Neonatal and Maternal Cranial Form

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SUMMARY

The mean cephalic index (CI) in the normally grown full-term neonate is in the lower eighties. Because intrauterine growth retardation causes a greater proportionate reduction in the biparietal than in the occipitofrontal diameter, the resultant CI is significantly lower \( (P<0.01) \) than in neonates who have grown normally. There is no significant correlation between maternal and neonatal cranial form as judged by the CI. In man, hereditary factors operate in the long period of postnatal growth and differentiation.


Neurocranial shape in the newborn was the subject of two earlier studies. The parameter of head shape investigated was the cephalic index (CI). The study groups consisted of South African Blacks, a population with a low mean adult value for this index. In both series the measurements were made on neonates delivered by Caesarean section without the prior occurrence of labour pains. Statistical analysis showed the difference between the two groups of data to be significant at the 5% level. There had been an apparent shift in the group norm in the period of 16 years which elapsed between the two studies.

Because the mean CI in the first series was significantly lower than that quoted in the literature, it was stated that this was consistent with the lower mean value of the adult Black population. The conclusion was that the cranial form of the newborn foreshadowed the adult cranial characteristics and that hereditary factors were important in determining the morphology of the neurocranium at birth.

The findings of the second investigation called for an adjustment of the main conclusion of the earlier study. Despite having been drawn from the same population, the results were significantly different. They were, moreover, consistent with the mean newborn cephalic indices determined by other workers in populations with high adult values for the index. The results of the second study thus supported the general belief that common human inheritance determines cranial form at birth, the value in the newborn being in the lower eighties, regardless of the adult cranial characteristics. In man, hereditary factors operate in the long period of postnatal growth and differentiation.

The only other noteworthy difference between the two series of cases was in birth size; the earlier series had a significantly lower mean birth weight than the later. A study of the birth weight trend in this population revealed that the difference between the two series was part of a secular trend. There was, in fact, a highly significant positive correlation with time \( (r = 0.995) \) for the period 1917 - 1970.

An investigation of the relation between birth weight and the cephalic index shows a significant positive correlation. With increasing full-term fetal size, the allometric enlargement of the brain and its neurocranium is not a proportionate but a differential process in which the enlargement of the biparietal diameter is greater than that of the occipitofrontal, thus accounting for the concurrent rise in the cephalic index. Differences in birth weight are, therefore, an important factor in the determination of the variability of the index in the newborn. In the present investigation, variations in headform in the newborn are studied in relation to the maternal cranial characteristics.

PATIENTS AND METHODS

Neonates satisfying the following criteria were selected for inclusion in the normal group.

Absence of Moulding

Only neonates delivered by elective Caesarean section without the prior occurrence of labour pains were measured. This decision imposed a serious limitation on the number of cases available for study. It was based on the author's earlier analysis of his own and other investigators' findings on the effect of parturition on the fetal neurocranium. The suggestion that a restoration of neonatal cranial configuration takes place early in the neonatal period, before significant postnatal growth and differentiation occur, was investigated. The finding was that in approximately one-third of infants distortion and asymmetry of the neurocranium persist until the second postnatal week, at which time significant neurocranial growth has already taken place. Asymmetrical neurocranial distortion was still present in some infants who were examined 6 weeks after birth. Ultrasonic determinations of the biparietal diameter in utero performed within 48 hours before vaginal delivery differed significantly from measurements taken at birth by means of a craniometer. A significant reduction of the biparietal diameter during parturition took place in 90% of 30 neonates who were studied.

Maturity

1. A calculated gestational age of 39 to 41 weeks was regarded as mature, provided that the antenatal record showed the fundal height to correspond with the calculated duration of gestation, based on the menstrual history in those with regular cycles.
2. A minimal fetal length of 48.5 cm (19 inches).
3. A paediatric gestational score corresponding to at least...
39 weeks according to the score sheets used in Groote Schuur Hospital paediatric units.

4. Additional data, sometimes available, were of help in establishing the age of the fetus: radiological evidence, information on the amniotic creatinine value, the amniotic sphingomyelin/lecithin ratio, and amniotic cytology.

Absence of Growth Retardation

In the normal group babies with growth retardation were excluded. The diagnosis was suspected on the basis of the following:

1. Failure of the mother to gain weight in a satisfactory manner in the course of antenatal supervision. The weight gain standards applied were those of Eastman and Jackson.

2. Failure of the fundus uteri to rise in the expected manner in the period of antenatal care.

3. Failure of the fetal biparietal diameter to follow the trajectory defined by Campbell and Dewhurst.

4. Multiparous subjects in their sixth and subsequent pregnancies were excluded from the normal group. Their exclusion is based on the observation that in this population birth weight rises significantly ($r = 0.78$) with birth order up to the fifth pregnancy, and thereafter falls.

The Abnormal Group

Cranial measurements were also taken on a group of neonates who did not satisfy the criteria for normal growth. The group consisted of full-term dysmature neonates who showed evidence of intra-uterine growth retardation during the period of antenatal observation. The diagnosis of inappropriate growth was confirmed at postnatal examination. All babies in the series were delivered by Caesarean section.

Measurements

All measurements were made within 24 hours of birth. Birth weight was recorded on the standard balance scales used in the University of Cape Town paediatric unit. Paediatric scoring of gestational age was carried out by the senior paediatrician. Newborn occipitofrontal and biparietal measurements were made with a standard craniometer. Cranial measurements on the mother were, as a rule, done in the postpartum period.

RESULTS AND ANALYSIS

Maternal and Neonatal Cephalic Index (CI) in the Normal Group

The results are summarised in Table I. The correlation between the maternal and neonatal CI has been determined in two ways.

First analysis. The data were grouped according to the value of the mother's CI by means of a class interval of one unit (Table I). This stratification produced 8 sub-populations of neonates for the corresponding maternal classes and $8 \choose 2 = 28$ possible pairs of newborn sample means for both birth weight and CI. These two variables were analysed statistically to test the null hypothesis ($H_0$) that the 8 groups have been drawn from the same population (i.e. with equal means). Analysis of variance and the

| TABLE I. STRATIFICATION OF DATA ACCORDING TO MATERNAL CEPHALIC INDEX BY MEANS OF CLASS INTERVAL OF ONE UNIT |
|---|---|---|---|
| Maternal data | Cephalic index | Mean CI | Range Birth weight | Mean (g) |
| Class interval | Mean | (SD = 0.07) | 2987 - 3675 | 3286.00 |
| 74.0 - 74.9$^*$ | 74.25 | 79.75 | 2987 - 3675 | 3286.00 |
| (N = 2) | (SD = 0.07) | (SD = 0.49) | (SD = 255.97) | (SD = 371.13) |
| 75.0 - 75.9$^*$ | 75.5 | 80.29 | 2797 - 3630 | 3236.15 |
| (N = 8) | (SD = 0.32) | (SD = 0.73) | (SD = 225.97) | (SD = 371.13) |
| 76.0 - 76.9$^*$ | 76.51 | 80.13 | 2880 - 3630 | 3236.15 |
| (N = 7) | (SD = 0.30) | (SD = 0.75) | (SD = 225.97) | (SD = 371.13) |
| 77.0 - 77.9$^*$ | 77.33 | 80.31 | 2779 - 3675 | 3236.15 |
| (N = 15) | (SD = 0.27) | (SD = 0.63) | (SD = 225.97) | (SD = 371.13) |
| 78.0 - 78.9$^*$ | 78.20 | 79.94 | 2935 - 3710 | 3236.15 |
| (N = 5) | (SD = 0.16) | (SD = 0.73) | (SD = 225.97) | (SD = 371.13) |
| 79.0 - 79.9$^*$ | 79.2 | 80.10 | 3271 | 3236.15 |
| (N = 1) | | | | |
| 80.0 - 80.9$^*$ | | | | |
| 81.0 - 81.9$^*$ | 81.2 | | | |
| (N = 1) | | | | |
| 82.0 - 82.9$^*$ | 82.05 | 80.85 | 2958 - 3690 | 3236.15 |
| (N = 2) | (SD = 0.07) | (SD = 3.19) | (SD = 255.97) | (SD = 371.13) |

CI = cephalic index.
method of simultaneous multiple comparisons gave test statistics within the acceptance range, i.e. they did not reject $H_0$ at the 0.05% level.

This analysis indicated that, even when there were significant differences in the value of the CI among the several groups of mothers, there were no significant differences in CI among their newborn infants. (The importance of accepting $H_0$ with respect to birth weight is discussed later.)

**Second analysis.** By this method a formal test of correlation between individual maternal and neonatal index values was performed. In the scattergram (Fig. 1) the co-ordinates of the plots are the maternal CI ($x$) and that of her newborn infant ($y$). The scatter of the data showed no apparent direction of covariability between maternal and neonatal values. The sample correlation coefficient, which is a maximum likelihood estimator of the population correlation coefficient ($\rho$), has the value of $r = 0.16$. A test of significance showed that the value of the sample correlation coefficient was not significant at the 0.05 level.

**Comparison of Growth-Retarded and Normal Neonates**

Data on the birth size and CI of normal and growth-retarded neonates are summarised in Table II. A test for homoscedasticity at the 0.01 level gives a test statistic in the acceptance range. A $t$ test for a significant difference between the means rejects the null hypothesis at the 0.01 level that the samples have been drawn from populations with equal mean values of the CI.

**DISCUSSION**

Birth weight is an important determinant of cranial form in the newborn human. In the present 'normal' series only fullterm neonates whose growth was normal were studied. There were no significant differences in birth weight among the different subgroups corresponding to the maternal classes stratified according to the CI. The neonates in this series were, therefore, a highly selected sample. The question arises as to how valid the conclusion of the study is, viz., that there is no significant correlation between maternal and neonatal headshape, as judged by the CI, and whether this observation is applicable to all subtypes of *Homo sapiens*.

Grosser's grading of placental development, based on the number of layers intervening between maternal and fetal circulations, defined 4 types, of which the haemochorial form represents the highest evolutionary development. Barcroft had reservations concerning the assumptions underlying this classification and Amoroso pointed out that all tissue components might not necessarily participate in the placental barrier. The advent of electron microscopy has made it possible to show that placentas rarely conform to any rigid classification with regard to their constituent layers and that placentas within the same general category differ markedly in fine structural organisation. While all higher primates share a common haemochorial placenta, significant histological differences are noted, for example, among the great apes, gibbons and man. They are most easily discernible early in placental ontogeny and are, to a large degree, erased at the conclusion of intra-uterine development. These distinctions are associated with quantitative and qualitative differences in placental function.

The specialised haemochorial placenta of man is an important part of the total mechanism which is responsible for his having the highest initial size constant in the neonatal maternal allometric formula among primates. Yet, the very intimacy of the relationship between the fetal and maternal circulations is also responsible for a peculiar sensitivity of the product of gestation to variations in the maternal condition. Under unfavourable conditions of child-bearing, the growth of the fetus may be retarded, despite the autonomy and homeostatic function of the fetoplacental unit. The numerous factors which may cause intra-uterine growth retardation include malnutrition, poor living conditions, and the whole host of entities subsumed under the title of poor socio-economic conditions. Intra-uterine growth retardation is encountered predominantly in poorer communities, viz. among the social classes desig-
nated IV and V according to the British classification. The direct effect of these factors, as well as their transgenerational consequences, were reviewed in an earlier work.\textsuperscript{1} There are indications that laboratory primates are eminently sensitive to conditions akin to our socio-economic and neonatal forms. Variation in birth weight among the progeny of Indian monkeys from India is very wide and it has been seen, although not documented, that in several species such variations correlate with the conditions under which the female grew up.

Not all human fetuses realise their full growth potential. Even in a socio-economically well-situated population like that of an American voluntary hospital, anywhere from one-third to one-half of all infants of low birth weight are not premature but growth-retarded.\textsuperscript{2,3} Stein and Ellis\textsuperscript{4} report that in the majority of 250 Cuban babies from a community of low economic status, the cause of low birth weight is intra-uterine growth retardation.

Intra-uterine growth retardation (IUGR) in poor communities is mainly due to protein energy malnutrition. It is described as being symmetrical or global, because both brain and bodily ponderal growth are reduced. The present study indicates that the effect of IUGR on the neurocranium is to restrict the enlargement of the biparietal diameter more than that of the occipitofrontal, thus lowering the CI. In determining the CI in any sample of neonates, the result will be influenced by the proportion of growth-retarded material. The exclusion of cases of IUGR is important in comparative studies, for the effects of this pathological condition will vary in different populations, depending on the intensity of the pathology and the ratio of normal to growth-retarded material.

Birth Size

An analysis\textsuperscript{4,5} of the relationship between birth weight and the CI in neonates whose growth is normal shows that with increasing neonatal weight the expansion of the neurocranium to accommodate the allometrically larger brain is a differential process in which the expansion of the biparietal diameter is greater than that of the occipitofrontal dimension. There is a significant positive correlation \((r = 0.67)\) between rising birth weight and the CI. The influence of birth size variations on the CI must be taken into account when comparing head form in neonates. It is desirable, as a rule, to use unselected cases when determining the characteristics of a variable in a population. Because differences in birth weight due to inappropriate growth (IUGR) and birth weight variations among neonates whose growth is normal are determinants of headform, two women of the same CI may give birth to infants of widely differing CI. In determining what the relationship between maternal and neonatal cranial form is, it is necessary to eliminate these exogenous influences. In the present study this has been done by the careful application of the obstetric criteria of normal intra-uterine development. The 8 subpopulations of neonates, corresponding to the different maternal groups stratified according to the value of the CI, do not differ significantly in birth weight. Statistical analysis of the CI values in these subpopulations of neonates reveals no significant differences among them. No significant correlation is present between the maternal and neonatal cephalic indices.

The Nature-Nurture Problem

The inheritance of cranial form has been the subject of much speculation. While it is clear that the cranial form of a population tends to be more or less uniform, much evidence has accumulated to show that changes in adult cranial morphology occur when members of a population are transferred to a new environment. It has often been assumed that population differences in skeletal characteristics are relatively unaffected by the environment and are attributable, therefore, to genetic variation. The possibility that some of the smaller differences commonly encountered in a population are environmental in origin needs serious consideration.\textsuperscript{6} The inheritance of anthropometric characteristics appears to depend on many genes. The appropoach to the problem of partitioning heritable from environmental influences has been to study resemblances and differences in twins and close relatives living in different environments. In the assessment of heritability, however, it must be remembered that the reaction to a given environment represents the interaction of the genotype of the population being studied with the environment. The estimate of heritability thus derived may be valid only for the population for which it has been determined. A comparison of the parental group with their progeny who have migrated to more favourable environments provides a wealth of illuminating and sometimes confusing information on the nature-nurture problem. The study on Japanese immigrants to Hawaii showed that the Hawaiian-reared offspring have an increase in several measurements, e.g., stature and head breadth, but a significant reduction in head length. The first Hawaiian-born generation had a higher adult CI than their parents.

Many investigations have been carried out on the cranial form of the newborn and contradictory opinions have been expressed concerning the presence at birth of an inherited cranial form. These investigations have been bedevilled by the presence of a uniquely human feature, viz., the presence of moulding in vaginally-delivered neonates. In this as well as in two previous studies this vitiating influence has been avoided by admitting to the study group only those infants delivered by elective Caesarean section. The conclusion of this analysis is that, when variations in the CI due to IUGR and birth weight differences are eliminated, no correlation between the maternal and newborn cephalic indices can be demonstrated. Whether this applies to other populations cannot be stated, for it cannot be assumed that the alteration in adult CI (if any) in association with IUGR and birth weight variations is the same in all populations.

REFERENCES

Chronic Granulomatous Disease of Childhood

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SUMMARY

Two boys and one girl suffering from recurrent severe bacterial infections were investigated. All 3 exhibited normal cellular and humoral immunity, normal neutrophil phagocytic ability, and defective neutrophil bacterial capacity. The clinical features and laboratory findings in these patients are diagnostic of chronic granulomatous disease. A sex-linked inheritance pattern was confirmed in 1 patient by the demonstration of a heterozygous carrier state in the mother.


Chronic granulomatous disease (CGD) is characterised by an inability of phagocytic cells to kill ingested catalase-positive micro-organisms. Patients with this defect rarely survive beyond adolescence. They suffer from recurrent severe infections which start early in life and are usually caused by organisms of low virulence. Suppurative adenitis, pneumonia, liver abscesses and osteomyelitis are common features. Subsequent development of pulmonary and reticuloendothelial granulomas is characteristic of CGD.

Following the initial descriptions of CGD in young males and the demonstration of an X-linked, recessive inheritance pattern, female patients with abnormalities of neutrophil function similar to those in the male patients were described. No heterozygotes could be demonstrated in the families of these female patients and the mode of inheritance was not clear. These girls are most probably representative of a separate disease entity which is biochemically and genetically different from that which affects males.

In this article we describe 3 patients, 2 boys and 1 girl, who were admitted to the Red Cross War Memorial Children's Hospital because of recurrent, severe infections. We have demonstrated diminished bactericidal capacity of neutrophil polymorphonuclear leucocytes in at least 3 patients. One boy had an X-linked inheritance pattern, typical of CGD. The relatives of the second boy were not available for investigation, but the clinical course and nature of the disease were characteristic of CGD. We were also unable to examine the family of our female patient; her clinical history was unusual in that symptoms only manifested at 3 years of age. However, her neutrophil bactericidal defect was in every way similar to that of the male patients.

PATIENTS AND METHODS

Patients

Patient 1. Shortly after birth this boy developed infantile eczema and a chronic nasal discharge. At the age of 10 months he presented with hepatosplenomegaly, acute weight loss and an inflammatory lesion of the finger. Cultures from the nose, finger and a specimen from the liver yielded Citrobacter freundii. A laparotomy revealed multiple liver and spleen abscesses and five of the largest of these were drained. Despite intensive antibiotic therapy, he developed...