body alone was associated with a better prognosis. The observation that the titre of antigen may fall during exacerbation of the illness and that clinical improvement may coincide with disappearance of antigen and appearance of antibody is compatible with the hypothesis of an immune complex mechanism for the pathogenesis of polyarteritis nodosa. Such a mechanism is also suggested by analogy with much of the symptomatology, including arthralgia, myalgia, urticaria, and glomerulonephritis, and the characteristic features of human or experimental serum sickness.

Mechanisms of immune complex induced nephritis

J. G. P. SISSONS (Department of Medicine, Royal Postgraduate Medical School, Hammersmith) The particular susceptibility of the kidney to involvement by circulating immune complexes (IC) results, at least in part, from its anatomical structure with high intracapillary pressure and blood flow; reduction of renal blood flow reduces IC deposition. However, the recent claim for a specific receptor for C3b in the human glomerulus suggests another potential mechanism of IC localization. Local release of vasoactive amines from platelets (Gelfand et al, 1975), brought about by the release of a platelet activating factor from basophils, increases glomerular basement membrane permeability and is one determinant of IC localization in experimental nephritis.

The mediation of allergic glomerular injury has been studied mainly in experimental acute IC nephritis and nephrotoxic serum nephritis. In the acute IC model, glomerular injury can occur independently of C and polymorphonuclear leucocytes (PMN) (Henson and Cochrane, 1971). In the chronic IC model, defibrination or massive heparinization prevents crescent formation (Thomson et al, 1975) but the role of C and PMN have not been assessed. However, in the nephrotoxic serum model PMN-mediated damage can occur independently of C5, possibly because PMN have an Fc receptor.

The size and rate of deposition of IC appear to determine the histological pattern of nephritis in experimental models, and morphological variations in human nephritis may occur on a similar basis.

It has been postulated that relative immunodeficiency may predispose to the development of spontaneous IC disease (Alpers et al, 1972; Peters and Lachmann, 1974). There is no direct evidence for this in human nephritis, except perhaps in rare patients with genetic C deficiencies. In the majority of patients with isolated nephritis of presumed IC aetiology definite antigens and circulating IC can still not be identified, making more logical approaches to therapy difficult.

References


Enzyme defects in mucopolysaccharidoses

I. C. BARNES and C. A. PENNOCK (Department of Chemical Pathology, Bristol Royal Infirmary, Bristol) The mucopolysaccharidoses are a group of inherited connective tissue disorders in which excessive cellular accumulation and urinary excretion of glycosaminoglycans (GAG) occur. They are now recognized as disorders of GAG degradation affecting metabolism of heparan sulphate, dermatan sulphate, and keratan sulphate. In the past three years all of the enzymes which are either absent or show diminished activity have been identified. Types I H (Hurler) and I S (Scheie) are deficient in α-L-iduronidase; type II (Hunter) in dermatan sulphate sulphatase; type III (Sanfilippo) subtype a in heparan sulphamidase, and subtype b in N-acetyl-α - D - glucosaminidase; type IV (Morquio) in N-acetyl-hexosamine - 6 - sulphate sulphatase, type VII (Maroteaux-Lamy) in N-acetylglactosamine-4-sulphate sulphatase, and type VII in β-glucuronidase.

The importance of these recent discoveries is that definitive diagnosis may be achieved, antenatal diagnosis is now available, and enzyme replacement therapy is possible. However, a number of practical difficulties may be encountered when the enzymes are assayed, especially on cultured amniotic fluid cells or cultured fibroblasts. Most of the enzymes require a natural substrate which may be difficult to purify, or a suitable artificial substrate which may be difficult to synthesise.

Advantages of the 'blind simulated clinical' specimens in quality control in microbiology

W. A. BLACK and SUE DORSE (Department of Microbiology, University Hospital, Ontario, Canada) The use of recognizable 'specimens' either in the form of lyophilized cultures or simulated clinical specimens is suitable for assessing the best performance of a laboratory in bacterial identification and antibiotic sensitivity testing. It may also be the only technique which is feasible when the participating laboratories are spread over a large geographic area. However, the test conditions are abnormal, and this method of control gives little indication to the laboratory director of the real quality of work in his laboratory.

Our regional programme compared data retrieved from 'blind, simulated clinical' specimens and lyophilized specimens using the same organisms in each specimen type. Six surveys were carried out over two years with an average of six simulated 'specimens' per survey, usually two 'urines', two 'faeces', and two 'pus swabs'. These specimens were introduced surreptitiously into the 17-20 participating laboratories. To arrange this properly, involved about 1000 miles of travel per survey. Major quantitative and qualitative differences in performance with simulated and lyophilized test specimens were noted. In particular, whereas the putative origin of the specimen did not affect performance with the lyophilized specimens, it played a major role in performance with the simulated specimens, showing for the latter deteriorating performance in the order faeces > pus > urine. Bacterial identification was noticeably better with lyophilized specimens where this depen-
The Association of Clinical Pathologists: 95th general meeting

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Leucocyte ascorbic acid in abnormal leucocyte states

G. M. G. BARTON AND O. S. ROATH (Department of Pathology, General Infirmary, Salisbury, and Department of Haematology, Southampton University) The leucocyte ascorbic acid (LAA) content is the most commonly used method of examining body vitamin C status, but no corrections or interpretations are made relating to the type or maturity of the leucocytes or whether a recognizable leucocyte disorder is present. Disorders with a high preponderance of one type of leucocyte were therefore investigated, noting that abnormal or immature cells might be present. The LAA was estimated in cases of infectious mononucleosis, reactive leucocytosis, and various types of leukaemia. Note was made of patients on cytotoxic drugs. Results show that the LAA content in most of the leukaemias, acute and chronic, was normally low. In infectious mononucleosis, some 50% were low. In patients with leucocytosis there was a wide scatter of levels. About half of the patients on cytotoxic drugs showed low levels. This might reflect their underlying condition. A significant depression of LAA values was found in pregnant patients. In none of these subjects was there any evidence of overt scorbuts or deficiency of vitamin C in the diet. It is therefore concluded from these studies that LAA resides largely in normal mature polymorphs, and that its assay in abnormal leucocyte states may be misleading as an index of body vitamin C status.

Value of microbiological examination at necropsy on the newborn

ROSA LINDE HURLEY AND J. PRYSE-DAVIES (Institute of Obstetrics and Gynaecology, Queen Charlotte’s Hospital for Women, London) Microbiological examination was made on material taken at necropsy on 585 of 613 (95.4%) neonates over a seven-year period. The specimens examined included cerebrospinal fluid, heart blood, and bronchial swabs. Bacteriological studies were made routinely, and virological studies where indicated by the necropsy findings. The microbiological findings, particularly those relating to neonatal meningitis or septicaemia, will be described briefly, and the value of these investigations as a routine adjunct to the necropsy will be illustrated.

Grade of histological differentiation, glutamate dehydrogenase activity and alphafetoprotein production in human hepatocellular carcinoma

P. P. ANTHONY (Bland-Sutton Institute of Pathology, Middlesex Hospital, London) C. L. VOGEL AND R. I. GLAZER (Emory University, Atlanta, Georgia, USA) and K. R. MCINTIRE (National Cancer Institute, Bethesda, Maryland, USA) Activity of glutamate dehydrogenase (GDH) in the liver and serum levels of alphafetoprotein (AFP) were correlated with the degree of histological differentiation in cases of human hepatocellular carcinoma to see if a metabolic behaviour pattern, similar to that seen in experimental animal tumours, could be detected.

GDH activity was measured spectrophotometrically in tumour tissue as well as in adjacent normal or cirrhotic liver in 19 patients. AFP levels were determined in these as well as in a further 163 patients by qualitative immunodiffusion and quantitative radioimmunoassay.

No differences in GDH activity were detected between normal or cirrhotic liver tissue. In hepatocellular carcinoma tissue, GDH enzyme activity was significantly reduced and this decrease was proportionately greater in poorly differentiated tumours. In this latter group qualitative immunodiffusion for AFP was more frequently positive and quantitative radioimmunoassay showed higher serum levels. Concurrent estimations of serum protocollagen, proline hydroxylase, glutamic-oxaloacetic transaminase, and alkaline phosphatase showed elevated levels in most patients irrespective of the grade of tumour.

These data suggest that patterns of metabolic behaviour exist in human hepatocellular carcinoma which can be related to the degree of differentiation and growth rate of the tumour.

Fatal post-traumatic vertebro-basilar ischaemia

R. A. GOODBODY (Department of Neuroradiology, Southampton University General Hospital) Hutchinson and Yates (1966) reported spasm and thrombosis of an extracranial carotid artery as being responsible for fatal cerebral infarction. Animal experiments have suggested that simple spasm of these arteries may be...