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 packed 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 monomyelo-

blastic. Reports of a preleukaemic state in acute 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 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 refractory cytopenia or monocytosis noted years before the definitive diagnosis; and relatively slight anaemia and toxæmia. Most cases show a mixed granulocytosis and monocytosis in the blood, the total WBC ranging from 10 to 100000. A cell with indeterminate morphology (the 'paramyeloid' cell) is particularly characteristic. Most cases are moderately thrombocytopenic, and some show bleeding tendency, leading to iron deficiency.

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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