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Paediatric Update

The adolescent with cancer

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1. Introduction

Particular challenges are posed for the adolescent with cancer and for the health care system that attempts to address them. Recent recognition of these special circumstances is exemplified by the decision to give additional attention to them in the columns of Medical and Pediatric Oncology [1,2], the organ of the International Society of Pediatric Oncology (SIOP). Within this initiative, a new mandate of the Children's Oncology Group has been proposed of a task force on cancer in adolescence [3].

This article will explore the issues of incidence and mortality, the spectrum of disease, elements of cancer control, the impact on the adolescent patient, and challenges for the health care system.

2. Incidence and mortality

As an extension of the internationally accepted definition of childhood, which, for the purposes of cancer registration, is 0–14 years of age [4], adolescence has been assigned to the 15–19 year age bracket by the SEER (Surveillance, Epidemiology and End Results) programme of the National Cancer Institute (NCI) in the USA [5]. Within the database of the SEER programme, the annual incidence rate of cancer in adolescence, at slightly more than 200 per million, is higher than in any younger age quintile [6].

More strikingly, in the period 1973–1995, the incidence rate in adolescents increased by 30%, while that in childhood rose by only 10%. This striking increase in incidence in adolescence was due mainly to malignant germ cell tumours and lymphoid neoplasms (Table 1). There were no significant changes in the incidence rates of the other cancers common in adolescents: Hodgkin's disease, central nervous system (CNS) tumours, thyroid carcinoma and malignant melanoma.

At the same time, the fall in the cancer-related mortality rate in adolescents has been less striking than in children (Table 2) such that, over the past 25 years, the prospects for cure in children now exceed that in the older (adolescent) age group. In particular, the survival rates for bone and soft-tissue sarcomas (STS) and for the acute leukaemias are lower in adolescents than in children. These diseases, together with CNS tumours and malignant germ cell tumours, account for more than 80% of cancer-related mortality in adolescence.

3. The spectrum of disease

There is an emerging consensus [7–9] that the classification of cancers in adolescents is better accomplished with the internationally accepted system designed for children [10], that is based mainly on histology, than with the primarily organ-based system (1CD-0) that is used widely for cancers in adults [11]. It may be useful to separate colorectal, lung and salivary carcinomas from 'other carcinomas' within the category of 'carcinomas and other epithelial tumours' in the former system [9]. A similar strategy could be adopted for carcinoma of the breast [3], although this is a rare disease in adolescents [12,13].

The most prevalent malignant diseases in the adolescent age group are listed in Table 3. The malignant lymphomas, germ cell tumours and brain tumours account for almost 50% of the total, a distribution different from that in children and quite distinct from that seen in adults. In adolescents, the incidence of acute myeloid leukaemia is almost equal to that of acute lymphoblastic leukaemia (ALL); diffuse large-cell lymphomas are more common than lymphoblastic and Burkitt's lymphomas; and, among the soft-tissue sarcomas, non-rhabdomyosarcomatous variants predominate

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Table 1
Cancer in adolescence: age-specific incidence rates

	1975–1979	1980–1984	1985–1989	1990–1994
Testicular germ cell tumours	22.1	26.7	24.9	28.4
Non-Hodgkin's lymphoma	10.7	14.5	14.4	16.3
Ovarian germ cell tumours	7.9	8.3	11.8	13.3
Acute lymphoblastic leukaemia	10.6	13.2	12.4	13.0
Osteosarcoma	6.6	8.9	9.7	9.3
Gonadal carcinomas	2.7	2.4	4.3	5.3

Source: Ref. [5].

[3]; again, a distinctly different disease distribution from that observed in children.

There are notable gender differences in the incidence rates of tumours in adolescence [5]. These are ranked in descending order of the M:F ratios in Table 4, ranging from a value of more than 2 for ALL to a striking reversal for thyroid carcinoma which occurs in young women much more frequently than in young men.

Racial differences in incidence rates are evident also. Overall, cancer is more common in white than black adolescents. For example, in the USA, the ratio for the respective incidence rates is 1.5 to 1.0 [5], higher rates being encountered particularly for germ cell tumours, thyroid cancer, malignant melanoma, ALL and Ewing's sarcoma (which is also rare in the Chinese). Similar findings have been reported from the UK [14].

Table 2
Cancer in childhood and adolescence: changes in cancer-related mortality rates

	Age	
	<15 years	15–19 years
1975	45%	36%
1990	25%	24%
2000	15%*	20%[a]

[a] Projected.
Source: Ref. [5].

Table 3
Cancer in adolescence: most prevalent diseases

	%
Hodgkin's disease	16.1
Germ cell tumours	15.2
CNS tumours	10.0
Non-Hodgkin's lymphoma	7.6
Thyroid cancer	7.2
Malignant melanoma	7.0
Acute lymphoblastic leukaemia	6.4

CNS, central nervous system.
Source: Ref. [5].

4. Elements of cancer control

These may be considered individually as follows:

1. Prevention: This assumes knowledge of aetiology, a matter on which there is limited information of good quality. A long list of rare or uncommon genetic diseases is associated with higher incidence rates of skin cancers, malignant lymphomas, sarcomas and liver tumours [3], although these are not limited to the adolescent age group. Regarding environmental exposures, there are clear associations between sunlight and malignant melanoma, in particular in Australia [15] and between maternal use of diethyl-stilboestrol during pregnancy and adenocarcinoma of the cervix/vagina in offspring [16]. The occurrence of second malignant neoplasms after chemo-radiotherapy represents an opportunity for reduction in risk among future patients by modification of primary treatment strategies.

Furthermore, adolescents should be targeted with information for cancer prevention in later life, particularly with respect to the use of tobacco and potential dietary interventions [2]. In this regard, it is disappointing to note that cigarette smoking and alcohol ingestion are as prevalent among adolescent survivors of cancer as these practices are among their peers in the general population [17].

Table 4
Cancer in adolescence: gender differences

Tumour type	M:F ratio
Acute lymphoblastic leukaemia	2.2
Non-Hodgkin's lymphoma	1.8
Ewing's sarcoma	1.8
Osteogenic sarcoma	1.6
Germ cell tumours	1.4
CNS tumours	1.3
Soft tissue sarcomas	1.2
Hodgkin's disease	0.8
Malignant melanoma	0.6
Thyroid carcinoma	0.1

CNS, central nervous system.
Source: Ref. [5].

2. Screening: Given the fact that cancer of the testes is the most common form of malignant disease in adolescent and young adult males, and that cure is attainable in the vast majority of cases if the disease is at an early stage [18], self-examination of the testes has been recommended in these populations [19], a practice that is regrettably seldom implemented. The rarity of breast cancer in adolescent females would appear not to support the promotion of breast self-examination in this age group, but it may be sensible to encourage the early instigation of this strategy, given the risk of the disease in later life.

The American Cancer Society has advised that Papanicolaou smears be collected routinely and regularly from women aged 18 years and older, and from even younger women who are sexually active. The prevalence of abnormal smears has exceeded 10% in sexually active adolescents in New York [20], perhaps related to the increasing occurrence of human papillomavirus (HPV) infection [21]. This is a particular problem among Latinas [20], reflected in the fact that Mexico has the highest recorded mortality rate in the world for carcinoma of the cervix [22].

3. Treatment: By far the most important factor in cancer control in adolescents is anti-neoplastic therapy. There is considerable evidence from North America that patients in this age group who have acute leukaemia enjoy a survival advantage if treated in co-operative study group institutions [23,24]. However, no such advantage exists in the UK [25]. Nevertheless, other reports attest to the importance of entering children and adults with cancer in therapeutic clinical trials [2].

Consequently, it is distressing to note the low accrual rates of adolescents and young adults to such studies [26]. Indeed, at 2% (Table 5), the rate for individuals in the 20–29 year old age bracket is as low as it is for adults in general. Here, surely, is an opportunity for improvement, yet recent experience in the UK attests to the refractoriness of the problem [27].

4. Supportive and palliative care: In common parlance, the term 'supportive care' encompasses medical issues such as the use of antiemetics, analgesia, blood products, antibiotics and nutritional supplementation. None of these raises issues peculiar to adolescents. Rather, the need in this age group is for particular attention to psychosocial support.

Table 5
Cancer in adolescence: (non) participation in clinical trials

	Age (years)		
Index	<15	15–19	20–29
Care at co-operative group institutions	95%	20%	<10%
Entry in clinical trials	65%	10%	2%

Promoting a sense of control and responsibility, effecting programmes in school re-integration, and encouraging/facilitating the development of peer groups are all vehicles for constructive interaction between adolescent patients and their healthcare team [2]. Fostering hopefulness [28] in these patients may be especially important [29], as it is among their peer group at large [30].

At best, palliative care in the adolescent with cancer is a vexatious matter. This is a complex challenge and one to which we have not risen adequately [31] as a community of healthcare providers. There is much to learn and more to be delivered in the end of life care for the young individual afflicted by terminal malignant disease.

5. Long-term follow-up: Otherwise known as 'surveillance and monitoring', its main purpose in the adolescent population is not the early detection of recurrent disease, but discerning the all-too-prevalent late effects of cancer therapy [32–34]. Additionally, this activity should stimulate health maintenance and quality of life, provide a forum for the education of clinicians and afford an environment conducive to the pursuit of research [2].

Regrettably, survivors of cancer in adolescence are poor participants in long-term follow up. The reasons appear to be an amalgam of unwillingness, uncertainty of the need and loss to further contact [35]. Such experiences have led to the recommendation for the establishment of specific adolescent oncology units [27,36] and designated facilities within which long-term follow-up can be undertaken [37,38].

5. Impact on the adolescent patient

In their perceptive review [39], Whyte and Smith list a series of maturational tasks facing and normally accomplished by adolescents (Table 6). The added burden of malignant disease at this age, quite predictably then, leads frequently to loss of self-esteem, control and independence [27]; perturbation of body image with related alteration of sexual identity [40]; and fear of peer rejection [41]; all resulting in reduced participation in

Table 6
Cancer in adolescence

As adolescents mature they:
Become more comfortable with their own bodies
• Work towards independence — from parents and other authority figures
• Build new and meaningful relationships with others of both sexes
• Develop a personal value system
• Learn to verbalise conceptually

Source: Ref. [39].

both physical and social activities [42]. In such circumstances, it is small wonder that many adolescents with cancer travel a difficult path in seeking a return to normality, some bearing permanent scars (both physical and emotional) from their journey.

6. Challenges to the healthcare system

While these may appear to be legion, several demand closer scrutiny in the particular context of cancer in adolescence. At this age, the newly diagnosed patient and his caregivers may be faced at the onset with the difficult issues of informed consent and assent [43]. Although these have received considerable attention from ethicists and legislators alike, and all manner of guidelines have been developed in recent years, there are a few influences that impact fundamentally on the process. These are timing (with respect to the introduction of the subject — very early being ill-advised), the developmental stage of the young participant and the evolving relationship between the patient and the physician [2].

Adherence and compliance, especially with respect to chemotherapy, are lower in adolescents than in younger patients [44–47]. In some measure, this may reflect the lesser influence of and supervision by parents. However, non-compliance is less of a problem when adolescents with cancer sustain a sense of control and responsibility over what is happening to them [48].

The most extreme example, outright refusal of therapy, poses one of the most difficult challenges. This is a complex problem that requires imagination and input from numerous stakeholders to effect a solution [49]; the outcome, even then, is not always accomplished to the satisfaction of all concerned.

Finally, there are the challenges of transitions in care [32]. These may be categorised as on-treatment to off-treatment (either resulting from completion of scheduled therapy or from the transfer of the focus of care to palliation); off-treatment to post-treatment (where the focus is moved from surveillance of the original disease to long-term follow-up); and the movement from child-centred to adult-oriented healthcare systems. Barriers to the successful accomplishment of these transitions have been identified [50]. Perhaps the most intransigent difficulty is posed by the paediatric-to-adult transition. While there is reasonable agreement that this is necessary and desirable [51] for most adolescents with cancer, it does not occur in a planned orderly fashion [35]. To an important degree, this reflects the lack of preparation of adult-oriented physicians at both the community [36] and institutional levels [50].

Much remains to be done to meet the needs of adolescents with cancer; a manifestly neglected population compared with younger patients. An increasing role for co-operative ventures between paediatric and adult study groups is envisaged [3] and holds considerable promise for the immediate future.

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Commentary

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Barr states correctly that "Much remains to be done to better meet the needs of adolescents with cancer", and the new focus on adolescent care in paediatric oncology is welcome and timely.

In all areas of healthcare, there is an increasing recognition of the special needs and problems of adolescents internationally [1]. Adolescents are the one age group in which mortality and morbidity has not decreased in the last three decades [2]. Diseases with social origins such as suicide, accidents and drug-related illnesses, have replaced communicable and congenital diseases as the largest source of mortality for those aged 12 to 17 years [2].

While cancer remains relatively rare in adolescents, the need for better services for teenagers with cancer is clear, particularly given Barr's observation that incidence rates for cancer in young people in the USA have

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