

Cancer and the Adolescent

Second edition

EDITED BY

T. O. B. Eden

Academic Unit of Paediatric Oncology, University of Manchester, Manchester, UK

R. D. Barr

Department of Paediatrics, McMaster University, Hamilton, Ontario, Canada

A. Bleyer

*Department of Paediatrics, The University of Texas MD Anderson Cancer Center,
Houston, Texas, USA*

M. Whiteson

Teenage Cancer Trust, London, UK



**Blackwell
Publishing**

BMJ
Books

**Cancer
and the
Adolescent**

Cancer and the Adolescent

Second edition

EDITED BY

T. O. B. Eden

Academic Unit of Paediatric Oncology, University of Manchester, Manchester, UK

R. D. Barr

Department of Paediatrics, McMaster University, Hamilton, Ontario, Canada

A. Bleyer

*Department of Paediatrics, The University of Texas MD Anderson Cancer Center,
Houston, Texas, USA*

M. Whiteson

Teenage Cancer Trust, London, UK



**Blackwell
Publishing**

BMJ
Books

© 2005 by Blackwell Publishing Ltd

BMJ Books is an imprint of the BMJ Publishing Group Limited, used under licence

Blackwell Publishing, Inc., 350 Main Street, Malden, Massachusetts 02148–5020, USA

Blackwell Publishing Ltd, 9600 Garsington Road, Oxford OX4 2DQ, UK

Blackwell Publishing Asia Pty Ltd, 550 Swanston Street, Carlton, Victoria 3053, Australia

The right of the Authors to be identified as the Authors of this Work has been asserted in accordance with the Copyright, Designs and Patents Act 1988.

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, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

First published 1996

Second edition 2005

Library of Congress Cataloging-in-Publication Data

Cancer and the adolescent.— 2nd ed. / edited by T. O. B. Eden . . . [et al.].

p. ; cm.

Includes bibliographical references and index.

ISBN-13: 978-0-7279-1810-9 (pbk.)

ISBN-10: 0-7279-1810-9 (pbk.)

1. Cancer in adolescence. 2. Tumors in adolescence.

[DNLM: 1. Neoplasms—therapy—Adolescent—Congresses. 2. Neoplasms—psychology—Adolescent—Congresses. QZ 275 C208 2005] I. Eden, T. O. B.

RC281.C4C345 2005

616.99'4'00835—dc22

2005008026

ISBN-13: 978-0-7279-1810-9

ISBN-10: 0-7279-1810-9

A catalogue record for this title is available from the British Library

Set in 9.5/12 pt Meridien by Graphicraft Limited, Hong Kong

Printed and bound in Harayana, India by Replika Press Pvt Ltd

Commissioning Editor: Mary Banks

Editorial Assistant: Mirjana Misina

Development Editor: Veronica Pock

Production Controller: Debbie Wyer

For further information on Blackwell Publishing, visit our website:

<http://www.blackwellpublishing.com>

The publisher's policy is to use permanent paper from mills that operate a sustainable forestry policy, and which has been manufactured from pulp processed using acid-free and elementary chlorine-free practices. Furthermore, the publisher ensures that the text paper and cover board used have met acceptable environmental accreditation standards.

Contents

List of contributors, vii

Introduction, ix

I. Gibson

Chapter 1 A right, not a privilege! 1

M. Whiteson

Part one: Patterns and perspectives

Chapter 2 Patterns of incidence of cancer in teenagers and young adults: implications for aetiology, 13

J. M. Birch

Chapter 3 Lack of participation of older adolescents and young adults with cancer in clinical trials: impact in the USA, 32

A. Bleyer, T. Budd and M. Montello

Chapter 4 Adolescents and cancer: perspectives from France, 46

L. Brugières

Chapter 5 Care of teenagers with cancer: a North American perspective, 50

R. D. Barr

Part two: Advances

Chapter 6 Leukaemia, 61

J. Nachman

Chapter 7 Advances in treatment for non-Hodgkin's lymphoma, 72

M. P. Gerrard

Chapter 8 Hodgkin's disease and adolescents: the lost tribe? 83

K. P. Windebank

Chapter 9 Adolescent CNS tumours: my brain has damaged my life, 96

D. A. Walker

Chapter 10 Ewing's sarcoma, 102

A. Craft

Chapter 11 Advances in osteosarcoma, 113

J. Whelan

Chapter 12 Osteosarcoma and surgery, 121

R. J. Grimer

Part three: Survivorship

Chapter 13 Subfertility in adolescents with cancer: who is at risk and what can be done? 133

W. H. B. Wallace and M. F. H. Brougham

Chapter 14 Body image, 155

M. Woods and L. Shearer

Chapter 15 The impact of cancer on adolescents and their families, 165

K. L. Neville

Chapter 16 Resilience in survivors of teenage cancer: a life-adaptive approach, 179

J. J. Spinetta

Chapter 17 Surviving with scars: the long-term psychosocial consequences of teenage cancer, 183

M. C. Self

Part four: Palliation

Chapter 18 Whose dying is it anyway? Palliative care in adolescence, 203

R. Hain

Chapter 19 The parent's perspective of teenage cancer, 214

R. Kanarek and V. Riley

Part five: Controversies

Chapter 20 Who should care for young people with cancer? 231

J. Arbuckle, R. Cotton, T. O. B. Eden, R. Jones and R. Leonard

Chapter 21 Patterns of care for teenagers and young adults with cancer: is there a single blueprint of care? 241

I. Lewis

Chapter 22 Managing professional relationships across the services, 259

S. Morgan

Chapter 23 The next 10 years in biomedical science and care for teenagers and young adults with cancer, 270

P. Selby, A. Shah, R. Yates and M. Leahy

Index, 283

List of contributors

Editors

- T. O. B. Eden**, Academic Unit of Paediatric Oncology, University of Manchester, Manchester, UK
R. D. Barr, Department of Paediatrics, McMaster University, Hamilton, Ontario, Canada
A. Bleyer, Department of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA
M. Whiteson, Teenage Cancer Trust, London, UK

Contributors

- J. Arbuckle**, Western General Hospital, Edinburgh, UK
R. D. Barr, McMaster University, Hamilton, Ontario, Canada
J. M. Birch, Cancer Research UK Paediatric and Familial Cancer Research Group, Royal Manchester Children's Hospital, Manchester, UK
A. Bleyer, The University of Texas MD Anderson Cancer Center and University of Texas Medical School, Houston, Texas, USA
M. F. H. Brougham, Royal Hospital for Sick Children, Edinburgh, UK
L. Brugières, Département de Pédiatrie, Institut Gustave Roussaay, Villejuif, France
T. Budd, Children's Oncology Group, Arcadia, California, USA
R. Cotton, Christie Hospital NHS Trust, Manchester, UK
A. Craft, Department of Child Health, Royal Victoria Infirmary, Newcastle upon Tyne, UK
M. P. Gerrard, Sheffield Children's Hospital, Sheffield, UK
I. Gibson, MP and Chairman of All Party Cancer Group, UK
R. J. Grimer, The Royal Orthopaedic Hospital NHS Trust, Birmingham, UK
R. Hain, Department of Child Health, University of Wales College of Medicine, Penarth, UK
R. Jones, South West Wales Cancer Institute, Singleton Hospital, Swansea NHS Trust, Swansea, UK
R. Kanarek, Teenage Cancer Trust Unit, The Middlesex Hospital, London, UK
M. Leahy, Teenage Cancer Trust Senior Lecturer, Cancer Research UK Clinical Centre, St James's University Hospital, Leeds, UK
R. Leonard, Cancer Institute, Swansea, UK
I. Lewis, St James University Hospital, Leeds, UK
M. Montello, The University of Texas MD Anderson Cancer Center and University of Texas Medical School, Houston, Texas, USA
S. Morgan, Teenage Cancer Trust Unit, St James's University Hospital, Leeds, UK
J. B. Nachman, Department of Pediatrics Hematology/Oncology, Chicago, Illinois, USA
K. L. Neville, Department of Nursing, Kean University, New Jersey, USA
V. Riley, Teenage Cancer Trust Unit, The Middlesex Hospital, London, UK
P. Selby, Cancer Research UK Clinical Centre, St James's University Hospital, Leeds, UK
M. C. Self, North West Cardiff Community Mental Health Team, Cardiff, UK
A. Shah, Non-Communicable Disease Epidemiology Unit, London School of Hygiene and Tropical Medicine, London, UK
L. Shearer, Poole, UK
J. Spinetta, San Diego State University, San Diego, California, USA

D. A. Walker, Faculty of Medicine and Health Sciences, University of Nottingham,
Nottingham, UK

W. H. B. Wallace, Royal Hospital for Sick Children, Edinburgh, UK

M. Whiteson, Teenage Cancer Trust, London, UK

K. P. Windebank, University of Newcastle upon Tyne and Royal Victoria Infirmary,
Newcastle upon Tyne, UK

J. Whelan, The Meyerstein Institute of Oncology, The Middlesex Hospital, London, UK

M. Woods, Manchester, UK

R. Yates, Statistical Information Team, Cancer Research UK, London, UK

Introduction

Thanks to the Teenage Cancer Trust, attention is at last being focused on the disadvantaged position of teenagers and young adults with cancer. Advances are now being made in their management.

The recognition of their needs, both medical and psychosocial, by the UK National Institute for Clinical Excellence is a key milestone. Work will result in their production of national guideline recommendations for this group of patients.

The third International Conference on Cancer and the Adolescent, organized and sponsored by the Teenage Cancer Trust, has thrown a spotlight on the issues for this cohort of young people. There are common problems for young people with cancer right around the world and we in the UK appear to be in the vanguard of championing their case.

Attention has been drawn to the low level of recruitment into clinical trials and the increasing incidence of cancer in the 16- to 24-years age group, a dearth of specialist facilities and multidisciplinary teams to look after such patients, and the relatively poor outcome for this group. In addition, it is clear that social and financial discrimination is experienced by many of the survivors. It is clearly now time for government as well as charities like the Teenage Cancer Trust to do something much more active. I would personally recommend that governments should offer financial support matching that given by, for example, the Teenage Cancer Trust to ensure that this group of teenage and young adult cancer patients receive the level of care to which they are entitled and which they deserve.

Dr Ian Gibson
MP and Chairman of the All Party Cancer Group

CHAPTER 1

A right, not a privilege!

M. Whiteson

In 1948, when the National Health Service was established in the UK, we were promised health-care ‘from the cradle to the grave’. No-one mentioned much about the in-between years. Here, and in many other countries, health-care is provided separately for children and adults. The age at which one becomes an ‘adult’ in this context varies from 12 to 18 years, and sometimes appears to be an arbitrary line drawn in the sand. In England and Wales this line divides the men from the boys (and the girls from the women) at 16 years. I am not sure why. We make other divisions about other issues; for instance, we may hold a child over 10 to be criminally responsible. In the field of education we separate infants from juniors, and all of them from the secondary stage at 11 years of age, and may even subdivide the 11 to 17/18 age group. In doing this, it is acknowledged that adolescents or teenagers have specific needs and must be dealt with differently.

We all know that the commercial world recognizes these ‘in-betweens’ and makes a great deal of money by meeting their needs. However, in the medical context, teenagers and young adults are a neglected group and suffer as a result. It is their right to have their special needs recognized and satisfied. This should not be seen as a privilege.

The Teenage Cancer Trust (TCT) was established formally in the early 1990s by a small group of charitably minded individuals who, having set up the first specialist unit for young cancer patients at the Middlesex Hospital, London, realized the yawning gap in the provision of treatment and care for this group of patients.

The vision of TCT is to supply a teen-friendly environment in which an expert and highly specialized team of health-care professionals provide their patients with the very best chance of recovery. TCT units are this and more. They espouse a philosophy of putting the patient first. This is not really a new idea, for, as Professor J. B. Murphy (1857–1916, Professor of Surgery, Northwestern University, Chicago, USA) pointed out some 100 years ago, ‘The patient is the centre of the medical universe around which all our work revolves, and toward which all our efforts trend.’ Within TCT units, the needs of young people are recognized and respected, and not just their needs as cancer patients. The emphasis is on the quality of life as well as its duration.

Teenage Cancer Trust Units
March 2004

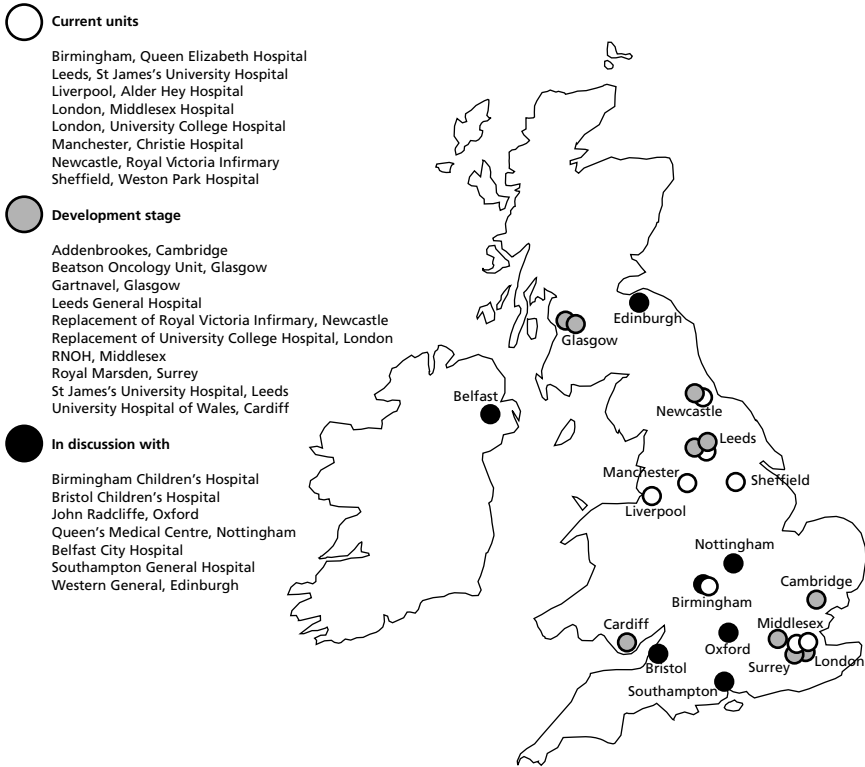


Fig. 1.1 Distribution of Teenage Cancer Trust units.

We have gone on to establish eight TCT units around the UK and are in the process of developing a further 17 (Fig. 1.1). Setting up these units is a slow process, and it is not the TCT that is causing the delay. Lack of government support, lack of recognition within the medical profession, failure of physicians to cooperate across the age divide, and conservative and unimaginative hospital managements are the main impediments.

In developing these units, we have learned that physically appropriate environments – where architecture and interior design not only provide pleasant surroundings but also add constructively to the well-being of the patient – really make a difference to the quality of patients' lives. In 2003 the TCT unit at Weston Park Hospital, Sheffield, received a commendation from the Commission for Health Improvement for its innovative design and for meeting patients' needs. Additionally, in 2003 the TCT unit at St James's University Hospital, Leeds, was the winner of one of the Department of Health's Health and Social Care Awards – the Cancer New Hope Award.

The growth of a network of units is beginning to allow specialization (and so expertise) within adolescent cancer medicine. There is a definite growth of interest in the field which can only benefit our patients.

We have also extended our sphere of work to support the basic concept of specialized units for youthful cancer patients. We sponsor the Teenage Cancer Trust Multidisciplinary Forum, organize conferences such as the International Conference on Cancer and the Adolescent, and also Find Your Sense of Tumour – a conference for young cancer patients. We are setting up a Family Support service, run an Education and Awareness team for schools and universities – and hope to be appointing the first Chair in Adolescent Cancer Medicine in the world, very shortly.

We consider we have played a considerable part in focusing attention on the needs of this hitherto neglected group of patients, world-wide. Attendance at our international conference has increased from the involvement of five countries to 18 countries, indicating the massive growth in interest. This is one field where the UK (and TCT) is showing the way!

World-wide, cancer service provision for those at such a sensitive and crucial stage of life appears generally inadequate and fails to meet all the needs of the patient. Cancer service provision, we would argue, is about more than treatment: it is also about the quality of care and life both during and after treatment. As in other social structures, this transitional stage of development of young people has to be recognized and our state health services have to make provision built upon good information and must be available to all who require them. Within the UK we appeal to our government and our National Health Service to work with TCT to meet that need.

Some people question whether there is a need for specialized care for adolescent and young adult cancer patients and ask whether teenagers get cancer. The common perception – not only among the general public but sometimes also among professional and political decision-makers – is that children get cancer and adults get cancer, but teenage cancer numbers are insignificant. Yet cancer is the commonest cause of non-accidental death in teens and young adults in both the USA¹ and the UK.² In the UK we are just below the European average for 5-year survival rates for children and teenagers with cancer, which leaves much room for improvement.³

What are the issues?

Cancer services are delivered by an out-of-date infrastructure that, by and large, fails teenagers and young adults.

- There are difficulties in obtaining reliable statistics.
- Teens and young adults are often subject to late diagnosis.
- Levels of skill and expertise vary between and within treatment centres and we need to know the effect of these variations on outcome.
- Young people have low enrolment in clinical trials.

- They are placed at the crossover between adult and childhood cancers and experience a different distribution of cancers from other age groups.
- This complexity is exacerbated by the usual division of child and adult services. In the UK (and elsewhere, too) the approach to children is generic, across the board, whereas for adults it is specific to the cancer site.
- Different protocols are used by adult and paediatric practitioners for the same diseases – the relative success of these needs to be evaluated.

Cancer patients in their teens and early adulthood tend to be disadvantaged at every stage.

Do we have the information?

Although statistics for this age group are still difficult to obtain, we are beginning to appreciate, contrary to common perception, that there are more young people with cancer in the 15–24 age group than in children aged 0–14 years. It is estimated that around 2000 new diagnoses are made per annum in the teenage and young adult (TYA) group in the UK. Some of those treated successfully for cancer during childhood go on to relapse during adolescence. About 75% of children with cancer are cured, but many continue to require physical and emotional follow-up in the long term. Because of the way we gather information in the UK and other countries, we do not actually know how many young people nationwide will be calling upon our cancer services.

In England and Wales the National Institute for Clinical Excellence is currently studying cancer services for children and young people. The National Public Health Service for Wales⁴ has data which suggest that the falling birth rate will result in a change in the population's demographic profile, with increasing numbers in the older age groups projected to 2011. Since the incidence rate of cancer is higher in the 15–24 age group (214 per million) than the 0–14 age group (134 per million), increased survival and a changing demography are likely to result in an increase in absolute numbers of incident and prevalent cancer patients aged 15–24. This suggests an increased need for services both in the short and longer term for the TYA group.

Why has this not been sufficiently considered by the medical profession? Failure to do so has hindered the reorganization of service delivery. Why has the National Health Service not made the necessary infrastructure changes to care appropriately for young cancer patients? Surely this is negligence! In the UK, it has taken a charity – TCT – to show the way and inspire change.

The numbers game

The problems of gathering statistics are, in part, due to the division of TYAs between child and adult services. This is a serious problem and an obstacle to the provision of sound information. It undermines the establishment of appropriate standards and systems of service delivery to the complex group of patients that make up the TYA sector. The work of Birch and colleagues⁵

highlights the value of detailed data in assessing the needs of and the provision of services to the hitherto neglected youth with cancer.

In order to fulfil our duty to young cancer patients, both as a profession and as a society, we need more focused information-gathering. The sector of the population with whom we are concerned presents many problems that would be addressed by more reliable information, and this information would also enable us to build structured approaches to treatment and help resolve the unique issues.

It may be too cynical to suggest that failure to identify this group of patients – so that true figures and information are not available – has resulted in the absence of demand for special facilities, treatment, research and funding. Defining this group out of existence might save governments, the National Health Service and the health trusts a great deal of money. You don't have to spend on what doesn't exist.

Late diagnosis

There is much anecdotal evidence and some factual indication regarding the issue of general practitioner delay. Many factors contribute to this impediment to speedy diagnosis and treatment.

- Teenagers themselves! Often they are hesitant or even reluctant to visit the doctor. In the USA it is observed that young adults have the lowest rate of primary care use.¹
- Young people are under-educated regarding their own health.
- Parents are less involved in their children's personal care at this stage of life.
- Few general practitioners have experience of adolescent and young adult cancers.
- Few general practitioners have cancer in their lexicon of possible diagnoses for young patients (the low profile of teenage cancer may contribute to this).
- There is not a clear pathway of referral, as there is for children. As a result, the locus of referral is something of a lottery. In turn, this influences the levels of experience and expertise that patients will find. We need to know how this affects the outcome.

Clinical trials

Relatively few teenagers and young adults with cancer are enlisted in clinical trials. Overall, the outcome for patients involved in trials tends to be more favourable. Results of clinical trials provide the information base for future treatment. They are the foundation upon which treatment can be improved and standardized. Therefore, once again young cancer patients are disadvantaged.

It is accepted that few TYAs are included in trials. The following factors contribute to their exclusion.

- The pharmaceutical industry dominates in this field. Pharmaceutical companies work on numbers, and we are talking about a relatively small group of patients. It is accepted that within each country the numbers are proportionally small, but world-wide there is a considerable total, enough to justify research. The pharmaceutical industry appears to show little interest in this age group.
- Governments, who are sizeable customers of the pharmaceutical companies, should place requirements on these organizations to test drugs to benefit young people. In the USA the Food and Drug Administration requires drug companies to evaluate their products for children in order to obtain a paediatric licence. This is an encouraging move.
- While eminent clinicians advocate clinical trials for young cancer patients, we in Europe are concerned about a European Union directive, due to come into force in May 2004, which will make clinical trials for children, adolescents and even young adults even less likely than they are now. If implemented, this directive will make trials more costly and the outcome will be that only the pharmaceutical companies will be able to afford to set up trials, and academic trials will be severely curtailed as a result. This can only further limit the involvement of young cancer patients in such research.
- Some of the cancers which TYAs experience are rare and so do not inspire trials.
- Clinicians often see young people as non-compliant, and there may be some validity in this argument – but insufficient to justify not involving them. A concentration of young people in specialist centres such as TCT units would assist in the setting up and management of clinical trials and help mitigate patient resistance.

It is vital that young people with cancer are actively involved in clinical trials, in order to ensure a consistent and enhanced standard of care.

Range of cancer services

The variety of cancers affecting the age group in question includes childhood and adult cancers. Imposing this diversity upon the rigid structure of childhood or adult centres and protocols raises further problems.

It is common practice in the UK for the approach to childhood cancer treatment to be generic while that for adult cancer is site-specific. These systems do not mesh well. As a result, those on the cusp may not get the appropriate approach to treatment. This is often exacerbated by a lack of cooperation between adult and paediatric practitioners. Unfortunately, this is sometimes my experience when working with hospitals in the UK, and having conducted a straw poll via nurses from a number of other countries I conclude that this glass wall exists in those countries too.

But TYA cancer patients should not be limited to either paediatric or adult services – there is another alternative. There is the transitional facility – such as TCT units – where the skills and expertise are focused on their specific needs.

Too many young people with cancer do not have the benefit of access to a specialized teenage unit – this is true abroad, and also here in the UK. We look forward to the day when TCT units and services are the norm, as paediatric services are now. Until then we need to call upon consultants to exhibit a generous degree of cooperation and flexibility and to bridge the discipline and age boundaries.

Generally, service provision for TYAs is supplied in two self-contained structures, with children in the paediatric box and all the rest in the adult box. For some, where there is a TCT unit, an alternative to the rigid two-box system is offered and this works best where practitioners show an elasticity of approach.

In declaring that we offer care from the cradle to the grave, we must ensure that needs are met at all ages. No-one questions paediatric medicine today – nor do they question geriatric medicine – so why do we fail to meet the needs of those at the most sensitive, transitional stage of life?

For teenagers and young people with cancer the appropriate situation is to have specialized staff with specific training in the management of the cancers affecting this age group, and nurses and other staff who have a particular interest in young people who are trained to deal with the medical and psychosocial issues affecting this group of patients.

Ideally (Fig. 1.2), genuinely concerned practitioners will endeavour to accommodate the needs of these patients by blurring the delivery edges. Keeping the patients central, the consultants will bring their particular expertise to the

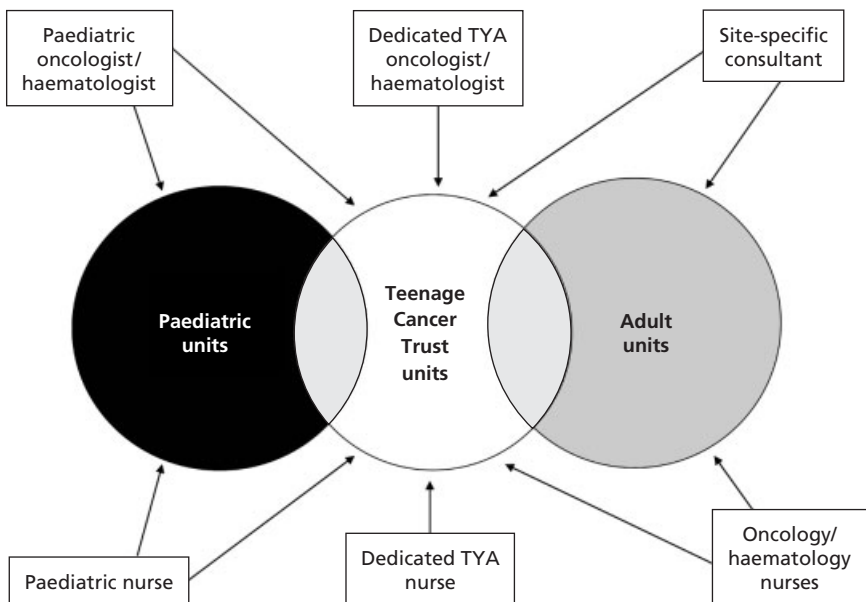


Fig. 1.2 Diagram of professional practitioner flow.

patients, and I envisage that, in all probability, there will always be a need for consultants in certain cancer types to be involved. Nurses specializing in adolescents with cancer will be supplemented by paediatric oncology nurses with an interest in the age group. This will be demanding, particularly where facilities for the very young and for the elderly are miles apart, but some movement in that direction must take place until a critical mass of practitioners specializing in adolescent cancer medicine is built up and we can provide every young person with cancer access to a specialized, age-appropriate facility and team.

Why is this group so special?

I have indicated already some of the particular issues complicating the diagnosis and treatment of young people with cancer. These people are going through a great many changes aside from the impact of their cancer: physical, psychological, emotional, educational and lifestyle alterations.

- *Staff* need different skills when dealing with these patients and also with their parents. Negotiations are far more complex when dealing with TYAs than with small children or fully independent adults. Who makes the decisions – patient or parent? What if they disagree?
- *Physical changes*. While any cancer patient will struggle with physical changes, these are so much more painful for the TYA patient. In our surveys, patients identify their appearance as of more concern than the possibility of death.
- *Fertility* is a vitally important concern for young people. It is a significant possibility that fertility will be impaired or lost as a result of treatment. This can cause major psychological and social damage. When young people are treated in a paediatric setting they are deemed to be children and are not offered advice on fertility. But even in adult centres patients are failed by a lack of fertility counselling.
- *Social relationships*. Peer groups are of primary importance during this period of life. Cancer diagnosis singles out and isolates the young patient. Youth can be a difficult stage to handle without the added complication of cancer. Lack of confidence (despite an often brash image) is not uncommon during the ‘in between’ years. Both self-perception and expectations can deteriorate. Life-threatening disease, change of image, loss of contact with contemporaries and possible loss of fertility can all undermine the fragile self-assurance of the young patient.

Many of our patients who have been treated in either children’s or adult wards have complained that their friends would not visit them – highlighting their sense of being different – and of isolation. In TCT units, friends are considered important and welcomed into the user-friendly surroundings.

- *Education*. It is the norm within the UK for education to be provided for children in hospital – that is, up to 16 years of age – but it is from that age that education and examinations become more serious and achievements at the 16 to early 20s stage can dictate future life work and lifestyle. There is

rarely any educational provision for 17-year-olds and over who are being treated in adult facilities.

- *Independence.* For this age group generally and for our patients in particular, family issues are complex to handle. Many of our patients will just be gaining independence and their illness will throw them back into dependency. Instead of becoming financially self-supporting, or even a contributor to the family coffers, they become a burden. The equilibrium of normal separation, both emotional and financial, will be unbalanced to the detriment of both parents and youngster.
- *Palliative care* too requires very special expertise when dealing with adolescents and young adults. The issues differ considerably from those relevant to other age groups with cancer, and appropriately trained staff for both patients and their families are necessary.
- *Long-term effects* for young people may be more far-reaching than for older cancer patients. Impaired image, fertility loss, neurological and psychological damage, loss of education and life chances, loss of independence and the sword of Damocles effect can all severely affect their future. Will having had cancer always affect their personal relationships, as it may their financial ones? Will potential partners be deterred from long-term relationships? Many insurers are unwilling to provide insurance (sometimes even holiday insurance) or mortgages for people they see as a risk. Or if they do, the premiums are unaffordable. In the USA it has been noted that the young adult age group is the least likely sector to have medical insurance anyway – they are not able to afford it and are too old to be included under their parents' policies. Having cancer when young can determine a survivor's pattern of life.

And now?

We cannot in all honesty say that cancer services, anywhere, are offering the very best to young people with cancer. There is much that is within our power to do and much that we have yet to learn. We know that having cancer at any age is tough, and to combine it with adolescence and young adulthood makes things even harder. We *can* do something about this – and to fail to do so is to fail our young citizens.

Within the UK we have a great advantage. We have the TCT, which for over 10 years has been highlighting the needs, showing the way, lobbying and bringing about change to reduce the disadvantage experienced by many young cancer patients – while successive governments have done nothing!

Although our government has given lip service to the needs of TYA cancer patients, what have they done? In discussion with colleagues from other countries the same or a worse situation seems to exist for them.

We are not even asking the British government for money. This has to be a first! We will continue, as we have over the years, raising money in pennies and pounds to fund our activities – but we *are* asking them for something!

It is hard to believe, but health trusts can take years to see the needs of their TYA cancer patients as any sort of priority. There are hospitals which, after 10 years of discussions, are still deliberating and denying their young patients the service they need and deserve. These institutions need the push that only the state can give. We are willing to go on providing specialized units, to develop expertise, to work on prevention, to encourage research, to provide staff and to continue many of the support services required, but without the backing of the government – without their requirement that health trusts make appropriate provision for young people with cancer – our work will continue to be uphill and slow.

Is the UK government going to sit on its hands and watch while young people with cancer continue to fall behind in the cancer lottery? There may have been some recent improvement overall in cancer death rates, but not necessarily in the young people with whom we are concerned. Funds have been given to support cancer services, but how much has this benefited TYA patients?

Our patients are dying for government recognition and support. It must be remembered that these young people are citizens of the UK; they are the future and current voters, taxpayers, workers, politicians and parents (as are their families) and cannot continue to be ignored.

The government has a responsibility here – one that it has an obligation to meet. It is time that our work was endorsed by the government. This would help accelerate the development of TCT units and services and hopefully improve patients' quality and chance of life.

Remember, it is our young patients' *right* – not just their *privilege* – to receive the best treatment, care and chance of recovery.

References

- 1 Albritten K, Bleyer WA. The management of cancer in the older adolescent. *Eur J Cancer* 2003; **39**: 2584–2599.
- 2 Office for National Statistics. *20th Century Mortality. 2000 Update*. London: ONS, 2000.
- 3 Gatta G, Corazziari I, Magnani C, *et al.*; EUROCARE Working Group. Childhood cancer survival in Europe. *Ann Oncol* 2003; **14** (Suppl. 5): v119–v127.
- 4 National Public Health Service for Wales (2003/4). <http://www.wales.nhs.uk/sites/documents/368/EXTNPHS0304.pdf>
- 5 Birch JM, Alston RD, Quinn M, Kelsey AM. Incidence of malignant disease by morphological type, in young persons aged 12–24 years in England, 1979–1997. *Eur J Cancer* 2003; **39**: 2622–2631.
- 6 Gatta G, Capocaccia R, De Angelis R, Stiller C, Coeburgh JW, EUROCARE Working Group. Cancer survival in European adolescents and young adults. *Eur J Cancer* 2003; **39**: 2600–2610.
- 7 Jeha S. Who should be treating adolescents and young adults with acute lymphoblastic leukaemia? *Eur J Cancer* 2003; **39**: 2579–2583.

Part one
Patterns and perspectives

CHAPTER 2

Patterns of incidence of cancer in teenagers and young adults: implications for aetiology

J. M. Birch

Introduction

Cancer is predominantly a disease of the late middle-aged and elderly, and 65% of all registered cancers (excluding non-melanoma skin cancer) in England are of patients aged 65 years and above. In the year 2000, 0.6% of all cancer registrations were for teenagers and young adults aged 15–24 years.¹ However, cancer is the most common natural cause of death in this age group and is exceeded only by accidents.² Since national cancer statistics are published in 5-year age groups, it is not possible to derive figures for younger teenagers. Little is known about the aetiology of cancers in such young people. It is likely that environmental agents account for the great majority of cancers in older age groups, following chronic exposures over many years,³ but in the young there is no opportunity for such long-term exposure. The mechanisms operating between exposure to a risk factor and the clinical onset of a cancer in the young may therefore be fundamentally different compared with late-onset cancers. In addition, the contributions of the various factors may be proportionally very different and it is likely that genetic susceptibility plays a greater role.

Although a coordinated national approach to the treatment of cancers in younger children was established many years ago,⁴ teenage and young adult cancer patients have not benefited from a similar policy.⁵ The teenage years and early twenties are a crucially important period in terms of educational, social and career development. Interruption of education, vocational and professional training following the diagnosis of cancer can have a lasting impact on later life. Furthermore, the potential late effects of cytotoxic treatment can have a greater and more lasting impact in the young than in the middle-aged and elderly. Loss of fertility, the development of treatment-induced second malignancies and organ failure are critical considerations in this age group. Furthermore, the types and distribution of malignancies presenting in teenagers and young adults are markedly different compared with those seen in young

children as well as in older patients.⁶ For all these reasons, the development of specialist services targeted towards teenage and young adult cancer patients is desirable and necessary to improve all aspects of outcome. In order to develop services tailored to the needs of this age group, it is necessary to define the extent and nature of the patient population through precise analyses of relevant population-based data.

Diagnostic classification

Cancer incidence data are usually presented in terms of the primary site according to the International Classification of Diseases (ICD).⁷⁻⁹ In general, this is satisfactory for the majority of cancers occurring in later life, which are mainly carcinomas, but in young people carcinomas are rare. Therefore, for epidemiological and service planning purposes data on cancers in young people should be presented mainly in terms of morphology.

A classification scheme which is specifically tailored to the teenage and young adult cancer groups has recently been published by our research team.⁶ The scheme is largely based on morphology, and diagnostic groups are specified in terms of the International Classification of Diseases for Oncology (ICD-O) morphology and topography codes.¹⁰ We proposed that the classification scheme should be used in future studies of cancers in teenagers and young adults to achieve a standard format for data presentation, to facilitate international comparisons and encourage an interest in research into these cancers. The scheme was applied to national cancer registration data for England for the years 1979–1997 for patients aged 15–24 years. In this age range the main cancers that occurred were lymphomas, leukaemias, bone tumours, central nervous system tumours, germ cell tumours, soft tissue sarcomas and carcinomas. In contrast to older age groups, where carcinomas of the lung, breast, large bowel and prostate account for more than 50% of all cases¹ at these sites, carcinomas represent only 2% of malignancies in 15- to 24-year-olds. However, certain ‘adult’ cancers are relatively more frequent in this age range. Melanoma and carcinoma of the thyroid represent 8% and 3% of all cancers respectively in 15- to 24-year-olds, but across all ages these cancers make up only 2% and 0.4% of the total.⁶

The classification scheme was subsequently applied to an extended age range, which included younger adolescents, and also presented incidence rates by more detailed morphological type.¹¹ These incidence rates have now been updated to include national cancer registrations for England up to 2000 and are presented below.

Data and statistical analyses

Anonymized national data on individual registered cancers for the years 1979–1992 were obtained from the Office for National Statistics on CD-ROM.¹² More recent data up to 2000 were supplied directly by the Office for National

Statistics. From 1979 to 1994 data are coded by the ICD-O first edition¹³ and the ICD ninth revision⁷ and from 1995 onwards by the ICD-O second edition (10) and the ICD tenth revision.⁸ National population estimates by single year of age, sex and calendar year were supplied by the Population Estimates Unit of the Office for National Statistics.

Eligible cases included all malignant tumours and non-melanoma skin cancers occurring in England from 1979 to 2000 in young persons aged 13–24 years. *In situ* cancers and neoplasms of uncertain behaviour were excluded, as were non-malignant CNS tumours. Individual cancer registrations were classified by type of cancer, age group (13–14, 15–19, 20–24 years), sex and time period (1979–1985, 1986–1992, 1993–2000). Cancer groups were defined by specific morphology and topography code combinations according to the scheme described by Birch *et al.*⁶ Algorithms for selecting tumour groups are given at <http://www.biomed2.man.ac.uk/crcpfcrg/CRUKPFCRG/PFCRG.htm>. Person years at risk for each subgroup were calculated from the population data. Age group, sex- and diagnostic group-specific annual incidence rates per 100 000 population were calculated. An age-standardized rate was calculated at each time period, using direct standardization to the world population.⁹ A combined rate for the entire time span was obtained using a weighted average of the separate standardized rates.¹⁴ The significance of variability by sex, age group and time period was assessed using Poisson regression. Changes in the incidence rate over time were assessed after taking into account variability in cancer rates by age and sex. It was assumed that the changes in incidence rates over time were consistent. All calculations were performed using the statistical package GLIM 4.¹⁵

Incidence rates by age and group

The study included 31,921 cases of malignant neoplasms, 3009 in the 13- to 14-year age range, 10,856 in 15- to 19-year-olds and 18,056 in 20- to 24-year-olds. The study population comprised a total of 178,082,000 person years at risk, including 28,085,000 in the 13- to 14-year age range, 73,197,000 in the 15- to 19-year age range and 76,800,000 in the 20- to 24-year age range (Table 2.1).

Table 2.2 shows the incidence and percentage distribution of malignant disease among the study population by age group and main diagnostic group. Among 13- to 14-year-olds, highest rates were seen for the leukaemias, with lymphomas second highest, then central nervous system (CNS) tumours and bone tumours. In this age group, soft tissue sarcomas, germ cell tumours, melanoma and carcinomas were relatively uncommon. In comparison with younger teenagers, the most striking difference in the 15- to 19-year-olds was a doubling of the incidence rates for lymphomas, which were the most common malignancies in this age group. Rates for leukaemias, CNS tumours and bone tumours were a little lower than those observed in the 13- to 14-year age group, but increases in rates relative to the younger age group were observed

Table 2.1 Registered cases of cancer by age group, time period and main diagnostic group in England, 1979–2000*

Age group (years)	1979–1985				1986–1992				1993–2000			
	13–14	15–19	20–24		13–14	15–19	20–24		13–14	15–19	20–24	
100 Leukaemia	249	575	429		191	546	496		241	523	469	
200 Lymphoma	185	1,023	1,258		185	1,007	1,576		256	937	1,506	
300 Malignant brain tumours	189	380	401		152	410	507		203	380	491	
400 Bone tumours	149	360	172		127	310	222		137	386	222	
500 Soft tissue sarcomas	55	237	269		65	228	300		66	214	279	
600 Germ cell neoplasms	38	297	825		28	332	1,007		63	410	1,215	
710 Malignant melanoma	20	164	405		27	202	664		31	279	752	
800 Carcinoma	75	440	1,141		78	341	1,233		84	448	1,436	
900 Miscellaneous tumours	21	51	54		17	47	67		26	39	48	
1000 Unspecified malignant neoplasms NEC	8	48	83		22	155	341		21	87	188	
All	989	3,575	5,037		892	3,578	6,413		1,128	3,703	6,606	
Population (1000s)	10,309	26,881	25,377		8,106	23,268	26,758		9,670	23,048	24,665	

*Excludes non-malignant CNS tumours and non-melanoma skin cancer. NEC, not elsewhere classified.

Table 2.2 Cancer incidence rates per 10⁵ and percentage distribution for main groups of cancers in young persons aged 13–24 years in England, 1979–2000

	Age group (years)					
	13–14		15–19		20–24	
	Rate	% all cancers in group	Rate	% all cancers in group	Rate	% all cancers in group
Leukaemia	2.42	22.6	2.25	15.1	1.82	7.7
Lymphoma	2.23	20.8	4.05	27.3	5.65	24.0
Malignant brain tumours	1.94	18.1	1.60	10.8	1.82	7.7
Bone tumours	1.47	13.7	1.44	9.7	0.80	3.4
Soft tissue sarcoma	0.66	6.2	0.93	6.3	1.10	4.7
Germ cell neoplasms	0.46	4.3	1.42	9.6	3.97	16.9
Malignant melanoma	0.28	2.6	0.88	5.9	2.37	10.1
Carcinoma	0.84	7.9	1.68	11.3	4.96	21.1
Miscellaneous tumours	0.23	2.1	0.19	1.3	0.22	1.0
Unspecified malignant neoplasms	0.18	1.7	0.40	2.7	0.80	3.4
Total	10.71		14.83		23.51	

in soft tissue sarcomas, germ cell tumours, melanoma and carcinomas. However, rates for these malignancies were still markedly lower than rates for leukaemia and lymphoma. There were distinct differences in the incidence pattern of cancers seen in the 20- to 25-year age range compared with younger age groups. There was a marked increase in rates of lymphomas, which were the most common malignancies, with a substantial decrease in rates for leukaemias. The ratio of lymphomas to leukaemias was approximately 1:1 in 13- to 14-year-olds, but in 20- to 25-year-olds this had increased to more than 3:1. However, the most striking differences were in the rates for carcinomas, germ cell tumours and melanomas, which were the second, third and fourth most common cancer groups observed in these young adults. In contrast, bone tumours were much less frequent compared with the younger age groups, but there was an increase in the incidence of soft tissue sarcomas. The incidence of CNS tumours was fairly similar across all three age groups. The pattern of malignancies that occur in 20- to 24-year-olds overall is therefore very different compared with the younger teenagers. The 15- to 19-year-olds show a transitional pattern. The incidence of all malignancies combined in the 20- to 24-year age group was more than double that observed in 13- to 14-year-olds.

Table 2.3 shows incidence rates for leukaemia subtypes and for non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD). In 13- to 14-year-olds most leukaemias were acute lymphoid leukaemia (ALL), which represented more than two-thirds of all cases. Acute myeloid leukaemia (AML) accounted for nearly all of the remaining cases. Among 15- to 19-year-olds, the pattern was similar, ALL being the most common; AML accounted for most of the

Table 2.3 Incidence of leukaemias and lymphomas per 10⁵ in young persons in England, 1979–2000

	Age group (years)		
	13–14	15–19	20–24
Acute lymphoid leukaemia	1.70	1.24	0.65
Acute myeloid leukaemia	0.57	0.73	0.80
Chronic myeloid leukaemia	0.07	0.13	0.23
Other unspecified leukaemias	0.08	0.16	0.14
Non-Hodgkin's lymphoma	0.91	1.22	1.52
Hodgkin's disease	1.32	2.84	4.13

remainder, but there was an increase in rates for AML and a decrease in ALL relative to the younger age group. However, among 20- to 25-year-olds, AML was the most frequent subtype, accounting for nearly 50% of the cases. Chronic myeloid leukaemia (CML) was relatively rare at all ages but showed increasing rates with increasing age. The incidence of CML in 20- to 25-year-olds was more than three times that seen in 13- to 14-year-olds.

In contrast to ALL, rates for NHL increased with increasing age. Only about half of all registered cases were coded to a specific subtype of NHL. The subtypes specified in the data set are inconsistent with the current international classification of lymphomas, as the classification of NHL has changed substantially during the period covered.^{16,17} However, in summary, nearly 80% of all cases with a specified subtype across the age range 13–24 years were classified as diffuse, about 10% as follicular/nodular and the remainder as other miscellaneous subtypes. The incidence of HD increased markedly with age, and the incidence among 20- to 25-year-olds was more than three times that seen in 13- to 14-year-olds. HD subclassification was consistent across the time period and was based on the Rye scheme.¹⁸ More than two-thirds of the HD cases were coded to a specified subtype. Of these, more than 70% were nodular sclerosing HD and this proportion did not differ markedly within age groups. Mixed cellularity HD comprised nearly 20% of all specified cases and was somewhat more frequent among 15- to 24-year-olds than in 13- to 14-year-olds. Lymphocyte-predominant HD formed less than 10% of all specified cases but was rather more frequent at younger than older ages. Lymphocyte-depleted HD was infrequent across all age groups.

Table 2.4 presents incidence rates of malignant CNS tumours. The most frequent CNS tumour was astrocytoma; in those with a specified subtype, low-grade astrocytomas were more common than glioblastoma and anaplastic astrocytoma in the 13- to 14-year-olds and 15- to 19-year-olds. However, the difference in rates between low-grade and high-grade astrocytoma was less marked in 15- to 19-year-olds than in the younger age group. In 20- to 25-year-olds, high-grade astrocytomas were more frequent than low-grade variants. Rates for ependymoma did not differ markedly among the age groups,