

# Surviving childhood cancer

The 5-year overall survival rate for children and adolescents diagnosed with cancer has dramatically improved in recent years and now stands at 80% (Ries et al, 2002). One estimate is that 1 in 900 people aged 15–44 years in the United States is a survivor of childhood cancer. Increasing numbers of successfully treated children and adolescents are growing up into adults, raising the question of survival, but at what cost?

Much of the improved outcome has rested on the introduction of multimodal treatment, which includes surgery, radiotherapy and more recently complex chemotherapy regimens. The toxicity of such treatment modalities has been pushed to the limit, but it is some time later before the true incidence of long-term toxicity and late sequelae can be realized.

A national UK network of late effects clinics focussing on the late morbidity of treatment has been established, with clinics based in each of the UK's major children's cancer centres. Comprehensive data are now accumulating, giving more information about the possible late effects of new treatment regimens. These data have also highlighted the successful treatment of low stage tumours, for example Wilm's tumour and Hodgkin's disease, resulting in reflection and a decrease in treatment intensity, in the hope of limiting late morbidity.

## LATE MORTALITY

It is well recognized that both the type and intensity of treatment as well as the patient's age at treatment are important factors in overall survival and late effects. Excessive mortality rates are now recognized in 5-year survivors of childhood cancer with studies (Mertens et al, 2001; Moller et al, 2001) reporting a 10.8-fold excess in overall mortality following treatment. The most common reason for death (6–7%) was primary tumour recurrence. An excess was also shown in females and those treated before the age of 5 years. The original diagnosis

was also important with a worse outcome for patients diagnosed with leukaemia or a brain tumour. The risk of treatment-related death including second malignancies is 2%, but worse for patients with Hodgkin's disease or Wilm's tumour.

## CHEMOTHERAPY

Chemotherapy was introduced in the early 1970s and intensified in the 1980s for the treatment of leukaemia. Much has been learnt about the late sequelae of these agents. Congestive cardiac failure is a complication of anthracycline therapy compounded by mediastinal radiation. Regular cardiac review is recommended for those patients exposed to such agents until such time that the dose-related toxicities are understood. Acute and chronic pulmonary fibrosis with long-term restrictive lung disease is recognized as a consequence of bleomycin exposure with or without lung radiation.

Renal toxicity resulting in tubular acidosis and renal rickets can be seen following ifosfamide and platinum treatment, resulting in long-term morbidity and the prospect of renal failure with transplantation. Alkylating agents are well recognized for their potential to induce malignancy, synergistic with the use of radiation.

## RADIOTHERAPY

The use of radiotherapy diminished in the late 1980s particularly for Hodgkin's disease, but also for other solid tumour types and leukaemia. Experience has shown an increase in CNS tumours some years after treatment in patients treated for leukaemia who were given CNS radiation prophylaxis treatment. Children who received CNS radiation younger than 5 years old have been left with substantial intellectual impairment in future years, making educational achievement and adult independence difficult. Limitation in growth of bone and soft tissues can result in major physical compromise as a result of radiotherapy at a very young age. Direct treatment

to the pelvis in girls and testes in boys results in infertility, and if given at a young age this does not allow modern technology to limit the late sequelae.

## SURGERY

Removal of tumours at primary and secondary sites remains an important part of planned treatment. Extensive surgery is more rare because chemotherapy is usually used to shrink large tumour volume and subsequent surgery is less extensive. One arena of success is that of titanium prosthetic replacements for those with limb bone tumours. However, while having a pleasing cosmetic result, function is not always optimum, and data are emerging of infective rates and revisions in the order of 10%, along with the need for replacement after 10–15 years.

## FERTILITY

Survivors of childhood and adolescent cancer are sub-fertile with an adjusted relative fertility of 0.85 compared with siblings. The adjusted relative fertility of male survivors is slightly lower than females. The most dramatic decline in fertility rates is seen in males treated with alkylating agents with or without sub-diaphragmatic radiation (Green, 2001). There is increasing interest in research on interventions aiming to prevent or circumvent the effects of chemotherapy and radiation therapy on gonadal function. Many ethical issues are raised concerning the preservation of gametes (Grundy et al, 2001), in particular cryopreservation of slices of ovarian cortex, immature oocytes, and testicular or epididymal aspiration all remain contentious. For those boys who are Gillick competent the possibility of sperm cryopreservation remains an option, while for other patients in-vitro fertilization or intracytoplasmic sperm injection are other options.

## PSYCHOSOCIAL

The psychological impact of a diagnosis of a malignancy has different ramifications depending not only on personal character and resilience, but

also on the age of diagnosis. For those less than 5 years of age the memory of treatment is pallid. Residual physical deficits may cause difficulty in the future and much depends on family and educational support.

Adolescence presents the other end of the spectrum with an indelible mark made with respect to the experience of receiving treatment. Personal development is suddenly blunted and in many cases it is difficult for individuals to resume a normal lifestyle. Loss of self-esteem, poor body image and erosion of confidence all contribute to long-term morbidity and difficulties of re-integration into society. Increased difficulty in forming personal relationships is well recognized, many patients remaining alone and experiencing dif-

ficulty in maintaining long-term employment. These problems can all be compounded in the presence of physical disability or the subsequent development of ill health as a result of toxic side effects of treatment.

### FUTURE GOALS

Successful treatment for childhood and adolescent malignancy should aim at achieving intact physical and psychological wellbeing. Modifications of present therapy protocols may reduce mortality and morbidity, but most probably major changes or new modes of treatment are required. Recognition by society that total cure and normal life achievements are possible following such a diagnosis would go some way in supporting these patients.

Offering the same opportunities as for the general population, for example life insurance and mortgages, would positively reinforce and recognize what is becoming more and more frequently an expected outcome for childhood and adolescent cancer treatment. The challenges for the survivor of childhood cancer are many. These do not cease concomitantly with active treatment but continue for life, each individual learning to live with the diagnosis and the consequences. **HM**

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### KEY POINTS

- Five-year overall survival for childhood and adolescent cancer is 80%.
- Long-term survival has been achieved using intensive multimodal treatment regimens.
- Long-term follow-up is unveiling significant late morbidity.
- Survivors have a 10.8-fold increased relative risk of mortality following treatment.
- The most likely cause of mortality is recurrence of the primary tumour.
- Second malignancies are associated with radiotherapy and some cytotoxic agents used in primary treatment.
- The younger the age of treatment, the more likely that severe late sequelae will occur.
- Morbidity can be encountered in all body systems. Long-term follow-up clinics continue to monitor these patients.

Green DM (2001) Preserving fertility in children treated for cancer. *Br Med J* **323**: 1201

Grundy R, Larcher V, Gosden RG et al (2001) Fertility preservation for children treated for cancer (2): ethics of consent for gamete storage and experimentation. *Arch Dis Child* **84**: 360-2

Mertens AC, Yasui Y, Neglia JP et al (2001) Late mortality experience in five-year survivors of childhood and adolescent cancer: the childhood cancer survivor study. *J Clin Oncol* **19**: 3163-72

Moller TR, Garwicz S, Barlow L et al (2001) Decreasing late mortality among five-year survivors of cancer in childhood and adolescence: a population-based study in the Nordic countries. *J Clin Oncol* **19**: 3173-81

Reis LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Edwards BK, eds (2002) *SEER Cancer Statistics Review, 1973-1999*. National Cancer Institute, Bethesda, MD ([http://seer.cancer.gov/csr/1973\\_1999/](http://seer.cancer.gov/csr/1973_1999/) accessed 22 July 2002)