J. F. N. TAYLOR introduced by DR. R. E. BONHAM CARTER (London). 'Prognosis Following Balloon Atrial Septostomy and Subsequent Management of Transposition of the Great Arteries.' In transposition of the great arteries the pulmonary and systemic circulations are independent; but there must be an adequate communication between the two circulations, preferably at atrial level. An adequate atrial septal defect may be created satisfactorily during the first 3 months of life by the technique of balloon atrial septostomy described by Rashkind and Miller (1966). This procedure carries a very much lower mortality in this age group than the Blalock-Hanlon operation.

During the ensuing months following satisfactory palliation there is a continuing declining survival, indicating the need for further treatment. Analysis of the first 150 operations for rearrangement of atrial flow by the Mustard technique performed since February 1965 shows that in simple transposition of the great arteries (i.e. with no additional lesions than an atrial communication) there is a 90% operative survival rate; age range 3 months to 20 years. The survival rate is similar if the infant group (children less than one year old) is separated out.

It is thus suggested that in simple transposition of the great arteries successful palliation by balloon septostomy should be followed by rearrangement of atrial flow at about one year of age (when most of the infants weigh 5-7 kg), as the survival rate from operation is at least as high as the natural survival rate during the ensuing year.

REFERENCES

- Rashkind, W. J., and Miller, W. W. (1966). Creation of an atrial septal defect without thoracotomy. A palliative approach to complete transposition of the great arteries. *Journal of the American Medical Association*, **196**, 991.
- Blalock, A., and Hanlon, C. R. (1950). Surgical treatment of complete transposition of the aorta and pulmonary artery. *Surgery, Gynecology, and Obstetrics, with International Abstracts of Surgery*, **90**, 1.
- Mustard, W. T. (1964). Successful two-stage correction of transposition of the great vessels. *Surgery*, **55**, 469.

J. M. H. BUCKLER (Leeds). 'The Growth Hormone Response to Exercise.' To be published.

G. J. A. I. SNODGRASS introduced by DR. L. STIMMLER (London). 'Intravenous Glucagon as a Test of Growth Hormone (GH) Secretory Capacity.' To be published elsewhere.

P. H. W. RAYNER (Birmingham). 'The Use of Clomiphene Citrate to Assess Pituitary Gonadal Function in Males with Delayed Puberty.'

Clomiphene citrate, a non-steroidal oestrogen analogue, is capable of inducing the release of luteinizing hormone (LH) from the pituitary in normal adult males. A preliminary assessment of the value of this response as a test of the pituitary Leydig cells axis has been performed in boys with delayed puberty or in whom abnormal pubertal development was anticipated.

The urinary and plasma testosterone response to the oral administration of clomiphene citrate (100 mg once daily for 6 days) has been measured by a competitive

protein binding assay in 12 male subjects (age range 9-22 years). Measurements were continued for 2 days after the drug was stopped. The following diagnostic categories were studied: (1) *hypogonadotrophic hypogonadism* 2 subjects, (2) *isolated pituitary GH deficiency* 2 subjects, (3) *constitutional short stature with delayed puberty* 3 subjects, (4) *Prader Willi syndrome* 2 subjects, (5) *cryptorchidism* 2 subjects, and (6) *penoscrotal hypospadias* 1 subject.

Basal urinary testosterone levels were below the normal pubertal range (0.4-6.0 $\mu\text{g}/24\text{ hr}$) in all except 2 patients. Both hypogonadotrophic patients and both patients with the Prader-Willi syndrome showed no response. The two youngest patients, aged 9 and 11 years, also showed no significant response. The remaining 6 patients showed maximal urinary testosterone levels after clomiphene stimulation ranging from 4.7 to 36.4 $\mu\text{g}/24\text{ hr}$ indicating a normal pituitary-Leydig cell axis; in 3 patients the maximum response occurred 2 days after clomiphene was discontinued. There was an increase in the maximum urinary testosterone levels recorded after clomiphene with increasing chronological age and increasing sexual maturity.

These results demonstrate that clomiphene citrate administration may provide a basis for a clinically useful test of pituitary-Leydig cell axis in males with pubertal abnormality. Further studies are required during normal puberty, and on the dose and duration of clomiphene required to obtain an optimum response.

D. C. L. SAVAGE, CONSTANCE C. FORSYTH, EILEEN McCAFFERTY, and JENNY CAMERON (Dundee). 'Excretion of Individual 17-oxosteroids and Corticosteroids in the Urine during Childhood and Adolescence.'

There are few reports of fractionation of adrenal metabolites in the urine of children. We have studied the individual 17-oxosteroids and the α -ketolic metabolites of cortisol and corticosterone during a 24-hour period in 83 normal children and adolescents and 10 adults by paper chromatography using Bush systems. The normal results, which have their own physiological interest, provide a basis on which the effect of various disease states on adrenal metabolism may be compared.

There is an increase as the child grows older in the excretion of the total 17-oxosteroids, the 11-deoxy-17-oxosteroids (dehydroepiandrosterone, aetiocholanolone, androsterone) and the 11-oxy-17-oxosteroids (11 β -hydroxy-aetiocholanolone, 11 β -hydroxyandrosterone, 11-oxo-aetiocholanolone, 11-oxoandrosterone). Dehydroepiandrosterone is detectable by this method at 6 years of age. During childhood the increase in excretion of the total 17-oxosteroids appears to be related to body weight but since below the age of 10 years 60% of the total assay is non-steroid chromogen interpretation of this data with respect to adrenal metabolite excretion must be cautious; furthermore, the 11-deoxy-17-oxosteroids show no such relationship. There is a preferential degradation of the 17-oxosteroids to 5 α derivatives initially before puberty is clinically detectable but which continues through puberty and occurs earlier in the girls than the boys.

The excretion of the total 17-hydroxycorticosteroids and the α -ketolic metabolites of cortisol (tetrahydrocortisol, allo-tetrahydrocortisol, tetrahydrocorticosterone) increases from infancy to adult life and when expressed per 100 kg of body weight show a close relationship. The corticosterone metabolites (tetrahydrocorticosterone, allo-tetrahydrocorticosterone, tetrahydro-11-dehydrocorticosterone) when expressed similarly show a marked fall during the first few years of life.

G. KOMROWER (Manchester). 'Experiences with the Scriver Technique as a Screening Procedure for Phenylketonuria and Other Amino Acid Disorders.'

D. N. RAINE introduced by DR. MARGARET I. GRIFFITHS (Birmingham). 'Screening for Several Amino Acidopathies in Neonates in Birmingham by Plasma Chromatography.'

A screening programme based on the plasma chromatographic method described by Scriver, Davies, and Cullen (1964) was established in Birmingham (population 1 million, 20,000 births per year) two years ago. The organization at domiciliary, laboratory, and City Health Department levels will be described. As a result of specific studies it has been found that:

1. The programme can be conducted with posted specimens as well as those analysed on the day of collection.
2. The time of collection of blood in relation to feeding, although leading to differences, does not present special problems.
3. Chromatography of plasma is superior to that of discs punched from paper soaked with whole blood collected for the Guthrie test.
4. When, at 6-9 days, tyrosinaemia is the only abnormality, further tests should be delayed until the age of 6 weeks when 95% will have become normal.
5. The cost of Scriver testing is similar to that of Guthrie testing up to 30,000 tests/year; above that, Guthrie testing will probably be cheaper.

Such a screening programme will lead to about 40 additional outpatient visits per year and 12 additional admissions for further investigations and treatment. Though this system can detect up to 19 amino acid disorders, the efficiency of this method and the optimal time for testing for those other than phenylketonuria has not yet been established.

REFERENCE

- Scriver, C. R., Davies, E., and Cullen, A. M. (1964). Application of a simple micro-method to the screening of plasma for a variety of amino acidopathies. *Lancet*, 2, 234.

MARGARET I. GRIFFITHS (Birmingham). 'Implications for Clinical Implementation of Results of Metabolic Screening for Amino Acidopathies in the Newborn.'

This paper discussed some of the problems that have arisen in the clinical follow-up of neonates examined in Birmingham, as described by D. N. Raine.

It was found essential that where there was any question of persisting aminoacidaemia that the babies should be examined and that they should be seen regularly at a follow-up clinic. The following aminoacidaemias presented clinical problems:

1. *Children with methioninaemia.* These comprise a group of 18 children, the majority of whom were immigrants, and the majority of whom were premature. The implications of this were discussed. In addition, some of the babies showed rickets and/or abnormalities in the liver function tests. The significance of this was discussed.
2. *Infants with histidinaemia.* So far three of these infants have been detected. As there is doubt as to the effect of histidinaemia all three have been put on a histidine-free diet and their speech and language development is being recorded.
3. *Prolinaemia.* Three children with prolinaemia have been found.

The implication of abnormal aminoacidaemia in early life is not yet clear. It is considered that it is most important that these children should be carefully followed up and, particularly, should be assessed at school age. It has been suggested (Woolf, 1968) that because the incidence of phenylalaninaemia is very much higher in the newborn than in the population in subnormality hospitals that many undetected cases of phenylalaninaemia are of normal intelligence. The converse may well be true and it may be that children who have had transient abnormalities of amino acid metabolism during the early months of life, may show permanent retardation for which no cause can be found, if they are only examined at a later age. This hypothesis was discussed.

REFERENCE

- Woolf, L. I. (1968). Mass screening of the newborn for metabolic disease. *Archives of Disease in Childhood*, 43, 137.

BARBARA E. CLAYTON (London). 'Experience with a screening service, using the Guthrie Test, in the North-West and North-East Metropolitan Regions.'

Infants in two metropolitan regions have been screened by the Guthrie test for raised phenylalanine (Phe) levels in blood. The results obtained in 117,446 infants were:

1. 8 infants had classical phenylketonuria (PKU), i.e. an incidence of 1 in 14,680 births. One of these had a hitherto undiagnosed PKU sib who was very retarded, and two had sibs already receiving dietary treatment for classical PKU.
2. 1 infant had atypical PKU with plasma phenylalanine levels of 20-27 mg/100 ml. He had a hitherto undiagnosed sib of normal mentality with Phe levels of 12-20 mg at age 2.2 to 2.6 years.
3. 391 infants (i.e. 0.33% of the total) had raised values when first tested, but on repeating about 1 week later these had fallen to normal.
4. 26 infants had raised values persisting after the second test. The maximum value was 15 mg and all except 2 infants had tyrosinaemia associated with prematurity, excessive protein intake, etc.