PROCEEDINGS OF THE
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AND IRELAND

5th and 6th January 1970

The one hundred and twentieth meeting of the Society was held at the Royal Postgraduate Medical School, London, on Monday and Tuesday, 5th and 6th January 1970

SYNOPSISES OF PAPERS

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Papers accompanied by a demonstration are indicated by an asterisk

1. ORGANIC CANALISATION AND VASCULARISATION OF DEEP VEIN THROMBI STUDIED WITH DYED-MICROPAQUE INJECTED AT NECROPSY

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Little is known about vascularisation and organic canalisation of thrombi in deep veins. It is uncertain whether they are the same or different processes. It is also uncertain whether or not the vascular spaces formed are connected with the vasa venorum. This might be important because of the possibility of arterio-venous shunting after canalisation. At necropsy Micropaque dyed with prussian blue was injected into the common iliac arteries. After this, thigh or calf veins containing thrombi were excised and sectioned. Histological examination showed prominent vasa venorum which contained the injection medium. Unequivocal communication was demonstrated between the vasa venorum and the vascular channels within the organising thrombi. Canalising channels in some thrombi also contained Micropaque, suggesting that they communicate with the arteries via the vasa venorum. The permanence of the arterio-venous communications is uncertain as scarred remnants of old venous thrombi showed injection of their intrinsic vessels but not of the vein lumen.

2. SOME HISTOPATHOLOGICAL, ENZYME-HISTOCHEMICAL AND ELECTRON-MICROSCOPICAL DATA ON HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

J. Snijder, J. de Jong and A. E. F. H. Meijer

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From both a clinical and a morphological point of view, as well as in respect of their aetiology, the so-called primary cardiomyopathies represent a group of heterogenous conditions. However, in recent years cases have emerged that constitute a clinically recognisable category. Cases of this type have been variously called hypertrophic obstructive cardiomyopathy or subaortic stenosis. Specimens of tissue removed surgically from the outflow tract of the left ventricle in a number of cases of hypertrophic obstructive cardiomyopathy have been studied morphologically. In addition to histopathological data, the results of enzyme-histochemical and electron-microscopical studies were reported.

The question was discussed whether or not, on the strength of the data available, the cases studied belong to a nosological entity.
3. AN EXPERIMENTAL STUDY OF ELASTIC-TISSUE FORMATION IN THE CHICK AND RAT AORTAS

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The mechanisms of normal and of pathological elastogenesis are not understood as fully as those of collagen fibre synthesis. In order to clarify the position elastogenesis has therefore been studied in the chick embryo and in the rat aorta. Intimal proliferation was induced in the rat aorta by painting with 4 per cent. HCl. The new intima that developed was investigated by light and electron microscopy and the nature and morphology of the cells present and the structure of the newly formed fibres and ground-substance defined. The features of young elastic material in the embryonic and newborn chick aorta, and in that of the rat, showed many similarities. Thus, on electron microscopy, elastic material was found to consist of clumps or aggregates measuring from 40 to 200 nm in diameter, with granules of 7–12 nm at their periphery. Also present were fine filaments of 1.5–3 nm in diameter; these and the electron-dense granules were sometimes present in the extracellular space at some distance from the elastic clumps or aggregates. The granules were arranged either as rows 7–12 nm in diameter or as tubelike structures formed by the circular arrangement of 4 or 5 granules. It is suggested that the formation of extracellular elastic structures may be related, both normally and during neo-intima formation, to the presence of cells with the characteristics of smooth muscle. There is no evidence that the presence of connective tissue cells is necessary for vascular elastogenesis.

4. GLOMERULAR FINE STRUCTURE IN AN ADULT CASE OF SO-CALLED MIXED MEMBRANOUS AND PROLIFERATIVE GLOMERULONEPHRITIS

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A renal biopsy from a 55-yr-old man with nephrotic syndrome of unknown aetiology was examined by light and electron microscopy. Light microscopy showed the entity called mixed membranous and proliferative glomerulonephritis. Electron microscopy revealed the following principal abnormalities: (a) very marked mesangial cell hyperplasia; (b) equally marked invasion of the peripheral capillary basement-membrane by mesangial cell cytoplasmic processes; (c) a modest increase of endothelial cells; (d) focal thickening, thinning, rarification and varying density of the capillary basement-membrane; (e) an excessive number of neutrophil polymorphonuclear leucocytes in the glomerular capillaries and direct contact between them and the basement-membrane, and (f) very occasional subendothelial deposits. Because this histopathological entity looks with the light microscope like a combination of an acute proliferative glomerulonephritis and late stage membranous glomerulonephritis in almost equal proportions, there has been a hesitancy to label the condition categorically as either. However, the majority of the fine structural changes in this case are in favour of a basically proliferative process. This is in agreement with recent similar evidence in a few cases of mixed glomerulonephritis in children. The present evidence indicates that the prognosis of such cases is relatively good despite the severe anatomical deformity of the glomeruli.

5. GLOMERULAR EPITHELIAL CELL COAT AND BASEMENT-MEMBRANE

F. Walker

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The possibility of a relationship between epithelial cell coat or “fuzz” and basement-membrane was investigated using the rat glomerulus as an experimental model. The
glomeruli, either labelled \textit{in vivo} with silver or stained \textit{in vitro} with ruthenium red, were examined electron microscopically. It was shown that a component of renal glomerular basement-membrane is secreted by the visceral epithelial cells. This component is secreted in the same manner and at the same time as, and shares certain staining affinities with, the cell coat that covers the visceral epithelial cells.

6. \textbf{THE EFFECT OF INJECTION OF A HETEROLOGOUS ANTI-KIDNEY-MITOCHONDRIAL ANTISERUM IN RATS MADE TEMPORARILY PROTEINURIC}

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Mild proteinuria was produced in rats by BSA-induced acute serum sickness or by a small dose of nephrotoxic serum. During the phase of transient proteinuria, a rabbit anti-rat-kidney mitochondrial antiserum was injected intravenously. From 4 wk onwards a progressive renal disease developed, which was similar to autologous immune-complex nephritis. Control groups, which included intact animals given an injection of the anti-kidney mitochondrial antiserum, did not develop the disease.

The significance of these experiments in relation to the pathogenesis of autologous immune-complex nephritis was discussed.

7. \textbf{PSEUDOMEMBRANOUS TRIGONITIS}

L. Henry and M. Fox

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Recurrent urinary tract infections and the urethral syndrome are frequently seen in young women, and may produce a distressing urgency and frequency. The urine is sterile and antibacterial therapy has little or no effect. On endoscopy the bladder neck shows an abnormal, greyish, heaped-up mucosa covering the distal part of the trigone but sometimes extending to the ureteric orifices or reaching into the upper urethra. The area has a serpiginous margin and a cuff of hyperaemia. Bleeding may occur during cystoscopy. The symptoms are usually eased by urethral dilatation, but recurrence is not uncommon. Diathermy of the area may be necessary. Biopsy was obtained in 31 cases, all female, with ages ranging from 15 to 70 yr. The tissue was invariably sterile on culture. The histology showed "vaginal" metaplasia of the epithelium with a high content of glycogen. The underlying tissue showed oedema and vascular dilatation but no significant cellular infiltrate. Minimal fibrosis is occasionally present with extension into the muscularis. The condition may be associated with adjacent areas of cystitis cystica, glandularis and follicularis. The aetiology is not known.

8. \textbf{THE TOTAL LENGTH OF TUBULES IN NORMAL AND ATROPHIC TESTES}

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The volume of testis can be estimated during life fairly exactly by measuring its three main diameters at the time of biopsy. Histometric measurements on the biopsy can then be translated into absolute figures for the quantity of any tissue in the whole testis: a method of this type for Leydig cells has already been published. It ought to be possible to determine the total length of the tubules in the testis in a similar manner. A useful first approximation can be obtained by multiplying the volume of the testis by the number of tubule cross-sections.
in unit area; this figure has the great advantage that it can be rapidly and relatively accurately obtained. The true length of the tubules is related to this figure by a factor that depends on the geometry of the tubules; its size has not yet been established, though some progress has been made. The approximate figure can serve, however, as a basis of comparison between different types of testicular disease, and its use has indicated that in the del Castillo type of tubular atrophy the tubules are reduced to 70 per cent. of normal, and in XXY Klinefelter's syndrome to 24 per cent. of normal.

9. FURTHER OBSERVATIONS ON THE PATHOLOGY OF CROHN'S DISEASE

H. Thompson, J. Burman, J. A. Williams and W. T. Cooke

University of Birmingham and General Hospital, Birmingham

Comparative studies in a large series of cases collected in Leeds and Birmingham were reviewed. Diagnostic criteria, localisation of the disease, recurrence rate and vascular changes were discussed. The possibility of a delayed hypersensitivity reaction being involved in pathogenesis was considered.

10. ULCERATIVE COLITIS IN RABBITS FED WITH DEGRADED CARRAGEENAN

J. Watt and R. Marcus

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We have recently reported the occurrence of ulcerative colitis in several species of experimental animals fed with carrageenan in their drinking water. Degraded carrageenan derived from the red seaweed Eucheuma spinosum produces severe ulcerative colitis, which affects the entire colon in the rabbit. The lesions in the colon are associated with loss of weight, diarrhoea, fresh or occult blood in the faeces, and anaemia. In a dose-response study we have found that ulcerative lesions occur in the colon of the rabbit when a daily dose as small as 0.07 g per kg body weight is given.

The results of the experiments were described and their significance discussed.

11. BIRTH TRAUMA TO THE CERVICAL SPINE AND VERTEBRAL ARTERIES

E. L. Jones, A. H. Cameron and W. Thomas Smith

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Spinal injury at birth can be latent clinically and often remains undetected because the spinal cord is examined infrequently during necropsies on neonates. In the past, birth injuries to the spinal structures were commonly reported, but more recently attention has centred on injuries to the brain. The cervical vertebrae and related structures in a series of 30 perinatal and neonatal deaths have been examined. Evidence of distortional birth trauma included spinal meningeal haemorrhages, tears and haemorrhages in nerve roots, spinal cord lesions and adventitial haemorrhages around the intra-osseous portions of the vertebral arteries. It is possible that ischaemia can be induced in the territory supplied by the basilar and vertebral arteries when the latter are involved, leading to damage to the brain-stem, cerebellum and/or temporal lobes.
12. ALKALINE PHOSPHATASE IN MENINGIOMAS

W. R. Timperley and T. W. Warnes

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Department of Medicine, Manchester Royal Infirmary

Five meningiomas were found by histochemical techniques to contain alkaline phosphatase. Alkaline phosphatase was extracted from the tumours with butanol and several of its biochemical properties, including electrophoretic mobility, inactivation by heat, and sensitivity to urea and L-phenylalanine were investigated. These biochemical properties were compared with those of two known isoenzymes of alkaline phosphatase, namely those of small intestine and of normal serum. In contrast to small-intestinal alkaline phosphatase, the meningioma isoenzyme was virtually uninhibited by L-phenylalanine and was remarkably heat-sensitive. It was also very much more inactivated by M-urea than intestinal alkaline phosphatase, the inactivation produced being of a similar order to that obtained with the alkaline phosphatase of normal serum. Electrophoretically the alkaline phosphatase of all 5 meningiomas produced a single band moving at the same rate as the main band seen in normal serum.

13. A RAPID METHOD FOR PRODUCING CIRRHOSIS OF THE LIVER IN RATS AND ITS EFFECT ON MICROSOMAL ENZYME ACTIVITY

Elizabeth K. McLean, A. E. M. McLean, W. J. Marshall and P. M. Sutton

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The toxicity of carbon tetrachloride (CCl₄) is dependent on its metabolism. Exposure to DDT or phenobarbitone induces synthesis of the enzymes that metabolise CCl₄ and greatly enhances its acute toxicity. We have given CCl₄ twice weekly by inhalation, with simultaneous dosage with phenobarbitone in the drinking water. All the surviving rats (50–80 per cent. of the initial groups) develop a severe cirrhosis of the liver in 4–8 wk. One to 8 weeks after cessation of CCl₄ dosage the rats were found to have ascites, splenomegaly, portal hypertension, gastro-intestinal bleeding and testicular atrophy, in addition to their cirrhosis. Studies of the microsomal hydroxylation enzymes that are concerned with detoxication of steroids and barbiturates showed that these were depressed only in the most severely cirrhotic livers. As a technique of producing experimental cirrhosis this has the advantage that it halves the time and increases the yield of cirrhotic animals in comparison with administration of CCl₄ alone.

14. GRANULOCYTES IN BILE DUCTS EQUALS CHOLANGITIS?

H. P. Meister

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In most textbooks inflammatory changes of bile ducts and ductules secondary to biliary obstruction are described as cholangitis. Some studies emphasise the haematogenous origin of cholangitis. Most of the references consider granulocytes in bile ducts or ductules as pathological. In this study the frequency of such inflammatory changes is determined. To improve the accuracy in detection and localisation of minimal changes, thin sections of methacrylate-embedded material from 100 consecutive liver biopsies were evaluated. The inflammatory changes of the intrahepatic biliary system were compared with the over-all histological lesion, in some cases with findings in previous biopsies and with clinical and laboratory data.

The significance of these changes was discussed.
15. **Electron microscopy of pulmonary lesions induced by metabolites of pyrrolizidine alkaloids**

W. H. Butler

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The pyrrole derivatives of the alkaloids monocrotaline and retrorsine on intravenous injection induce in the lung a proliferative lesion of the alveoli that is progressive over a period of 3–4 wk. The fully developed lesion consists of an interstitial oedema and a fibroblastic response. The alveolar capillary endothelium is increased and abnormal nuclei are present. The alveolar epithelial cells have a more complex form and their basement-membrane is greatly thickened and tortuous. There is no significant increase of granular type-II pneumonocytes.

The development of this lesion was described.

16. **Paraquat poisoning***

W. A. Harland, W. G. S. Spilg, P. G. Toner and J. M. Vetters

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Paraquat, a bipyridylum weedkiller, is known to be highly toxic in man and experimental animals. It usually produces a rapidly progressive pulmonary fibrosis. A fatal case is presented in which the development of the lung lesion was studied by biopsy and electron microscopy. The lesion is apparently irreversible and treatment therefore depends on rapid elimination of the poison by dialysis or forced diuresis, followed by lung transplantation when evidence of pulmonary damage appears.

17. **Hyperparathyroidism with local amyloid deposition***

D. J. Pollock and P. W. Leedham

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The finding of material giving the staining reactions for amyloid in the parathyroids of a patient with primary parathyroid hyperplasia prompted the search for this material in other similar cases. Amyloid was found, deposited in a concentric fashion in the centre of parathyroid follicles, in 6 cases out of 54 examined. Five of these came from two separate families and at least one member of each had the multiple endocrine adenoma syndrome.

The significance of this finding in relation to amyloid in islet cell tumours and medullary carcinoma of the thyroid was discussed.

18. **Hereditary amyloidosis of the cornea**

A. Garner

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Of the several categories of hereditary corneal dystrophy, two are described in which there is patchy deposition of abnormal protein material within the substantia propria. In one of these there is good evidence that the material is amyloid; in the other the deposits consist of a non-collagenous granular protein of as yet undetermined nature, whose components include appreciable amounts of tyrosine, arginine and sulphur-containing amino acids. The occasional finding of recognisable amyloid within the deposits of the latter condition raises the possibility that the granular material may be a related protein, perhaps a precursor or forme fruste.
19. The effects of glucagon and insulin on the hypoglycaemia following total pancreatectomy and partial hepatectomy in the rat

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In previously reported experiments we have shown that rats subjected to the combination of total pancreatectomy and partial hepatectomy (and not fed post-operatively) become fatally hypoglycaemic some hours after the operation, with only a trace of glycogen remaining in their livers. There is, of course, a close functional relation between the liver, the pancreas and carbohydrate metabolism—the liver as the major site of glucose production and the endocrine portion of the pancreas as the source of both insulin and glucagon. We now report experiments on the effects of administering these hormones to rats undergoing total pancreatectomy with partial hepatectomy. Giving glucagon did not prevent the animals from becoming hypoglycaemic under these circumstances, whereas the administration of insulin accelerated the onset of hypoglycaemia. The cause of this experimentally induced hypoglycaemia therefore remains unknown.

20. Virus-like particles in a malignant lymphoma of the tonsil

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A woman aged 43 yr, born in Guyana, was first seen in this country in August 1969 with a history of tonsillitis 2½ months earlier, which did not settle as usual; and she had noticed enlargement of the left cervical nodes and of the left tonsil. There were hard matted glands on the left side of her neck and the left tonsil was enlarged, with a central necrotic area. Later, both the tonsil and cervical lymph-nodes increased in size and some nodes appeared on the right side of her neck. Biopsy was done and the diagnosis of malignant lymphoma-reticulo-sarcoma confirmed. The condition responded well to radiotherapy, but mediastinal and abdominal masses developed and these were treated with cytotoxic drugs. Electron microscopy revealed multiple intracellular vacuoles or inclusion bodies in the cytoplasm of the neoplastic cells. They contained large numbers of virus particles 60–70 nm in diameter. The particles had a double membrane and were surrounded by a corona of smaller units and resembled coronaviruses. Serological tests gave a titre of over 320 to the EB-virus. Similar particles have been noted in another case of lymphosarcoma of the tonsil.

21. Myelocyte proliferation in pernicious anaemia

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A combination of quantitative cytochemical measurement of DNA and tritiated thymidine autoradiography has been used to study myelopoiesis in pernicious anaemia. An arrest of myelopoietic cells in the post-synthetic phase (G2) has been demonstrated, this defect being maximal in the giant metamyelocytes. Protein synthesis in the myelopoietic cells has been investigated by autoradiographic analysis of 3H-leucine incorporation. The origin of the hypersegmented polymorphonuclear leucocyte and the question of ineffective myelopoiesis in pernicious anaemia were discussed in the light of these results.
22. THE INFLUENCE OF GERM-FREE STATUS AND ANTILYMPHOCYTE SERUM ON TUMOUR DEVELOPMENT IN MICE EXPOSED TO CHEMICAL CARCINOGEN

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Tumour development has been studied in C3H mice maintained in germ-free (GF) isolators or kept in a minimum-disease (MD) animal facility. In some experiments mice were exposed to the chemical carcinogen 7,12-dimethylbenz (a) anthracene (DMBA); others were given no treatment. A course of injections of horse anti-mouse lymphocyte serum (ALS) was given to DMBA-treated mice in one experiment. The main findings so far are: (1) GF-status reduces the risk of development of liver-cell adenomas in response to DMBA in male mice; (2) GF-status delays the development of sarcomata at the site of subcutaneous injection of DMBA; (3) 8 out of 17 MD female mice treated with DMBA at birth and with ALS between 32 and 39 wk had neoplasms (of lung, liver and reticuloendothelial system) when killed at 42 wk as compared with none out of 17 similarly treated GF female mice.

The results of experiments still in progress were presented and the findings as a whole were discussed.

23. THE "NON-SPECIFIC" INFLAMMATORY RESPONSE TO SUBCUTANEOUS TRANSPLANTS OF THE EHRlich CARCINOMA

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In untreated mice subcutaneous growth of the Ehrlich tumour is of infiltrative type and is accompanied by an acute inflammatory response. When this response is abrogated by treatment with phenylbutazone the growth pattern changes, becoming expansive rather than infiltrative. It can be demonstrated that the inflammatory response is biphasic: an initial period of inflammation in the first 3-4 days after transplantation is followed by a period up to day 14 in which less reaction is present. At 14 days the response appears anew.

The possible causes of this biphasic reaction were discussed.

24. CHANGES IN THE ELECTROPHORETIC MOBILITY AND GROWTH PATTERN OF EHRlich CARCINOMA CELLS FOLLOWING TRANSPLANTATION IN TUMOUR-BEARING MICE

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When an intraperitoneal injection of Ehrlich ascites carcinoma cells is given to mice bearing a subcutaneous transplant of the same tumour, growth of the intraperitoneal transplant differs from that in control non-tumour-bearing mice, in that less fluid exudate is formed. The tumour cells from the ascites in the mice with subcutaneous transplants show a higher electrophoretic mobility than those from controls. On further transplantation to normal mice these tumour cells fail to elicit an acute inflammatory response until several days after transplantation, in contrast with tumour cells from the controls, which elicited a response from the first day.

The host-tumour relation in these normal mice was discussed.
25. FEATURES OF THE GROWING EDGE OF A TRANSPLANTED TUMOUR IN MOUSE LIVER

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The growth of solid Landschutz tumour in mouse liver was studied by electron microscopy and by histochemical methods for acid phosphatase and non-specific esterase. Pseudopodia from the tumour appear to be important in its growth and can be seen indenting the plasma membrane of otherwise intact host cells. Lysosomes in the liver are increased in number, especially at the tumour edge. This increase is probably not due to direct absorption of lysosomal enzymes from the tumour, since the latter contains very little histochemically demonstrable acid phosphatase or esterase. Desmosomes are relatively well preserved, even between liver cells that are otherwise severely damaged. It is probable, therefore, that trypsin-like enzymes do not play a major part in the spread of this tumour.

26. HEPATOCELLULAR NECROSIS FROM DIETARY SILVER IN VITAMIN E-DEFICIENT RATS

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Addition of 0.15 per cent. silver acetate to drinking water produces hepatocellular necrosis in vitamin E-deficient rats. Sequential studies showed that the lesion first appeared on the 14th day of treatment and was rapidly fatal. It was visible at necropsy as haemorrhagic areas. The lesion was irregularly distributed so that some lobes of the liver were severely affected, and others appeared normal. Histologically necrosis appeared first in the centrilobular areas, the remainder of the lobule rapidly becoming affected. By light microscopy, nuclear and cytoplasmic damage appeared to occur concurrently. Ultrastructurally, the mitochondria appeared to be affected at an early stage. Histochemically, the lysosomal changes observed were consistent with those found in cell damage from other causes. The latent period and histological features of the lesion are closely similar to those observed in dietary liver necrosis from a combined deficiency of vitamin E and selenium. This similarity suggested that the silver might interfere with the availability of selenium in the vitamin E-deficient rat, leading to a deficiency state of both vitamin E and selenium. This suggestion seems to be supported by reports stating that dietary supplements of selenium (0.05–1.0 p.p.m.) afford partial protection against high doses of silver (1000 p.p.m.) and full protection against low doses (3–30 p.p.m.).

27. THE PATHOLOGY OF THE MOTOR END-PLATE

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28. CHANGES INDUCED BY 4-ETHYLSULPHONYLNAPHTHALENE-1-SULPHONAMIDE IN THE URINARY BLADDER EPITHELIUM

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The compound 4-ethylsulphonylnaphthalene-1-sulphonamide (ESNS) has a toxic effect on the transitional epithelium lining the urinary bladder of the rat. Necrosis is followed by
an increased mitotic rate and this leads to hyperplasia which is maintained as long as the
ESNS is administered. Such ESNS-treated bladders have an increased susceptibility to
chemical carcinogens. The early epithelial changes in the rat bladder in the first 5 days after
a single dose of ESNS have been studied by electron microscopy. Initial damage was most
pronounced in the superficial cells. They responded by proliferation and dedifferentiation
of the Golgi complex with an attendant failure in the supply of the thick luminal membrane.
There was an increased production of lysosomes and autophagic vacuoles. In some areas
cytoplasmic dissolution was followed by cell death; in others the cells survived, but their
specialised luminal barrier membrane was replaced by one that was unspecialised and
thinner.

These observations were discussed in relation to the co-carcinogenic action of ESNS in
the rat bladder.

29. EARLY CHANGES IN THE TRANSITIONAL EPITHELIUM OF RAT
URINARY BLADDER INDUCED BY NITROSOMETHYLPYRURIA

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Nitrosomethylurea (NMU) is carcinogenic in all species tested and produces tumours in
different organs depending on its route of administration. Its carcinogenicity in the rat
urinary bladder is being investigated after direct intracystic injection of a single dose of 13 mg
per kg. The early changes in epithelial structure in the first few months following injection
of NMU into the bladder have been examined by light and electron microscopy. The normal
bladder epithelium is three cells thick and each cell layer may be characterised by the degree
of specialisation and differentiation of its subcellular organelles. The single dose of NMU
is cytotoxic and within 2 days focal necrosis of all cell layers is common, and 5 days later
complete desquamation of regions of the epithelium is seen. Subsequently a cyclic process
of repair and necrosis is established, which persists for a period of months. There are subtle
changes in the fine structure of the cells during this time and the thickness of the epithelium
is very variable.

The possible significance of these findings was discussed in the context of carcinoma of
the bladder epithelium.

30. ULTRASTRUCTURAL CHANGES INDUCED IN THE RAT KIDNEY BY
DIMETHYLNITROSAMINE AND THEIR RELATION TO THE
DEVELOPMENT OF NEOPLASIA

G. C. Hard and W. H. Butler

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Following the demonstration by light microscopy of a sequence of renal cortical lesions
in the protein-depleted rat after a single injection of 50–60 mg DMN per kg (a dose that
induces up to 100 per cent. of renal tumours), the ultrastructural events were traced from
24 hr after treatment until the time of tumour appearance. Certain cells of the afferent
arteriole were identified as a specific target of injury at 24 hr. This was followed by changes
in the proximal tubules and the formation of hypercellular interstitial foci around damaged
tubules and arterioles. An attempt was made to characterise the elements of the persisting
cellular foci at various intervals in order to relate acute damage with the inevitable neoplastic
development.
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31. EARLY CHANGES AND NEOPLASTIC RESPONSE AT THE SITE OF REPEATED SUBCUTANEOUS INJECTION OF CARCINOGENS

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An aqueous solution of the carcinogens methylnitrosourea, nitroquinoline-N-oxide or butyrylethylenimine was injected twice weekly into the subcutaneous tissue of rats and mice. The early tissue reaction was studied and the neoplastic outcome recorded. An initial destructive effect on the subcutaneous tissue was seen after the first injection with all 3 compounds and was most severe with nitroquinoline-N-oxide. The reparative response was atypical and delayed from the normal 2–3 days after initial injury to about 14 days. Fibroblastic response and capillary formation were poor. A number of the fibroblasts were abnormal in size, or nuclear structure, or both. Mammary tumours arose at the injection site of methylnitrosourea and nitroquinoline-N-oxide after 12 wk, and after 18 wk in the butyrylethylenimine experiment. Sarcomas appeared at the site of injection by 22 wk with the first 2 compounds. The initial lesion and the neoplastic response are in keeping with the results obtained by the subcutaneous administration of polycyclic aromatic hydrocarbon carcinogens, but differ markedly from those produced by the repeated injection of surface active or hypertonic solutions.

32. PATHOLOGICAL EFFECTS IN HAMSTERS OF MURINE SARCOMA VIRUS (MSV HARVEY)*

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Under certain conditions Moloney's strain of leukaemia virus (MLV) is capable of inducing inflammatory lesions and sarcomas in mice. The virus or mixture of viruses responsible have been called murine sarcoma virus (MSV) and named after the investigator originally describing them, e.g., Harvey, Moloney or Kirsten. Preparations of murine sarcoma virus (Harvey) injected into newborn hamsters lead to the development of the following lesions: (1) solid tumours containing multinucleate giant cells in the subcutaneous tissue and muscle near the site of inoculation of virus; (2) distant tumours particularly in the limbs, with involvement of their bones; (3) lymphadenectasis similar to that seen in rats given an injection of some strains of Rous sarcoma virus; (4) accumulation of milky fluid in the pleural cavities; (5) polymorphonuclear leucocytosis and anaemia. Virus can be recovered from some of the tumours.

The pathological and biological features of the primary and transplantable tumours were discussed and in particular whether they should be regarded as inflammatory or neoplastic lesions.

33. HISTOCHEMICAL AND ELECTRON-MICROSCOPIC STUDIES OF MULTINUCLEATE CELLS IN HAMSTER TUMOURS INDUCED BY MURINE SARCOMA VIRUS (MSV HARVEY)*

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We have studied the cellular relations between the multinucleate giant cells and the MSV-induced tumours of the golden hamster in which they are found. By histochemical
techniques the similarity was demonstrable between the giant cells of the "early" subcutaneous tumours and the surrounding tumour cells and also the giant cells found in some human granulomas. Electron microscopy showed that there were two types of giant cell in the subcutaneous tumours and that possible precursor cells made up much of the cellular bulk of the tumours at this stage. In tumours involving striated muscle three types of giant cell were seen: (1) multinucleate degenerating striated muscle; (2) multinucleate macrophages; (3) another multinucleate cell probably related to striated muscle. Results indicate that the giant cells in tumours involving muscle arise in response to or as part of the extensive cellular destruction caused by the infiltrating tumour.

34. THE DEVELOPMENT OF "SPONTANEOUS" MALIGNANT CHANGE
IN VITRO IN CELLS FROM YOUNG AND OLD MICE

L. M. Franks

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The ability of mouse cells to produce malignant tumours when retransplanted into syngeneic hosts after cultivation in vitro was used as a system for testing the tumour-producing potential of cells from animals of different ages. Thirty-six cell lines were established from various organs of embryo (18 days), young (3-20 days) and old (28-34 mth) C3H and C57(a1) Icrf mice. Six of 14 lines from young mice and 9 of 21 lines from old mice have so far produced tumours on subcutaneous inoculation into syngeneic mice. There did not seem to be a constant relation between malignant transformation and the length of the lag phase before rapid in-vitro growth began, the growth rate, the method of initiation or transfer of cultures, extensive cell contacts, or age and strain of the donor tissue. Virus particles (C type) were present in both tumour and non-tumour lines.

35. NATURALLY OCCURRING TUMOURS AND OTHER LESIONS OF THE DIGESTIVE TRACT IN UNTREATED C57BL MICE

C. Rowlatt, L. M. Franks, M. U. Sheriff and F. C. Chesterman

Imperial Cancer Research Fund, London, W.C.2

A wide range of tumours of the intestinal tract was found in 97 old C57BL mice in a series of 962 mice in which a full autopsy was carried out. The epithelial tumours included polyps of the forestomach (2), glandular stomach (1), duodenum (41), ileum (2), caecum (5), and colon (2). Carcinomas were found in the forestomach (1), duodenum (4), jejunum (7), ileum (8), and caecum (2). There were two disseminated carcinomas. Nineteen hypertrophic duodenal plaques were also found. In addition, there were four neurofibromas, one haemangioma and nine reticulo-endothelial tumours localised in the intestinal tract.

36. NEOPLASIA IN FISH

L. E. Mawdesley-Thomas and D. H. Barry

Departments of Pathology and Histochemistry, Huntingdon Research Centre, Huntingdon

Neoplasia in fish has until recently been considered extremely uncommon, although the liver cell tumour in rainbow trout is one of the notable exceptions. However, a detailed literature search has shown that over 500 documented references to fish neoplasia exist to date. During the past 5 years, several hundred fish have been examined in these laboratories, many of which had neoplasms. The distribution of neoplasia throughout this vertebrate group is widespread and many fundamental questions arise. In contrast with mammals, in fish tumours of mesenchymal origin are most common, followed by the ectodermal epidermal
Neoplasms of the central nervous system do not appear to have been reported. The current interest in aflatoxins has indicated a marked species difference in the Salmonidae, between the extremely sensitive rainbow trout (Salmo gairdnerii) and the resistant brown trout (Salmo trutta). Some enzyme histochemical methods have been investigated in livers from these two closely related species. A marked difference in the distribution of acid and alkaline phosphatase has been found.

†37. THE DETECTION OF MYOVID CELLS IN THE HUMAN FOETAL AND NEONATAL THYMUS BY IMMUNOFLUORESCENCE

A. Hayward

Department of Morbid Anatomy, University College Hospital Medical School, University Street, London, W.C.1

38. LOCALISATION OF TISSUE ANTIGENS AT THE ULTRASTRUCTURAL LEVEL WITH PEROXIDASE-COUPLED ANTIBODIES

Ph. J. Hoedemaeker

Pathologisch-Anatomisch Laboratorium, Groningen, Holland

39. A COMPARATIVE STUDY OF HUMORAL AND CELL-MEDIATED IMMUNITY INDUCED IN THE GUINEA-PIG BY THE GINGIVAL AND SYSTEMIC ADMINISTRATION OF ORAL BACTERIA

J. M. A. Wilton

Department of Microbiology, Guy's Hospital Medical School, London, S.E.1

40. THE FINE STRUCTURE OF GRANULOMAS IN SARCOIDOSIS, KVEIM TEST AND TUBERCULOSIS

W. Jones Williams, D. A. Erasmus, E. M. Valerie James and T. Davies

Department of Pathology, Welsh National School of Medicine, Cardiff

41. GRANULOMA FORMATION IN LYMPH-NODES

J. L. Turk and S. M. Gaafar

Department of Immunology, Institute of Dermatology, London, E.9

42. OBSERVATIONS ON STIMULATED LYMPHOCYTES WITH THE SCANNING ELECTRON MICROSCOPE

J. Clarke, D. A. Willoughby and J. Salsbury

Departments of Anatomy, Pathology and Haematology, St Bartholomew's Hospital Medical College, London, E.C.1

43. PROPERTIES OF THE HUMAN RETICULAR CELL

A. Edna Davidson and A. E. Stuart

Department of Pathology, University of Edinburgh

† Synopses of microbiological and immunological papers are printed in the Journal of Medical Microbiology.
44. Antibody production in the chicken after injection of human serum albumin (HSA) in complete Freund-type adjuvant
Valentine I. French, J. M. Stark and R. G. White
Department of Bacteriology and Immunology, University of Glasgow

45. Production of opacity in serum by group-A streptococci and its association with the presence of M-antigen
Jean P. Widdowson, W. R. Maxted and Doris L. Grant
Central Public Health Laboratory, London, N.W.9

46. Bacterial iron metabolism and resistance to infection
J. J. Bullen and Henry J. Rogers
National Institute for Medical Research, Mill Hill, N.W.7

47. Distribution of anaerobic sarcinae in human faeces
J. S. Crowther
Wright-Fleming Institute, St Mary's Hospital Medical School, London, W.2

48. Phage-typing for coagulate-negative staphylococci
R. E. O. Williams and Jean Corse
Wright-Fleming Institute, St Mary's Hospital Medical School, London, W.2

SPECIALIST GROUP IN IMMUNOPATHOLOGY
Convener: E. J. Holborow
The cytoarchitecture of lymphoid tissues in relation to function
Chairman: Professor R. G. White

49. Experimental definition of the thymus-dependent lymphoid cell population
Delphine M. V. Parrott and M. A. B. de Sousa
Department of Immunology, Western Infirmary, Glasgow

50. The relationship between afferent lymph cells and germinal centres
R. Kelly
National Institute for Medical Research, London

51. The localisation of altered IgG and soluble immune complexes in germinal centres in guinea-pigs and mice
E. J. Holborow and J. C. Brown
M.R.C. Rheumatism Research Unit, Taplow
52. **Morphology of lymph-nodes in Waldenström's macroglobulinaemia**

   C. V. Harrison
   
   *Royal Postgraduate Medical School, London, W.12*

53. **The background changes in the Hodgkin's lymph-node**

   A. G. Stansfeld
   
   *St Bartholomew's Hospital Medical College, London, E.C.1*

54. **The test for SH-Australia antigen in viral hepatitis**

   G. C. Turner and G. B. Bruce White
   
   *Public Health Laboratory, Liverpool L3 5SU*

55. **The growth of viruses in organ cultures of intestinal epithelium**

   D. Rubenstein and D. A. J. Tyrrell
   
   *Clinical Research Centre Laboratories, Mill Hill, London, N.W.7*

56. **Studies on influenza virus type C**

   A. K. Prasad and J. W. Czekalowski
   
   *Division of Virology, Bacteriology Department, School of Medicine, Leeds 2*

57. **Immunity to Louping-ill: a British arbovirus model of general interest**

   J. G. Brotherston
   
   *Moredun Research Institute, Edinburgh EH17 7JH*

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**DEMONSTRATIONS**

58. **Hyperplasia of bronchial muscle in chronic bronchitis**

   S. Hossain and B. E. Heard
   
   *Department of Pathology, University of Edinburgh*

59. **The histogenesis of tubule formation during resorption of autotransplanted liver fragments**

   A. A. Shivas and A. McL. Jenkins
   
   *Department of Pathology, University of Edinburgh*
60. Problems in thyroid carcinoma

I. Doniach, G. Sclare and E. D. Williams

London Hospital, London, E.1, Bangour General Hospital, West Lothian, and Welsh National School of Medicine (Thyroid Tumour Panel)

61. Quantitation of tissue components in lung and bone by a new automated technique

M. Coyne, F. H. Doyle, G. R. Massarella, E. D. Williams and A. Tha Aung

Royal Postgraduate Medical School, London, W.12, and The Welsh National School of Medicine