meetings every six months throughout the ensuing five years, to give a broader understanding of the problems and successes with such patients and the skills and attitudes needed in achieving these results.

[1] Arthritis and Rheumatism Council, Workshop on Undergraduate Education in Rheumatology, Manchester, 1979.

Cell surface markers in chronic lymphatic leukaemia

Chronic lymphatic leukaemia (CLL) is the most common leukaemia seen in Western countries, though characteristically it is found in elderly patients. In about a third of cases the disease is diagnosed by accident when blood tests are done for other reasons or when splenomegaly or lymphadenopathy is detected on routine examination. Some degree of clinical and morphological overlap exists between CLL and other lymphoproliferative disorders, and the identification of immunological markers on the lymphocyte cell surface is becoming increasingly valuable in separating these diseases. Lymphocytes can be classified by their reaction with sheep erythrocytes to form E-rosettes (T cells) or by the presence of surface immunoglobulin (B cells). Other cell surface markers have already helped in subclassifying acute lymphoblastic leukaemia[1 2] and may help to classify unusual cases of CLL.[3]

IgM and later IgD appear on the lymphocyte surface in fetal life,[4] so that cells possessing both surface immunoglobulins may be assumed to be more mature than those with IgM only. The cells that proliferate in CLL are monoclonal B lymphocytes that possess both IgM and IgD on their surface[5] as well as complement receptors. In vitro these cells are able to synthesise immunoglobulin light chains,[6 7] and occasionally patients are found to have a monoclonal immunoglobulin, usually IgM, in the serum. In these cases the serum immunoglobulin appears antigenically identical with that on the cell surface.[8] Though the CLL lymphocyte is thought to be incapable of further differentiation, some patients show a picture of light-chain excretion, amyloidosis, and sometimes IgM paraproteins, suggesting a link with Waldenström's macroglobulinaemia and the mature plasma cell.[9]

In a few patients with CLL the lymphocytes form E-rosettes, antibodies have been found against T-cell-specific antisera,[10–12] and there are no surface immunoglobulins. These patients often have small or impalpable lymph nodes but a moderate degree of hepatosplenomegaly. Leukaemic skin infiltration is usual, and the central nervous system is occasionally affected.[12] The morphology of the lymphocytes is variable, but often there is a folded nucleus and copious cytoplasm containing azurophilic granules. Nevertheless, these patients do not have the mediastinal lymphadenopathy characteristic of T-cell acute lymphoblastic leukaemia (T-ALL) and of lymphoblastic lymphoma.[13] The lymphocytes do not contain the enzyme terminal transferase[12] present in T-ALL cells,[14] and this T-cell variant of CLL appears to result from proliferation of a mature lymphocyte clone.[12]

Diffuse lymphocytic lymphomas of well-differentiated cell type (WDLL) occur predominantly in older patients and are usually widespread at diagnosis. The appearances of lymph node biopsy samples are indistinguishable from those of the tissue infiltrates of CLL,[15] and WDLL has close clinical similarities too. Immunological studies have shown that in WDLL the lymphocytes bear monoclonal B-cell markers identical with those found in B-cell CLL,[16–19] and indeed WDLL is now thought to represent CLL without extension to the blood.

In the past it has been difficult to define CLL in terms of an absolute lymphocyte count because of the difficulty of separating CLL from benign lymphocytosis. Patients with total lymphocyte counts below $15 \times 10^9/l$ are still usually excluded.[29] Early CLL can now, however, be distinguished from benign lymphocytosis by cell surface marker studies. Patients with non-neoplastic lymphoid proliferations have a symmetrical increase in both B and T cells, whereas patients with early CLL have lymphocytes that almost exclusively show the B-cell markers of the typical disease.[21]

In a few patients with lymphosarcoma primitive lymphoid cells appear in the blood in the terminal stages of the disease. This clinical picture is usually easy to recognise, but the occasional patient who shows such cells early on presents diagnostic difficulties. Lymphosarcoma cells are often larger than mature lymphocytes, and contain variable amounts of clear grey-blue cytoplasm and a cleft or indented nucleus that usually has a characteristically primitive chromatin pattern.[22] Considerable morphological variability exists, however, and the large amounts of immunoglobulin that are seen on the surface of lymphosarcoma cells contrast with the sparse amounts found in both CLL and WDLL. This distinction provides a reliable means of separating CLL from lymphosarcoma-cell leukaemia.[17]

Prolymphocytic leukaemia (PL), first described by Galton,[23] is an unusual disease occurring predominantly in elderly men and occupying a position between CLL and lymphosarcoma-cell leukaemia. It is usually characterised by tiredness, loss of weight, sweats, fevers, massive splenomegaly, and moderate hepatic enlargement, but little or no lymphadenopathy. The blood contains many large lymphocytes with a moderate amount of cytoplasm and well-condensed nuclear chromatin with a single prominent nucleolus. Most patients have B-cell markers on the cell surfaces,[24] but Catovsky and his colleagues have shown differences in surface receptors between B-cell-CLL and B-cell-PL that may help differential diagnosis[25 26]—principally the formation of a high proportion of rosettes in the reaction with mouse red cells in CLL, but not in PL.

Other lymphoproliferative disorders that occasionally may be confused with CLL include the Sézary syndrome and hairy-cell leukaemia. The Sézary syndrome was the first clearly identified T-cell neoplasm[27] and is now known to be a malignant proliferation of T helper cells.[28 29] Its characteristic skin lesions[30] will nearly always distinguish it from CLL. On the other hand, the origin of hairy cells has been hotly debated[26] and, though they are probably B cells,[31] the diagnosis is made by methods other than surface marker studies.[26]

The identification of lymphocyte surface markers, then, is no longer the exclusive province of research workers but a practical diagnostic tool for all specialist haematology laboratories. Nevertheless, as Brouet and Seligmann[1] have recently emphasised, membrane marker studies have to be interpreted with knowledge of the methodological problems and pitfalls; no single test, or even small group of tests, is likely to give an absolutely clear indication even between T and B membrane markers. Using a panel of markers is essential for accurate conclusions. We know little so far about how membrane markers evolve on neoplastic cells, but distinct changes are known to occur—for example, cell membrane markers may

alter at relapse in childhood ALL.[32] The present classification of leukaemias and lymphomas must be extremely crude, and the advances in our knowledge that are likely to come will make some revision inevitable.

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Consultant contract improvements

Last week the CCHMS unanimously approved the improvements in consultants' contracts which its leaders had negotiated with the new Government.[1] No doubt, to most of the consultants discussing the DHSS's draft circular at the meeting (see p 949) such an outcome would have seemed improbable in the aftermath of the Review Body's disappointing pricing[2] of the revised work-sensitive contract.[3] That contract had been agreed with the previous Government only after tough and protracted negotiations. But, refusing to retreat after this medicopolitical reverse, Mr A H Grabham and Mr D E Bolt, then the chairman of the CCHMS and its Negotiating Subcommittee, returned to impress on the new Secretary of State the importance of acting to boost consultants' low morale. As well as persuading Mr Patrick Jenkin to make a joint approach with the BMA to the Review Body to obtain redistribution to consultants' basic incomes of the £8m earmarked for the now rejected emergency recall fees,[4] they secured worthwhile improvements to the existing contract. Indeed, the new package may have greater appeal than the rejected contract to those doctors with reservations about the possible effect of the latter on their professional status.

What are the principal changes in the latest package? Firstly, consultants holding a maximum part-time contract will be paid 10/11 instead of 9/11 of the whole time salary, with no change in their existing NHS commitments. Secondly, in future full-time consultants may do some private practice—with a limit in these earnings of 10% of their gross whole-time salary, including any distinction award. Finally, the opportunity to take the nine-session part-time contract (paid at the same rate as for the present maximum part-time contract) is to be offered for those consultants preferring a more defined NHS commitment. In that case a consultant's obligation to give substantially the whole of his time to the NHS and to give it priority at all times—described in the option agreements of 1955 and 1961—would not apply. In addition to these major changes a full-time consultant will in exceptional circumstances be able to do one paid (non-superannuable) extra session—for example, during the prolonged unexpected absence of a colleague or when a sudden increase in overall work load occurs. Two other useful changes are improved openings for consultants wishing to do less than nine sessions and top-of-the-scale starting salaries for posts that are hard to fill. Finally, the DHSS has accepted BMA proposals for reforming the distinction award system. The profession hopes that the changes will start on 1 January 1980.

The latest agreement has been criticised by some consultants. In particular, the NHS Consultants Association—which, Mr Bolt told his committee, has a membership of around 150—is worried that the Review Body will take into account the whole-timer's 10% private earnings when assessing consultants' pay. The result, the association claims, would be a relative 10% cut for those not doing private practice—and some have no opportunity or, indeed, the wish to do any. Judged by his recent letter to senior hospital staff,[5] however, the new CCHMS chairman is confident that this will not happen. The HCSA, in an unusually low-key criticism, asks why the CCHMS negotiators did not go further towards obtaining a properly priced notional half day, equal work for equal pay, and complete freedom for consultants to do what they wished with their free time. The answer is that the negotiators went for an attainable objective. The arrival of a Secretary of State keen to improve consultants' morale offered a fleeting political opening that had to be exploited quickly. Indeed, to seal his side of the bargain in an NHS that is battling with cash limits Mr Jenkin may well have had a rougher passage with his Cabinet colleagues than with the profession's representatives. The extra money needed (up to £3 million is the informed estimate) will not come from consultants' present global pay—Mr Jenkin has promised joint BMA/DHSS evidence to the Review Body on that point—though it will have to come within cash limits.

Having heard its regional representatives' views, the CCHMS was right in accepting the deal so promptly without a delaying ballot. As well as providing some welcome extra money for consultants, in future their contracts will more realistically reflect their NHS commitments. In his September letter[1] to the negotiators Mr Jenkin concluded "... I should like to stress the importance which my ministerial colleagues and I attach to improving the morale of consultants.... It is fundamental that we should restore the professional spirit which the events of recent years have done so much to shake." This deal is a first step towards both objectives.

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