disease, and to B lymphocyte reactions in this disease.

Esterase and Acid Phosphatase in the Identification of Cell Type in Leukaemia

V. JAMES AND P. W. PRICE (*University of Sheffield*) Since the evolution of different treatment regimes for the various leukaemias, it has become more important to make the initial classification as accurate as possible. The identification of cell type in leukaemia based only on the appearances of Romanowsky-stained blood and bone marrow films aided by the well established cytochemical reactions (peroxidase, PAS etcetera), can be difficult and often unreliable.

Esterase histochemistry can provide valuable assistance towards the identification of granulocytes, monocytes, lymphocytes, and their precursors¹. Using a variety of naphthol esters as substrate various patterns were obtained. The best differentiation between granulocytes and cells of the monocyte series was observed following the sequential use of naphthol AS-D chloroacetate and α -naphthol acetate, employing azocouplers of different colours. Applying these techniques, we were able, in some cases, to make diagnoses which could not have been reached without the results of esterase histochemistry.

Seven isoenzymes of acid phosphatase have been isolated from human leucocytes, of which isoenzyme 5 alone exhibits marked resistance to inhibition by 0.05 M L(+) tartaric acid. Isoenzyme 5 is demonstrable in the abnormal cells in 'hairy cell' leukaemia whereas most other haemopoietic cells do not contain cytochemically detectable amounts². We have demonstrated tartrate-resistant acid phosphatase in the abnormal cells of a number of patients previously diagnosed as suffering from one of the lymphoproliferative malignancies, thereby establishing the diagnosis of 'hairy cell' leukaemia in these cases.

In the light of these findings we feel that increased use of these techniques would enable accurate diagnoses to be reached in more patients.

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The Heparin-thrombin Clotting Time in Clinical Medicine

J. R. O'BRIEN, M. ETHERINGTON, AND P. LAWFORD (*Central Laboratory, Portsmouth*) We report that the heparin-thrombin clotting time of plasma is abnormally long in all cases of idiopathic thrombocytopenic purpura studied and abnormally short in diffuse intravascular coagulation. This suggests that this test, the heparin-thrombin clotting time, is influenced by platelet turnover and supports the concept that platelets are disposed of in an entirely different manner in these two conditions. These findings also suggest that a short heparin-thrombin clotting time may reflect intravascular platelet breakdown and depend on liberated platelet factor 4.

The heparin-thrombin clotting time is shorter than normal in patients after recovery from myocardial infarction, in atherosclerosis with no history of myocardial infarction, in patients with a history of deep vein thrombosis, and in an assorted group of patients with malignant disease. In the first patient with recurrent pulmonary embolization studied in detail heparin and probably aspirin normalized the heparin-thrombin clotting time. It seems this test may have an important place in assessing platelet abnormalities in vascular disease.

The Kidney in Diabetes Mellitus

D. B. BREWER (*Department of Pathology, University of Birmingham*) The renal lesions characteristically associated with diabetes mellitus are: (1) Armani-Ebstein change; (2) necrotizing papillitis; (3) diabetic glomerulosclerosis.

Armani-Ebstein change, deposition of glycogen in the tubules, although very specific, appears to be of no functional significance.

Necrotizing papillitis is an important and serious complication. It appears to result from a combination of urinary tract infection and diabetes. It accounts for a large proportion of all cases of necrotizing papillitis seen at necropsy. The figures vary from 44 to 73% but will obviously vary with the incidence of other causes of necrotizing papillitis, such as analgesic nephropathy.

The glomerular changes are very common. The important lesions are the nodular and diffuse forms of diabetic glomerulosclerosis. Although they are

morphologically distinct they probably result from the same underlying process. The incidence of the changes increases with the duration of the diabetes.

The clinical manifestations of these glomerular changes are proteinuria, oedema, hypertension, and renal failure. However, the correlation between the histological appearances and clinical manifestations is not very close although in general, patients with the most severe glomerular damage have the most severe clinical manifestation.

Similarly, the correlation both between prognosis and rate of progression of the renal disease and the extent of the glomerular damage as seen in the initial biopsy is not very good. Although as would be expected, in general, those with the most severe lesions have the worst prognosis.

The Freeze-etching Approach to the Study of Islet Pathophysiology in Diabetes

L. ORCI (*Institute of Histology and Embryology, University of Geneva, Switzerland*) Freeze-etching was used to investigate possible abnormalities of membrane systems in islet cells from diabetic Chinese hamsters. Age- and sex-matched animals were classified according to their past history as 'control' (aglycosuric), non-ketotic diabetic, and ketotic diabetic respectively. Comparison of islet cells by thin-section and freeze-etch electron microscopy revealed that A-cells could be unambiguously identified in freeze-etching by the presence of characteristic bundles of thick filaments in the perinuclear region. In fracture faces of the plasma membrane of B-cells, obvious alterations were found in the number, size, and distribution of membrane-associated particles. In B-cells from 'control' animals, these particles ($1217 \pm 29/\mu^2$) were distributed in a random pattern and had a mean size of $95.0 \pm 0.6 \text{ \AA}$. In B-cells from diabetic and ketotic animals, the particles were aggregated leaving completely smooth areas in the membrane; their mean number and size were also altered ($767 \pm 60/\mu^2$; $102.1 \pm 1.1 \text{ \AA}$ in ketotic animals, $p < 0.005$ for both values). In addition to these changes in the plasma membrane, an augmentation in the number of nuclear pores was observed in A- and B-cells of diabetic and ketotic animals. These findings point to alterations in membrane systems as possible determinants for insular dysfunction in diabetes mellitus.