Propionicacidaemia in twins. F. Cockburn, M. D. Cohen, J. A. B. Darling, M. Giles, R. A. Harkness, and A. D. Nicol. (*Departments of Child Life and Health and Paediatric Biochemistry, University of Edinburgh, and Simpson Memorial Maternity Pavilion, Royal Infirmary, Edinburgh.*) A few infants with a serious metabolic disease associated with increased concentrations of propionic acid in the plasma have been reported. The majority of these infants have died in the neonatal period. Ketoacidosis and hypotonia have been presenting features. We describe such a syndrome in nonidentical twins.

The parents are first cousins and come from Pakistan. The mother's 4 previous pregnancies had resulted in an abortion, an anencephalic stillbirth, and two children who died in the neonatal period. One of these children was reported by Gompertz *et al.* (1970) to have had propionicacidaemia.

During pregnancy the mother's urinary oestriol concentrations had been consistently low. Labour occurred spontaneously at 37 weeks. Amniotic fluid from each sac and umbilical venous plasma from each twin had normal concentrations of amino acids and propionic acid. Twin I, a girl, weighed 1.7 kg, and twin II, a boy, 2.7 kg. Both followed an almost identical course of progressive hypotonia, apathy, and diminished reflexes, merging into coma and death. Twin I died on day 10 and twin II on day 13. Long chain ketones and acetone were present in their urine from the first day of life, in association with a mild metabolic acidaemia. Plasma propionic acid concentrations increased markedly, 6.0 mM in twin I and 4.8 mM in twin II, by day 7. Hydroxyproline, serine, asparagine, glycine, isoleucine, leucine, and ornithine concentrations were increased in the plasma of twin I. Asparagine, aspartic acid, glycine, citrulline, leucine, and lysine concentrations were increased in the plasma of twin II.

Propionyl coenzyme A carboxylase activity in liver mitochondria from each twin was less than 10% of control levels in human, rabbit, and rat liver mitochondria.

Biotin, pantothenic acid, and carnitine were without demonstrable clinical or marked biochemical effects.

It is suggested that the twins had clinical and biochemical abnormalities similar to cases previously described as having idiopathic ketotic hyperglycinaemia, methylmalonic acidaemia, and propionicacidaemia.

REFERENCE

- Gompertz, D., Storrs, C. N., Bau, D. C. K., Peters, T. J., and Hughes, E. A. (1970). Localisation of enzymic defect in propionicacidaemia. *Lancet*, 1, 1140.

Plasma copper and zinc in acute leukaemia. F. W. Alexander, H. T. Delves, and H. Lay (*introduced by C. G. D. Brook*). (*Institute of Child Health, 30 Guilford Street, London WC1N 1EH.*) The concentrations of copper and zinc have been measured in the plasma of leukaemic children before and after treatment and compared with healthy controls.

The plasma copper concentrations were higher and

the plasma zinc concentrations were lower for the untreated leukaemic children than for the other 2 groups. The concentrations of both metals were altered after treatment—the copper was lowered and the zinc increased—to values approaching the normal range.

The plasma Cu : Zn ratio discriminated well between the 3 groups of children and would be valuable both in the diagnosis and response to treatment of leukaemia in childhood. There was no correlation between this ratio and the total white cell or peripheral blast cell count. However, the ratio was proportional to the extent of the leukaemic process.

Further work is necessary to determine the roles which Cu and Zn play in leukaemia in children.

Familial hypobetalipoproteinaemia. A. S. Fosbrooke, S. Choksey, and B. A. Wharton (*introduced by B. A. Wharton*). (*Institute of Child Health, 30 Guilford Street, London WC1N 1EH.*) A 2-year-old boy admitted to hospital with gastroenteritis was further investigated because of small stature. He had low serum cholesterol (73 mg/100 ml) and reduced beta lipoprotein cholesterol (20 mg/100 ml). Faecal fat, jejunal biopsy, and red cell morphology were normal. Plasma growth hormone and thyroxine were also normal, and it was concluded that small stature was the result of hereditary and/or psychosocial factors.

A family study showed a similar lipoprotein abnormality in the patient's mother; her serum cholesterol was 79 mg/100 ml and beta lipoprotein cholesterol 34 mg/100 ml. Analysis of the beta lipoprotein fraction in both child and mother showed it to have abnormal lipid composition; the cholesterol/phospholipid ratio was 1.0 and 0.8 respectively (normal 1.7), and within phospholipid components the proportion of sphingomyelin was markedly reduced (11% and 5%; normal 30%). These findings differ from previous reports that the composition of beta lipoprotein is normal. Familial hypobetalipoproteinaemia has been shown to be inherited as an autosomal dominant, and our findings are in agreement.

Though a few individuals with this condition have been reported to have some though not all of the features associated with abetalipoproteinaemia, neither our patient nor his mother had any gastrointestinal, haematological, or neurological abnormalities.

Dystrophia myotonica in infancy and childhood. Victor Dubowitz. (*The Department of Child Health, University of Sheffield.*) Though characteristically a disease of adolescence and adult life, there have been several case reports in recent years of dystrophia myotonica in infancy and childhood.

Cases were presented illustrating the wide variation in clinical pattern. These included a boy, aged 10 at the time of diagnosis, with early features (myopathic facies), whose mother had a classical syndrome, thus making clinical diagnosis easy; a young man of 30 with a classical syndrome whose muscle symptoms date from birth; a girl of 13 presenting with scoliosis, who at birth had unexplained asphyxia and bilateral talipes, and

subsequent delay in motor milestones, and her 10-year-old sister with bilateral pes cavus and talipes equinovarus, otherwise symptom-free, who was also found to have facial weakness and EMG evidence of myotonia; two floppy infants with delayed milestones whose related mothers have a subclinical (almost) involvement; and a 6-year-old boy who presented with bilateral facial palsy and whose symptom-free mother and grandfather have EMG evidence of myotonia.

The typical EMG pattern is readily missed, unless carefully searched for in distal as well as more proximal muscles. Muscle biopsy may be histologically normal in these children, but may show selective type 1 fibre atrophy with histochemical enzyme reactions.

Late onset form of globoid cell leucodystrophy. Desmond Patrick and John Wilson (introduced by John Wilson). (*Department of Biochemistry, Institute of Child Health, 30 Guilford Street, London WC1N 1EH.*)

Elevated erythrocyte 2,3-diphosphoglycerate concentration in primary trisomic Down's syndrome. Elizabeth Nelson and Philip F. Benson. (*Department of Clinical Haematology, University College Hospital Medical School, London W.C.1, and Paediatric Research Unit, Guy's Hospital, London S.E.1.*) The level of 2,3-diphosphoglycerate (DPG) in erythrocytes is an important factor in regulating oxygen delivery to the tissues. It does this by binding to deoxyhaemoglobin and has the effect of lowering the haemoglobin affinity for oxygen. DPG is a glycolytic intermediate and its concentration is dependent upon the activity of the enzymes in the pathway. In Down's syndrome there is a marked increase in the activity of erythrocyte phosphofructokinase, a unidirectional enzyme which plays an important role in the regulation of glycolytic rate.

We have therefore investigated the possibility of a concomitant rise in erythrocytic DPG concentration.

The DPG level was higher in 20 subjects with primary trisomic Down's syndrome (12 males, 8 females, mean age 17.6 years, range 9 to 26 years; mean $5.37 \mu\text{moles/ml RBC}$; SD 0.625) than in 20 matched controls (mean $4.32 \mu\text{moles/ml RBC}$; SD 0.368 ; $P < 0.001$).

Changes in DPG concentration may be influenced by red cell pH and conditions of hypoxia as well as glycolytic activity. Anaemia was excluded in our patients (mean PCV = 43.1% ; SD 3.4 ; mean Hb concentration 14.7 g/100 ml ; SD 1.498).

One can calculate that the observed increase in DPG concentration would produce a 14% increase in P_{50} when associated with Hb-A. Though there would not be such a significant difference with Hb-F we do not know the effect of DPG on embryonic Hbs and further studies are necessary to determine the DPG level in Down's fetuses and to assess any possible effects that changes might have on fetal growth and development.

Creatine phosphokinase (CPK) in the CSF: its value in the management of children with

myelomeningocele and hydrocephalus. Margaret B. Drummond and Neville R. Belton (introduced by J. Keith Brown). (*Department of Child Life and Health, and Royal Hospital for Sick Children, Edinburgh.*) A need exists for a reliable test which will indicate 'brain damage' during the course of acute or chronic neurological disease. A number of studies have previously investigated the level of enzymes and other suitable substances in the CSF.

Creatine phosphokinase is present in high concentration in brain as well as in skeletal and heart muscle. Previous studies (Herschkowitz and Cumings, 1964; Nathan, 1967) have suggested increased CPK activity in a number of neurological diseases, particularly in patients with progressive hydrocephalus and symptomatic epilepsy. Sherwin, Norris, and Bulcke (1969) have shown that CSF contains only the brain isoenzyme of CPK.

In this study, which is part of a wider investigation of CSF-CPK in children with neurological disorders, all 65 children studied had a myelomeningocele and hydrocephalus. CPK was estimated, along with routine bacteriological and biochemical estimations, and pressure measurements taken whenever a ventricular tap was indicated clinically. CSF was withdrawn during the investigation and treatment of increased intracranial pressure, ventriculitis, and blocked shunts. Serum CPK levels were estimated concurrently in 11 cases.

The main findings were: (1) No correlation was found between serum and CSF levels of CPK, or between CSF-CPK and protein levels or pressure readings. (2) Newborn infants with myelomeningocele have increased levels of CPK in CSF. (3) Increased CSF-CPK levels are also found in most cases of raised intracranial pressure and in ventriculitis where they tend to parallel the clinical course of the infection. (4) CPK levels in the myelomeningocele lesion fluid were much higher than those in ventricular CSF on concurrent specimens.

Thus there are indications that CSF-CPK determinations can be useful in the management of blocked or malfunctioning shunts but may not add additional information in the management of ventriculitis.

REFERENCES

- Herschkowitz, N., and Cumings, J. N., (1964). Creatine kinase in cerebrospinal fluid. *Journal of Neurology, Neurosurgery and Psychiatry*, **27**, 247.
Nathan, M. (1967). *Journal of Neurology, Neurosurgery and Psychiatry*, **30**, 52.
Sherwin, A. L., Norris, J. W., and Bulcke, J. A. (1969). Spinal fluid creatine kinase in neurologic disease. *Neurology (Minneapolis)*, **19**, 993.

Fat absorption in children with chronic liver disease.* J. F. T. Glasgow (introduced by I. J. Carré, Belfast). The digestion and absorption of dietary fat in 15 children (aged 2-90 months) with varying degrees of chronic liver disease has been investi-

*Carried out in co-operation with Drs. J. R. Hamilton and A. Sass-Kortsak, The Hospital for Sick Children, Toronto, Canada.