

PAEDIATRIC PATHOLOGY CLUB

Proceedings of the Sixth Annual Meeting

The sixth meeting of the Paediatric Pathology Club was held in the Pathology Department of the Royal Hospital for Sick Children, Glasgow, on October 21 and 22, 1960, under the chairmanship of Dr. A. Macdonald. Twenty-two members and 21 guests signed the register.

The following papers were presented.

Summaries of Original Papers

T. E. PARRY (Cardiff). 'Aminoaciduria in Childhood Due to Causes Other than Liver Disease.' Four cases of phenylketonuria, one of cystinuria, one of the Fanconi syndrome, a case of dermatomyositis with severe malnutrition and two cases of unexplained aminoaciduria were investigated chromatographically.

Phenylalanine was demonstrated in the urine in all, and in the blood in two of the phenylketonurics.

The typical pattern of cystine-lysine-arginuria was demonstrated in the cystinuric after cystine crystals had been discovered incidental to infective hepatitis. Chromatograms of whole blood, plasma and packed red cells were normal. Aspartic and glutamic acids were present in higher and valine and leucine in a lower concentration in the packed cells than in the plasma. Glycine, serine, threonine, alanine, glutamine and tyrosine were present in about equal concentration in both. The distribution of amino acids between cells and plasma was identical to that observed by the author in normal subjects.

Two cases of generalized unexplained aminoaciduria were encountered. (1) A large male infant who died at 36 hours; hyperplasia of the islets of Langerhans was a striking feature at necropsy. The aminoaciduria was considered to be in excess of the physiological aminoaciduria at this age. (2) A boy of 2½ years with a history of 'fits' presented with unilateral cataracts. He was normal physically and mentally. He excreted large quantities of glycine, threonine, alanine, glutamine, valine and leucine with small quantities of histidine, tyrosine, phenylalanine and asparagine.

H. E. C. WILSON (Glasgow. Introduced by A. Macdonald). 'The Mode of Action of Dexamethazone and Chlorothiazide in the Treatment of Nephrotic Oedema.' The diuretic effect of dexamethazone and chlorothiazide in nephrosis was demonstrated in respect of water and electrolyte excretion. Chlorothiazide produced a marked diuresis within a few days with no remission of the albuminuria. Dexamethazone caused diuresis after a latent period of five to nine days. The

albuminuria gradually diminished from the fifth to the ninth day. The diuresis preceded any increase in total protein or albumin in the serum. The concentrations and total excretions of Na and K at the commencement of the diuresis did not justify a conclusion as to whether it was due primarily to a diminution of an ADH factor or aldosterone secretion. A few experiments on animals indicated that dexamethazone depressed the excretion of an ADH (pitressin) factor.

O. H. WOLFF, A. H. CAMERON and H. B. SALT (Birmingham). 'Veno-occlusive Disease in Protein-losing Enteropathy.' A 2½ year-old boy presented with generalized oedema and gross enlargement of the liver. Liver biopsy suggested the diagnosis of veno-occlusive disease. It then came to light that the patient was in the habit of nibbling various plants, his favourite being groundsel (*Senecio vulgaris*).

The oedema was due to hypoproteinaemia with depletion of albumin and all the globulins, particularly gamma globulin. The hypoproteinaemia was found to be the result of a protein leak into the gut: after an intravenous injection of ^{131}I -labelled polyvinylpyrrolidone (P.V.P.) 12.5% of the dose appeared in the faeces (Dr. W. F. R. Pover). On treatment with prednisolone the serum proteins returned to normal, the oedema cleared and only 1% of an intravenous dose of P.V.P. appeared in the faeces—a normal result. After 21 months of steroid treatment the patient still requires prednisolone to maintain normal serum protein levels.

Possible relationships between the protein-losing enteropathy and the veno-occlusive disease were discussed.

D. BIALESTOCK (Melbourne). 'Microdissection of the Kidney.' The historical background and technical details of the method of microdissection as applied to the infant kidney were outlined. Use of the method was demonstrated by slides of nephrons from cases of cystic disease, pyelonephritis, hydronephrosis and the nephrotic syndrome in babies.

The study of the nephron in its entire length in the baby reveals bizarre, multiple abnormalities and final interpretations of the significance of these in clinical manifestations are, as yet, not at all clear.

A. H. CAMERON (Birmingham). 'Intestinal Biopsy in Coeliac Disease.' Sixty-nine per-oral biopsies of the duodenum and jejunum have been performed at the Birmingham Children's Hospital in the past 18 months. By measuring the surface area and relating this to the

obliteration of the intervillous spaces a mathematical index of the degree of abnormality can be established. This has proved useful in the diagnosis and follow-up of cases of coeliac disease. Gluten-free diet improves the appearances and the index number becomes normal in about two-thirds of cases. Striking improvement is seen after five months' treatment. Clinical response to treatment is not always accompanied by histological response. Intestinal biopsy is regarded as the most reliable single investigation in coeliac disease and is a safe procedure even in young infants.

J. J. BODDAERT (Ghent, Belgium). 'The Pathology of Human Thyroid Aplasia with Special Reference to the Changes in the Endocrine Organs.' Two cases of congenital absence of the thyroid gland in female infants were studied. At necropsy no thyroid gland could be found. In one case, 3 months of age, the organs of the neck were studied completely on serial sections, while in the case aged 28 months numerous blocks of tissues were taken at both sides of the trachea for microscopical study.

In the region where the thyroid should have been found, groups of small cysts located laterally to the trachea were observed on microscopic examination. The cysts were closely associated with small islets of poorly differentiated 'thyroid' tissue and with the parathyroids, whose size and structure were normal.

The cysts and islets could be remnants of the lateral thyroid anlage contributing to the formation of the normal thyroid gland.

The following changes were observed in the endocrine organs: the pituitary was normal in weight but in both cases the acidophils were decreased and an increased number of sparsely granulated and degranulated modified acidophils resembling thyroidectomy cells was found. In addition, in the case aged 28 months, the basophils were increased in number.

The thymus was markedly atrophic. In one case (28 months) myoid cells with cross striations were present. The adrenals were of normal weight and morphology for this age.

The islets of Langerhans in the pancreas were large and in some instances hypertrophic. The ovaries contained atretic follicle cysts.

S. A. DOXIADIS, PH. FESSAS and T. VALAES (Athens, Greece). 'Glucose-6-phosphate Dehydrogenase Deficiency; a new aetiological factor of neonatal jaundice.' In about one-third of all cases of severe neonatal jaundice in Greece there is no Rhesus or ABO incompatibility. This type of jaundice not due to iso-immunization may cause kernicterus if not treated by exchange transfusion. Many clinical and laboratory features point to an increased postnatal haemolysis; there is also a familial incidence and a preponderance of males.

In their search for an inherited haemolytic factor they were able to show, using the technique described by Motulsky and Campbell, that the great majority of these babies had deficiency of the glucose-6-phosphate dehydrogenase of their red cells. The incidence of this

enzyme defect in a group of controls was minimal. They postulate that G-6-PD deficiency may be an important aetiological factor of severe neonatal jaundice in some countries where this enzyme defect is prevalent.

A. MITHAL and J. EMERY (Sheffield). 'The Effect of Birth on the Heart Ventricles.' Diverse opinions are expressed concerning the growth of the right ventricle after birth. Authors that have shown right ventricular atrophy have used cases of doubtful maturity at birth and included wasted children.

After careful exclusion of pathological material and infants of uncertain gestation, ventricular weights from 122 children with ages from birth to 12 years were analysed. In children born prematurely the right ventricle continues to grow at the same rate as if the child had been *in utero*, but the left ventricle grows at a greater rate.

After full-term birth, the right ventricle continues to grow uniformly, there being no phase of atrophy.

R. F. JENNISON and F. A. LANGLEY (Manchester). 'Perinatal Lung Infection.' Previous work from St. Mary's Hospital has shown that three types of perinatal pneumonia can be distinguished:

- (a) Foetal pneumonia, occurring in foetuses at or near term;
- (b) Later perinatal pneumonia, in infants dying after the first day but before the second week;
- (c) An intermediate type in infants dying during the first day.

The present investigation was undertaken to study the bacteriology of perinatal pneumonia in relationship to pathogenesis. After searing the surface of one lung a fragment was incubated in Brewer's medium and on a blood agar plate. A smear was also examined microscopically. The efficiency of this method of isolating organisms was estimated at about 91% and the 'laboratory contamination' rate at between 1.2% and 5.4%.

Organisms were found in only about half the lungs showing histological evidence of pneumonia. The possible reasons for this were discussed. During the period 1955 to 1959 organisms were found in about 18% of lungs which showed no pneumonia. This is termed 'pulmonary soiling'. Analysis of the types of organisms present shows that the flora in pulmonary soiling is similar to that of the parturient vagina and also of foetal pneumonia. The bacterial flora in later perinatal pneumonia can be resolved into two components: (1) That due to pulmonary soiling about the time of birth, and (2) that derived from the environment later, especially *Staphylococcus pyogenes* in the hospital.

P. D. HOLLAND (Dublin). 'Ward Trial of the Bacteriological Effect of Hexylresorcinol Aerosol.' Control air bacterial counts showed that about 30% of the air bacteria were potentially pathogenic staphylococci with antibiotic resistances comparable to those of organisms isolated from cross infections in the ward. Dust samples from each room and cubicle also were tested for antibiotic sensitivity.

After seven, nine and 14 days' exposure of the ward to the hexylresorcinol aerosol (Aerovap), air bacterial counts indicated a marked and sustained reduction of the bacterial air count in the central corridor of the cubicle ward.

The cubicles showed a reduction in bacterial air counts not as convincing as that in the central corridor, due probably to inadequate penetration of the aerosol.

Post-aerosol sampling showed that the dust flora had been favourably influenced by the aerosol.

Nasal swabs from the nursing staff showed no change in the percentage of carriers nor in the sensitivity of the strains isolated after 14 days' exposure to the aerosol.

No toxic effects were noted.

It is clear the hexylresorcinol aerosol is bactericidal and that its maximum effect is demonstrated where adequate air concentration can be maintained, i.e. in closed corridors and in individual rooms and cubicles.

K. B. ROGERS and N. SLATER (Birmingham). 'A New Method of Disposal of Soiled Nappies.' Nappies from babies in hospital, especially those of babies suffering from gastro-enteritis, may help to spread infection between the time when they are taken from the baby and when they arrive in the laundry and are placed in washing machines. A German technique has been adapted to solve this problem, using disposable polythene bags which are sewn along one side with an artificial protein thread.

Soiled nappies in these bags are transported to the laundry and are thrown unopened into a washing machine in which there is a solution of a proteolytic enzyme. In this the special protein thread is dissolved, allowing the bags to fall open. After a quarter of an hour, the contents of the washing machines are boiled. The effluent from this washing machine contains no viable non-sporing organisms. The proteolytic enzyme helps to remove adherent faeces allowing the nappies to be washed more easily and more efficiently than with conventional methods but eliminating much of the offensive odour associated with the washing of these soiled nappies. The enzyme, thread and the made-up bags are all now being manufactured in England.

R. A. OSBORN (Derby). 'Intestinal Perforation in Three Children with Polyarteritis Nodosa.'

Case 1: A boy, aged 8, was admitted with tonsillitis followed by melaena and a purpuric rash and later abdominal pain, haematuria and convulsions with a blood pressure of 160/100 mm. Hg. Laparotomy revealed 18 in. of gangrenous and perforated small bowel, with undermining ulcers and polyarteritis nodosa in the less affected areas. Progress was slow. Persistent haematuria and hypertension were treated with prednisone and mecylamine. He is now well and symptom free.

Case 2: A full-term normal girl was constipated and vomited after birth; a tight anal sphincter was dilated. Abdominal distension increased on the 11th day and fluid levels were seen in the erect radiograph of the abdomen.

A 4-in. segment of gangrenous splenic flexure of colon was resected. She died 10 hours after operation. Necropsy showed hard, brown faecal masses in the rectum and lesions of polyarteritis nodosa in the bowel wall and around the ovaries. There was calcification of striated muscle fibres in the diaphragm end of the distal convoluted tubules of the kidneys.

Case 3: A full-term normal girl whose mother was a diabetic. An infected umbilicus was treated with streptomycin. At 3 weeks she developed melaena with vomiting and a temperature of 102° F. She died one week after admission. Necropsy revealed a general peritonitis due to perforation of the jejunum. The small bowel showed numerous small ulcers. An abscess 1 cm. in diameter was present near the umbilicus. There was a large haemorrhage into the right adrenal. Polyarteritis nodosa was seen in the small bowel and adrenals. There were numerous venous thromboses in the kidneys and around the peritoneum. Calcification was present in the umbilical vessels and alongside the thromboses in the renal veins.

J. M. A. LENIHAN and J. M. WARREN (Glasgow. Introduced by A. Macdonald). 'Radioactive Strontium in Human Bone—Glasgow Measurements for 1959.' Radioactive strontium ⁹⁰Sr, produced in fall-out from distant nuclear weapon explosions, is being deposited over the earth's surface (more particularly over the Northern hemisphere) at the present time. Local concentrations depend largely on rainfall but ground contamination is otherwise fairly uniform between latitudes 40° and 60° N.

Some of the ⁹⁰Sr is incorporated in grass and other growing crops, from which it passes into animal and human food chains. Milk, vegetables and wheat products are the main sources in human diet.

A proportion (about 25%) of the ⁹⁰Sr ingested by an infant is incorporated in the growing bone. Present indications are that the amounts accumulated are well below the danger level, but long-term studies are clearly desirable. The amount of ⁹⁰Sr in an infant femur may be as little as 10⁻¹³ g. (0.1 μμg.). The separation of this material from the accompanying several grams of calcium is a difficult exercise.

The radioactive strontium is prepared as carbonate on a small planchet and assayed by a specially built low-background Geiger counter system.

During 1959, 125 bone samples (femur) were obtained. One hundred and three were prepared and assayed in Glasgow; 22 were analysed at Woolwich for comparison purposes.

Detailed studies of the 1959 results have been published by the Medical Research Council.

P. ROBB (Dumfries. Introduced by A. Macdonald). 'The Development of the Islets of Langerhans in Man.' The present study was based on 36 pancreases from fetuses ranging between 10 and 42 weeks' gestation and weighing between 34 g. and 3,600 g. Four stages were observed in the development of the islets; these over-

lapped, so that in any one pancreas, there were islets in more than one stage.

1. *Stage of budding islets*: In the third and fourth gestational month, islets consisting of a central cluster of B cells surrounded by ungranulated cells and occasional L cells, budded off from the ducts. The B cells predominated.

2. *Bipolar Stage*: From the fifth to eighth month, bipolar islets were seen, with the B cells at the tip and the L cells at the base (nearest the duct).

3. *'Mantle-islet' Stage*: The proliferating L cells grew round the B cells to form 'mantle-islets' with a kernel of B cells and a shell of L cells. The L cells now greatly outnumbered the B cells. 'Mantle-islets' dominated the picture from the sixth month onward.

4. *Stage of Mature Islets*: From the eighth month, a few islets were seen with the haphazard distribution of L and B cells characteristic of the mature adult islet.

A point of particular interest in these observations was the presence of differentiated L and B cells in the islets of the smallest (34 g.) foetus.

DOUGLAS BAIN (Edinburgh). Mast cells were obtained from the tissue culture of a tumour from a newborn infant. The tumour was multifocal and undifferentiated.

G. S. ANDERSON and T. BIRD (Newcastle). 'Congenital Iodopyrine (Felsol) Goitre.' Evidence recently presented by Morgans and Trotter (1959) strongly suggests that Felsol, a drug commonly taken by asthmatics, may be goitrogenic due to the iodopyrine it contains. Two infants (binovular twins) with congenital goitres, born of a mother with asthma and a goitre considered to be due to Felsol, were presented. One infant died at 10 hours with a thyroid of 11 g. showing large irregular vesicles filled with colloid but with signs of epithelial activity. The other twin died at 38 days with a thyroid weighing 7 g. showing small vesicles, poorly filled with colloid and a flat epithelium. It was suggested that the iodides liberated from iodopyrine in the maternal gut crossed the placenta to block the iodine-binding power of the foetal thyroids. Since Felsol was withdrawn nine days before delivery the histology was con-

sidered to support the view that iodides caused a colloid type of goitre, but that epithelial activity soon occurred when iodides were stopped. Neither death was attributable to the goitres.

REFERENCE

Morgans, M. E. and Trotter, W. R. (1959). Iodopyrine as a cause of goitre. *Lancet*, 2, 374.

K. M. LAWRENCE (Cardiff). 'Sarcoma of Pelvis.' A large pelvic tumour that had invaded the bladder and grown along the inferior vena cava; it was thought to be an embryonic sarcoma, possibly a rhabdomyosarcoma originating from the prostate.

H. B. MARSDEN (Manchester). 'Metachromatin Leucodystrophy.' A male child with a normal sibling began to have attacks of pyrexia at the age of 16 months. He eventually lost the use of his arms and legs, developed opisthotonos and died after repeated fits at the age of 2 years 10 months. The E.C.G. showed generalized dyspolycythuria and the C.S.F. had a protein level of 100 mg. %.

At necropsy the brain appeared relatively normal to the naked eye, but showed extensive gliosis of the white matter. Sudanophilic material was minimal and present only as small perivascular collections.

On staining with toluidine blue abundant metachromatic material was present in the brain, peripheral and spinal nerves, kidneys and to a lesser degree, in the liver, pancreas and adrenal medulla. Clinical analysis of the brain (Professor J. N. Cunningham) revealed loss of phospholipid and cholesterol with increase of hexosamine in the white matter. Numerous needle-shaped crystals were found in the adrenal cortex.

J. L. EMERY (Sheffield). 'Congenital Hypothyroidism—presenting clinically as intestinal obstruction.' A child was described having a minute aberrant lingual thyroid only who presented clinically as intestinal obstruction? congenital megacolon. Other instances of congenital thyroid deficiency presented in this way were referred to.

W. W. PAYNE (London). 'Apparatus and Method of Ultra Micro Chemical Techniques.' Description and demonstration.

Erratum

It is regretted that in the paper 'Observations on the Clinical Course and Treatment of One Hundred Cases of Still's Disease' by B. E. Schlesinger, C. C. Forsyth, R. H. R. White, J. M. Smellie and C. E. Stroud, which appeared in this journal (Volume 36, pages 65-76) Figs. 9a and 9b were transposed.