pregnant. At about 8 months gestation she developed lupus nephritis and was treated with prednisolone and frusemide. She delivered a male infant spontaneously at 36 weeks.

The infant was 'small-for-dates', developed hypoglycaemia, and died on the fourth day. At necropsy extensive pulmonary haemorrhage was found. There was calcification of the fat in the neck, the intima of the pulmonary arteries, the aorta, and the circle of Willis. There was arborizing calcification of the kidney. There was hyperplasia of the islands of Langerhans of the pancreas and also of the adult cortex of the adrenal. The kidney showed fibrosis of the subcapsular zone, destruction of some tubules, and dilatation of others. Large foci of calcification were seen. The bones showed depressed osteogenesis.

Liver Damage after Treatment with THAM via Umbilical Catheter. J. D. Elema (*Pathologisch-Anatomisch Laboratorium, Oostersingel 63, Groningen, Holland*).

Symposium on the Early Detection of Phenylketonuria

The Organization of a Large-scale Guthrie Screening Programme. S. F. Cahalane (*Department of Pathology, The Children's Hospital, Temple Street, Dublin, Eire*).

Early Detection of Phenylketonuria and Other Aminoacidopathies in a Large City Using Plasma Chromatography. D. N. Raine (*Department of Biochemistry, The Children's Hospital, Birmingham B16 8ET*). Capillary blood has been collected from infants, mainly at 6 to 9 days of age, born in the City of Birmingham (population 1 million; 20,000 births per year), for the past 18 months and the plasma subjected to paper chromatography as described by Scriver, Davies, and Cullen (1964). Midwives take the samples to one of 12 collecting centres and all are delivered to the laboratory by midday. All subsequent work is done by one person whose only laboratory training has been in this procedure. The interpretation is checked by a biochemist.

Studies have established that the results on specimens posted to the laboratory, although different from those delivered immediately, can be interpreted satisfactorily. The optimum age for repeating initial tests which show only increased tyrosine has been established as six weeks, irrespective of whether the infant is premature or not. Administration of ascorbic acid has not shortened this period by a useful amount.

In 18 months the diagnoses that have been made include phenylketonuria 3, histidinaemia 3, prolineaemia 2, and hyperlipidaemia 1. There have been 14 infants showing hypermethioninaemia, mostly transient, but four required admission and one died with a possible diagnosis of 'tyrosinosis'.

The initial test needed to be repeated in 6% of all cases. Three-quarters of the repeats were required because the initial pattern was abnormal, and 66% of the abnormal patterns were due to tyrosine. The remaining one-quarter were repeated for technical

reasons (haemolysis, specimen collected before 6 days, and laboratory mishaps).

REFERENCE

Scriver, C. R., Davies, E., and Cullen, A. M. (1964). Application of a simple micromethod to the screening of plasma for a variety of aminoacidopathies. *Lancet*, 2, 230.

Screening for Phenylketonuria on a District Hospital Scale. L. R. Davis (*Department of Pathology, The Belgrave Hospital for Children, Clapham Road, London S.W.9*). A report was presented on the experience gained in the first year's work on screening infants born in the King's College Group of Hospitals and the neighbouring Borough of Southwark. The reasons for undertaking small scale screening were given. Over the year 3500 Guthrie tests had been performed. The procedures for minimizing the clerical and technical work were described. Technical difficulties had been confined to attempting quality control of the results because of the variation in the amount of growth with different batches of medium and on different plates. Ways of allowing for this variation were suggested. Only two positive tests were discovered, but about 0.5% of tests gave results about the upper limit of normal and required repeating. No true cases of phenylketonuria were detected during the year.

Management of Hyperphenylalaninaemia (HPA) in Northern Ireland. Nina A. J. Carson (*Nuffield Department of Child Health, The Queen's University of Belfast, Grosvenor Road, Belfast BT12 6BJ*). For a period of 1 year and 9 months, from 1 January 1969 to 30 September 1970, 56,257 newborn infants were screened in Northern Ireland for phenylketonuria (PKU) by the use of the Guthrie inhibition assay.

Specimens were collected on the 7th day of life by midwives, health visitors, or hospital staff and all tests were carried out in one centre in Belfast under the direction of the Consultant Bacteriologist of the Royal Victoria Hospital, Dr. George Gibson.

In all babies with phenylalanine levels of 4 mg/100 ml and above, repeat tests were requested and those with rising levels were investigated further. In these infants venous blood was examined for aminoacids by the use of an automatic aminoacid analyser, and a sample of urine examined for aminoacids and phenylketones. 17 infants showed levels persistently above 4 mg/ml. 8 infants were found to have classical PKU with phenylalanine blood levels in excess of 25 mg/100 ml, and phenylketones in the urine. A daily intake of phenylalanine of less than 300 mg was required to keep their blood phenylalanine levels between 2-8 mg/100 ml. 9 infants had persistently high blood levels varying from 12-23 mg/100 ml. On initial testing, urinary phenylketones were not found in this group. All were started on treatment, those with lower levels being given a low natural-protein diet; those with levels nearer 20 mg/100 ml, a hydrolysate mixture as in classical PKU. Up to the time of writing, three of these children could tolerate a normal diet and the remaining six were still

under treatment, requiring 350–1150 mg phenylalanine daily to keep their blood levels between 2–8 mg/100 ml.

The treatment of these children was monitored by the use of Guthrie tests collected by the health visitor in the home at the request of the paediatrician, the frequency of testing depending on the efficiency of control of blood levels. In the HPA infants (excluding PKU) when blood phenylalanine levels registered as <2 mg/100 ml on two or more consecutive occasions, a trial period of 2–3 days on a normal diet was given and the Guthrie test repeated.

In distinguishing classical PKU from persistent HPA, phenylalanine load tests may be helpful in doubtful cases. In the normal child, blood and urinary phenylalanine levels revert to normal basal levels 4 hours after a dose of 100 mg/kg phenylalanine. In PKU, infants' peak levels are found between 1 and 4 hours after giving the load, and the basal level is not reached until 24–48 hours. It has been reported that in HPA peak levels are reached as in PKU between 1 and 4 hours, but basal levels are regained within 24 hours.

It is of the utmost importance that those undertaking the management of infants with HPA are aware of the variants that occur within this group. Apart from classical PKU, insufficient data are available to classify these different types. Liver biopsy for the estimation of phenylalanine hydroxylase is the only means of studying them at present and this is not a practical procedure. Nor do we know what is the critical level of blood phenylalanine that results in brain damage. It is our policy at present to treat all infants whose blood phenylalanine is persistently 12 mg/100 ml or higher. Until more is known about these variants, there is a case for centralization, for both Guthrie testing and management of these infants. It is apparent that apart from classical PKU, these patients with HPA variants may at any time become capable of metabolizing phenylalanine in a normal manner and if this is not recognized, there is a

danger of developmental retardation and failure to thrive due to prolonged hypophenylalaninaemia.

Herpes Zoster Serum in Chicken-pox Contacts with Depressed Immunological Responses. A. E. Caunt, E. G. Hall, and D. Mainwaring (*Department of Pathology, Alder Hey Children's Hospital, Liverpool L12 2AP*). Chicken-pox occurring in patients during the course of treatment of malignant disease, including leukaemia, with cytotoxic agents and steroids may be a severe and sometimes fatal disease. The ineffectiveness of human normal immunoglobulin and convalescent chicken-pox immunoglobulin in the treatment of such cases was illustrated. The high and persisting levels of neutralizing antibody to varicella-zoster virus after clinical herpes zoster indicated that post-zoster serum might be more effective. Promising results were reported following the treatment of each of 4 patients with approximately 400 ml of post-zoster serum. 5 further patients who had been exposed to chicken-pox were treated during the incubation period with 200 ml of serum. None of these developed the disease.

The Virulence of Group B Streptococci in the Newborn, and Possible Difficulties in their Identification. K. B. Rogers (*Department of Microbiology, The Children's Hospital, Ladywood Middleway, Birmingham B16 8ET*).

Medical Research Council Trials of Treatment in Neuroblastoma and Nephroblastoma. A. E. Claireaux (*Department of Pathology, The Hospital for Sick Children, Great Ormond Street, London W.C.1*). The current position regarding the arrangements for these trials was reported, and matters which would involve pathologists were discussed.

Familial Gaucher's Disease. D. G. Fagan (*Department of Pathology, The University, Dundee*).