

WORLD HEALTH ORGANIZATION



INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

BURKITT'S LYMPHOMA: A HUMAN CANCER MODEL

Proceedings of a Symposium organized by the IARC and
co-sponsored by the WHO Regional Office for Africa, the General Motors
Cancer Research Foundation and the Association pour
le Développement de la Recherche sur le Cancer,
held in Lyon, 6-9 December 1983

EDITORS

G.M. Lenoir

G.T. O'Connor

C.L.M. Olweny

IARC SCIENTIFIC PUBLICATIONS No. 60

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

LYON 1985

The International Agency for Research on Cancer (IARC) was established in 1965 by the World Health Assembly, as an independently financed organization within the framework of the World Health Organization. The headquarters of the Agency are at Lyon, France.

The Agency conducts a programme of research concentrating particularly on the epidemiology of cancer and the study of potential carcinogens in the human environment. Its field studies are supplemented by biological and chemical research carried out in the Agency's laboratories in Lyon and, through collaborative research agreements, in national research institutions in many countries. The Agency also conducts a programme for the education and training of personnel for cancer research.

The publications of the Agency are intended to contribute to the dissemination of authoritative information on different aspects of cancer research.

Distributed by
Oxford University Press, Walton Street, Oxford OX2 6DP

London New York Toronto
Delhi Bombay Calcutta Madras Karachi
Kuala Lumpur Singapore Hong Kong Tokyo
Nairobi Dar es Salaam Cape Town
Melbourne Auckland

and associated companies in Beirut Berlin Ibadan Mexico City Nicosia

Oxford is a trade mark of Oxford University Press

Distributed in the United States by Oxford University Press, New York

ISBN 0 19 723057 1

ISBN 92 832 1160 X (Publisher)

© International Agency for Research on Cancer 1985

The authors alone are responsible for the views expressed in the signed articles in this publication. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior permission of Oxford University Press

PRINTED IN FRANCE

CONTENTS

Foreword.....	1
Introduction.....	3
Participants.....	5

I. HISTORICAL BACKGROUND

The beginnings of the Burkitt's lymphoma story D.P. Burkitt.....	11
Historical background: Burkitt's lymphoma and Epstein-Barr virus M.A. Epstein.....	17

II. DEFINITION OF THE TUMOUR

Morphological definition of Burkitt's tumour: historical review and present status C.W. Berard	31
Histogenesis of Burkitt's lymphoma: a B-cell tumour of mucosa-associated lymphoid tissue D.H. Wright.....	37
Immunologic markers of Burkitt's lymphoma cells J.L. Preud'homme, K. Dellagi, P. Gugliemi, L.B. Vogler, F. Danon, G.M. Lenoir, F. Valensi & J.C. Brouet.....	47
Cytogenetics of Burkitt's lymphoma-leukaemia: a review R. Berger & A. Bernheim	65
<i>Rapporteur's Report</i> D.H. Wright.....	81

III. CLINICAL ASPECTS

Clinical features of Burkitt's lymphoma: the African experience F.K. Nkrumah & C.L.M. Olweny	87
Burkitt's lymphoma in Algeria M. Aboulola, B. Boukheloua, Y. Ladjadj & F.Z. Tazerout	97
Burkitt's lymphoma in Europe T. Philip	107
Clinical features of Burkitt's lymphoma in the USA I.T. Magrath & E. Sariban	119
Burkitt's lymphoma in the Middle East E. Anaissie, S. Geha, C. Allam, J. Jabour, M. Khalyi & P. Salem	129
Burkitt's lymphoma in Japan I. Miyoshi	135
<i>Rapporteur's Report</i> J. Lemerle	149

IV. EPIDEMIOLOGY

Geographic distribution of Burkitt's lymphoma D.M. Parkin, R. Sohier & G.T. O'Connor	155
Epstein-Barr virus and Burkitt's lymphoma worldwide: the causal relationship revisited G. de-Thé	165
Epidemiological evidence for the role of falciparum malaria in the pathogenesis of Burkitt's lymphoma R.H. Morrow, Jr	177
The latent period of Burkitt's lymphoma: the evidence from epidemiological clustering N.E. Day, P.G. Smith & B. Lachet	187
Epidemiology of Burkitt's lymphoma: other risk factors A.S. Evans	197
A preliminary report of epidemiological studies of Burkitt's lymphoma, Epstein-Barr virus infection and malaria in North Mara, Tanzania A. Geser & G. Brubaker	205
Burkitt's lymphoma in the USA: cases reported to the American Burkitt Lymphoma Registry compared with population-based incidence and mortality data P.H. Levine, R.R. Connelly & F.W. McKay	217
<i>Rapporteur's Report</i> P.G. Smith	225

V. ETIOLOGY

Role of Epstein-Barr virus in the etiology of Burkitt's lymphoma D.T. Purtilo, G. Manolov, Y. Manolova, S. Harada, H. Lipscomb & E. Tatsumi	231
Cell-mediated immunosurveillance mechanisms and the pathogenesis of Burkitt's lymphoma C.M. Rooney, A.B. Rickinson, D.J. Moss, G.M. Lenoir & M.A. Epstein	249
The cytogenetics of human B lymphoid malignancy: studies in Burkitt's lymphoma and Epstein-Barr virus-transformed lymphoblastoid cell lines C.M. Steel, J.E.N. Morten & E. Foster	265
Prevention of endemic Burkitt's lymphoma M.A. Epstein & A.J. Morgan	293
<i>Rapporteur's Report</i> G. Klein	303

VI. LABORATORY APPROACHES

The use of lymphomatous and lymphoblastoid cell lines in the study of Burkitt's lymphoma G.M. Lenoir, M. Vuillaume & C. Bonnardel	309
Immunological characterization of Burkitt's lymphoma cell lines J.P. Magaud, P.A. Bryon, J.Y. Cohen, C. Vincent & J. Brochier	319
Biochemistry of latent Epstein-Barr virus infection and associated cell growth transformation E. Kieff, K. Hennessy, S. Fennewald, T. Matsuo, T. Dambaugh, M. Heller & M. Hummel	323
Translocations among antibody genes in human cancer P. Leder	341
<i>Ras</i> oncogenes in human tumours: identification, mechanism of activation and cooperative role in transformation J.M. Cunningham & R.A. Weinberg	359
<i>Rapporteur's Report</i> I.T. Magrath	365

VII. TREATMENT AND FUTURE PROSPECTS

Treatment of Burkitt's lymphoma: the African experience C.L.M. Olweny & F.K. Nkrumah	375
Treatment of B-cell non-Hodgkin's malignant lymphomas of childhood in Europe: recent and on-going studies J. Lemerle	383

The treatment of diffuse undifferentiated non-Hodgkin's lymphoma in children: the Childrens Cancer Study Group experience R.D.T. Jenkin, J.R. Anderson, R.R. Chilcote, P. Coccia, P. Exelby, J. Kersey, C.R. Kjeldsberg, J. Kushner, A.T. Meadows, S. Siegel, J.F. Wilson & D. Hammond.....	399
Advanced stage (III-IV) Burkitt's lymphoma and B-cell acute lymphoblastic leukaemia in children: kinetic and pharmacologic rationale for treatment and recent results (1979-1983) S.B. Murphy, W.P. Bowman, H.O. Hustu & C.W. Berard.....	405
Massive therapy and autologous bone-marrow transplantation in very bad prognosis Burkitt's lymphoma T. Philip, P. Biron, I. Philip, M.C. Favrot, G. Souillet, N. Philippe, P. Hervé, E. Plouvier, J.L. Bernard, C. Reybaud, D. Frappaz, F. Freycon, B. Crozet & M. Brunat-Mentigny	419
Autologous bone-marrow transplantation for Burkitt's lymphoma: marrow purging with anti-Y 29/55 monoclonal antibody and complement C. Baumgartner, B. Delaleu, P. Imbach, A. Lüthy, R. Olavic, G. Brun del Re, U. Bucher, H.K. Forster, A. Hirt & H.P. Wagner	435
Indication for bone-marrow harvesting and purging in Burkitt's lymphoma: a three-year experience I. Philip, T. Philip, M.C. Favrot, P. Biron & G.M. Lenoir.....	441
Immunophenotypic classification of 28 Burkitt cell lines with monoclonal antibodies and reagent selection for bone-marrow purging M.C. Favrot, I. Philip, T. Philip, H. Cabrilat, C. Pinatel, J.-F. Doré & G.M. Lenoir ..	447
Reactivity pattern of the B-leukaemia-associated monoclonal antibody anti-Y 29/55 H.K. Forster, J.-P. Obrecht & F.G. Gudat	453
38.13: a monoclonal antibody directed against a Burkitt's lymphoma-associated antigen and its use as a carrier for toxins J. Wiels, A. Balaña & T. Tursz.....	457
<i>Rapporteur's Report</i> T. Philip	465

IX. CONCLUSIONS

Concluding remarks S. Murphy.....	471
The state of and prospects for molecular genetics in Burkitt's lymphoma P. Leder.....	475
AUTHOR INDEX	477
SUBJECT INDEX	479

FOREWORD

The Agency's interest in Burkitt's lymphoma dates back early in its history. Following the establishment of a relationship between infection by the Epstein-Barr virus and the development of infectious mononucleosis, the suggestion was made in 1968 that the Agency was well placed to organize studies, including sero-epidemiological surveys in Africa, to investigate the relationship between infection with that virus and the development of Burkitt's lymphoma. Thus, a large survey was initiated in Uganda to determine the serological patterns preceding the development of Burkitt's lymphoma and to make comparisons with serological profiles of controls. A study of the relationship between malaria and Burkitt's tumour was also set up. These studies led to the establishment at the Agency of a large number of cell lines, which are available to scientists all over the world, enabling them to carry out laboratory investigations that may help to elucidate the mechanisms by which this tumour develops.

The primary reason for carrying out research on Burkitt's lymphoma is that it represents the major tumour for children between 0 and 14 years in equatorial Africa. It has also been shown to be a model for the study of other human cancers, because the induction and evolution of lymphoid neoplasms, as tumours of the immune system, are strongly influenced by those environmental factors, such as infection and nutrition, which affect the immune response.

The Agency therefore felt it of great importance that a Symposium be organized to review current knowledge in the field of this tumour and is pleased to be able to publish these proceedings with the goal of preventing not only this cancer but others of similar type.

L. Tomatis
Director,
IARC

INTRODUCTION

The first description of the tumour now called Burkitt's lymphoma (BL) was published exactly 25 years ago. Its recognition by workers in Uganda as a distinct clinical and pathological entity that occurs with high frequency in African children led to epidemiological observations that suggested a possible viral etiology and an association with holendemic malaria. Subsequently, in 1963, the Epstein-Barr virus (EBV) was discovered; and its relationship to endemic BL, and its association with other neoplastic and non-neoplastic diseases, has been the subject of intensive study involving many scientific disciplines during the last two decades.

BL occurs throughout the world with varying frequency, but everywhere it represents a significant proportion of malignant lymphomas in children. In non-endemic areas, the association with EBV is infrequent, but specific karyotypic anomalies characterize the tumour wherever it is found. Recently, these chromosomal rearrangements have been related to key molecular events involving certain genes, and these studies have provided further insight into mechanisms of malignant transformation at the subcellular level.

Advances in the clinical management of BL have paralleled those made in basic laboratory investigations, so that what was primarily a rapidly fatal disease in virtually all cases can now be considered curable in well over 50% of patients receiving appropriate therapy.

The very rapid progress in the many disciplines relevant to the study of this tumour created a need to bring clinical and laboratory scientists together in order to review the disease in its entirety; and there has not been a major international conference dealing with all aspects of Burkitt's lymphoma for more than ten years.

The proceedings of this Symposium represent a comprehensive 'state-of-the-art' reference source for this tumour and provide information on the recent developments in molecular biology and in clinical management and give recommendations for future work.

The Editors

LIST OF PARTICIPANTS

M. Aboulola	Service de Chirurgie Pédiatrique, Centre Hospitalier Universitaire Mustapha, Alger, Algeria
E.J. Anaissie	American University Medical Centre, Beirut, Lebanon
C. Baumgartner	Clinique de Pédiatrie, Hôpital de l'Île, 3010 Bern, Switzerland
C. Berard	Chairman, Division of Pathology, St Jude Children's Research Hospital, 332 North Lauderdale, PO Box 318, Memphis, TN 38101, USA
R. Berger	Laboratoire de Cytogénétique, Hôpital Saint-Louis, Centre Hayem, 2 place du Dr Fournier, 75475 Paris Cedex 10, France
P. Biron	Centre Léon-Bérard, 28 rue Laënnec, 69373 Lyon Cedex 08, France
G. Bornkamm	Institute of Virology, Hygiene Centre, Hermann-Herderstrasse 11, 7800 Freiburg, Federal Republic of Germany
G. Brubaker	Shirati Hospital, Private Bag Musoma, Musoma, Tanzania
P.A. Bryon	Hôpital Edouard-Herriot, Service d'Hématopathologie, Pavillon E bis, 5 Place d'Arsonval, 69374 Lyon Cedex 08, France
D. Burkitt	The Old House, Bussage, Stroud, Glos GL6 8AX, United Kingdom
J. Cohen	INSERM U.80, Hôpital Edouard-Herriot, Pavillon P, 5 place d'Arsonval, 69374 Lyon Cedex 08, France
J. Cunningham	Center of Cancer Research and Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
N. Day	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France
G. de-Thé	Directeur de Recherche, CNRS, Faculté de Médecine Alexis-Carrel, rue Guillaume-Paradin, 69372 Lyon Cedex 02, France

K. Dellagi	INSERM U.108, Hôpital St Louis, 2 place du Dr Fournier, 75475 Paris Cedex 10, France
M.A. Epstein	Head, Department of Pathology, University of Bristol, The Medical School, University Walk, Bristol BS8 1TD, United Kingdom
A.S. Evans	Department of Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, PO Box 3333, New Haven, CN 06510, USA
M. Favrot	INSERM U.51, Centre Léon-Bérard, 28 rue Laënnec, 69373 Lyon Cedex 08, France
K. Forster	Central Research Units, Hoffman-La Roche & Co. Ltd, 4002 Basel, Switzerland
A. Geser	La Dombarière, 49 chemin de Grandvaux, 69130 Ecully, France
N. Goldblum	Hebrew University, Jerusalem, Israel
V. Gurtsevitch	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France
O. Hasan-Kasule	Department of Epidemiology, Harvard University, 677 Huntington Avenue, Boston, MA 02115, USA
H. zur Hausen	Director, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 6900 Heidelberg 1, Federal Republic of Germany
R.D.T. Jenkin	Director, The Ontario Cancer Foundation, Toronto-Bayview Clinic, Sunnybrook Medical Centre, 2075 Bayview Avenue, Toronto, M4N 3M5, Canada
E. Kieff	Departments of Medicine and Microbiology, Section of Infectious Diseases, University of Chicago, Pritzker School of Medicine, 910 East 58th Street, Chicago, IL 60637, USA
G. Klein	Department of Tumor Biology, Karolinska Institute, 10401 Stockholm, Sweden
J. Ladjadj	Clinique de Chirurgie Pédiatrique, Centre Hospitalier Universitaire Mustapha, Alger, Algeria
P. Leder	Chairman, Department of Genetics, Harvard Medical School, 45 Shattuck Street, Boston, MA 02115, USA
J. Lemerle	Service de Pédiatrie, Institut Gustave-Roussy, rue Camille-Desmoulins, 94805 Villejuif, France
G. Lenoir	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France

P.H. Levine	Clinical Epidemiology Branch, 5121 Landow Building, National Institutes of Health, Bethesda, MD 20205, USA
J.P. Magaud	Laboratoire d'Hématologie, Pavillon N, Hôpital Edouard-Herriot, 5 place d'Arsonval, 69374 Lyon Cedex 08, France
I. Magrath	Senior Investigator, Pediatric Branch, National Cancer Institute, Building 10, Room 13N240, Bethesda, MD 20205, USA
E. Mark-Vendel	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France
I. Miyoshi	Kochi Medical School, Okohcho, Nankoku, Kochi 781-51, Japan
R.H. Morrow	Secretary, Scientific Working Group on Epidemiology, World Health Organization, 1221 Geneva 27, Switzerland
S.B. Murphy	St Jude Children's Research Hospital, 332 North Lauderdale, Memphis, TN 38101, USA
F. Nkrumah	Department of Paediatrics and Child Health, University of Zimbabwe, PO Box A178, Avondale, Harare, Zimbabwe
G. O'Connor	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France
C. Olweny	Visiting Consultant, Tropical Disease Research Centre, PO Box 71769, Ndola, Zambia
M. Parkin	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France
I. Philip	Centre Léon-Bérard, 28 rue Laënnec, 69373 Lyon Cedex 08, France
T. Philip	Service de Pédiatrie, Centre Léon-Bérard, 28 rue Laënnec, 69373 Lyon Cedex 08, France
J.L. Preud'homme	Laboratoire d'Immunologie et d'Immunopathologie, CHU La Miétrie, BP 577, 86021 Poitiers, France
D.T. Purtilo	Chairman, Department of Pathology and Laboratory Medicine, University of Nebraska Medical Center, 42nd and Dewey Avenue, Omaha, NE 68105, USA
A. Rickinson	Cancer Research Campaign Laboratories, Department of Cancer Studies, The Medical School, Birmingham B15 2TJ, United Kingdom
L. Robison	Division of Epidemiology, University of Minnesota, Mayo Memorial Building, 420 Delaware Street SE, Minneapolis, MN 55455, USA

M.C. Rooney	Department of Pathology, University of Bristol Medical School, University Walk, Bristol BS8 1TD, United Kingdom
H. Sieverts	RWTH Aachen, Abteilung für Kinderheilkunde, Goethestrasse 27-29, 5100 Aachen, Federal Republic of Germany
P.G. Smith	Tropical Epidemiology Unit, London School of Hygiene and Tropical Medicine, Keppel Street (Gower Street), London WC1E 7HT, United Kingdom
R. Sohier	International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 08, France
M. Steel	MRC Clinical and Population Cytogenetics Unit, Western General Hospital, Crewe Road, Edinburgh EH4 2UX, United Kingdom
A. Stern	Inselspital, Bern, Switzerland
T. Tursz	Groupe d'Immunobiologie des Tumeurs, Pavillon de Recherche, Institut Gustave-Roussy, rue Camille-Desmoulins, 94805 Villejuif Cedex, France
J. Wiels	Groupe d'Immunobiologie des Tumeurs, Pavillon de Recherche, Institut Gustave-Roussy, rue Camille-Desmoulins, 94805 Villejuif Cedex, France
O. Williams	Consultant Haematologist and Medical Oncologist, Department of Haematology, University College Hospital, Ibadan, Nigeria
D. Wright	Faculty of Medicine, The University of Southampton, South Laboratory Pathology Block, Southampton General Hospital, Tremona Road, Southampton SO9 4XY, United Kingdom

I. HISTORICAL BACKGROUND

