PAEDIATRIC PATHOLOGY CLUB

Proceedings of the Eighth Annual Meeting

The eighth meeting of the Paediatric Pathology Club was held at Cardiff on October 20 and 21, 1962, under the joint presidency of Dr. T. Parry and Dr. M. Laurence. The meeting on October 20, a symposium on abnormalities of red cells, was held at Cardiff Royal Infirmary, where the Guest Chairman was Dr. M. C. G. Israels. The meeting on October 21 was held at Llandough Hospital, Penarth. Twenty-seven members and 34 guests signed the attendance book.

Scientific Communications

The following papers were read at Cardiff:

D. Brynor Thomas (Cardiff). ‘The “Leuco-erythroblastic” Anaemia of the Human Foetus.’ During the second quarter of gestation the human foetus is ‘anaemic’ in that the erythrocyte content of the blood is low in comparison with that of the adult blood and the haemoglobin concentration is reduced, but to a lesser degree. The reduced blood viscosity, which can be inferred from the relatively low packed cell volume, may be an important factor in maintaining the flow of blood through the placental circulation. The mean corpuscular haemoglobin of foetal erythrocytes is greater than that of adult erythrocytes, but the mean corpuscular volume is greater in comparison with adult values than the mean corpuscular haemoglobin. The serum vitamin B₁₂ concentration of foetal blood is double that of maternal blood, and as erythropoiesis in the bone marrow is normoblastic during the period under consideration both vitamin B₁₂ and folic acid appear to be present in adequate concentrations and to be utilized normally. Throughout the second quarter of gestation foetal blood contains erythroblasts and granulocyte precursors, the presence of which, together with numerous reticulocytes, may simply reflect the extreme activity of the foetal haemopoietic tissues.

E. Blanche Butler (Cardiff). ‘The Blood Picture During the First Week in the Normal Infant.’ The material consisted of one to five specimens of blood taken from 39 babies. A total of 118 specimens was examined and these included 12 cord bloods. The results were presented as scattergrams in which the average trend during the first week of life was also shown. The mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration were shown as graphs in which the indices were compared with graphs of factors from which they were derived.

The average cord blood haemoglobin was 14·3 g. This rose to 19·6 g. as the average for the 0–6-hour period and fell to 17·5 g. in the 6–12-hour period. This was followed by a further gradual fall. It was suggested that this pattern reflected a temporary haemoconcentration after birth superimposed on the effect of the placental transfusion received by the child at birth.

Attention was drawn to the dramatic fall in nucleated red cells which were virtually absent by the fourth day.

The scatter of the absolute lymphocyte count was shown to be very narrow, particularly when compared with the wide scatter of the total granulocyte counts. It was also noted that in this small series there was an increase in total white cells and total granulocytes at the seventh day in bottle-fed babies, but not in breast-fed babies. This difference was not seen in the lymphocyte counts.

T. E. Parry (Cardiff). ‘Nutritional Megaloblastic Anaemia in Infancy.’ The haematological aspects of a 6-month-old male phenylketonuric infant who developed a nutritional megaloblastic anaemia due to folic acid deficiency when on a low phenylalanine diet were presented [Royston, N. J. W., and Parry, T. E. (1962). Arch. Dis. Childh., 37, 430].

A further case, uncomplicated by phenylketonuria, in a premature (33 weeks' gestation) 7-week-old male infant was also described. Both these infants had been on diets that were shown by biochemical assay to be deficient in folic acid.

The fairly high incidence of the syndrome in the age group 2–4 months amongst the published cases was noted as well as the frequent absence of macrocytosis in the peripheral blood. The latter findings may delay the diagnosis unless marrow biopsy is resorted to in any unexplained anaemia in this age-group when the diet is normally low in folic acid. This is particularly important in cases complicated by prolonged infection or gastro-enteritis.


Low serum folate concentration and positive FIGLU
findings in congenital haemolytic Haemolytic genital boy an infant with grossly haemolytic secondly, suggested B12 level by the liver removed neither for hereditary fragility, the the R. M. SEPHTON (Penarth), 'Radioactive Isotopes in the Investigation of Congenital Haemolytic Anaemias.' Congenital haemolytic anaemia due to red cell defects may be usually diagnosed by means of a small range of tests on the peripheral blood. Radioactive chromium studies may be of value in determining the site of red cell destruction, particularly in atypical cases when splenectomy is under consideration.

In early infancy the degree of anaemia may be further aggravated by the reduced erythropoiesis frequently found in the first two months of life, and transfusion may be required urgently. If this is done without preliminary investigation, diagnosis will not be possible afterwards as the circulating red cells will be predominantly donor in origin.

In two such transfused infants radioactive iron was of great diagnostic help. Measurement of the rate of plasma clearance provided evidence that the anaemia was haemolytic in type: in one of the cases the osmotic fragility of the patient's own labelled red cells was found to be increased and this suggested a diagnosis of hereditary spherocytosis at a time when no abnormality could be detected in the blood using conventional techniques.

In both patients in vivo counting revealed that red cell destruction was taking place predominantly in the spleen and provided a rational basis for splenectomy.

G. T. STEWART (London). 'A Case of Congenital Spherocytosis without Jaundice.' The features of the absence of jaundice despite repeated haemolytic episodes were discussed particularly in relation to the increased hepatic excretion of bilirubin and failure of reduction of bilirubin in the gut. Urobilinogen was therefore absent in the stool and the urine. In this case the red cell glucose-6-phosphate dehydrogenase failed to rise with the reticulocytes.

The following papers were read at Penarth:

J. K. STEWART (Manchester). 'Tumours of the Nervous System in Children.' Approximately one-third of all children's tumours arise from some part of the nervous system: the glia, the sympathetic or the retina. Those arising from the sympathetic nervous system have the worst prognosis; in Manchester the neuroblastoma has a survival rate of only 16%. Histologically the neuroblastoma may also be a diagnostic problem; often an anaplastic tumour may have some features of a neuroblastoma yet the evidence may not be enough to allow the pathologist to be certain. Closely bound up with the diagnostic difficulties is the problem of the nature of 'Ewing's tumour.' The finding that neuroblastomas may be hormonally active offers the hope that a more precise diagnosis may be possible in some of these controversial cases and that the treatment of children with neuroblastoma may be controlled biochemically.

H. B. MARSDEN (Manchester). 'Neuroblastomas and Catecholamines.' A study of 55 neuroblastomas seen over a 10-year period was made. During the past two years tumour tissue has been fixed in chromate as well as formalin, but none have shown a chromaffin reaction. The developing neurones stain green with azur-eosin after chromate fixation only, which could be evidence of catecholamine production. In addition, a mature
ganglioneuroma showed excessive elaboration of these substances so that the presence of undifferentiated cells would not be needed to account for catecholamine formation.

Blood pressure records were obtained in 16 patients with evidence of hypertension in nine. One case had hypertensive encephalopathy and one showed attacks of excessive sweating. Manipulation of the tumour at operation caused a rise in blood pressure which fell on cutting the tumour pedicle.

Diarrhoea was only mentioned in three of the 55 cases, whereas constipation was a feature in seven, the remainder having normal bowel action.

It is felt that Ewing's tumour still remains an entity, and possible distinguishing features were discussed, together with the normal excretion of catecholamines in these cases.

M. Bell (Manchester). ‘Clinical Chemistry of Neuroblastoma.’ After a brief review of the synthesis and metabolism of the catecholamines, particular attention was paid to the inclusion of dopamine. Results were presented for a series of 18 cases of neuroblastoma investigated in the past two years. Total catecholamines, normetadrenaline + metadrenaline and 4-hydroxy-3-methoxy mandelic acid were estimated and an attempt was made to classify the tumours according to their chemical excretion pattern. Response to therapy was illustrated by reference to four cases followed for periods up to 18 months and, using a combination of grouping and response to therapy, tentative suggestions were made regarding possible prognosis. Finally, two relatively simple screening methods for total catecholamines and 4-hydroxy-3-methoxy mandelic acid were presented, and it was shown how these could be used in the diagnosis and classification of neuroblastoma.

Eight cases of Ewing's tumour where there was active tumour present at the time of the investigation gave negative results for all the tests employed.

R. M. Norman (Bristol). ‘Neonatal Anoxic Brain Damage.’

L. L. R. White (Manchester). ‘Brain Biopsy.’ Some of the results of diagnostic brain biopsy were reviewed. Biopsies were taken through cranial burr-holes of about 1.5 cm. diameter, and, where indicated, cerebellum and cerebral cortex was sampled. After fixation, frozen sections (20μ) were examined by multiple staining procedures.

The value of the technique in children with progressive mental and neurological disorders was illustrated by a number of cases. These included four examples of cerebral lipidosis, a child with metachromatic leukodystrophy, two instances of demyelinating disorders and an infant with tuberous sclerosis.

Although some observations had also been made in other conditions such as acute infantile hemiplegia and static mental deficiency, it was in the groups of progressive disorders that the most useful diagnostic information had been obtained. Such information was of clinical value in regard to prognosis and genetic advice. The technique also provided an opportunity for histochemical investigations of fresh brain tissue.

W. I. H. Sheddin (Sheffield). ‘Meningitis due to Serratia marcescens.’ Three children developed meningitis and septicaemia following the insertion of a Holter valve for the treatment of hydrocephalus associated with spina bifida cystica. The organism responsible was Serratia marcescens. The biochemical properties of the organism were detailed. The paper adds to the weight of evidence that Serr. marcescens may be an important human pathogen. It is emphasized that non-pigmented variants of this organism may be wrongly identified as atypical Escherichia coli in the laboratory.

S. F. Cahalane (Dublin). ‘Specificity of Foetal Lesions in Premature Detachment of the Placenta.’ Tardieu spots are non-specific lesions found in cases of mechanical asphyxiation due to strangulation and drowning as well as in infections and poisonings. They may be found in the sudden death of infants.

Examination of 560 perinatal necropsies in Dublin shows that such lesions were present in 72-4% of cases of premature separation of the normally situated placenta. Of all the cases showing such anoxic lesions a history of premature detachment could be obtained in 84%.

By attempting to grade both the severity of the clinical condition and the distribution of the petechiae, evidence was presented from which the following deductions were made. (1) Classical abruption of the placenta is accompanied by petechial haemorrhages of the visceral and parietal pleura, the epicardial surface of the heart and great vessels and the anterior surface of the thymus.

(2) Cases of marginal placental separation and haemorrhage show a lesser degree of intrathoracic haemorrhages, and in most cases these involve the lungs and thymus only and in a few cases the lungs and heart, while only one clear-cut case showed the distribution described by Potter.

In the group of cases designated accidental haemorrhage in which the foetus did not show these typical lesions, it is suggested that either the foetus had already died at the time of placental separation or else the diagnosis of premature separations was doubtful. It is also possible that haemorrhage into other sites may prevent development of the surface petechiae which fail to develop in some cases of abruption.

N. France and L. Butler (London). ‘A Hypotonic Child with XXY Chromosome Pattern.’ A child, now aged 11 months, had been noted to be hypotonic at the age of 3 months; this was most marked in the proximal muscle groups so that the acromion processes could be almost approximated. The hips were unusually lax. Movements of the hands were made with extended elbows and pronated wrists. He had an unusual facial appearance with bilateral epicanthic folds and a mongoloid slant of the palpebral fissures. The fifth fingers were relatively short and there was a left transverse palmar crease: both feet showed poorly developed
Brushfield's lines and a minor degree of syndactyly of digits 2 to 5.

Electromyography was suggestive of a myelopathetic lesion affecting the deltoid muscles, which showed uniform mild atrophy on biopsy.

Chromosome preparations obtained from peripheral blood and skin cultures showed counts of 47 with six chromosomes in Group VII. Analysis of karyotypes showed a normal pairing of Nos. 21 and 22, which often showed satellites, while the other two chromosomes were morphologically similar to Y.

A. D. Bain and I. Smith (Edinburgh). 'Some Anomalies of the Larynx.' A series of congenital anomalies of the larynx has been collected in the Paediatric Pathology Centre, Edinburgh. Four anomalies were demonstrated: laryngeal atresia, in which serial sections showed cartilaginous malformation, and persistence of the pharyngo-tracheal duct. Other anomalies, which presented clinically as stridor from birth and resulted in sudden death in infancy, were aberrant thymus within the larynx, congenital cyst of the larynx and haemangioma of the larynx.

M. Lawrence and P. A. Davies (Penarth). 'The Incidence of Central Nervous System Malformations in South Wales.' It has been the clinical impression that congenital malformations are particularly prevalent in South Wales. This was confirmed by some of the preliminary results of the 1957 Perinatal Mortality Survey. A local social genetic study was being carried out on major central nervous system malformations. In a population of 800,000, 769 families had been found where a child with a major central nervous system malformation had been born since 1956. As findings were not yet complete, this figure was not a total. There were 295 anencephalics, 253 with spina bifida cystica and 115 hydrocephalics, but some of the latter may be excluded and others classified with the spina bifidas.

The spina bifida and anencephalic ratio was the reverse of that found in other investigations: the reason for this was not clear at the moment. The figures suggest an incidence of at least 10 per 1,000 total births, an incidence greatly in excess of any other in the British Isles (with the possible exception of Dublin). Regional variations in South Wales were even more striking with incidences varying from 8.2 to 24 per 1,000 in four selected townships.

J. S. Elwood (Liverpool). 'Pancreatic Curiosities.' Two cases of aberrant pancreas were shown, one in a Meckel's diverticulum in a mongol and the other in a thoracic intestinal duplication in a child with a gross heart malformation. A third case, from which no adequate explanation was forthcoming, was a boy of 6 months with cardiac failure and severe cyanotic attacks, who was found to have hyperglycaemia and an elevated C.S.F. sugar (212 mg./100 ml.) shortly before death. At necropsy the pancreas was congested with white opaque plaques on its surface ('fat necrosis'). Microscopic examination showed chronic inflammatory infiltration of the stroma, but no apparent changes in the parenchyma or islet tissue.

F. Storrington (Cardiff). 'Multiple Pulmonary Cysts with Masses of Heterotopic Nervous Tissue in an Infant of 3 Months.' A female infant with hare-lip and cleft palate was admitted with a history of three severe cyanotic attacks within 24 hours, temperature of 104° F. (40° C.) and the radiological findings of a tension cyst in the right lung. Thoracotomy was performed and three pulmonary cysts were removed, the largest from the right upper lobe and two smaller ones from the right lower lobe. The cysts measured approximately 7 cm., 2.5 cm. and 2 cm. in diameter respectively.

Histological examination of the cysts revealed that they contained, in their walls, what appeared to be heterotopic neuroglial tissue. Sections stained with haematoxylin and eosin, van Gieson, P.T.A.H. and Luxol-fast blue were shown. Stains for neuroglia (Cajal's gold chloride sublimate, Weil Davenport and Holzer, etc.) gave negative results. Sections of the cyst walls showed, in addition, a large amount of calcified and amorphous material. The chest radiographs after the operation showed two further cysts in the left upper lobe.

(Note: All members who saw these sections thought the tissue in the lung to be similar to the heterotopic nerve tissue seen in meningoceles.)