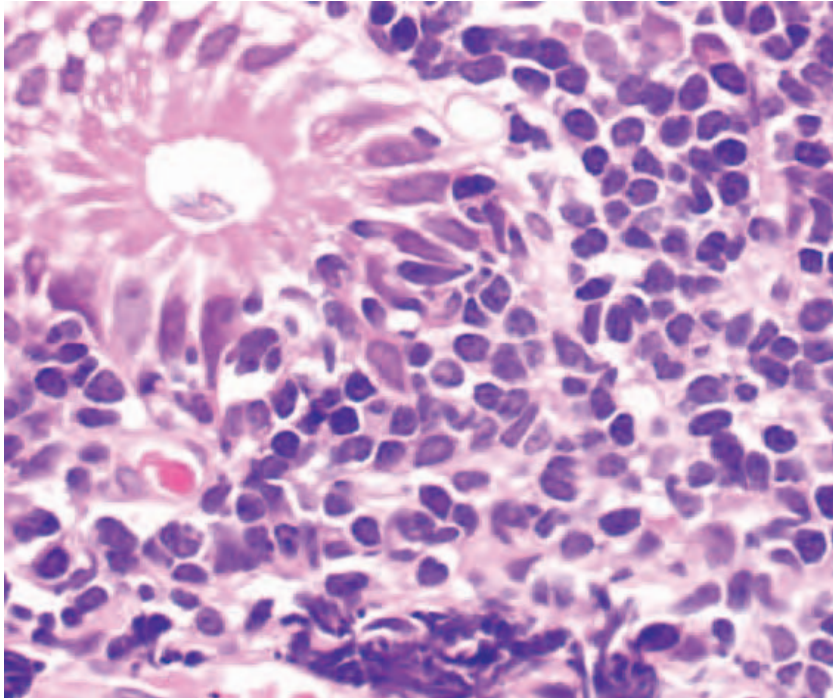


Fast Facts



Fast Facts: Lymphoma

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Fast Facts: Lymphoma



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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com

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the mucosa-associated lymphoid tissue (MALT) lymphoma subtype.

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Glossary of abbreviations

ALK: anaplastic lymphoma kinase	L&H: lymphocytic and histiocytic
ALL: acute lymphoblastic leukemia	LBL: lymphoblastic lymphoma
ATLL: adult T-cell leukemia/lymphoma	LDH: lactate dehydrogenase
CD4: (cluster of differentiation 4) glycoprotein marker for T-helper cells	LGL: large granular lymphocyte
CD8: (cluster of differentiation 8) glycoprotein marker for cytotoxic T cells	LPL: lymphoplasmacytoid lymphoma
cHL: classical Hodgkin lymphoma	MALT: mucosa-associated lymphoid tissue
CLL: chronic lymphocytic (or lymphatic) leukemia	MHC: major histocompatibility complex (protein)
CNS: central nervous system	NHL: Non-Hodgkin lymphoma
CSF: cerebrospinal fluid	nLPHL: nodular lymphocyte-predominant Hodgkin lymphoma
CT: computed tomography	PD: progressive disease
DLBCL: diffuse large B-cell lymphoma	PET: positron emission tomography
EBV: Epstein–Barr virus	PR: partial remission
EDTA: ethylenediamine tetra-acetic acid	PTLD: post-transplant lymphoproliferative disorder
FISH: fluorescent in-situ hybridization	REAL: Revised European American Lymphoma (classification)
FLIPI: Follicular Lymphoma International Prognostic Index	rHuEpo: recombinant human erythropoietin
GCB: germinal-center B cell	SD: stable disease
G-CSF: granulocyte colony-stimulating factor	SEER: Surveillance, Epidemiology and End Results
HAART: highly active antiretroviral therapy	SLL: small lymphocytic lymphoma
HLA: human leukocyte antigen	SLVL: splenic lymphoma with villous lymphocytosis
HRP: horseradish peroxidase	SVC: superior vena cava
HRS: Hodgkin/Reed–Sternberg	TCR: T-cell receptor
HTLV-1: human T-cell lymphotropic virus 1	WHO: World Health Organization
IPI: International Prognostic Index	

Chemotherapy regimens

ABVD: doxorubicin (adriamycin), bleomycin, vinblastine, dacarbazine

BEACOPP: bleomycin, etoposide, adriamycin (doxorubicin), cyclophosphamide, oncovin (vincristine), procarbazine, prednisone

CHOP: cyclophosphamide, hydroxydaunorubicin (doxorubicin), oncovin (vincristine), prednisolone

CODOX-M: cyclophosphamide, oncovin (vincristine), doxorubicin, methotrexate

CVP: cyclophosphamide, vincristine, prednisolone

EPOCH: etoposide, prednisone, oncovin (vincristine), cyclophosphamide, hydroxydaunorubicin (doxorubicin)

ESHAP: etoposide, steroid (methylprednisolone), high-dose ara-C (cytarabine), platinum (cisplatin)

HyperCVAD-MA: high-dose, fractionated cyclophosphamide, vincristine, adriamycin (doxorubicin), dexamethasone, methotrexate, cytosine arabinoside

IVAC: ifosfamide, etoposide, ara-C (cytarabine)

R-CHOP: rituximab plus cyclophosphamide, hydroxydaunorubicin (doxorubicin), oncovin (vincristine), prednisolone

R-CVP: rituximab plus cyclophosphamide, vincristine, prednisolone

R-DHAP: rituximab plus dexamethasone, high-dose ara-C (cytarabine), platinum (cisplatin)

R-ESHAP: rituximab plus etoposide, steroid (methylprednisolone), high-dose ara-C (cytarabine), platinum (cisplatin)

R-FMD: rituximab plus fludarabine, mitoxantrone, dexamethasone

R-ICE: rituximab plus ifosfamide, carboplatin, etoposide

Introduction

Lymphoma is an interesting and significant disease in a number of respects. It can affect young patients, and, in some cases, may be curable. Certain forms are increasing in incidence and it is now one of the commonest malignancies of the Western world. However, this is not where its significance ends. The developments in basic and applied sciences have been used in the clinical setting nowhere more notably than in the management of patients with hematologic malignancies. The CHOP chemotherapy regimen in the 1970s constituted a major breakthrough in the treatment of non-Hodgkin lymphomas and, indeed, paved the way for the development of the specialty of medical oncology; this in turn heralded the beginning of truly effective chemotherapy. Simultaneously, improved radiotherapy methods defined early stage Hodgkin lymphoma as a curable entity.

It was on this background that, in the 1980s and 1990s, the development of immunophenotyping and molecular diagnostic techniques allowed greater precision in the classification of lymphoproliferative diseases and a still more rational approach to their management. Targeted biological agents such as rituximab exemplify this approach, and the effects in terms of improved overall survival of patients with lymphoma have been dramatic. Staging techniques have similarly advanced from surgical laparotomy to positron emission tomography.

Fast Facts: Lymphoma aims to outline both a historical and up-to-date perspective of the diagnosis and management of Hodgkin and non-Hodgkin lymphomas. Fundamentally, this book should impart a clear understanding of the nature of lymphoma and the principles of its management. It should therefore be of use to training doctors and specialist nurses in the field of hemato-oncology, as well as being of interest to the inquiring patient or carer who wishes to know more about lymphoma.

Lymphoma is a malignancy of lymphocytes and their progenitors. The term lymphoma encompasses a broad range of lymphoid malignancies, which is reflected in the complexity of the classification systems (see page 140). Consequently, it is difficult to present an all-encompassing overview of the epidemiology of lymphoma. The task is further hindered by weaknesses inherent in the classification systems available. For example, although the current World Health Organization (WHO) and Revised European American Lymphoma (REAL) classification systems are clinically useful, it is likely that some of the broader categories, such as diffuse large B-cell lymphoma, include several distinct entities, each with its own unique epidemiological and etiologic profile. The most accurate epidemiological data come from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute in the USA, which has provided most of the data discussed here.

Incidence

The annual incidence of lymphoma in the USA between 1995 and 1999 was 19.1/100 000, making it the fifth most common cancer. The incidence is slightly lower in Western Europe.

Factors affecting incidence

Age. Overall, incidence increases with age. However, children are more susceptible to certain forms of lymphoma (Table 1.1).

TABLE 1.1

Characteristics of lymphomas in children

- Less common than in adults: annual incidence approximately 0.8–1/100 000
- More often high grade (e.g. lymphoblastic lymphoma, Burkitt lymphoma, anaplastic large-cell lymphoma)
- Decreasing mortality

Sex. The incidence is 50% higher in men. However, certain lymphoma subtypes have a predisposition to affect men or women. For example, mantle cell lymphoma particularly affects men (> 70% of cases), whereas primary mediastinal B-cell lymphoma is more common in women.

Ethnicity. The incidence of non-Hodgkin lymphoma (NHL) is 50% higher in white Americans than black Americans.

Geography. It has long been recognized that certain forms of lymphoma have an increased incidence in certain parts of the world (Figure 1.1). This association is particularly striking for endemic Burkitt lymphoma and adult T-cell leukemia/lymphoma; however, similar associations are also well established for other subtypes. Overall, NHL is most common in the USA, Western Europe and Australia (possibly reflecting the age demographics of these populations). However,

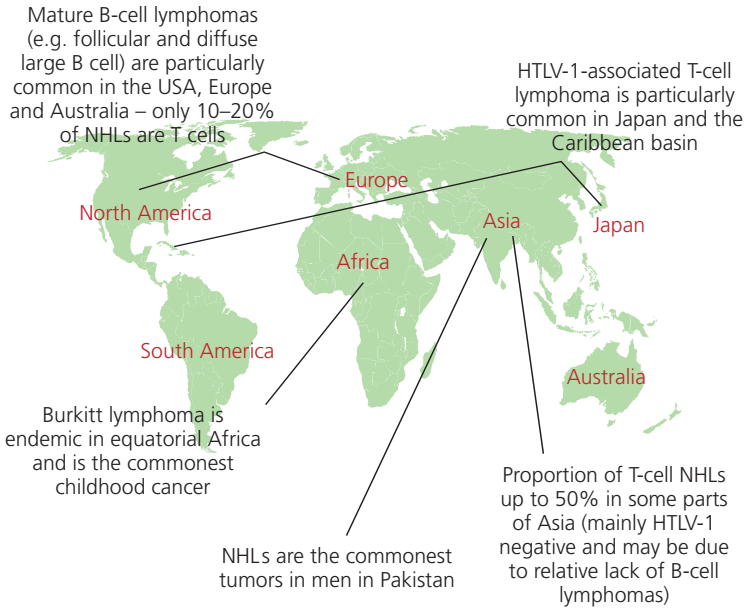


Figure 1.1 Geographical variation of non-Hodgkin lymphoma (NHL) subtypes. HTLV-1, human T-cell lymphotropic virus 1.

Accurate diagnosis is essential in order to successfully treat any disease. This is a major issue in the case of lymphoma due to the existence of so many different subtypes, many of which respond differently to a given treatment modality. Recent advances in cellular and molecular techniques have revolutionized our understanding of lymphoma as a disease and have paved the way for improved diagnosis and treatment.

Flow cytometry and immunophenotyping

Flow cytometry and immunophenotyping can be used to establish the following characteristics of any particle or cell:

- size
- complexity (for a cell this means its granularity)
- surface characteristics (for a cell this means the proteins expressed on the cell surface).

A flow cytometer is capable of analyzing cells one at a time provided the cells are in a fluid phase. Flow cytometry is therefore ideally suited to the analysis of blood samples. However, the technique is also increasingly used to analyze diseased lymph nodes, though the tissue must first be disrupted. Each blood or lymph-node cell scatters a beam of light from a laser in two different ways (Figure 3.1): the forward scattering reflects the size of the cell and the sideways scattering reflects the granularity of the cell. Lymphocytes are small, agranular cells and therefore tend to exhibit a low forward and sideways light scattering.

To determine the proteins expressed on the cell surface, the cells are first mixed with an antibody specific to the protein (antigen) in question. This antibody is linked to a fluorescent marker, which will emit light if it is bound to the cell when it passes through the flow cytometer. The strength of the emitted light is measured by a detector, which then provides information about the relative amount of antigen expressed on the cell surface. More than one protein can be assessed at the same time, as each antibody being used can be linked to markers that emit light of different frequencies. The process of using antibodies to

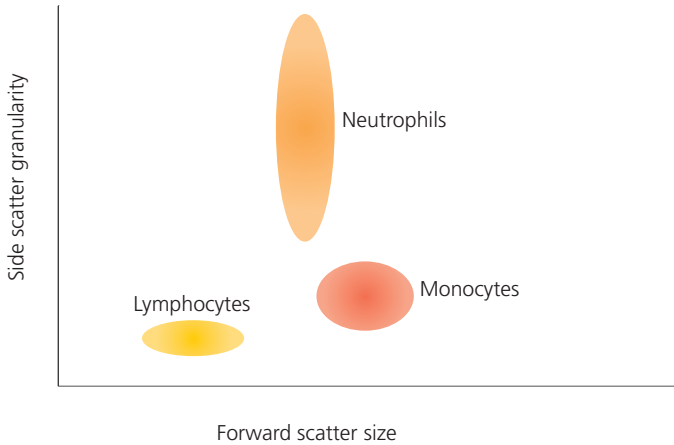


Figure 3.1 Normal forward and side scattering of light by white blood cells, measured by a flow cytometer. The greater the forward scatter, the bigger the cell and the greater the side scatter, the more granular the cell.

define the phenotype of a cell is called immunophenotyping. The immunophenotypes of normal mature T cells and B cells are listed in Table 3.1.

Immunophenotyping is invaluable in the diagnosis of lymphoid disorders. It can help determine:

- clonality
- disease subtype.

Clonality. In B-cell lymphoproliferative disorders, clonality is demonstrated when all of the lymphocytes express either κ or λ light chains. No such test is available to demonstrate the clonality of T cells; clonality is shown by molecular tests that demonstrate a single pattern of rearrangement of the genes of the TCR.

Disease subtype. Certain subtypes of lymphoproliferative disorders are associated with specific patterns of cell surface protein expression, which can be detected by immunophenotyping. In many instances, the pattern is thought to reflect the stage of lymphocyte development at which the malignant change occurred (Table 3.2).