

CHAPTER 1 FOREWORD AND INTRODUCTION

It seemed logical that guidelines be developed for the management of malignant lymphomas. Based on 2001 incidence and mortality data, malignant lymphoma (including non-Hodgkin lymphoma and Hodgkin lymphoma) represents the sixth most common cancer in both incidence and mortality in Australia. Incidence figures were of the order of 4300 new cases in Australia in 2001, with some 1680 deaths.

Data from the Cancer Council of Victoria's publication *Trends in cancer mortality, Australia 1910–1999* note that mortality from non-Hodgkin lymphoma has more than doubled since 1950 in both sexes, with annual increases of around 4% consistent with international trends. In contrast, the Hodgkin lymphoma mortality has fallen by about 2% annually and faster since the 1970s, due to improved chemotherapy. This increase in mortality from non-Hodgkin lymphoma is matched in other western countries. For example, over the last 50 years, mortality in the United States has increased from 3.2 per 100,000 person years to a rate of seven. Similarly, the Hodgkin lymphoma mortality rates decreased from 1.7 to 0.4 deaths per 100,000 person years.

There have not been any systematic surveys of lymphoma management in Australia. However, it is hard to imagine a more complex category of diseases than malignant lymphoma. The classification system is evolving rapidly. Management aims vary from curative for certain subtypes to simple palliative approaches (albeit with long survival) for other subtypes. Lymphomas represent some of the most curable of malignancies and have been a prototype for the development of multi-modality approaches to the management of cancer. The complexity of integrating surgery, radiotherapy and medical treatments is well recognised.

A major impetus for the development of appropriate guidelines is the economic burden created by the lymphomas, not only in terms of the morbidity of the disease process and its economic implication, but the costs of many of the modern treatments that employ the latest fruits of biotechnology.

A working party to develop guidelines for the management of the malignant lymphoma was assembled with assistance from Emeritus Professor Tom Reeve and Mrs Christine Vuletich of the Australian Cancer Network. It met for the first time in Melbourne in 2001. Members of the working parties (diagnostic and clinical) were selected because of their areas of expertise and to ensure a wide geographic representation reflecting the national nature of the project.¹ Separate working parties developed parts of the diagnostic process and clinical sections. In the clinical section, for simplicity and clarity, it was elected to group the various lymphomas into a clinical concept of low-, intermediate- and high-grade while using the World Health Organization (WHO) pathological classification system. The working parties decided that the management of multiple myeloma and chronic lymphocytic leukaemia would not be part of its brief.

The evidence would be researched and assigned to a level according to the following scale:

- I Evidence obtained from a systematic review of all relevant randomised controlled trials.
- II Evidence obtained from at least one properly designed randomised control trial.
- III.1 Evidence obtained from well-designed pseudo randomised controlled trials (alternate allocation or some other method)
- III.2 Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case control studies, or interrupted time series with a control group.
- III.3 Evidence obtained from comparative studies with historical control, two or more single arm studies or interrupted time series without a parallel control group.
- IV Evidence from case series, either post-test or pre-test and post-test.

In general level III evidence has not been subclassified, however, in some instances where it was possible, some subclassifications of level III evidence have been defined.

Apart from specific guidelines, key points are used in various chapters. These are items felt to be of considerable importance or recommendations, but not as strong as guidelines with specific levels of evidence.

For some clinical scenarios, high-level evidence supporting one intervention over another may not be available. Where this is the case, the guidelines say so, and make recommendations about the further research that is required. The biological and clinical complexity of lymphoma is reflected in its classification into some 30 subtypes. This has led to a massive literature (there are over 30,000 papers published in this field since 1966). It is not feasible to conduct detailed Cochrane-style analyses of the evidence available with current resources.

The recently evolving molecular, pathological and clinical subtypes, as well as new therapeutic modalities emerging from biotechnology, have resulted in some 7500 publications since 2000.

The rapid appearance of new information makes it difficult to maintain appropriately up-to-date guidance. We have included a chapter on late-breaking news, in particular, the implications of new therapeutic breakthroughs, especially with the wider use of the monoclonal antibody, rituximab.

In certain areas, the therapeutic recommendations in these guidelines may be ahead of the Australian Department of Health's funding and marketing recommendations. Clearly, with rapidly emerging new knowledge, the guidelines will need to be revised in the next few years.

It is important to note that it is implicit in the preparation of these guidelines that where possible, practitioners participate in clinical trials of the management of patients with lymphoma.

Another problem identified in the guidelines is that for many of the diagnostic studies, particularly immunological and molecular studies, and new imaging studies such as PET scanning, there are no specific sources of funding through the traditional and current route, that is, the Australian Department of Health. Here again, the guidelines are ahead of the Commonwealth funding process.

The guidelines frequently stress the need for multidisciplinary clinics in the management of patients with lymphoma. We recommend that readers refer to the National Breast Cancer Centre's document on multidisciplinary care models.

In considering the evidence, the working party has taken into account the effectiveness of an intervention rather than its cost.

The guidelines were presented to a public meeting in March 2004 and the working parties have considered the resulting recommendations. The draft manuscript was made available for public comment before its final editing and publication. They will need to be evaluated to assess their effect on the management of patients with lymphoma, in terms of both clinical and economic outcome, and then revised to ensure they reflect contemporary knowledge. It is planned to have a general review in two to three year's time. As well, if critical new information arises, specific topics will be revised in the electronic version. Meanwhile, a late-breaking chapter to address recent developments has been inserted as Chapter 25.

The Working Party hopes that health practitioners and consumers will find the *Guidelines for the diagnosis and management of lymphoma* a useful resource in the management of this difficult group of diseases. Feedback is welcomed on any aspect of the publication.

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References

- 1 National Health and Medical Research Council. A guide to the development, implementation and evaluation of clinical practice guidelines. Canberra, AGPS, 1999.

