

## CLASSIFICATION OF NON-HODGKIN'S LYMPHOMAS

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While the Rye classification of Hodgkin's disease is widely used by pathologists and clinicians alike, there is as yet no universally accepted classification of the non-Hodgkin's lymphomas.

### Rappaport Classification<sup>1</sup>

The Rappaport classification of the non-Hodgkin's lymphomas is based on two morphological features, viz. the overall geographical pattern of the tumour in the lymph node and the cytological characteristics of the lymphoma cell population. It was the first classification to divide the non-Hodgkin's lymphomas into nodular (**follicular**) and diffuse groups. Clinical studies have shown a marked difference in survival between these two groups: the nodular type, irrespective of cell type carries a better prognosis than the diffuse type.

In evaluating cell size, the nucleus of the tissue macrophage or endothelial cell is used as the reference standard. If the nuclei of the lymphoma cells are smaller than the reference nuclei, the lymphoma is called a lymphocytic lymphoma. Well-differentiated lymphocytic lymphomas have small, round, regular nuclei while poorly differentiated lymphocytic lymphomas have indented irregular nuclei. If the nuclei of the lymphoma cells are as large as or larger than the reference nuclei, the lymphoma is classified as a histiocytic or undifferentiated lymphoma. If a heterogeneous population of cells is present the tumour is called a mixed cell (lymphocytic and histiocytic) lymphoma.

To be acceptable, a classification must not only provide the clinician with information that is clinically significant but be based upon morphological criteria which are sufficiently distinctive that, when applied by non-expert pathologists, they will be highly reproducible when compared with expert interpretations. The Rappaport classification meets both the above two requirements. The classification is

highly reproducible because of its simplicity. It also has clinical significance in that the prognosis in the nodular lymphoma group is relatively good while all patients with diffuse lymphomas (apart from the well differentiated lymphocytic group) uniformly have a poor prognosis.

The main fault with the Rappaport classification is that it was proposed prior to the current vogue in immunological testing to determine the precise origin of the tumour cells. The criticism therefore is that the Rappaport classification is not biologically correct. The large cells present in the mixed lymphocytic and histiocytic cell lymphoma, for instance, are not histiocytes but are transformed B lymphocytes. Immunological studies have shown, in fact, that true lymphomas of histiocytic origin are uncommon.

Several new classifications of the non-Hodgkin's lymphomas have recently been proposed.

Rappaport classification

Nodular	Diffuse
	Lymphocytic, well-differentiated Lymphocytic, poorly differentiated Mixed cell (lymphocytic and histiocytic) Histiocytic Undifferentiated

### Lukes and Collins classification<sup>2</sup>

This classification interprets morphology in terms of immunological function and therefore essentially requires specialised immunological techniques for its application. It suffers at the present time by the inescapable fact that the majority of practising pathologists are not in the position to apply nor to interpret these

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immunological techniques. Furthermore the morphological distinction between the numerous types of lymphomas in this classification is very fine and the criteria for distinguishing between them are difficult for the vast majority of pathologists to apply in their daily diagnostic work. One often has to rely on imprints, plastic-embedded sections, special stains, immunological techniques and electron microscopy to come to a final decision even the experts often disagree on the diagnosis. The classification also lacks any direct indication to guide the clinician as to whether he is dealing with a high or low grade malignant lymphoma. Therefore although the Lukes-Collins classification is biologically accurate, it is cumbersome, not readily reproducible and not as clinically significant as the Rappaport classification.

Kiel classification<sup>3</sup>

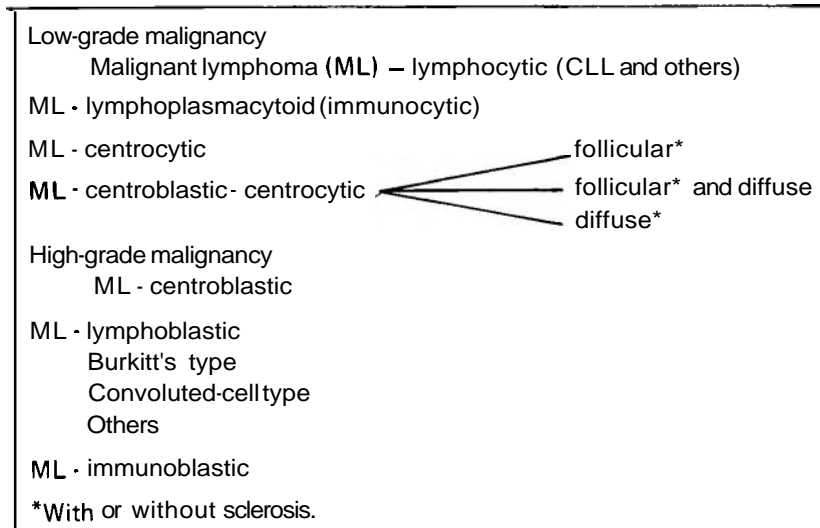
Another recent classification is the Kiel classi-

fication. The accurate categorisation of tumours is based upon precise morphological identification by means of Giemsa stained preparations together with cytohistochemical techniques; immunological function is implied according to the cell type recognised. This classification has the merit of indicating low and high grade tumours. Unfortunately this decision is based on cytological factors rather than on the architectural pattern (nodular or diffuse), as the exponents of this classification believe that the alteration in pattern does not necessarily affect the prognosis adversely and that the cytological type is of greater import in this regard. This surmise has yet to be proven. Furthermore such is the precision required in the identification of cell types that to the pathologist inexperienced in the sophisticated techniques involved rather a high proportion of tumours are allocated to the unclassifiable category.

Lukes and Collins classification

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| <p>I. U-cell (undefined) type</p> <p>II. T-cell types</p> <p>1) Mycosis fungoides and Sezary's syndrome</p> <p>2) Convolutated lymphocyte</p> <p>3) ? Immunoblastic sarcoma (of T cells)</p> <p>4) ? Hodgkin's disease</p> <p>III. B-celltypes</p> <p>1) Small lymphocytic (CLL)</p> <p>2) Plasmacytoid lymphocytic</p> <p>3) Follicular centre-cell types (follicular, diffuse, follicular and diffuse, and sclerotic)</p> <p>a) small cleaved</p> <p>b) large cleaved</p> <p>c) small non-cleaved</p> <p>d) large non-cleaved</p> <p>4) Immunoblastic sarcoma (of B cells)</p> <p>IV. Histiocytic type</p> <p>V. Unclassifiable</p> |
|---|

Kiel classification



British National Lymphoma Investigation classification<sup>4</sup>

This is relatively simple and reproducible and is based primarily on cell morphology at both light and ultrastructural levels. An important aspect for the clinician is the separation of the different groups into the Grade 1 (lower) and Grade 2 (higher) malignant categories. However since electron micrographs are essential for the precise categorization of tumours, the general histopathologist without a keen interest in lymphomas may be reluctant to follow this classification unless there is clear evidence that this classification is superior to a simpler classification as far as clinical significance is concerned.

International Histological (WHO) Classification<sup>5</sup>

This classification, while incorporating some of the new terms such as "immunoblastic", becomes retrogressive when it employs the terms "lymphosarcoma" and "reticulosarcoma". It is a modification of the Rappaport classification. Although the WHO monograph is well illustrated, the classification does not appear to have universal appeal.

Clinicians have been regarding this intransigence amongst pathologists with dismay. The clinician basically wants to know, in simple and familiar terms, whether the patient has a lymphoma or

some other disease, and, if it is a lymphoma, whether it is of a type likely to respond to treatment. Rightly or wrongly, he is not particularly interested in the terminology: his interest is in the patient's condition and what can be done to improve it. It is the pathologist's duty to interpret pathology for the clinician in terms that the latter can understand. It is probably best therefore to leave the controversies in semantics to the experts and to stick to a simple classification until a classification emerges that is not only reproducible and clinically significant but is also biologically accurate.

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British National Lymphoma Investigation classification

FOLLICULAR LYMPHOMA	)	
Follicle cells predominantly small	)	
Follicle cells mixed small and large	)	
Follicle cells predominantly large	)	Grade
DIFFUSE LYMPHOMA	)	I
LYMPHOCYTIC, WELL DIFFERENTIATED (small round lymphocyte)	)	
LYMPHOCYTIC, INTERMEDIATE DIFFERENTIATED (small follicle lymphocyte)	)	
LYMPHOCYTIC, POORLY DIFFERENTIATED (lymphoblast)	)	
a. Non-Burkitt lymphoma	)	Grade
b. Burkitt's tumour	)	II
c. Convoluted cell mediastinal lymphoma	)	
LYMPHOCYTIC, MIXED SMALL AND LARGE CELL (mixed follicle cells)	)	
'UNDIFFERENTIATED' LARGE CELL (large lymphoid cell)	)	
HISTIOCYTIC CELL (mononuclear phagocytic cells)	)	Grade
PLASMA CELL (extramedullary plasma cell)	)	I & II
UNCLASSIFIED		

Plasmacytoid differentiation in lymphocytic tumours, and banded or fine sclerosis recorded

WHO classification

Lymphosarcoma
Nodular lymphosarcoma
<b>P</b> rolymphocytic
Prolymphocytic, lymphoblastic
Diffuse lymphosarcoma
Lymphocytic
Lymphoplasmacytic
<b>P</b> rolymphocytic
Lymphoblastic
Immunoblastic
Burkitt's tumor
<b>M</b> ycosis fungoides
Plasmacytoma
Reticulosarcoma
Unclassified malignant lymphomas