The Association of Clinical Pathologists: 93rd general meeting

The 93rd general meeting was held at Imperial College, London, from 18 to 20 September 1973. Abstracts of most of the scientific communications and of some of the papers read at symposia on 'Some aspects of diabetes' (Chairman: Professor V. Marks), 'Urinary tract infections in paraplegics' (Chairman: Dr A. Percival), and 'Granulocyte function' (Chairman: Dr H. E. M. Kay) follow. A fourth symposium, 'Clinical pathology in other parts of the world' (Chairman: Dr M. G. Rinsler) was held on the morning of 19 September. The Presidential Address, 'Beyond "cogwheel" doctors and the management of the National Health Service', was given by Dr Frank Hampson. Dr P. I. A. Hendry, President both of the Royal College of Pathologists of Australia and of the World Association of Societies of Pathology, gave an illustrated talk on the forthcoming 9th Congress of the World Association of Societies of Pathology, to be held in Sydney in October 1975.

Chronic Granulocytic Leukaemia in Pregnancy

H. G. H. RICHARDS AND A. S. D. SPIERS (*Lincoln County Hospital, Lincoln, and Royal Postgraduate Medical School, Hammersmith*) Chronic granulocytic leukaemia (CGL) was diagnosed in two young women during early pregnancy as a result of routine blood examinations. Both responded satisfactorily to splenic irradiation with shielding of the uterus. The pregnancies proceeded uneventfully and each was successfully delivered of a normal and subsequently healthy baby. Both mothers later underwent elective splenectomy during a period of satisfactory haematological control; no operative or postoperative complications occurred. Although both patients have shown some thrombocytosis and peripheral blood basophilia since splenectomy, they remain well 60 and 30 months after diagnosis and 32 and 20 months after splenectomy on a continuous regime of chemotherapy in which the antileukaemia agent was varied (busulphan, 6 mercaptopurine, 6 thioguanine, and dibromomannitol). Attempts to reduce chemotherapy severely have always provoked leucocytosis with marked basophilia and some increase in immature granulocytes, marked thrombocytosis, and an outpouring of large nuclei fragments resembling those of megakaryocytes. No thrombotic complications occurred, but in one case temporary acne rosacea, herpes simplex, and erythema nodosum developed following prolonged oxytetracycline and chemotherapy. Bone marrow studies before treatment and during remission phases provided interesting cytological and histological contrasts.

Plasma Erythropoietin Values in Patients with Renal Failure¹

SYLVIA W. DAVIES AND EVELINE GLYNNE-JONES (*Area Department of Pathology, Exeter*) The post-hypoxic mouse method (Camiscoli and Gordon, 1970) has been used to measure plasma erythropoietin. Values expressed as percentage uptake of ⁵⁹Fe in mice after 1.0 ml test plasma are: normal males, mean $7.42 \pm 6.73\%$; normal females, mean $6.79 \pm 4.71\%$; males: females $p > 0.7$. These values are equivalent to 0.3 ± 0.25 and 0.27 ± 0.17 units of standard reference B human urinary erythropoietin.

Plasma of patients with chronic renal failure gave mean values of $9.71 \pm 7.28\%$ ⁵⁹Fe uptake per ml equivalent to 0.4 ± 0.3 units standard erythropoietin. The significance of our results will be discussed.

Reference

Camiscoli, J. F., and Gordon, A. S. (1970). In *Regulation of Hemopoiesis*, vol. 1, *Red Cell Production*, edited by Albert S. Gordon, p. 369. Appleton-Century Crofts, New York.

¹This work was carried out with the help of a research grant from the South-West Regional Hospital Board.

The Development of Myelomatosis in a Case of Existing Hodgkin's Disease

J. C. CAWLEY, A. H. GOLDSTONE, AND JEANNE ARNO (*Addenbrooke's Hospital, Cambridge*) This paper describes the clinical and pathological features of a patient with Hodgkin's disease treated by chemotherapy alone who developed fulminating myelomatosis approximately 26 months after the initial diagnosis of Hodgkin's disease.

This previously fit man presented at the

age of 65 years with fever and bilateral cervical adenopathy. Biopsy showed nodular sclerosing Hodgkin's disease, and staging without laparotomy or liver biopsy indicated the presence of at least stage IIIB disease. He was treated with six courses of MOPP (mustine, oncovin, procarbazine, and prednisone) chemotherapy, and this was followed by continuous chlorambucil. He went into a good clinical remission after the third course of combination chemotherapy, and this remission continued for approximately two years when biopsy-proven relapse in the tonsil occurred. Treatment with MOPP therapy was started once more, but he rapidly became pancytopenic, and remained so for the last six weeks of his life despite steroid, and later oxymethalone therapy.

Immediately before this period of pancytopenia, the total protein level was 6.3 g%, there was no definite serum paraprotein, and marrow aspirate contained less than 5% plasma cells. However, six weeks later the total protein was 10 g%, there was a full monoclonal γ peak, and the marrow aspirate was extensively replaced by plasma cells. The paraprotein proved to be IgGk in type, and immunoglobulin showed moderate immune paresis; no Bence Jones proteinuria was demonstrated. Shortly after the diagnosis of myelomatosis, the patient died as a result of pulmonary aspergillosis and probable fungal septicaemia, before antimyeloma therapy could be introduced.

The possible significance of this association between HD and myelomatosis is discussed in relation both to the previous literature concerning the development of a second malignancy in Hodgkin's

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.

References

- ¹Li, C. Y., Lam, K. W., and Yam, L. T. (1973). Esterases in human leukocytes. *J. Histochem. Cytochem.*, **21**, 1-12.
- ²Yam, L. T., Li, C. Y., and Finkel, H. E. (1972). Leukaemic reticuloendotheliosis: the role of tartrate-resistant acid phosphatase in diagnosis and splenectomy in treatment. *Arch. intern. Med.*, **130**, 248-256.

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 membranes, 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 of insular dysfunction in diabetes mellitus.