radiation therapy, surgery and bone marrow transplantation have been made. However, current challenges include diminishing therapy-related morbidity and late effects and improving patients' quality of life. Advances in molecular biology, surveillance of minimal disease and novel chemotherapeutic agents may further improve the cure rates.

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Commentary

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As one of the lead investigators with the French LMB Group, Dr Patte has been involved in setting the pace for improving outcome in Burkitt's lymphoma over several years. In her useful overview she has highlighted the key areas in childhood NHL where progress has been made and those where there are still further challenges.

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Despite Burkitt's lymphoma being one of the first cancers in which clearly defined molecular mechanisms have been identified, causal mechanisms are still speculative. The recent upsurge of interest in the role of Epstein–Barr virus associated with lymphoproliferative disorders (LPD) in transplant recipients and AIDS patients will undoubtedly shed further light on this subject. With the increase in number of solid organ transplant procedures being done in children and the

ever present problem of vertical transmission of HIV, the diagnosis and management of LPD in these patients is likely to be an increasing problem. In this context the U.S. Pediatric Oncology Group (POG) registry of HIV-associated lymphomas in children and the registry of post-transplant LPD run by the UKCCSG are of particular importance.

The persisting problem of terminology was discussed by Dr Patte and the fact that the REAL classification has now been accepted in the collaborative study by the SFOP, UKCCSG and USCCG should be emphasised. If we are to take advantage of this classification and start 'talking the same language', then we should try and get used to using this slightly different terminology. In the past, the terms 'lymphoblastic' and 'large cell lymphoma' have led to confusion and difficulty in comparing treatment strategies and outcome in different national groups. Only the term 'Burkitt' has been used in common and this has been retained in the REAL classification. Distinguishing Burkitt from 'Burkitt-like' is a morphological refinement of little practical relevance. In the new classification, which is based on the previous Kiel classification, i.e. combining immunophenotyping and morphology, tumours are divided on the basis of whether the malignant cells correspond to precursor cells or peripheral cells of T and B lineage. Thus the term 'lymphoblastic' is used both for B and T lineage tumours, which mirror early precursor lymphoblastic populations. In contrast, the peripheral B tumours, namely Burkitt, Burkitt-like and diffuse large B cell, correspond to more mature lymphocytes, as do the group of peripheral T-lymphomas, which include anaplastic large cell and PTL unspecified. The continued use of the term 'lymphoblastic' when referring to pre-cursor T-lymphoblastic lymphoma is confusing and should probably now be dropped. Similarly, the loose association of a group of lymphomas under the umbrella term 'large cell NHL' is no longer useful, particularly as the anaplastic large cell subgroup has now been clearly identified, both immunologically and cytogenetically as an entity distinct from diffuse large B cell lymphoma.

The need for reliable prognostic factors is still a priority in all subgroups of childhood NHL. In pre-cursor T-lymphomas where, although the outcome in most national series is encouraging, around one third of patients still relapse. It is important to identify those patients in whom treatment intensity should be increased. No useful biological parameters have been identified to date, although the simple observation of a slow response on plain chest radiograph has been suggested to be of use. The apparently superior results from the BFM group are hard to explain as the chemotherapy strategy differs little from other national groups. Retention of CNS irradiation, an explanation for improved systemic disease control, is difficult to accept.

In peripheral B-lymphoma, both Burkitt, Burkitt-like and diffuse large B cell, where the overall cure rate now approaches 90% irrespective of stage, the priority is to identify those patients in whom treatment intensity can be decreased. There is little doubt that, with the current intensive regimens, both in Europe and the United States, a significant proportion of patients with stage II and stage III disease are being over-treated and will suffer late sequelae, such as infertility and cardiomyopathy. It could be argued that the great leap forward in cure rates for peripheral B-lymphomas in childhood, which followed the dose escalation of cyclophosphamide, methotrexate and cytarabine, in addition to a focus on minimal delay in delivery of chemotherapy, was achieved at the expense of children with localised disease whose cure rates could have been increased by a slightly more modest increase in treatment intensity. The recently published POG protocol 8106 demonstrated, in a randomised study, a significant improvement in outcome in stage III peripheral B-lymphoma, associated with fractionation and increased dose cyclophosphamide and introduction of high dose AraC. However, this was a relatively small study and it was not possible to pick out specific subgroups in whom such dose escalation was unnecessary. With the European experience where, in the late 1980s, cure rates for stage III patients began to exceed 90% and reached almost 100% for stage II disease, it became increasingly difficult to persuade oncologists to cut back on treatment intensity. The new collaborative venture between the SFOP, UKCCSG and USCCG is an important step forward, taking advantage of a large pool of patients in order to try and rapidly answer questions concerning which patients can be cured with less treatment.

The issue of how to manage ALCL (anaplastic large cell lymphoma) and to what extent this disease covers more than one biological entity is also being addressed in an international collaborative study. The recently formed Anaplastic Large Cell Intergroup is analysing retrospective data from several national groups and is involved in planning prospective randomised trials in this challenging disease. Moreover, it is hoped that the biological relevance of the t(2;5) translocation will be defined. It is clear that the Murphy staging system is inappropriate for ALCL and a new staging system based on sites of disease, as discussed in Dr Patte's review, is undergoing evaluation.

With the current battery of highly effective chemotherapeutic agents, there is little need for new conventional agents. Even the majority of patients with Burkitt's lymphoma presenting with CNS disease, who in the past had a grave prognosis, are now cured with the use of more intensive intrathecal chemotherapy and high-dose AraC. Ifosfamide has been introduced into first line protocols but the logic of using an agent which is not only inconvenient to administer but also carries additional toxicity is unclear.

The debate about the management of patients with localised pre-cursor B and pre-cursor T-lymphomas continues. Although it may seem excessive, the conventional policy of using prolonged ALL (acute lymphoblastic leukaemia) regimens for both of these groups is almost certainly necessary. Because of the comparative rarity of localised tumours, an international prospective randomised trial would be of value to determine if a shorter or less intensive treatment was appropriate for certain patients.

Although the overall cure rate, particularly for B lineage NHL, is impressive, these are tumours where there is the opportunity for novel approaches. In B NHL which is exquisitely sensitive to anything that triggers apoptosis, alternatives may be safer and effective, enabling further curtailment of toxic chemotherapy. Evaluation of such strategies may prove difficult because of a reluctance to risk any compromise on cure rate, but cytolytic or radiolabelled monoclonal antibodies, immunotherapy with anti-idiotype vaccines and antisense oligonucleotides directed against tumour specific intron sequences of c-*myc* have all shown promise and may have potential future applications.