in perivascular spaces. Many remaining neurones contained one or more spherical concentric hyaline inclusion bodies of Lewy. Ultrastructurally these consisted of fibrillary and granular material with the fibrils more abundant at the periphery where they tended to be radially arranged. The granular component usually predominated in the centre where it formed a compact mass corresponding with the refractile and strongly acidophilic central core. Some Lewy bodies appeared larger and more homogeneous without any central core and these were composed entirely of uniformly dispersed fibrillar material. There was no evidence from electron microscopy that altered melanin granules entered into the composition of the inclusions, but occasionally degenerating organelles, particularly mitochondria, were seen in these structures, suggesting that they represented areas of cytoplasmic degeneration within the neurones.

Corpora amylacea, frequent in the substantia nigra of these cases, differed from the Lewy bodies both in situation and in ultrastructure, being composed of larger, coarser granules and fibrils partially enclosed by a limiting membrane. Although there was reduction in number of melanin granules in Parkinsonism no significant structural difference in the granules was found on electron microscopy in comparison with those from normal control material of similar age. Although chemically different, the ultrastructural similarity between melanin and lipofuscin was striking.

A CLINICO-PATHOLOGICAL AND FAMILY STUDY OF POLYCYSTIC DISEASE OF THE KIDNEYS AND LIVER IN CHILDREN

H. M. BLYTH AND B. G. OCKENDEN (M.R.C. Clinical Genetics Unit and Department of Morbid Anatomy, Institute of Child Health, Guilford Street, London) The purpose of this study was to define those types of cystic disease of the kidneys occurring in children which carry a high risk of recurrence within the family. Difficulty had been experienced with genetic counselling for these conditions.

Index patients, having cystic malformation of the renal tubules and intrahepatic bile ducts (polycystic disease of the kidneys and liver), were ascertained (a) from surgical and postmortem material examined at The Hospital for Sick Children and (b) from families referred to the Genetic Clinic at the hospital over the past 20 years. The latter were included only if the diagnosis could be confirmed histologically in at least one member of the family.

Twenty-nine cases in 24 families were studied in which the diagnosis was confirmed histologically; in three of these families a further six relatives have been included on clinical and/or radiological grounds.

Dominant inheritance is certain in one family and three others come into this ‘adult’ type on the histological criteria of focal cystic malformation of renal tubules and hepatic bile ducts. In 20 families an autosomal recessive pattern of inheritance is indicated. In this ‘childhood’ type the cystic malformation affects all the intrahepatic bile ducts and the renal tubular lesions are uniformly dispersed throughout both kidneys. On clinico-pathological grounds the 25 cases in these families fell into four contiguous groups. The most easily recognized groups were those presenting earliest in the perinatal and neonatal periods, with bilateral large kidneys. A contrasting group presents in childhood with hepatomegaly and portal hypertension. Between these is a group presenting in infancy with hepatosplenomegaly and developing renal insufficiency later. Within individual families the type of disorder breeds true, suggesting that each group represents a recessive condition, but that a different mutant gene is involved in each group.

This paper will be published in full.

A CASE OF FATAL CLOSTIDIUM WELCHII TOXAEAMIA DUE TO WARD INFECTION

J. G. ALEXANDER (Royal Infirmary, Hull) A 14-day-old male baby had a small sacral meningocoele repaired in a neurosurgery theatre. There was no adrenaline in the local anaesthetic. He collapsed 20 hours later with meningitis due to Clostridium welchii (toxin type A serologically untypable). Intravenous ampicillin and cloxacillin did not prevent death from acute haemolytic anaemia 27 hours after operation. The organism was not present in his faeces. Histological examination of the wound edges showed morphological Clostridium welchii. From a large number of swabs from the theatre suite, the ward, and the portable incubator in which the baby travelled from (but not to) the theatre, there were seven toxin type A serologically untypable strains isolated. A rabbit antiserum made against the baby's strain agglutinated two strains from the incubator and one from the baby's cubicle but none from the theatre. The incubator was not infected from the baby because of an impermeable Nobecutane plastic film over the wound (causing tissue anaerobiosis). Previously, patients whose wounds yielded Clostridium welchii had not shown toxicity. Such a patient was the incubator's previous occupant and her Clostridium welchii had not been kept. This (or another ward strain) must have got on to the patient's skin in the ward. The bath used to bathe him preoperatively had been previously wiped with Savlon. Three applications of 0·5% chlorhexidine in 70% spirit to the operation area in the theatre did not prevent the infection. The local anaesthetic, Nobecutane spray, and dressings were sterile. Clostridium welchii strains were not found in the theatre air inlet ventilators or anywhere in the neurosurgery theatre.

SIGNIFICANCE OF THE GIANT ORTHOCROMATIC ERYTHROBLAST

H. B. GOODALL (Royal Infirmary, Dundee) The giant orthochromatic erythroblast is a greatly enlarged polyploid red cell precursor, usually multinucleate with dense chromatin, sometimes with a single hyperchromatic nuclear mass and with mature, well haemoglobinized cytoplasm. This characteristic morphological change may occur in the bone marrow in a wide range of clinical circumstances: as an inborn defect associated with ineffective erythropoiesis; as an accompaniment of neoplasia of erythroblasts or lymphoreticular cells; in deficiency of
cyanocobalamin or folic acid; during treatment with antimitotic drugs or irradiation; in reactive change, as in haemolytic anaemias; in the course of acute infections, particularly hepatitis. The change has also been described in pigs made experimentally deficient in vitamin E. The giant erythroblasts in the bone marrow smear are usually accompanied by scanty macrocytes in an otherwise normochromic normocytic peripheral blood film.

This paper describes such changes in two dissimilar types of case: in refractory sideroblastic anaemia which in many cases should be regarded as a myeloproliferative disorder; and as a transient phenomenon in cases of acute infection, particularly in two patients with acute hepatitis and an antitoxoplasma dye test titre of 1 in 256. Only one previous instance of an association between hepatitis and polyploid erythroblasts has been reported. There is a case for regarding this change as one of the cardinal signs of morphological haematology, a sign of varied pathological significance, but probably due to a failure of cytoplasmic division, which may in turn be brought about by inadequate synthesis of the cell membrane.

LABORATORY ASPECTS OF PHENYLKETONURIA DETECTION AND TREATMENT

S. F. CAHALANE (Children’s Hospital, Dublin) Mass screening of newborns by the Guthrie and other blood techniques lead to the detection of hyperphenylalaninaemia. The possible causes of this in the newborn may be condensed into six situations: classical phenylketonuria (PKU); mild or atypical PKU; transient tyrosinaemia; delayed maturation of the phenylalanine hydroxylase system; maternal PKU; and finally a number of rarer enzyme defects.

The choice of a screening method depends on such criteria as simplicity of specimen collection and transport; simplicity of test; sensitivity and specificity of test; applicability to all newborns and finally inexpensiveness of the programme.

The available techniques are based on microbial inhibition, paper chromatography, and automated fluorimetry. The microbial inhibition test of Guthrie seems to present to meet the criteria most comprehensively. Screening centres should be based on adequate catchment areas and should not be set up for small units.

The laboratory investigation of the presumptive positive test depends in the first place on the initial blood level and the age at testing. The commonest cause for an elevated test is transient tyrosinaemia, generally associated with prematurity and seldom showing test levels greater than 8 mg of phenylalanine.

Newborns with classical PKU tend to achieve levels of 30 mg or higher in a short time. The interpretation of intermediate levels is more difficult and may depend on some or all of the following methods: (1) repeat quantititative serum phenylalanine and tyrosine; (2) testing for urinary phenylpyruvic acid and O-hydroxyphenylacetic acid; (3) sibling and maternal blood tests and history; (4) phenylalanine tolerance tests on parents and/or infant; (5) enzyme assay on liver biopsy.

All cases of classical PKU and possibly all doubtful cases should be placed on a restricted diet. The doubtful cases can be reevaluated at about 3 or 4 months of age. Treatment must be monitored by regular biochemical assay of blood phenylalanine for which a number of reliable techniques are available.

CHLOROQUINE-RESISTANT P. FALCIPARUM INFECTIONS

A. R. T. LUNDIE (Singapore) The evidence of chloroquine-resistant P. falciparum malaria in Vietnam and Thailand is well known and has recently been reviewed by Peters (1969). Montgomery and Eyles (1963), Sandosham (1967), and Kellett, Cowan, and Parry (1968) have described evidence of resistant strains in the north of west Malaysia. Singapore is a malaria-free area. Since 1966 the British Army Medical Services have been conducting an investigation into the incidence of drug-resistant malaria in Malaya. McKelvey, Lundie, Williams, Moore, and Worsely (1968) reported the first evidence of chloroquine-resistant strains of P. falciparum from further areas, including south Johore. Investigations continue in cooperation with the Walter Reed Army Institute of Research in Washington and the Institute of Medical Research in Kuala Lumpur.

Laboratory studies were complementary to careful management by medical and nursing staff of a reference hospital in a malaria-free area to ensure that the World Health Organization field trial (1965) was applied. In addition to the examination of thick and thin blood films, on the first seven, the 14th, and 28th days of illness, Haskins’ (1958) test was carried out on urine daily on the first seven days. Urine was also tested for proguamit (Gage and Rose, 1946) on admission.

The extension of the area in which chloroquine-resistant P. falciparum malaria may be acquired emphasizes the need for adequate laboratory investigation of patients with pyrexia of unknown origin who have been in west Malaysia.

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Significance of the giant orthochromatic erythroblast.

H B Goodall

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