Paediatric Pathology Society

Proceedings of the Twenty-third Annual Meeting

The Twenty-third Annual Meeting of the Paediatric Pathology Society was held at the University Hospital, Groningen, The Netherlands, on 23–24 September 1977.

Paediatric pathology and its place in prenatal diagnosis. A. D. Bain and I. I. Smith. Department of Pathology, Royal Hospital for Sick Children, Edinburgh EH9 1LF.

Until recent years paediatric pathology has been largely equated with the provision of a diagnostic biopsy service for infants and children and with the identification of a cause of death at necropsy. Developments in technology have greatly altered this concept and health care developments in modern obstetric and paediatric practice owe much to the work of pioneers in paediatric morbid anatomy. Developments in cytogenetics and biochemistry, and the application of technology in these fields to prenatal diagnosis and perinatal pathological screening have put paediatric pathology in the forefront of preventative medicine. Exceedingly diverse demands are made on paediatric pathologists in the provision and development of a regional diagnostic service based on high standard technology and enhanced precision in pathological diagnosis.


Three fetuses and their placentas of 19, 21, and 38 weeks' gestation from pregnancies complicated by Mycoplasma hominis or Ureaplasma urealyticum infections were studied. These organisms affected the fetus (1) indirectly, causing severe chorioamnionitis which stimulated abnormal uterine contractions leading to fetal anoxia; (2) directly, by infection of the fetal lung and GI tract, and by damage to fetal organs including cardiomyopathy thought to result from release of toxic products by infective organisms.

Ureaplasma urealyticum isolated from the trachea of a stillborn fetus was used to infect organotypic cultures of human trachea. Examination of the cultures by electron microscopy at intervals from 5 minutes to 42 hours disclosed numerous individual or aggregated small particles with occasional filaments characteristic of mycoplasma absorbed to ciliated and microvillous cell surfaces. Cell shedding, particularly of ciliated cells, and deterioration of cilia occurred between 2 and 7 hours. After 18 to 25 hours focal elevation of cell borders and clumping of microvilli on nonciliated cells were prominent and aggregates of filaments and small vesicles were present on these surfaces. Cell shedding and epithelial separation progressed further at 42 hours. Control tracheal rings from the same fetus incubated without mycoplasma showed normal epithelial structure.

Aortic thrombosis in the newborn period. G. T. Knowlson and H. B. Marsden. Department of Pathology, Royal Manchester Children's Hospital, Manchester M27 1HA. Published in full in the Archives, 53, 164–166.

Meckel's syndrome. A. A. M. Gibson, J. M. Scott, and H. A. Tait. Department of Pathology, Royal Hospital for Sick Children, Glasgow G3 8SJ.

Liver biopsy in neonatal cholestasis: a retrospective study. M. Lendon and H. B. Marsden. Department of Pathology, Royal Manchester Children's Hospital, Manchester M27 1HA.

A total of 60 liver biopsies from 46 children presenting with neonatal cholestasis were examined from the surgical histology files of this hospital for the years 1969–1977. They were assessed for various histological parameters and the results correlated with the findings at laparotomy and the outcome in each case. A special study was done to identify those children with α1-antitrypsin deficiency liver disease using histochemical and immunohistochemical methods. The findings were compared with series from south-east England; Melbourne, Australia; and Michigan, USA.

Pathological changes in infants after Intralipid hyperalimentation. D. G. Fagan. Department of Pathology, Hospital for Sick Children, Toronto M5G 1X8.

Eighteen cases of preterm and term infants given Intralipid during total parenteral nutritional therapy
were studied post-mortem, 8 retrospectively and 10 prospectively. Sections from fresh, frozen, and formalin-fixed, paraffin processed tissues were examined to ascertain the extent and degree of both soluble lipid deposition in the reticuloendothelial system and ceroid formation in the liver and reticuloendothelial system.

Ceroid was defined as Sudan Black B positive material resistant to hot, alcoholic, or paraffin processing extraction. This material was usually Ziehl-Neilsen and PAS positive, and when fresh exhibited autofluorescence. Abnormal amounts of soluble lipid were found in the macrophages of the lung, lymph nodes, spleen, and liver. This, and the pattern of soluble lipid deposition in the hepatocytes, suggested a primary metabolic disorder rather than secondary neutral lipid accumulation.

Ceroid deposition was often associated with soluble lipid deposition in extrapathic sites, and the clinical data were examined to see if any correlation existed between this and various growth characteristics, underlying disease, or Intralipid dosage. Candida and other low grade pathogens were often isolated in blood cultures both in vivo and post-mortem.

**Fat embolism complicating Intralipid infusion.** A. J. Barson. Department of Pathology, St. Mary's Hospital, Manchester M13 0JH.

Numerous pulmonary fat emboli were found post-mortem in 4 infants who had received prolonged intravenous infusion of Intralipid 20%. One infant had in addition a focal softening of a temporal lobe which was probably a consequence of a paradoxical fat embolus. Although such emboli are best demonstrated by fat stains in frozen sections of fresh or wet formalin-fixed tissue, they can also often be recognised in sections from paraffin processed material. The emboli have a characteristic bubbly, transparent, refractile appearance and are contained in capillaries which are unnaturally perfectly circular and distended. In each case the total daily dose of Intralipid was within the limits recommended by the manufacturer but there had been transient periods when the infusion rate had been high. It was felt that this was a factor in the aetiology of Intralipid embolism.

**Effects of neonatal feeding in development of the endocrine pancreas: possible relevance to sudden infant death.** J. S. Wigglesworth, J. M. Polak, and M. V. McCrossan. Departments of Paediatrics and Histochemistry, Institute of Child Health and Royal Postgraduate Medical School, London.

The distribution and concentration of cells producing hormones including insulin, somatostatin, glucagon, and pancreatic polypeptide were studied by immunocytochemistry in 32 pancreata from fetuses and infants. Studies using the Quantimet 720D showed no relationship between gestational age and percentage area of pancreas staining for any hormone. Pancreata of 4 preterm infants who survived 10 days or more of intensive care had a significantly larger percentage tissue area staining for insulin than did other cases. The pancreata of those fed IV had relatively small islets, whereas those fed by jejunal tube had pronounced islet hyperplasia with intense pancreatic polypeptide staining. Similar islet hyperplasia was seen in one of 5 sudden infant deaths. It is concluded that the mode of feeding preterm infants may affect endocrine pancreatic development and that neonatal feeding practices might have a role in pathogenesis of islet cell changes reported in some sudden infant deaths.

**Cerebral white matter lesions in SIDS.** J. Huber, S. Takashima, D. Armstrong, and L. Becker. Department of Pathology, Hospital for Sick Children, Toronto M5G 1X8.

There is increasing evidence that cot death babies have not been completely normal before their sudden and unexpected death. An example is the finding of subcortical leucomalacia (SL) in 16% of 84 SIDS infants. SL is a triangular white-matter lesion occurring beneath deep sulci between secondary gyri, in watershed areas between major cerebral arteries. Lesions consist of rarefaction of neuropil, increased perivascular spaces, and slight astrogliosis. An age-matched control group of 63 infants with congenital heart disease showed similar lesions in 13% of cases, and in contrast, a group of 45 infants who had died from acute disease and trauma showed this lesion in 4% of cases.

**Endocardial fibrosis in apparently normal infant hearts.** R. B. Williams and J. L. Emery. Department of Pathology, Children's Hospital, Sheffield S10 2TH.

A method has been devised for quantitating the endocardium of the heart and a reproducibility test was done. A survey was later carried out from a sequential series of 262 hearts from children in whom no congenital abnormalities of the heart or fibroelastosis was diagnosed naked-eye at necropsy. The findings indicate that there is a group of children showing thickening of the endocardium of both the left and right ventricles dying between the ages of 2 and 3 months.

**Is the incidence of SIDS in The Netherlands changing?** J. P. A. Baak, L. M. Friden, R. Donner, J. J. van der Harten, and J. Huber. Free University Hospital,
Amsterdam; Central Bureau of Statistics, Voorburg; and Hospital for Sick Children, Toronto.

In a previous paper (Baak and Huber, 1974), an attempt was made to assess the incidence of SIDS in The Netherlands by investigating death code numbers 795.0, 796.0, 796.3, 796.9, E913.0, and E913.9 (ICD, 1965, 8th rev). A rate of 0.42/1000 live births (90 cases yearly) was found for the years 1969–1973. In 1974 there was an increase to 0.71 and in 1975 to 0.90 (160 cases). This increase is due to an ‘increase’ of cases diagnosed as sudden death, cause unknown (795.0). This increase, which is probably the result of the publicity about SIDS, is not correlated with a decrease of cases diagnosed as suffocation (E913.0). Analysis of the change in the frequency of other causes of death makes it likely that the ‘increase’ of sudden deaths is not correlated with a decrease in one other single cause of death.

Reference


Further observations in serum uracil levels in acute childhood and chronic adult leukaemia. T. E. Parry. Department of Haematology, Llandough Hospital, Penarth CF6 1XX.

Pretreatment serum uracil levels were raised and the range widened in 47 cases of acute childhood leukaemia (AL) compared with 97 normal controls (mean 22·1 µmol/l, range 7·2–77·1 µmol/l, SD 17·3 in AL; mean 15·7 µmol/l, range 5·7–40·5 µmol/l, SD 5·23 in controls; P<0.025, F ratio 10·8, P<0.001). In 10 cases (21%) the level was more than 3 SD and in 5 more than 8 SD above the normal mean. Uracil correlated with both the leucocyte (r = 0.7894, P<0.001) and the blast cell count (r = 0.710, P<0.001) but not with the blood urea, uric acid, vitamin B12, or folate. Grossly raised uracil levels of 90 and 87 µmol/l returned to normal or near normal levels in 24 and 36 hours respectively in 2 cases of AL after treatment and was accompanied by an equally precipitous fall in the leucocyte and blast cell counts. Normal uracil levels were encountered in 14 cases (8 chronic lymphoblastic leukaemia and 6 chronic myeloid leukaemia) of chronic adult leukaemia.

Renal retention, increased DNA catabolism, and enzymatic deamination of cytosine were considered and excluded as possible causes. It is suggested that the raised uracil is a function of the circulating blast cell. The results are consistent with the hypothesis that in some cases of leukaemia there is an impairment in the amination of uracil to form cytosine akin to its impaired methylation in the megaloblastic anaemias.

Beckwith’s syndrome with renal neoplasia and alphafetoprotein secretion. N. J. Brown and D. J. Goldie. Department of Pathology, Southmead Hospital, Bristol BS10 5NB.

A 5-year-old boy with previously diagnosed Beckwith’s syndrome presented with an inoperable mass in the right kidney; biopsy showed only dysplastic renal tissue. Serum alpha-fetoprotein (AFP) was greatly increased (1600 µg/l). After chemotherapy the mass shrank to operable size and was removed together with the kidney. Histologically the tumour was a nephroblastoma and biochemical assay showed it to contain AFP. Postoperatively serum AFP fell to normal.

Bone metastasising renal tumours. H. B. Marsden, W. Lawler, and P. Kumar. Department of Pathology, Royal Manchester Children’s Hospital, Manchester M27 1HA.

Out of 219 primary renal tumours of childhood diagnosed as nephroblastomas, 7 showed bone metastasis. The figure of 3·2% is within the range of most published series of Wilms’s tumours. However, only one case had a typical histological appearance of nephroblastoma. 4 of the 7 cases had a similar morphological appearance, indicating a distinct entity. Two identical tumours without bone metastases were also found in the series, although in both cases postoperative survival was very short. The incidence of these tumours was considered to be the same as that of mesoblastic nephroma in the Manchester experience.


Six children with synovial sarcoma have been seen in this hospital since 1969. Histologically all 6 were spindle celled tumours containing differentiation, the so-called biphasic appearance. In 4 of the tumours large numbers of mast cells were present. All 4 patients with mast cells in their tumour had complained of exquisite hypersensitivity over the tumour as the presenting symptom. In the most recent case the electron microscope confirmed the presence of large numbers of mast cells. The differential diagnosis is from fibrosarcoma, leiomyosarcoma, vascular leiomyoma, clear cell sarcoma of tendon sheath origin, and from some rhabdomyosarcomas.
Congenital neoplasia: the Society's experience.
A. J. Barson. Department of Pathology, St. Mary's Hospital, Manchester M13 0JH.

All Society members were canvassed for examples of neoplasia which had presented clinically or pathologically within one month of birth. A total of 285 cases were reported. The commonest tumours to be found in the newborn were teratomata (67 or 24%), more than half of which were sacrococcygeal in location. Almost equally common were neuroblastoma (64 or 23%). A heterogeneous group of rhabdo-, leio-, and fibrosarcomas arising in a wide variety of locations accounted for 8% of the total; Wilms's tumours and mesodoblastic nephromata constituted 7%; just over 6% of congenital tumours arose within the central nervous system (this figure excludes teratomata); and 6% of the total were cases of congenital leukaemia. The remaining tumours reported accounted individually for less than 5% each of the total, and included cases of histiocytosis X, haemangioma, hepatoblastoma, retinoblasto- 

Lung lesions in the premature rabbit neonate induced by brief periods of artificial ventilation: prophylactic effect of surfactant. R. Nilssen, G. Grossman, and B. Robertson. Department of Paediatric Pathology, Karolinska Institutet, and Research Laboratory, Department of Pathology, St. Görans Sjukhus, Stockholm.

Premature newborn rabbits (gestational age 27 days), were tracheotomised and treated with intermittent positive-pressure ventilation (IPPV) for periods varying between 1 and 60 minutes. Tidal volume was registered by a body plethysmograph and adjusted to 10 ml/kg body weight, and insufflation pressure recorded. Histological lung sections showed necrosis of bronchiolar epithelium in all animals ventilated for more than 1 minute; the degree and extent of these lesions increased with the duration of IPPV. A separate group of animals, ventilated for 19-60 minutes, received an intratracheal deposition of 50 μl of homologous surfactant suspension, prepared by centrifugation of lung wash from adult rabbits; littermates with empty tracheal tube served as controls.

In this series the mean quasistatic compliance of the lung-thorax system was higher among surfactant-treated animals than in controls (mean ± SD 0.42 ± 0.09 and 0.27 ± 0.04 ml/cm H2O per kg, respectively, P<0.002). Morphometric analysis of lung sections showed that the alveolar compartment was better expanded in surfactant-treated animals than in controls, and that necrosis and desquamation of bronchiolar epithelium were absent or scarce in the surfactant-treated animals but prominent in controls. Findings indicate that bronchiolar epithelial lesions can be induced in the preterm neonate by short periods of IPPV, and that these lesions can be prevented by deposition of surfactant in the upper airways before onset of ventilation.

Abnormalities in the structure of the trachea in children with tracheo-oesophageal fistula. P. Wailor and J. L. Emery. Department of Pathology, Children's Hospital, Sheffield S10 2TH.

A quantitative study has been carried out on the size, the amount of cartilage, and length of muscular tissue in standard blocks of the tracheae from children coming to necropsy. From these data, means and a normal range were devised. Serial blocks were taken throughout the length of the tracheae from a total of 50 cases of tracheo-oesophageal fistulas. Measurements from these have been compared with the controls and this indicates that a considerable number of children with tracheo-oesophageal fistula have abnormalities in the structure of the trachea throughout its whole length.

Is short segment Hirschsprung's disease a new entity? J. L. J. Gaillard. Department of Pathology, 1 Medical Faculty, Rotterdam.

Intramural colonic hamartoma: unusual cause of chronic constipation with segmental distalation of the colon. J. N. Cox, P. Braun, and D. Nusslé. Departments of Pathology, Paediatrics, and Genetics, Hôpital Cantonal, 1211 Geneva 4.

Radiological investigations in a 7-year-old girl, who had had chronic constipation from birth, showed localised dilatation of the sigmoid colon with functional obstruction and narrowing of the distal portion. Several rectal biopsies taken in the perinatal period showed normal ganglion cells, thus excluding Hirschsprung's disease. The resected segment had muscular abnormalities of the bowel wall and the accompanying vessels, consistent with a 'hamartoma' of the distal segment. Radiological, surgical, and pathological aspects were considered in relation to segmental dilatation of the colon and pseudo-Hirschsprung's disease.
Seminiferous tubules during infancy related to children dying with hydrocephalus. J. A. Mendez and J. L. Emery. Department of Pathology, Children's Hospital, Sheffield S10 2TH.

A quantitative study was carried out on the diameter of the seminiferous tubules and of the proportion of pregerminal and Sertoli cells in a series of 115 boys dying with hydrocephalus and spina bifida, and 162 children stillborn and dying during infancy.

There was a progressive increase in the diameter of the seminiferous tubules throughout the period under study. There is a great increase in the number of pregerminal cells around the time of birth; which disappear progressively after birth. In some children with hydrocephalus there is an increase in the number of pregerminal cells suggesting that the testis is in a state of abnormal hypothalamic stimulation.

Tubular lesions in focal sclerosing glomerulopathy. T. Ishidate and J. Huber. Department of Pathology, Hospital for Sick Children, Toronto M5G 1X8.

134 kidney biopsy specimens of primary nephrotic syndrome were reviewed with particular regard to the tubular changes, using light microscope and immunofluorescent findings. The age of the patients ranged from 6 months to 16 years (80 males, 54 females). Beside tubular atrophy, cast formation, and dilatation of tubular lumen, some biopsies showed marked proliferation of epithelial cells, often surrounding the casts in dilated or collapsed distal tubules and often accompanied by calcium deposition in adjacent interstitium. These changes were observed more often in focal glomerulosclerosis (FGS) (17 out of 36), compared to minimal lesion (5 out of 61), membranoproliferative glomerulonephritis (2 out of 11), and membranous glomerulopathy (1 out of 8). Out of 8 cases with these extensive tubular lesions in the FGS group, 6 patients were under 2 years of age at the time of onset of nephrotic syndrome.

Histopathology of lymphoid tissue in 15 cases of DiGeorge syndrome. J. J. van der Harten and J. Huber. Pathologisch Instituut, Vrije Universiteit, Amsterdam; and Department of Pathology, Hospital for Sick Children, Toronto M5G 1X8.

In children who suffer from the III-IV pharyngeal pouch or DiGeorge syndrome and in whom the congenital cardiac anomaly usually predominates, there is a disturbance of the cellular immunity because of the concomitant aplasia or hypoplasia of the thymus. This disturbance has clinical as well as pathological-anatomical manifestations.

Histopathological changes of the lymphatic tissue were found in a series of 15 cases with survivals ranging from 1 day to 7 months. (1) Gestational age and time of survival determine the morphology of the lymphatic tissue in lymph nodes and spleen. (2) The variability of the lymphocyte density and size of the paracortical areas in lymph nodes and perierteriolar lymphocyte sheaths in the spleen (thymus-dependent areas) did not permit us to distinguish between hypoplasia or aplasia of the thymus (partial or complete DiGeorge syndrome, respectively). (3) In the cases of less than 1-month survival where careful post-mortem examination failed to uncover thymic tissue, thymus-dependent areas in the lymphoid tissue could still be recognised.

Suppressor thymus-derived (T) lymphocytes in the human fetus: protective mechanism against rejection? L. B. Olding, R. A. Murgita, M. B. A. Oldstone, and H. Wigzell. Departments of Immunology and Pathology, University of Uppsala; and Scripps Clinic & Research Foundation, La Jolla, California.

The fetus inherits genetic materal from its father and, accordingly, should be recognised as alien, 'non-self', by the mother's immunocompetent cells and subsequently rejected. Obviously rejection does not occur in the vast majority of pregnancies. The reason is still unclear but presumably several protective mechanisms are involved. We have found so-called suppressor T lymphocytes in the cord blood of the human newborn which are able to abrogate the proliferation of mitogen-induced maternal lymphocytes in vitro. The suppression can be elicited by means of cell-to-cell contact between maternal and neonatal cells or by low molecular weight soluble factor(s) released by activated neonatal T lymphocytes. The newborn's suppressor cells seem to harbour in a subpopulation of T cells carrying surface receptors for IgG and are able to inhibit both cell-mediated and humoral responses in vitro.

Similar immunosuppressive activities both in vitro and in vivo have been reported in neonatal mice by other authors. One may speculate that maternal lymphocytes coming into contact with the fetal antigenically alien trophoblastic cell layer in the placenta are prohibited from responding by host-versus-graft reaction. This effect might be exerted either by fetal lymphocytes that travel through the placental barrier, or by the release of suppressive soluble substance(s) by fetal lymphocytes circulating in the capillaries in the chorionic villi. The low molecular weight soluble substance(s) found in our experiments might easily diffuse through the thin barrier between the fetal capillaries and the inter villous space in the placenta.