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Pituitary-adrenal function in thalassaemia major. N. McIntosh. Whittington Hospital, London N.19.

Thalassaemia major is an iron-loading disease produced by gastrointestinal iron absorption and by the iron load of repeated transfusions. The distribution of iron is similar to that seen in haemochromatosis with the notable absence of iron deposition in the skin, despite the invariable slate grey skin colour seen in the condition. An investigation was undertaken of the effect of iron deposition in the pituitary and adrenal glands in 9 children with thalassaemia major. The age range of the children was 6 to 13 years. 8 were treated by a high transfusion regimen, the 9th has only been transfused once; 6 of the 9 have been chelated with their transfusions, and 5 of these are chelated daily. All chelation is with desferrioxamine B.

Pituitary function tests have shown no evidence of decreased secretion; in all the children high levels for 9 a.m. immunoreactive adrenocorticotrophic hormone have been found.

24-hour 17-ketosteroid and 17-hydroxycorticoid excretion was normal. Plasma cortisol levels taken after stimulation with 40 units Acthar Gel showed a normal response in 6 patients and a diminished response in 3. The physiological tetracosactrin stimulation test (Landon *et al.*, 1967) showed impaired cortisol response in all subjects after administration of 31.25 and 62.5 ng, and in 5 out of 8 subjects after 125 ng. All children had a normal response to 0.25 mg.

These results suggest that in children with thalassaemia major there is partial adrenal insufficiency with high circulating adrenocorticotrophic hormone levels. This probably accounts for the skin pigmentation in this disease.

REFERENCE

Landon, J., James, V. H. T., Wharton, M. J., and Friedman, M. (1967). Threshold adrenocortical sensitivity in man and its possible application to corticotrophin bioassay. *Lancet*, 2, 697.

Adrenocortical function in normal, precocious, and delayed puberty. C. Forsythe, D. C. L. Savage, J. Cameron, and E. McCafferty. Department of Child Health, University of Dundee, Dundee.

There is a steady rise in the 24-hour urinary excretion of the 17-hydroxycorticosteroids and, more specifically, of the α -ketolic metabolites of cortisol throughout infancy, childhood, and adolescence which is directly related to body weight.

In contrast, there is a steep rise in the 24-hour urinary excretion of the 17-oxosteroids and more specifically, of dehydroepiandrosterone, aetiocholanolone, and androsterone in relation to puberty. This increase is much greater than could be explained on a body weight basis, and it occurs late in delayed puberty and early in precocious puberty.

The metabolic degradation, which takes place chiefly in the liver, of the adrenal androgens alters at puberty, favouring the production of 5 α -steroids rather than 5 β -steroids. The rise in the 5 α /5 β ratio with age for the 17-oxosteroids measured by our method is statistically significant, and the rise in this 5 α /5 β ratio occurs early in precocious puberty and late in delayed puberty.

Data were presented from 62 normal infants, children, and adolescents and, in addition, from 10 patients with early or precocious puberty and from 7 patients with delayed puberty on which the above conclusions are based.

The changes in adrenocortical function at puberty are thought to be associated with activity of the gonadal axis, but the precise relation is not fully understood.

Plasma and urine testosterone responses to human chorionic gonadotrophin (HCG) in children with delayed puberty. B. T. Rudd, P. H. W. Rayner, and S. K. M. Jivani. Department of Paediatrics, the Children's Hospital, Birmingham 16.

The plasma testosterone and/or urine testosterone levels after 1500 units HCG for 4 days were measured in 29 male children with clinical evidence of delayed puberty due to the following causes. 10 children with constitutional delayed puberty (11 years 11 months to 16 years); 10 with cryptorchidism (6 bilateral) (9 years 8 months to 16 years); 4 with Prader-Labhart-Willi syndrome (11 to 13 years 6 months); and 5 with primary testicular atrophy (8 years 6 months to 16 years 2 months). 2 of the children in this group were anorchid on surgical exploration. The 10 children with constitutional delayed puberty and all but 3 of the 10 children with cryptorchidism had similar mean incremental rises in testosterone (range for plasma testosterone 33–298 ng/100 ml, urine 1.1–28.3 μ g/24 hr).

Of 4 children with Prader-Labhart-Willi syndrome, 3 had a poor urine testosterone response to HCG (incremental rise 0.1–2.1 μ g/24 hr). The 5 children with primary testicular atrophy failed to respond to HCG and were clearly separated from the other three groups. There was a small but positive correlation between the

plasma and urine testosterone incremental changes after 4 days of HCG for all patients, suggesting either urine or plasma testosterone measurements under these conditions are suitable indices of testicular function. Basal levels of urine testosterone were no direct guide as to expected response to 4 days of HCG.

Eight children with normal pubertal development on follow-up and 3 children with constitutional delayed puberty had base-line plasma testosterone and 4-hour levels after a single injection of HCG (1500 units), directly proportional to their maturational status (Tanner I-V). The less mature (Tanner I-II) had very low basal plasma testosterone levels which did not change significantly at 4 hours. Good responses 24 to 48 hours after the single injection of HCG were, however, shown. This may be a useful alternative test of gonadal function to the 4-day stimulation test.

Congenital postural scoliosis. P. M. Dunn. University of Bristol, Department of Child Health, Southmead Hospital, Bristol.

Between 1960 and 1966, 19 infants were observed to have a smooth persistent, lateral curvature of the spine without bony malformation soon after birth (Dunn, 1969). 9 (47%) of these infants presented by breech at delivery. 2 infants, both born to women with marked oligohydramnios, died shortly after birth; their spines were examined closely at necropsy and the presence of scoliosis without malformation was confirmed.

Of the 19 cases of scoliosis, 9 were noted during a personal study of 6756 infants born consecutively in hospital during a 3-year period (Dunn, 1972), giving an incidence of approximately 1/1000. (The true incidence may be only half as great, as this was a selected hospital population.) 8 of these 9 infants (all without teratological malformation) had associated postural deformities ($P < 0.0001$) including plagiocephaly ($P < 0.0001$), facial deformities ($P = 0.0002$), contracture of the sternomastoid muscle ($P < 0.0001$), congenital dislocation of the hip ($P < 0.0001$), and congenital deformities of the feet ($P = 0.0025$). In 2 cases there was unilateral dislocation of the hip on the side of the convexity of the curve. These facts, taken together with other clinical observations regarding these cases, and the well known high rate at which spontaneous resolution takes place during the first 3 years of life strongly support the frequently challenged belief of the late Sir Denis Browne (1965) that scoliosis may be caused by mechanical factors responsible for persistent lateral curvature of the spine during intrauterine life.

REFERENCES

- Browne, D. (1965). Congenital postural scoliosis. *British Medical Journal*, 2, 565.
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Renal function studies in first week of life. B. J. N. Z. Danesh and I. B. Houston. Department of Child Health, St. Mary's Hospital, Manchester.

Accurately timed specimens of urine were collected

from newborn infants by a new technique. Collection was done continuously during the first 3 days and the 7th day of life, and blood samples were taken on the 1st, 2nd, 3rd, 5th, and 7th days; infants were studied only after an explanation to the parents and confirmation of their unqualified approval was obtained.

Renal function was studied in 23 babies, 8 term (39-41 weeks' gestation), 8 small-for-dates (37-39 weeks' gestation), and 7 prematures (33-36 weeks' gestation). The three groups showed maximum clearance of creatinine and urinary excretion rate (UV) of solutes (creatinine, urea, sodium, and chloride) within the first 12 hours of life, falling considerably during the next 60 hours and partially recovering by the 7th day of life. Urine flow rate and urinary sodium excretion expressed as a percentage of filtered load (%ENa) also showed a similar pattern. Though there was a marked variation in creatinine clearance, excretion rate, and %ENa in individual infants, statistical analysis did not reveal a significant difference between the three groups.

In the infants studied there was a linear relation between %ENa and PCV, suggesting that the degree of sodium excretion is related to the size of placento-fetal transfusion which occurs immediately after delivery. The rapid initial fall in %ENa may be a reflection of the postnatal need to conserve sodium as opposed to the probable intrauterine need for a large urine flow rate (and %ENa) to maintain amniotic fluid volume.

Development of mammalian fast muscle: dynamic and biochemical properties correlated. D. M. Johnston introduced by L. Taitz. Department of Child Health, the Children's Hospital, Sheffield.

Relation between granulocyte phenylalanine content and degree of neuropsychiatric disability in phenylketonuria. T. M. Andrews, R. O. McKernan, K. McPherson, and R. W. E. Watts introduced by H. B. Valman. Divisions of Metabolism and of Computing and Statistics, Medical Research Council Clinical Research Centre, Watford Road, Harrow.

The exact cause of brain damage in phenylketonuria is not understood, and we are unable to distinguish clearly in neonates between classical phenylketonuria and variant forms in which persistent hyperphenylalaninaemia does not result in neurological injury. This makes it difficult to assess the value of dietary treatment (Birch and Tizard, 1967), to identify those infants requiring strict control of blood phenylalanine levels, and to decide when dietary control can safely be relaxed.

It has been shown (Aoki and Siegal, 1970; Swaiman, Hosfield, and Lemieux, 1968) that experimental hyperphenylalaninaemia impairs ribosomal protein synthetic activity in the developing brain of neonatal rats. This suggested to us that intracellular levels of phenylalanine might be of more direct pathophysiological significance than extracellular concentrations, and might correlate more closely with the degree of brain damage in phenylketonuria than do plasma levels.