

MICROCEPHALY

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The head is relatively large at birth, the brain making up 12% of the body weight compared with 2% in the adult. This gives the normal newborn baby a somewhat top-heavy appearance. In severe mental deficiency the size of the head tends to be reduced. Fig. 1 shows the distribution of cranial circumference in 100 successive admissions to the Fountain Hospital. The cases are charted in terms of standard deviations from the norm for the age and sex. As will be seen, in a number of cases there is a very marked deviation below the norm. For our purpose we have considered in relation to microcephaly all those cases which fall more than three standard deviations (S.D.) below the norm. These make up 26% of our admissions. If instances of mongolism are excluded, the figure is 20%. For the purpose of a recent survey (Brandon, Kirman and Williams, 1959a), we were able to study 130 microcephalics, so defined and excluding mongolism. The admissions to the Fountain Hospital consist almost exclusively of children in the idiot and imbecile range of intelligence.

Time of Onset

In a number of cases of microcephaly, the head is obviously small at birth, for example, in patient G.A.F. it was 25.4 cm., and in patient M.I.H. 30.5 cm. at 7 weeks, i.e. 5.6 S.D. below the norm. Indeed, extreme smallness of the head is one of the few conditions that enable severe mental defect to be determined with certainty at birth (Kirman, 1958). The brain grows relatively faster than the remainder of the body in intrauterine life. Nevertheless, as shown in Fig. 2 (Westropp and Barber, 1956), a great deal of further growth in cranial size takes place after birth. Theoretically it would be possible for a child to fall into the microcephalic category on the above definition merely by failure to grow after birth. In fact this has happened in a number of our children. In patient C.B. the head circumference was 1 S.D. below the norm at 10 weeks and again at 7 months, whereas at 2 years and 10 months it was $3\frac{1}{2}$ S.D. below the norm. In L.R. at 2 years

and 5 months on admission to hospital, the head circumference was 46.3 cm. Eight years later, at the age of 10 years, it was 47 cm. Virtually, therefore, it had not grown in the interval, and in consequence the boy had become classifiable as microcephalic, whilst not so on admission, being now 4.5 S.D. below the norm for 10 years. In C.B. there was a history of very doubtful birth injury. L.R. had primary optic atrophy, and at autopsy the brain at 11 years weighed 832 g. and showed some ulegyria.

None the less, it is probable that all the more extreme cases of microcephaly are established as such in intrauterine life. At first sight it might seem that those cases which are already microcephalic at birth might be genetically determined and that those which fail to grow at a later stage are due to environmental factors. In fact this is not always so. In the cases described by Sylvester (1959), the abnormality consisted much more of a failure to grow after birth, but in these two cousins the defect was almost certainly due to genetic causes. On the other hand, in the two pairs of identical twins described previously (Brandon, Kirman and Williams, 1959b) the smallness of the head, while established before birth, must be ascribed to external factors, since only one twin was affected in each case.

Relation to Stature

Ashby and Stewart (1933), in considering reduction in size of the brain in mental defect, have suggested that this is merely part of the general reduction in stature. We, at the Fountain Hospital, are prepared to go a little further than this and to ascribe to the brain a leading role in the matter, considering that in a large number of cases of severe mental defect the reduction in size of the body is secondary to the abnormality of the brain. It is true that, in such inborn errors of metabolism as phenylketonuria, the chemical activity of every cell in the body is affected directly by the accumulation of abnormal metabolites. Two of our examples of microcephaly were cases of this syndrome. It might

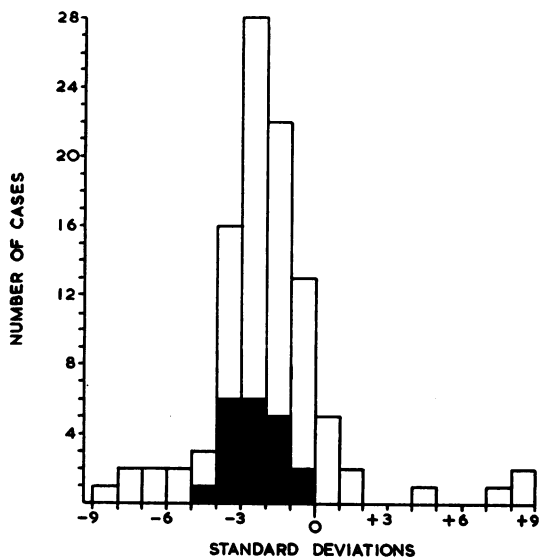


FIG. 1.—One hundred consecutive admissions to Fountain Hospital showing distribution of head circumference in relation to mean. Cases of mongolism are shown in black.

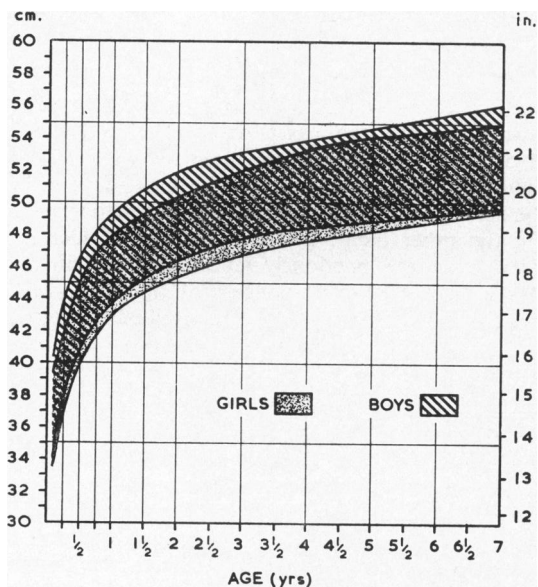


FIG. 2.—Normal channel of growth of head circumference. The upper margins of the shaded zones in this figure represent the lines drawn between serial values of the mean head circumference plus their standard deviations multiplied by 1.96 ($M + 1.966$) and the lower margins the lines between serial means minus 1.966. This 'normal' channel covers all but 5% of the original measurements so that, although any children with microcephaly will fall below the lower range shown, some normal children will also be excluded. Based on serial measurements of 331 boys and 333 girls in Oxford Survey (Westropp and Barber, 1956).

be considered that in them delay in growth of the brain is but a part of the general reduction in size. Similar considerations apply to mongolism, since all or most of the cells of the body presumably contain an additional chromosome in this condition (Jacobs, Baikie, Court Brown and Strong, 1959). In cases of microcephaly due to maternal rubella on the other hand, damage is apparently localized to the brain and sense organs in many cases, and these patients may not be markedly reduced in general stature. Among 10 instances of defect ascribed to maternal rubella in our series, two were microcephalic. In patient P.H. the height and weight at 5 years were 41½ in. (43.3 in.) and 37½ lb. (41.7 lb.) respectively; the corresponding figures in patient A.D. were 54 in. (48.9 in.) and 32 lb. (54 lb.) at 7 years. Figures in parentheses are norms. Birth injury is a difficult matter to assess retrospectively and the subject needs further study, but we have suggestive evidence that severe birth injury can cause both moderate microcephaly and reduction in stature as a secondary consequence.

Relation to Face

Koch (1959a), following other workers, includes as microcephalics only those cases where there is disproportion between the cranium and the face. He does not state, however, that he adopts any objective criteria in making this assessment. Since the degree of disproportion varies very widely, it is obvious that such a method of classification will depend upon subjective factors and may include a variable number of extreme cases. In addition, there is no good evidence that cases characterized by such disproportion are aetiologically distinct from those where there is a proportionate reduction of cranium and face. Similar criticisms apply to any other method of differentiating an 'essential' type of microcephaly, and until more evidence is available it seems advisable to pay attention to all cases in which the head is very small.

Usefulness of Concept

If this course is followed, it will be seen that the material covered in a survey will be extremely heterogeneous. It may in fact be questioned whether any useful purpose is to be served in surveying the microcephalic cases separately from other forms of cerebral anomaly. Until more information on aetiology and classification is available, it seems useful to do this since some factors such as mongolism (Fig. 3) and rubella are specially prone to cause microcephaly, while meningitis (Fig. 4) rarely does so, and none of our cases of kernikterus had very small heads (Fig. 5). Similarly, consideration

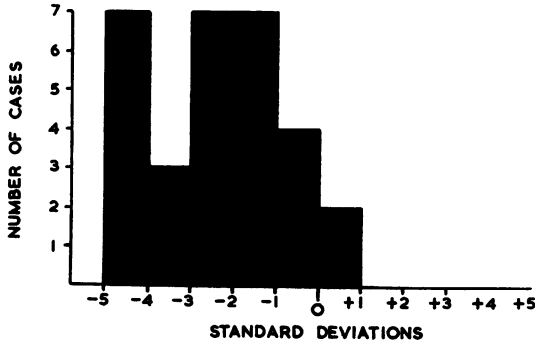


FIG. 3.—Thirty cases of mongolism showing cranial circumference assessed in terms of standard deviations from the mean for age and sex.

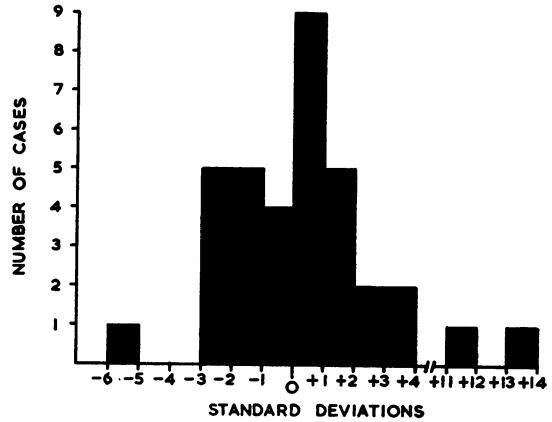


FIG. 4.—Thirty-five cases of infantile meningitis and mental defect showing cranial circumference assessed in terms of standard deviations from the mean for age and sex.

of the familial cases suggests strongly that the concept of microcephaly is useful. Of 10 mentally defective siblings of our microcephalic patients, nine were microcephalic (Table 1).

Familial Microcephaly

It seems fairly certain that there are a number of distinct forms of familial microcephaly. Koch (1959b) suggests that cerebral palsy is more likely to occur among the exogenous cases and that, where it is found in familial cases, it may be a superimposed complication. Our findings (Table 2) suggest that, among the familial cases, it is commoner to find children with cerebral palsy than without this complication. We also found a tendency for microcephalics with cerebral palsy to have microcephalic siblings similarly affected, while microcephalic children who do not have cerebral palsy tend to have affected siblings who are also able-bodied. The diversity of the pathology of the brain even in the familial cases further supports the view that a number of separate genetic factors

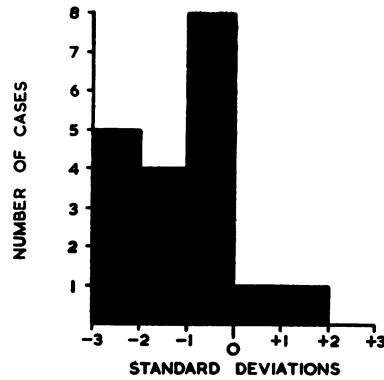


FIG. 5.—Nineteen cases of icterus gravis neonatorum showing effect upon cranial circumference assessed in terms of standard deviations from the mean for age and sex.

TABLE 1
TEN MENTALLY DEFECTIVE SIBLINGS OF MICROCEPHALICS

Case No.	Microcephalic	Spastic	Epilepsy	Head Circumference (S.D. below mean for sex and age)
1	—	+	P	1.2
2	+	Death at 8 days certified as microcephaly	—	4.3
3	+	—	—	—
4	+	Died at 25 days, hemiplegic, head and brain small	—	—
5	+	—	—	3.9
6*	+	+	—	6.6
7*	+	+	—	5.3
8*	+	+	+	3.3
9	+	—	—	5.9
10	+	+	+	3.5

P = Petit mal.

* One sibship

TABLE 2

MICROCEPHALIC PATIENTS AND THEIR MENTALLY DEFECTIVE SIBLINGS WITH REFERENCE TO CEREBRAL PALSY

Case No.	Cases	Affected Siblings
1	+	Ø
2	+	?
3	+	+
4	+	++
5	+	+++
6	+	++
7	+	?
8	+	?
9	+	O
10	+	+
11	+	+
12	+	Ø
13	+	Ø
14	O	Ø ¹
15	O	O
16	O	Ø ¹
17	O	+ ¹
18	O	Ø
19	O	Ø

+ = microcephaly and cerebral palsy.
 O = microcephaly without cerebral palsy.
 Ø = mentally defective without microcephaly or cerebral palsy.
 1 = half sibling.

may produce a small brain. Since none of the parents of our cases was microcephalic, it seems reasonable to suppose that, with the exception of the special case of mongolism, such genetic factors operate in a recessive manner.

Intelligence in Microcephaly

As mentioned, nearly all the patients whom we surveyed in connexion with microcephaly were

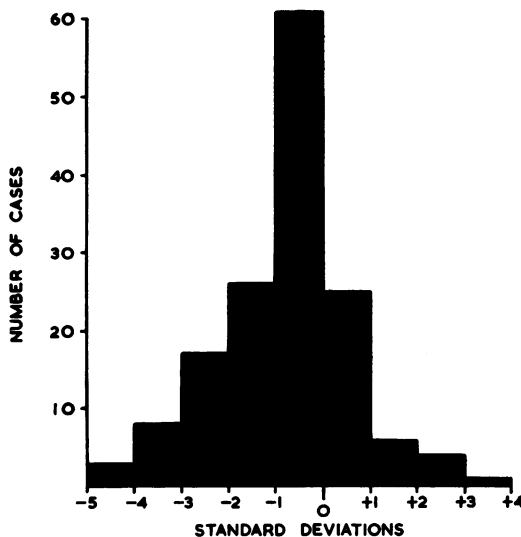


FIG. 6.—Cranial circumference in 151 feeble-minded women.

imbeciles and idiots. Three of our total of 108 cases in whom intelligence was formally assessed had a quotient above 50. There was a significant correlation in these 108 patients between head size and intelligence. In view of the mode of selection of our cases, it is likely that a group of mental defectives containing a proportion of feeble-minded patients might show some mild cases of microcephaly in that mental range. One of Penrose's (1954) male cases had an intelligence quotient of 80 with an estimated cranial capacity of 1,000 to 1,099, and three female patients with I.Q.s of 70 were in the same range of cranial circumference. In the same author's Colchester survey (1938), two of his 'traditional' microcephalics, about whom details of head measurements are given, had I.Q.s assessed in the 50-59 range.

Feeble-minded Microcephalics

For the purpose of this paper, we noted the recorded head circumference on admission of 151 feeble-minded patients discharged from South Side Home, Streatham. For this purpose, we took into account all those patients who had at any time on any test been credited with an intelligence quotient of 50 or more. In fact some of them had an intelligence well within the normal range. The results of this survey are shown in Fig. 6. Of this group of 151 patients, 11 fell into the microcephalic range. The available test scores on different occasions were scrutinized by Dr. Mary Woodward who considered that in three cases the overall results warranted classification as imbecile rather than as feeble-minded, leaving eight microcephalic feeble-minded patients. Two of the eight cases with Wechsler quotients of 77 and 78 fell into the range of microcephaly of 4-5 standard deviations below the norm, while for the six cases in the 3-4 standard deviations below the norm range, the quotients were 58, 59, 75, 76, 88 and 100. The woman with a Wechsler quotient of 100 has unfortunately since died, removing the possibility of further measurement. She was described as 'petite', and was employed as a domestic worker in a hospital. One of these patients was congenitally deaf and another had a marked degree of hypertelorism. The former is now in a convent, the latter is doing domestic work. Another case has a congenital abnormality of the heart and is not working, being fostered out. The other microcephalic cases are employed in factory or domestic work. One of these with a Stanford-Binet quotient of 58 is said to have earned up to £10 a week in factory work.

These discharged patients are now adults, but the original measurements were taken in some cases

whilst they were children. They have therefore been rechecked. Of the surviving seven patients, three now fall into the range of 3-4 standard deviations below the norm, while four are in the range of 2-3 below. For this purpose the figure kindly supplied by Professor Penrose for women students was used as a norm. From this small group of cases it appears possible that there is a tendency for the degree of deviation from the norm to be reduced as a result of the bony changes in the skull in adolescence.

There is surprisingly little information on the pathology of feeble-mindedness, and the above findings suggest that a more detailed survey of head size, among other matters, would be useful. It seems likely that those cases who are frankly microcephalic will prove on final analysis to be suffering from some more tangible clinical syndrome than many of the feeble-minded who elude more precise classification.

Summary

About a quarter of idiots and imbeciles have heads more than three standard deviations below the norm, or 20% if mongolism is excluded. In many cases the microcephaly is present at birth. In a number of the milder cases marked slowing of growth of the head, resulting in microcephaly, takes place after birth. Although the remainder of the body may be reduced in size in mental defect, we attach a leading role to the smallness of the brain. In some general metabolic disorders all tissues are directly affected. In microcephaly due to rubella the remainder of the body may not be particularly

small. Microcephaly so defined is of mixed aetiology, but some genetic and environmental factors are particularly prone to produce smallness of the head so that the concept of microcephaly is useful in a study of aetiology. Of the 108 cases in the previous survey, only three were above imbecile level, but this may have been due to selection. To test this, 151 case records of the 'feeble-minded' were studied, of these eight were microcephalic on a single measurement, two of these with other abnormalities were not employed and six were earning their living.

Our thanks are due to Dr. Mary Woodward, principal psychologist; to Dr. L. T. Hilliard whose patients we examined at South Side Home; and to Mrs. M. W. G. Brandon for information on the feeble-minded patients deriving from her survey (Brandon, 1960).

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