sufficient to damage the brain. A fit man of 23 received manipulation for a minor neck injury from an osteopath. Two hours later he was dizzy and nauseated before collapsing. Headache followed and he became drowsy and comatose. Investigations suggested a brain stem lesion but he died in coma undiagnosed after 38 hours.

Necropsy revealed bilateral symmetrical cerebellar infarction but the vertebral-basilar arterial tree was healthy and patent. One vertebral artery was surrounded by a recent haematoma within its canal. Microscopy showed acute haemorrhagic cerebellar infarction and widespread anoxic ischaemic damage in the medulla and distal pons. Brain stem lesions were symmetrical and included generalized acute congestion and acute haemorrhagic infarction of the floor of the fourth ventricle. At the cellular level damage varied from acute neuronal swelling to ischaemic change and homogenizing change. Myelin sheaths were swollen and beaded.

This case demonstrates that injury to the neck may be followed by arterial spasm sufficiently severe and prolonged to result in fatal cerebral infarction. The potential danger of manipulative therapy to a healthy young subject is illustrated. The recognition of arterial spasm is of great importance in treating these cases.

Serial liver biopsies in hepatitis B antigen carriers

E. TAPP (Department of Pathology, Withington Hospital, Manchester) Initial liver biopsies from asymptomatic antigen-positive blood donors showed a range of histological appearances varying from minor parenchymal lesions to cirrhosis. Twenty of these individuals have now been followed up for periods of between two and four years and during that time have had at least one further liver biopsy.

The histological appearances of these biopsies will be described and it will be seen that while the one case which showed cirrhosis initially and one which showed chronic aggressive hepatitis initially now have les inflammatory cell activity in the liver, there are two cases of chronic aggressive hepatitis which appear to have progressed to cirrhosis and one which now shows increased inflammation of the liver. Further evidence of the progressive nature of the liver disease is seen in two cases which showed chronic persistent hepatitis initially and which now have evidence of aggressive hepatitis, and three cases which showed only focal parenchymal lesions in the first biopsy and which now have the portal tract infiltrations of chronic persistent hepatitis.

Incidence of auto-immune thyroiditis

T. BIRD (Department of Pathology, Newcastle General Hospital) An area near Newcastle upon Tyne, whose adult population is closely matched for age, sex, and socioeconomic groups to the population of Great Britain, has been studied for the prevalence of subclinical hypothyroidism and its possible association with hyperlipidaemia and ischaemic heart disease. A random one-sixth of the population, 2779 adults, were seen in 1973-74. Antibodies to thyroglobulin and thyroid cytoplasm were present in 6-8% (2-7% of men and 10-3% of women). Serum thyroid stimulating hormone (TSH) was raised above 6mU/l in 5%, and 3-5% had both thyroid antibodies and raised TSH. Thus half of the people with antibodies were regarded as having evidence of subclinical hypothyroidism (Evered et al, 1973). One thousand consecutive adults, 590 men and 410 women, coming to necropsy in Newcastle General Hospital in 1974 were specially examined for lymphocytic infiltration of the thyroid and for thyroid antibodies in postmortem blood. A preliminary study had shown that antibodies could be demonstrated post mortem and this was confirmed during the survey. The lymphocytic infiltration has been graded similarly to that of Williams and Doniach (1962). Minor degrees of infiltration with only occasional small foci were seen in 10-8% of men and 19-5% of women, with more severe grades in 2-7% of men and 14-8% of women. A close correlation was demonstrated between the degree of infiltration and the presence of antibodies. Of the men 2-7% and of women 13-4% had antibodies but only seven patients of 144 with minor infiltration had antibodies, while 62 out of 85 with more severe infiltration had antibodies.

These results help to confirm the suggested association between lymphocytic infiltration of the thyroid, usually demonstrated at necropsy, and the presence of thyroid antibodies, usually demonstrated in different groups of living patients.

References


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their clinical significance. A study of the pumps in actual use in renal units demonstrated many variables, which made an initial clinical evaluation impracticable. A review of the literature revealed small numbers of experiments using complex circuits and relatively large volumes of blood to simulate clinical practice.

A simple sterile circuit was designed containing 35ml, constructed from standard medical grade plastic tubing and fittings. The volume was such that the required number of circuits to test all the pumps could be filled from one unit of fresh anticoagulated blood obtained from the Blood Transfusion Service. The general physical characteristics of the pumps were noted in order to relate them to variations in haemolytic rates. The induced flow pattern was investigated with an electromagnetic transducer in the circuit.

Blood was pumped under standard conditions and together with an unpumped control was tested for haemolysis. Immediate red cell damage was indicated by plasma haemoglobin and lactate dehydrogenase levels. The pumps fell into four groups with increasing haemolysis. In a sequence of tests on any pump the haemolysis was found to be proportional to the pumped cell volume. Sublethal or delayed damage to red cells was measured by the autohaemolysis test, which placed the pumps in only two groups, the first showing only minimal haemolysis. While laboratory in vitro testing has shown differences between pumps, the clinical relevance has yet to be established.

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Preleukaemia and smouldering leukaemia

GILLIAN MILNER (Department of Haematology, Manchester Royal Infirmary) The problems of delineation of the preleukaemic states are well known, and an absolute diagnosis can be made only in retrospect on evolution of a full-blown leukaemic state. Certain conditions carry an above average risk of developing leukaemia. These include states where initial marrow damage appears to predispose in some cases towards the later emergence of a leukaemic clone. Such conditions include Fanconi’s anaemia, paroxysmal nocturnal haemoglobinuria, aplastic anaemia, and pure red cell aplasia. In all such cases the type of leukaemia which evolves is nearly always acute myeloblastic or monomyeloblastic. Reports of a preleukaemic state in active lymphoblastic leukaemia are rare.

Some cases which later evolve to acute leukaemia present with no preceding haematological disorder but with an increased proportion of immature granulocytes in the bone marrow. This type has been variously termed smouldering leukaemia, or refractory anaemia with excess myeloblasts. Here the diagnosis may be less in doubt, but nevertheless the course may be very chronic, and as these patients are often elderly, death may occur from other pathology or as a result of the effects of anaemia, neutropenia or thrombocytopenia before evolution to a more acute disease takes place.

Diagnostically the most difficult group of patients are those presenting with one or more refractory cytopenias. Certain features which may indicate a preleukaemic rather than a benign state can be described.

There is at present no readily available method of predicting imminent evolution to full-blown leukaemia. The course of such conditions is very variable. Observation, with appropriate supportive therapy, is probably indicated for the majority.

Colony studies in refractory cytopenia

N. G. TESTA AND T. M. DEXTER (Patterson Laboratories, Christie Hospital, Manchester) Cell culture methods presently available allow the study of progenitor cells in the haemopoietic tissues by measuring their capacity of producing granulocytic and erythroid colonies in vitro. The granulocytic precursor cells of patients with overt leukaemia have been extensively studied, but little is known about the behaviour of such cells in haemopoietic abnormalities, which in some cases precede the development of acute leukaemia.

A group of 24 patients with refractory cytopenias (both with and without excess of marrow myeloblasts) have been studied by measuring the colony-forming capacity of granulocytic and erythroid progenitor cells.

Granulocytic colony-forming cells were absent, or greatly diminished in number, in 18 of these patients. They also tended to have small numbers of cells able to form erythroid colonies. This defect in colony formation (which occurs also in acute leukaemias) was found in the absence of clinical or morphological evidence of leukaemic change and was maintained unaltered for several months.

During the course of the study (18 months) two patients developed acute granulocytic leukaemia preceded or accompanied by a marked increase in the number of granulocytic clusters (smaller than colonies) which develop in vitro.

Chronic myelomonocytic leukaemia

C. G. GEARY (Department of Haematology, Manchester Royal Infirmary) Myelomonocytic leukaemia is usually regarded as one of the morphological variants of acute myeloid leukaemia, having certain distinctive, though not pathognomonic, clinical features, such as gum hypertrophy and lysozymuria, but leading a rapidly fatal course if a remission is not achieved.

However, a minority of patients, mostly elderly, have a form of the disease which leads to a relatively chronic or even ‘benign’ course. Because of the poor results of intensive chemotherapy in the elderly, it is important to recognize this group. They show the following features: an insidious onset—in some cases a refractory cytopenia or monocytosis is noted years before the definitive diagnosis; and relatively slight anaemia and toxemia. Most cases show a mixed granulocytosis and monocytosis in the blood, the total WBC ranging from 10 to 10000/µl; a cell with indeterminate morphology (the ‘paramyeloid’ cell) is particularly characteristic. Most cases are moderately thrombocytopenic, and some show a bleeding tendency, leading to iron deficieny.

The marrow is characteristically hypercellular, shows granulocytic hyperplasia, and, in contrast to the ‘mature’ peripheral blood picture, the percentage of blasts and promyelocytes is high. Most have high serum and urinary lysozyme levels. The value of cytochemistry, particularly the combined esterases method, will be discussed.

Myelomonocytic leukaemia can be regarded as a disease with an extremely wide spectrum, ranging from florid, acute disease to the indolent form described here and probably including those forms of the preleukaemic state which are characterized by defective granulocyte maturation and monocytoid features in the marrow. It is of interest that several of our patients eventually died with the picture of acute leukaemia.

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