregnancy and delivery cannot be implicated in the aetiology of the 71 children with mongolism. Of the rest, 147 children had varying degrees of mental handicap but no other abnormalities, apart from minor defects of common occurrence in the general population, such as squints, hernias, haemangiomas, and minor foot defects, and 125 exhibited other developmental anomalies (i.e. anomalies which must have arisen at an early stage of gestation), cerebral palsy, and epilepsy, alone or in combination. A further

breakdown of the cases in this category is shown in Table II. In this composite group developmental anomalies were present in 56%, cerebral palsy in 38%, and epilepsy in 54%.

For some comparisons, a control group is included of 90 hospital-born children who had been followed up from birth to 7 years or older in another study (Drillien, 1964). All control children had IQs of 85 or more and were doing classwork in school, appropriate to their age; none had any major developmental anomaly. Control children were selected so that the birthweight and sex distribution of the group and the proportion of single and multiple births was that of the general population of Edinburgh births in 1953–54 (Drillien and Richmond, 1956). The incidence of late pregnancy and delivery complications in the control group cannot be used for comparison with that of the mentally handicapped group, as control children were all delivered in two maternity hospitals, giving priority to mothers with complications. For this and some other comparisons, the control data used are those provided by the British Perinatal Mortality Survey (Butler and Bonham, 1963) which gives information about pregnancies and deliveries in a general population of births in 1958.

In three-quarters of the total the survey child was delivered in maternity hospital or nursing home

TABLE I
Clinical Categories

Clinical Category	No. of Children	%
Mental handicap of postnatal origin ..	24	6.5
No other abnormalities, IQ 55–69 ..	112	30.5
No other abnormalities, IQ <55 ..	35	9.6
Mongolism	71	19.3
Other developmental anomalies, cerebral palsy, epilepsy, alone or in combination	125	34.1
Total	367	100.0

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* One child with a severe hemiplegia and gross mental defect following a road accident at 9 years, included in the postnatal category in Part I, has been reclassified as *No other abnormalities*, IQ 55–69, which was his status before the accident.

TABLE II
125 Cases with Developmental Anomalies, Cerebral Palsy, and Epilepsy, alone or in Combination

	No.	%	No.	%
<i>All Cases with Developmental Anomalies</i>			71	100·0
Developmental anomalies only			37	52·1
" " and epilepsy			12	16·9
" " and cerebral palsy			9	12·7
" " , epilepsy, and cerebral palsy			13	18·3
All cases with epilepsy	25	35·2		
All cases with cerebral palsy	22	31·0		
<i>All Cases with Cerebral Palsy</i>			47	100·0
Cerebral palsy only			11	23·4
" " and epilepsy			14	29·8
" " and developmental anomalies			9	19·1
" " , epilepsy, and developmental anomalies			13	27·7
All cases with epilepsy	27	57·4		
All cases with developmental anomalies	22	46·8		
<i>All Cases with Epilepsy</i>			68	100·0
Epilepsy only			29	42·7
" and cerebral palsy			14	20·6
" and developmental anomalies			13	19·1
" , cerebral palsy, and developmental anomalies			12	17·6
All cases with cerebral palsy	27	39·7		
All cases with developmental anomalies	26	38·2		

(or admitted with the mother shortly after birth) and the obstetric records were available for scrutiny. In one-quarter no obstetric records were available and it was necessary to accept the history of events in pregnancy and delivery as given by the mother. It is likely that in some instances this history was

inaccurate. However, as is shown in Table III, the proportion of births having obstetric records available was very similar in all clinical categories. It seems unlikely that bias has been introduced by inaccuracy of reporting being more prevalent in some categories than in others.

TABLE III
Place of Birth by Clinical Category

Clinical Category	Place of Birth								Total	
	Hospital/Nursing Home				Home		Not Known			
	Records									
	Available		Not Available							
	No.	%	No.	%	No.	%	No.	%	No.	%
Postnatal	22	91·7	—	—	2	8·3	—	—	24	100·0
No other abnormalities, IQ 55–69										
Social Grade 1, 2, 3	*36	75·0	2	4·2	10	20·8	—	—	48	100·0
Social Grade 4, 5	*49	76·6	1	1·6	9	14·0	5	7·8	64	100·0
No other abnormalities, IQ <55										
Social Grade 1, 2, 3	15	68·2	4	18·2	3	13·6	—	—	22	100·0
Social Grade 4, 5	10	76·9	—	—	3	23·1	—	—	13	100·0
Mongolism	47	66·2	11	15·5	12	16·9	1	1·4	71	100·0
Developmental anomalies, cerebral palsy, epilepsy, alone or in combination	†97	77·6	1	0·8	27	21·6	—	—	125	100·0
Total	276	75·2	19	5·2	66	18·0	6	1·6	367	100·0

* Includes 1 case admitted to hospital after birth.

† Includes 2 cases admitted to hospital after birth.

It was shown in the previous paper that when survey children had no abnormalities apart from mental handicap there were significantly more coming from poor or very poor homes (Social Grades 4 and 5) than from middle class and superior or average working class homes (Social Grades 1, 2, and 3). For this reason, place of birth for these two clinical categories is given separately by social grade. There is no indication that poorer type women, who might be less likely to give an accurate history, were more often confined at home. Obstetric records were least likely to be available for mothers of mongol children and mothers of severely handicapped children without other abnormalities in the higher social classes, because of an increased number of older middle class women confined in private nursing homes.

Maternal Reproductive Capacity

The reproductive histories of mothers of mentally handicapped children in different clinical categories were compared with those of mothers of normal control children by applying certain arbitrary criteria of relative infertility to all groups. These criteria are described in detail elsewhere (Drillien, Ingram, and Russell, 1962) and essentially consist of a history of difficulty in conceiving, with long unwanted gaps after marriage or between conceptions, and/or frequent abnormal outcome in other conceptions.

Fertility of 27 of the survey mothers could not be assessed; in 14 instances the survey child was illegitimate and in 13 contraceptive habits of the parents were not known, or the marriage had not lasted long enough for an assessment of maternal fertility to be made. In 1 control case contraceptive habits were not known.

Table IV gives the incidence of relative infertility of control mothers and mothers of mentally handicapped children. Mothers of children with mental handicap only and no other abnormalities have been divided by social grade. The incidence of maternal infertility was little different for mothers of control children and mothers of survey children whose handicap was of postnatal origin. In the two clinical categories without other abnormalities, there was no increase in infertility of mothers from the lowest social grades, but there was an increase in superior and average grade mothers. This increase was just below the accepted level for statistical significance in mothers of children in the IQ range 55-69, and just above this level in mothers of children with IQ levels of 54 and under. In all other clinical categories there was a highly significant excess of maternal infertility.

Complications of Pregnancy

Table V gives the incidence of threatened abortion in the first six months of pregnancy and of potentially hypoxia-producing complications of later pregnancy.

Mothers who reported some 'spotting' of blood during early pregnancy, or slight post-conceptional bleeding at the expected date or dates of menstruation, were not included as cases of threatened abortion. There was an increase in the incidence of threatened abortion in some clinical categories, more especially in mothers having children with cerebral palsy and epilepsy, but the incidence figures are based on few cases.

As compared with mothers of mongol children and those whose handicap was of postnatal origin, mothers of children in other clinical categories (particularly those with no other abnormalities and those with cerebral palsy) showed an increased incidence of severe late pregnancy complications, but again these incidence figures are based on small numbers. The incidence of moderate or severe toxæmia in a general population of births in 1958 (Butler and Bonham, 1963) is given as 9.2%, and the incidence of antepartum haemorrhage as 3.1%.

Chronic diseases coincident with pregnancy are enumerated in Table VI. The 5 mothers suffering from active tuberculosis were on drug therapy throughout pregnancy. The 4 with migraine had all required inpatient hospital treatment.

The increased incidence of chronic disease in the clinical category 'No other abnormalities IQ 55-69' is accounted for by 6 cases of severe anaemia of which 5 were due to iron deficiency. This is not unexpected in a group of women coming predominantly from poor homes.

The highest incidence of chronic disease was reported for mothers of mongol children. In 5 instances the mother suffered from endocrine disturbances; 2 were receiving treatment for thyrotoxicosis, 2 for hypothyroidism, and 1 suffered from Cushing's syndrome due to an adrenal neoplasm. The incidence of endocrine disturbances was more than 10 times as great in mothers of mongols as in mothers of other mentally handicapped children.

Complications of Labour and Delivery

Table VII gives the method of delivery of survey patients and of a general population of births in 1958. In Table VIII an arbitrary grading was applied to total complications of labour and delivery to give some indication of severity. For example, mid-forceps and assisted breech delivery rated 1, when preceded by manual rotation or

TABLE
Incidence of Relative Infertility in

Clinical Category	No. of Cases	Fertility Not Known	Normally Fertile	
			No.	%
Postnatal	24	2	16	72.7
No other abnormalities, IQ 55-69				
Social Grade 1, 2, 3..	48	2	28	60.8
Social Grade 4, 5 ..	64	4	48	80.0
No other abnormalities, IQ <55				
Social Grade 1, 2, 3..	22	—	10	45.5
Social Grade 4, 5 ..	13	1	9	75.0
Mongolism	71	4	25	37.3
All with other developmental anomalies	71	8	33	52.4
All with cerebral palsy	47	8	18	46.2
All with epilepsy	68	7	24	39.3
Control	90	1	69	77.5

NS, not significant.

internal version, 2. Additional complications such as prolapsed cord, prolonged labour, or post-maturity rated a further 1 point.

Both Tables VII and VIII indicate that complications of labour and delivery were not increased during births of mongol children, and very little

increased during births of children with no abnormalities other than mental handicap. A more marked increase in complications was seen in the categories of children presenting with developmental anomalies, other than mongolism, cerebral palsy, and epilepsy.

TABLE V
Incidence of Pregnancy Complications

Clinical Category	No. of Cases	Threatened Abortion		Toxaemia and/or Antepartum Haemorrhage	
		No.	%	No.	%
Postnatal	24	1	4.2	2	8.3
No other abnormalities					
IQ 55-69	108	2	1.9	16	14.8
IQ <55	35	2	5.7	8	22.9
Mongolism	70	5	7.1	5	7.4
All with other developmental anomalies	71	5	7.0	10	14.1
All with cerebral palsy	47	7	14.9	10	21.3
All with epilepsy	68	11	16.2	10	14.8
Developmental anomalies, cerebral palsy, epilepsy, alone or in combination	125	12	9.6	16	12.8
Control	90	2	2.2	—	—

IV

Methers of Control and Survey Children

Infertile				1 + 2		Total Infertile		Significance of Difference from Controls p
1 Difficulty in Conceiving		2 Frequent Abnormal Conceptions						
No.	%	No.	%	No.	%	No.	%	
5	22.7	1	4.5	—	—	6	27.3	NS
12	26.1	5	10.9	1	2.2	18	39.1	NS
7	11.7	3	5.0	2	3.3	12	20.0	NS
12	54.5	—	—	—	—	12	54.5	<0.05
2	16.7	—	—	1	8.3	3	25.0	NS
38	56.7	3	4.5	1	1.5	42	62.7	<0.001
19	30.2	8	12.7	3	4.8	30	47.6	0.001
12	30.8	6	15.4	3	7.7	21	53.8	<0.001
24	39.3	10	16.4	3	4.9	37	60.7	<0.001
15	16.9	5	5.6	—	—	20	22.5	

Table IX gives delivery complication score for further subdivisions of patients in the composite group. There was a marked excess of complications of labour and delivery in the birth histories of children with epilepsy only as compared with those of mongol children and children in the postnatal category, and an even more marked excess in the histories of children with epilepsy and cerebral palsy, but when the epileptic child had associated developmental anomalies with or without cerebral palsy the increase in complications was much less. Children presenting with cerebral palsy only and all groups with developmental anomalies with or without neurological defects showed an increase in complications of the same order as that for children with epilepsy and developmental anomalies.

Birthweight, Intrauterine Growth, and Gestation Period

Table X gives birthweight distribution in different clinical categories, and birthweight of surviving infants in a general population of births in 1958. Since women from a poor social background are more likely to give birth to infants of low birthweight, the clinical categories of mental handicap with no other abnormalities are subdivided by social grade. In all categories except postnatal and mongolism, there was an increase in survey subjects having

birthweights of 2000 g. or less, amounting to between 6 and 10 times the incidence observed in the general population. There was a smaller increase in all categories of birthweights between 2001 and 2500 g.

Table XI shows the proportion of survey children in different clinical categories, who would be considered to show marked intrauterine growth retardation, in that their birthweight for gestational age was below the 10th centile, using the Denver, Colorado Scale (Lubchenco *et al.*, 1963). It is likely that birthweights given for Colorado infants born at different gestational ages are rather lower than those reported from Great Britain. The incidence of retarded intrauterine growth was 2-3 times as high as would be expected in those children with additional developmental anomalies. The apparent increase in all with cerebral palsy and all with epilepsy was accounted for by the association of these neurological defects with developmental anomalies in some cases. There was no increase when children with cerebral palsy and/or epilepsy and additional developmental anomalies were omitted from these clinical categories.

Table XII gives the distribution by gestation period of pregnancies resulting in mentally handicapped children and pregnancies in a general population. As would be expected from the birth-

TABLE
Chronic Diseases Coinciding*

Clinical Category	No. of Cases	Cardiac	Respiratory
Postnatal	24	—	—
No other abnormalities			
IQ 55-69	108	1	2
IQ <55	35	—	—
Mongolism	70	1	—
All with other developmental anomalies	71	—	—
All with cerebral palsy	47	—	—
All with epilepsy	68	1	—
Developmental anomalies, cerebral palsy, epilepsy, alone or in combination ..	125	1	—
Control	90	—	—

weight distribution, there was an increase in all clinical categories of pregnancies terminating at or before 36 completed weeks of gestation. This increase is small in the postnatal and mongolism categories. There was also an increased incidence of postmature births (gestation period >41 completed weeks) in children presenting with developmental anomalies, cerebral palsy, and epilepsy, alone or in combination, but not in children presenting with no other abnormalities, mongolism, or those whose handicap was of postnatal origin.

Discussion

In this series of 406 mentally handicapped children clearly defined syndromes and/or definite causes of handicap were found in one-third; 17% suffered from mongolism, 10% from other well-defined conditions including kernikterus, and in 6% the handicap appeared to have originated postnatally. In two-thirds of the total the cause of handicap was obscure; in 31% the children presented with neurological defects and/or developmental anomalies, and in 36% no other defects were

TABLE VII
Method of Delivery

Clinical Category	No. of Cases	Method of Delivery							
		Spontaneous Vertex		Forceps		Breech		Caesarean	
		No.	%	No.	%	No.	%	No.	%
Postnatal	24	20	83.3	2	8.3	2	8.3	—	—
No other abnormalities									
IQ 55-69	108	89	82.4	11	10.2	7	6.5	1	0.9
IQ <55	35	31	88.6	1	2.9	2	5.7	1	2.9
Mongolism	70	65	92.9	1	1.4	4	5.7	—	—
All with other developmental anomalies	71	56	78.9	5	7.0	7	9.9	3	4.2
All with cerebral palsy	47	32	68.1	4	8.5	4	8.5	7	14.9
All with epilepsy	68	49	72.1	6	8.8	5	7.4	8	11.7
Developmental anomalies, cerebral palsy, epilepsy, alone or in combination	125	95	76.0	11	8.8	9	7.2	10	8.0
General population perinatal mortality survey			88.2		4.7		2.3		2.7

VI

with Pregnancy

Endocrine	Tuberculosis (drugs)	Migraine	Anaemia	Other	Total	
					No.	%
—	—	—	—	2	2	8.3
1	1	—	6	2	13	12.0
—	—	1	—	1	2	5.7
5	—	3	1	1	11	15.7
1	2	—	—	2	5	7.0
—	1	—	—	—	1	2.1
—	2	—	—	2	5	7.4
1	4	—	—	3	9	7.2
—	—	—	—	4	4	4.4

detected apart from minor anomalies of common occurrence in the general population.

In any attempt to assess the significance of obstetric factors in the aetiology of mental and neurological handicaps an immediate difficulty arises from the fact that the same clinical picture may result from developmental malformation originating in early pregnancy; from adverse factors operating on a potentially normal central nervous system during later pregnancy and in the perinatal period; from environmental factors after

birth; or from a combination of adverse factors operating at different times on infants who, for other reasons (such as genetic constitution), may be predisposed to suffer damage.

The presence of developmental anomalies which must have arisen at an early stage of intrauterine existence (even when these anomalies are not themselves the cause of mental handicap) suggests that the total picture is more likely to be due to some adverse factor operating in early pregnancy than to later damage.

TABLE VIII
Labour and Delivery Complications Scored for Severity

Clinical Category	No. of Cases	Delivery Score							
		0		1		2		3 and over	
		No.	%	No.	%	No.	%	No.	%
Postnatal	24	18	75.0	3	12.5	2	8.3	1	4.2
No other abnormalities									
IQ 55-69.. .. .	108	74	68.5	28	25.9	4	3.7	2	1.9
IQ <55	35	26	74.3	8	22.9	—	—	1	2.8
Mongolism	70	60	85.7	10	14.3	—	—	—	—
All with other developmental anomalies.. .. .	71	40	56.4	24	33.8	5	7.0	2	2.8
All with cerebral palsy	47	22	46.9	16	34.0	4	8.5	5	10.6
All with epilepsy	68	30	44.1	24	35.3	7	10.3	7	10.3
Developmental anomalies, cerebral palsy, epilepsy, alone or in combination	125	62	49.6	44	35.2	11	8.8	8	6.4

TABLE IX

Delivery Score in Different Combinations of Developmental Anomalies, Cerebral Palsy, and Epilepsy

Clinical Category	No. of Cases	Delivery Score							
		0		1		2		3 and over	
		No.	%	No.	%	No.	%	No.	%
Epilepsy only	29	11	37.9	12	41.4	4	13.8	2	6.9
Epilepsy and cerebral palsy	14	5	35.7	4	28.6	1	7.1	4	28.6
Epilepsy ± cerebral palsy	43	16	37.2	16	37.2	5	11.6	6	14.0
Epilepsy and developmental anomalies	12	7	58.3	5	41.7	—	—	—	—
Epilepsy, developmental anomalies, and cerebral palsy	13	7	53.8	3	23.1	2	15.4	1	7.7
Epilepsy and developmental anomalies ± cerebral palsy	25	14	56.0	8	32.0	2	8.0	1	4.0
Cerebral palsy only	11	6	54.5	4	36.4	1	9.1	—	—
Cerebral palsy and developmental anomalies	9	4	44.4	5	55.6	—	—	—	—
Cerebral palsy ± developmental anomalies	20	10	50.0	9	45.0	1	5.0	—	—
Developmental anomalies only	37	22	59.5	11	29.7	3	8.1	1	2.7
All with developmental anomalies	71	40	56.4	24	33.8	5	7.0	2	2.8

The incidence of developmental anomalies is higher in low weight infants than it is in the general population. In addition, low weight infants with developmental anomalies are more likely to present with later handicaps (the most common being mental retardation and/or neurological defects) than are infants of like birthweight without anomalies.

However, this is not the case when later handicaps are attributable to severe pregnancy complications. In a study of the later status of infants of birthweight 2000 g. or less (Drillien, 1968), a comparison was made of the incidence of developmental anomalies in children with or without moderate or severe handicaps at 7 years, divided into those whose

TABLE X
Birthweight Distribution

Clinical Category	No. of Cases	Birthweight (g.)									
		2000 g. and under		2001 g.—2500 g.		Total 2500 g. and under		2501 g.—4000 g.		4001 g. and over	
		No.	%	No.	%	No.	%	No.	%	No.	%
Postnatal	24	—	—	3	12.5	3	12.5	20	83.3	1	4.2
No other abnormalities, IQ 55–69											
Social Grade 1, 2, 3	48	5	10.4	6	12.5	11	22.9	32	66.7	5	10.4
Social Grade 4, 5	58	5	8.6	6	10.3	11	19.0	45	77.6	2	3.4
All social grades	106	10	9.4	12	11.3	22	20.8	77	72.6	7	6.6
No other abnormalities, IQ <55											
Social Grade 1, 2, 3	22	1	4.5	1	4.5	2	9.1	17	77.3	3	13.6
Social Grade 4, 5	13	3	23.1	1	7.7	4	30.8	8	61.5	1	7.7
All social grades	35	4	11.4	2	5.7	6	17.1	25	71.5	4	11.4
Mongolism	70	3	4.3	9	12.8	12	17.1	56	80.0	2	2.9
All with other developmental anomalies	71	8	11.3	11	15.5	19	26.8	47	66.2	5	7.0
All with cerebral palsy	47	7	14.9	6	12.7	13	27.6	31	66.0	3	6.4
All with epilepsy	68	7	10.3	7	10.3	14	20.6	47	69.1	7	10.3
General population surviving infants			1.5		4.3		5.8		84.5		9.7

mothers had no complications of pregnancy to account for the premature delivery and/or low birthweight, and those whose mothers suffered from severe toxæmia or chronic disease. In most of this group premature delivery was iatrogenic, pregnancy being terminated because of the mother's condition. When premature delivery was due to these pregnancy complications there was no significant difference in the incidence of developmental anomalies in children with handicap (20%) and children without handicap (26%). However, in the absence of maternal complications there was a highly significant difference; 49% of children with handicap had developmental anomalies and only 22% of those without handicap.

In this series of mentally handicapped children minor anomalies of common occurrence in the general population were omitted, but it is of possible significance that among the 147 children classified as mentally handicapped only, 29% had minor anomalies compared with 9% of the control children, a difference that is highly significant ($\chi^2 = 12.991$, $p < 0.001$). In the composite group of 125 children with developmental anomalies, cerebral palsy, and epilepsy, alone or in combination, more serious and/or less common developmental anomalies were present in 56%.

Impaired reproductive capacity of mothers has been demonstrated as a significant association with a number of developmental anomalies. Infertility

TABLE XI
Incidence of Intrauterine Growth Retardation

Clinical Category	No. of Cases	Intrauterine Growth <10th Centile	
		No.	%
Postnatal	24	2	8.3
No other abnormalities			
IQ 55-69	107	11	10.2
IQ <55	35	3	8.6
Mongolism	70	8	11.4
All with other developmental anomalies	71	16	22.5
All with cerebral palsy	47	8	17.0
All with cerebral palsy and no developmental anomalies	25	2	8.0
All with epilepsy	68	10	14.7
All with epilepsy and no developmental anomalies	43	3	7.0

was reported by Murphy (1947) in his study of the reproductive histories of all mothers of infants with fatal congenital malformations born in a 5-year period in Philadelphia; by Record and Edwards (1958) studying congenital dislocation of hip in Birmingham; and by Drillien, Ingram, and Wilkinson (1966a) studying cleft lip and palate in Edinburgh. In a study of the prenatal histories of infants of low birthweights (Wilson, Parmelee, and Huggins, 1963) by means of multiple regression and single variable analysis computer programs, the

TABLE XII
Distribution by Gestation Period

Clinical Category	No. of Cases	Gestation Period (wk.)							
		32* and under		33-36*		37-41*		over 41*	
		No.	%	No.	%	No.	%	No.	%
Postnatal	24	—	—	2	8.4	19	79.1	3	12.5
No other abnormalities									
IQ 55-69	107	6	5.6	9	8.4	81	75.7	11	10.3
IQ <55	35	3	8.6	2	5.7	27	77.1	3	8.6
Mongolism	70	—	—	6	8.6	61	87.1	3	4.3
All with other developmental anomalies	71	1	1.4	9	12.7	45	63.4	16	22.5
All with cerebral palsy	47	5	10.6	4	8.6	26	55.3	12	25.5
All with epilepsy	68	5	7.4	7	10.3	34	50.0	22	32.3
Developmental anomalies, cerebral palsy, epilepsy, alone or in combination	125	7	5.6	10	8.0	73	58.4	35	28.0
General population of surviving infants			1.0		4.3		82.2		12.5

* Completed weeks of gestation.

most significant association with the lowest birth-weights was previous infertility, defined as an infertile period of at least 3 years of attempted pregnancy.

In the study of low weight infants quoted above (Drillien, 1968), in the absence of pregnancy complications 60% of mothers of children with and 31% of mothers of children without moderate or severe handicaps were considered to be relatively infertile. When low birthweight was attributable to severe pregnancy complications the incidence of infertility was 33% for mothers of children with and 26% of mothers without handicap.

In this series of mentally handicapped children there was no increase in maternal infertility in the postnatal group, nor in those with no other abnormalities coming from poor or very poor homes. In all other clinical categories there was an increase in maternal infertility, particularly marked if the child had other abnormalities. With the exception of mothers of mongol children, the increase in mothers having difficulty in conceiving, and those having frequent abnormal outcome in their other conceptions, was of the same order. The very high incidence of difficulty in conceiving reported by mothers of mongol children may be artificially exaggerated by the fact that, though no mother was rated as infertile if contraception had been used to prevent or delay pregnancy or if the parents had wished to avoid pregnancy and were 'being careful' (while taking no active measures), it may well be that intercourse was infrequently practised by some older parents. Nevertheless, it is of interest that in this group of mothers of mongol children, average age at marriage and average age at the births of preceding normal sibs was not much different from that of mothers of like social class having children of like birth rank in the general population. The older age of mothers at the births of their mongol children was frequently accounted for by a long period of apparently involuntary infertility preceding the birth of the mongol child. Thus, one might argue that older age of mother is of secondary importance in the aetiology of mongolism, the primary factor involved in the chromosomal aberration being some physiological disturbance in the mother (possibly endocrine) demonstrated by relative infertility.

There was an increase in threatened abortion during the pregnancy in all clinical categories except those with no other abnormalities IQ range 55-69, and in the postnatal group. Threatened abortion was most common when the survey child had epilepsy or cerebral palsy. In spite of small numbers of cases, the increase as compared with

controls rated as significant in both these clinical categories ($\chi^2 = 9.978$, $p < 0.01$; $\chi^2 = 11.023$, $p < 0.001$).

An increase in threatened abortion has been reported in other studies of developmental malformations (e.g. Record and McKeown, 1949; Worcester, Stevenson, and Rice, 1950; Drillien *et al.*, 1966a).

The incidence of potentially hypoxia-producing complications of late pregnancy is not much different from that reported for a general population of births. However, as compared with the pregnancy histories of mothers of mongols and of children in the postnatal category, the incidence of complications would be considered significantly increased in the pregnancies of mothers having children without other abnormalities ($\chi^2 = 4.349$, $p < 0.05$) and children with cerebral palsy ($\chi^2 = 5.652$, $p < 0.02$). In some cases in these two categories late pregnancy complications were associated with very low birthweight.

The increased incidence of chronic disease coincident with pregnancy reported by mothers of mongols (15.7%) would be considered significantly different from the incidence of 8.9% reported by mothers of all other mentally handicapped children ($\chi^2 = 4.904$, $p < 0.05$). However, it might be argued that chronic disease would be more likely to be found in any population of older women, though the fact that 1 in 14 of the mothers of mongol children was under treatment for endocrine disturbance during pregnancy may be of some significance.

In contrast to the small increase in pregnancy complications, there was a marked increase in complications of labour and delivery in some clinical categories. In the postnatal group, labour and delivery were uncomplicated in 75%. In spite of the older age of mothers of mongol children, no complications were reported in 86%. There was little increase in complications in the two categories of children without other abnormalities, but there was a marked increase when the survey child had additional neurological defects. As compared with the postnatal and mongolism categories, the difference in distribution of adverse delivery score was highly significant for children with epilepsy only ($\chi^2 = 23.765$, for 3 d.f., $p < 0.001$) and for children with epilepsy and cerebral palsy ($\chi^2 = 26.235$ for 3 d.f., $p < 0.001$). When the epileptic child had associated developmental anomalies the increase in complications and the level of significance of the difference in complication score compared with the postnatal and mongolism categories were much less ($\chi^2 = 8.593$ for 3 d.f., $p < 0.05$). In cases where epilepsy and cerebral palsy were found

in association with definite developmental anomalies it seems reasonable to suppose that mental, physical, and neurological defects were all due to developmental malformation rather than to later damage. These findings suggest that severe complications of labour and delivery were not primarily responsible for mental handicap in many cases but might have caused additional cerebral damage resulting in epilepsy and/or cerebral palsy.

The small but consistent increase in delivery complications noted in children with cerebral palsy only, developmental anomalies only, or combinations of these conditions with or without epilepsy, may be associated in part with increase in maternal infertility, in that the obstetrician may be more likely to decide on elective caesarean section or apply forceps earlier in the case of the much wanted baby. However, there is some evidence from other studies that there may be an excess of abnormalities of delivery in infants having fetal malformations even when the malformation itself does not present any particular problem at delivery (Potter and Adair, 1939; Drillien *et al.*, 1966a).

The incidence of low birthweight is increased in all clinical categories except those whose handicap appeared to be of postnatal origin. The increase of low birthweight in survey children without other abnormalities is not accounted for solely by the excess of women from poor or very poor homes in these two categories, the incidence of birthweights of 2500 g. or less being 18.6% of infants born to women graded as middle class and superior or average working class, and 21.1% of those born to poor or very poor working class women. The excess of very low birthweights of 2000 g. or less was most marked in all clinical categories, except for mongol children who were more likely to weigh between 2001–2500 g. The raised incidence of mental and neurological defects in children who were of low weight is well recognized but it does not follow that these defects are due primarily to premature delivery and/or low birthweight. It is equally probable that these factors may be secondary to developmental malformation in the fetus.

In view of the present discussions about the effects of fetal malnutrition and retarded intrauterine growth on the growing brain (Dobbing and Widdowson, 1965), it is of interest that in this series of mentally handicapped children, only those with additional developmental anomalies showed any noticeable increase in the incidence of intrauterine growth retardation. The incidence of intrauterine growth retardation in all children with developmental anomalies was 22.5% compared with 10.7% of those without these anomalies ($\chi^2 = 8.841$,

$p < 0.01$). In these cases the fetal growth retardation is likely to be secondary to developmental malformation rather than causative of handicap.

A highly significant increase in the incidence of prolonged pregnancy was noted for children with developmental anomalies, cerebral palsy, and epilepsy, alone or in combination (28.0%), as compared with the incidence of 8.5% in other clinical categories ($\chi^2 = 24.123$, $p < 0.001$). The highest incidence (37%) was recorded for children with epilepsy with or without cerebral palsy. Since postmaturity is known to be associated with a 50% increase in fetal wastage, particularly from intra-partum hypoxia (Butler and Bonham, 1963), it is reasonable to suppose that prolonged pregnancy led to hypoxic cerebral damage in some children who later presented with neurological defects in addition to mental handicap. However, the incidence of prolonged pregnancy was nearly twice as high in survey children with developmental anomalies but no neurological defects (21.6%) as in the general population (12.5%). Postmaturity was also found to be associated with fetal malformation in the British Perinatal Mortality Survey (Butler and Bonham, 1963) and in a study of cleft lip and palate in Edinburgh (Drillien *et al.*, 1966a).

Why infants with developmental malformations should be more likely to be delivered prematurely or postmaturely is by no means clear, but equally there is no clear explanation as to why over 80% of infants in the general population are born between 37 and 41 weeks. Perhaps some physiological disturbance in the mother is associated with both prematurity or postmaturity in her offspring.

Summary

Obstetric factors are not implicated to any noticeable extent in those mentally handicapped children (mostly in the IQ range 55–69) from poor or very poor homes. In these cases a combination of poor genetic endowment of intelligence and adverse postnatal environment is probably the primary cause of later handicap. Those without other defects from adequate homes have an increased incidence of low birthweight, premature delivery, pregnancy complications, and maternal infertility but not of delivery complications.

Apart from children with recognizable syndromes, the rest of the survey children presented with developmental anomalies, cerebral palsy, and epilepsy, alone or in combination, as well as mental handicap which was usually severe (IQ < 55). Complications of labour and delivery were associated with additional neurological defects but not with the mental handicap itself. The fact that over one-half

of this composite group exhibited developmental anomalies which must have arisen at an early stage of gestation suggested that the total picture of handicap was due to developmental malformation in many cases. Such malformations may have been caused by physiological (possibly endocrine) disturbances in the mother demonstrated by maternal infertility, prematurity and postmaturity, and difficulties during labour and delivery.

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