BEHIND THE HEADLINES

Behind the Headlines reproduces selected clinical articles which have been published online in *The Bulletin* in the preceding quarter, in order to disseminate this topical clinical information to a wider audience (including those Fellows and Members without internet access).

The reproduced articles aim to educate and inform the wider College membership about specialist items that have been reported in the international medical and mainstream media: to the non-specialist it may not always be clear how accurately such stories – whether reporting results of scientific studies or issues of concern to health professionals – have been reported. To clarify such situations, expert clinical comments are commissioned on matters that are recurring in the international media, or about which different reports have caused conflicting messages for those practising in other specialties.

It is hoped that this section will, in time, become an invaluable source of independent and authoritative advice for Fellows and Members interested in updating their knowledge of new developments in other specialties.

IN THIS ISSUE

- Obesity in childhood – much more than a cosmetic problem; and
- Treating childhood cancer – the cost of a cure.

OBESITY IN CHILDHOOD – MUCH MORE THAN A COSMETIC PROBLEM

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BACKGROUND

While significant media coverage and medical reporting has been, and continues to be, devoted to the global increase in obesity in adults, this article was commissioned in response to the increasing problem of childhood and adolescent obesity. This followed a number of reports which highlighted that childhood and adolescent obesity had reached epidemic levels and also followed the publication of the SIGN guideline on the *Management of obesity in children and young people*.

CHILDHOOD OBESITY IN CONTEXT

There has been much publicity about the health consequences of obesity in adult life in recent years, but there is less appreciation of the issues surrounding obesity in children and adolescents. There is a widespread perception that childhood obesity is largely a cosmetic problem, with only minor clinical effects. We were involved in the publication of a SIGN guideline in April 2003, entitled *Management of obesity in children and young people*.[1] The reasons for the production of the guideline were various: the lack of any evidence-based guideline on childhood obesity; the fact that diagnosis of obesity in childhood is less robustly performed than for adults, and therefore a wide variation in practice occurs; and the mislabelling of some large children as obese, with needless further referral and treatment, while some very obese children are not recognised, nor have appropriate referral or treatment. The rise in the prevalence of childhood obesity in the UK has been appropriately labelled an epidemic,[2] and it continues to this day. The adverse consequences of childhood obesity are increasingly recognised, as is the tendency for childhood obesity to persist into adult life. Despite its rapid rise in prevalence, there have been few prevention trials of childhood obesity, and treatment of childhood obesity has had only limited success, resulting in a negative approach to treatment strategies.

Obesity in children is different from obesity in adults in various ways. The most obvious difference is that children and adolescents need to grow – during puberty, adolescents will double their weight and increase their height by 20%. This will have consequences for the diagnosis of childhood obesity, and also for the management strategies for prevention and treatment of obesity in childhood. In adulthood, obesity is simply expressed as body mass index (BMI – weight in kilograms divided by height in metres squared). For example, a BMI of 26–30 kg/m^2 is considered overweight, a BMI of 30–40 is considered obese, and a BMI greater than 40 is considered morbid obesity. Given the

variation in growth throughout childhood, such a simple expression of obesity, unrelated to age, sex or ethnic background, is not possible. Regarding intervention, over-enthusiastic management may result in restriction of dietary energy, and could compromise normal growth and development. Unlike treatment of adult obesity, weight maintenance is therefore often a suitable goal for children.

Clinical nutrition assessment in childhood and adolescence revolves around energy balance – energy intake (food) minus energy outputs (resting metabolic rate plus activity). In contrast to adult life, where balance should be zero, children need a small continuing positive energy balance to support normal growth. An excess continuing positive balance of energy will lead to excess stores of energy, and thus obesity. It is not only fat which accumulates, but also excess lean body mass. The sources of chronic energy-positive balance leading to obesity are increased energy intake and reduced energy expenditure, by either lack of physical activity or an increase in sedentary behaviour. This simple energy-balance equation is poorly understood by the families of these children, who often believe their children have metabolic problems.

DEFINITION OF CHILDHOOD OBESITY

Subjective assessment of childhood obesity has been shown in both clinical practice and publications to be inadequate, and therefore we need to perform objective assessment. Weight itself is an inadequate measure, given its relation to height, but BMI has been shown in childhood not only to screen for excess fatness, but also to be related to morbidity.[1] This makes it an excellent choice of instrument for the definition of childhood obesity. Body mass index changes with age and differs between the sexes, so age and sex-specific centile charts are needed for childhood and adolescence, with use of cut-off levels. There is widespread support for the use of BMI in childhood,[1] using the UK 1990 Growth Reference Charts.[3] High cut-off levels of BMI centile have a low false-positive rate, so they do not misclassify children who are merely 'big' or 'muscular', but they have a more modest false-negative rate. This means that there are children who are falsely labelled as non-obese with a BMI less than, for example, the 90th centile. Recent work has shown that the BMI centile can also be used for the diagnosis of undernutrition in epidemiological and clinical practice.[4]

PREVALENCE OF OBESITY

In the UK, the adult obesity epidemic began in the late 1970s whereas work by various authors has suggested that it probably started ten years later in children. Cole *et al.*[3] collected growth data for children and teenagers in the UK in 1990, and published these in 1995. We therefore use these UK 1990 nationally representative data for our definitions of overweight and obesity. The Health Survey for England[4] was a nationally representative sample, which showed that in 1996 the prevalence of obesity (defined as BMI >95th centile for age and sex) was nearly 10% at six years of age, 12% at ten years of age, and 17% at 15 years of age. This has now been replicated in multiple other cohort and cross-sectional surveys.[1] In Scotland, data from National Child Health Surveillance Programme in 1999 showed that 9% of children in the first year of primary school were obese (BMI >95th percentile of UK 1990 reference data) and this had risen to 16% at age 15 years.[4] It can therefore be truly stated that obesity is the most common disorder of childhood and adolescence. Epidemiological studies have been less clear at finding high-risk groups in the UK for obesity. There is a definite link with socioeconomic deprivation in Scotland.[5] The issue of whether breast feeding is protective against later development of obesity remains a controversial area.[6]

CONSEQUENCES OF OBESITY IN CHILDHOOD

The answer to the question of 'does childhood obesity matter?' is that it does, both in the short term (for the child) and the long term (in adulthood). The evidence has recently been appraised and summarised in a systematic review.[7] The most common side-effect is psychological morbidity; the major work on psychological ill-health in childhood obesity has come from North America, while adequate research in the UK has not been performed. Very importantly, there is an increase in a cluster of cardiovascular risk factors, such as hyperlipidaemia, high blood pressure, abnormalities in left ventricular mass, hyperinsulinaemia, and prevalence of Type II diabetes.[1,7] Links to the development of asthma have been recognised, and rarer complications occur, such as orthopaedic problems and development of fatty liver.[7] The consequences of childhood obesity for adult life are persistence of obesity, significant increase in cardiovascular risk factors, socioeconomic effects and long-term morbidity and mortality.[7]

PREVENTION, TREATMENT AND MANAGEMENT OF CHILDHOOD OBESITY

The literature on prevention and treatment of childhood obesity has been reviewed recently both in the SIGN guideline[1] and in a pair of Cochrane reviews.[8,9] The disappointing outcome is that there have been few randomised controlled trials (RCTs), and most of these have major methodological deficiencies. Only one high-quality RCT has been identified for prevention of childhood obesity.[1] No high-quality RCTs have been identified for treatment of childhood obesity, and there is no evidence at all on drug therapy, surgery or residential treatments.[1] Despite this

gloomy literature review, we know that there are currently well-designed RCTs being performed in Scotland. MAGIC (funded by the British Heart Foundation and Glasgow City Council) is a prevention trial of childhood obesity in three to five-year-old children in nursery schools in Glasgow, and is a cluster RCT of 580 children which targets activity and inactivity. SCOTT (funded by the Scottish Executive) is an RCT of 140 primary-school-aged children in Central Scotland, which targets increasing activity, reducing inactivity, plus diet.

Given the lack of evidence base, consensus criteria for management of the obese child has been adopted.[1] We have concluded that complex interventions may be the best bet, with reduction in sedentary behaviour, increased lifestyle physical activity, a dietary approach, and family involvement.[1] There is also a strong argument that childhood obesity is a societal problem, rather than one that we can expect individual children and their parents to solve.[10] Useful resources are available for further reading, such as the SIGN guideline,[1] Cochrane reviews[8,9] and the RCPCH Guide to treatment of obesity in primary care.[11]

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TREATING CHILDHOOD CANCER – THE COST OF CURE

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BACKGROUND

This article was commissioned following the publication and media coverage of a report by the US Institute of Medicine in August 2003, which highlighted the complications and delayed side-effects which can be experienced by long-term survivors of childhood cancer and, as such, may be of interest to adult physicians in a number of specialties.

Treatment of childhood cancer is a success story and the chance of five-year survival for a child developing cancer today is nearly 80%. Much of the gain in survival has been achieved through intensifying treatment, particularly through the 1970s and early 80s, using multiple chemotherapeutic agents in addition to modalities such as irradiation and surgery. The main aim was to cure the child of the disease and improving survival rates were seen as proof of success. However, as children became survivors of cancer, the cost of that intensive treatment became apparent with sequelae occurring both directly related to the disease itself but also as a consequence of the therapy.[1] It is estimated that currently about 1 in 1,000 young adults is a survivor of childhood cancer, and attention is beginning to focus to an increasing extent on long-term follow-up of these children so that the excellent survival rates can be maintained and the late effects minimised. Late effects of treatment can be manifest in many ways and include secondary neoplasms, organ damage such as cardiotoxicity, problems with fertility and neurocognitive defects. Effects of these on future quality of life, including education, employment and social standing, may be more subtle. By increasing awareness of such effects amongst not only oncologists but also primary carers, patients and their families, strategies to institute appropriate counselling, follow-up, screening and referral can be implemented.[1,2]

Most information is known in children who have been treated for leukaemia and lymphoma as they constitute about 40% of those with malignancy and the majority does well. Hodgkin lymphoma has also been successfully treated with survival rates now around 90%, and thus there is mature information in this group of patients. As an example of how treatment has changed in the light of experience, not all children with acute lymphoblastic leukaemia now have cranial irradiation.[3] It became apparent that those who had irradiation suffered significantly more side-effects than those treated with chemotherapy alone. Cranial irradiation in acute lymphoblastic leukaemia is associated with an increase in neurocognitive problems which are manifest as difficulties with mathematics, abstract reasoning, memory and concentration. Central nervous system (CNS) irradiation is also associated with second malignancies, particularly CNS tumours.[3,4] This treatment modality has now been reserved for those in the highest risk subgroups or those with CNS involvement. In contrast, by introducing combined modality therapy in Hodgkin lymphoma, excellent treatment outcomes have been achieved with reduced incidence of treatment sequelae by utilising lower doses and smaller volumes of radiation therapy, and fewer cycles of less toxic chemotherapy.[4] It is recognised that irradiation in Hodgkin lymphoma is associated with a significant increase in secondary malignancy. For instance, secondary thyroid cancer is associated with a 36-fold increased risk in those who have had irradiation over the general population and there is a 55-fold increased risk of developing breast cancer in women who have had mantle radiotherapy. On the other hand, high-dose chemotherapy using alkylating agents may increase the risk of complications of myelosuppression at the time of therapy and gonadal dysfunction and secondary leukaemia later on. The degree of gonadal dysfunction depends on the drugs used, and can vary from sterility in the majority of patients to recovery of gonadal function in the majority of patients. This has led to the introduction of alternating combination chemotherapy regimens with less gonadotoxic drugs. Overall, the cumulative risk of developing a second malignancy in someone who has been treated for Hodgkin lymphoma ranges from 7·6% at 20 years to 18% at 30 years.[4] As ever, a balance between therapies, survival and late effects must be achieved and collection of data, from diagnosis, staging and treatment initiation through to many years off treatment, is imperative. The commonest malignancy following treatment for cancer in children is leukaemia which accounts for just over one-third of cases and is associated with the use of high doses of alkylating agents such as cyclophosphamide and topoisomerase II inhibitors such as etoposide. Brain and spinal malignancies account for a further 25% with bony tumours, soft tissue sarcomas and carcinomas making up 10% of the total cases each. The solid malignancies most often occur within or just at the edge of any field of irradiation. Advice can be given to pay particular attention to any symptoms or signs developing in such areas and to investigate appropriately.

Treatment of cancers other than leukaemia and lymphoma often require both chemotherapy and localised irradiation. The irradiation will carry an increased risk of secondary malignancy as outlined above but other significant late effects can occur with irradiation, including growth retardation, endocrine abnormalities and decreased fertility and damage to various organs such as the heart and lungs. Knowing the field of irradiation is essential when predicting possible secondary effects and thus directed screening for them. Monitoring growth, endocrine function or referral for specialist reproductive advice may allow early and more effective therapy. Drug regimens that use anthracyclines are particularly associated with cardiotoxicity, which may present gradually with signs of congestive cardiac failure or as a catastrophic event during increased stress such as pregnancy and labour or increased physical activity. The incidence of anthracycline-induced cardiomyopathy is dose-dependent and reduced cumulative doses have resulted in reduced toxicity. However, subclincal toxicity may be present even in those who have had comparatively safe doses.[4] It is important that patients and their doctors understand the increased risk of possible myocardial dysfunction so that function can be assessed by echocardiography in situations such as early pregnancy or prior to commencing such activities as long-distance running or weightlifting.

Treatment protocols are continually being modified to intensify the therapy for those in high-risk groups and to reduce therapy in the good-risk groups. More information on the biology of tumours and their drug sensitivity can help determine risk as well as more accurate methods to detect extent of disease. Sensitive methods of monitoring disease progress and response, e.g. at the molecular level in leukaemia, are being developed and implemented to enable stratification of patients into such groups. Risk-adapted therapy can then be instituted with the aim of maintaining an excellent disease-free survival with a reduction in late effects. There is an ongoing responsibility for those treating children for cancer to follow up the survivors in a systematic way to test whether these new treatment strategies deliver what is hoped. This careful surveillance should be conducted within the context of scientifically valid research, which will inevitably require cooperation between multiple institutions with agreed guidelines for follow-up.

But is it just the responsibility of oncologists to ensure adequate follow-up of these patients? As well as specialist follow-up clinics, education of the patient, carers and primary care physicians is of paramount importance so that reporting of symptoms or signs and appropriate referral or investigation can occur without delay. Specific

information on the possible late side-effects of drugs and any irradiation (including the field) should be given, preferably in written form as some of the problems can occur decades after the treatment. While not wanting to cause increased anxiety in survivors of childhood cancer when they develop minor ailments, it is important that the possible significance of what otherwise might be considered a trivial or unusual complaint is realised. For instance, breathlessness may be secondary to lung fibrosis or cardiomyopathy; back pain may be secondary to a developing osteosarcoma or tiredness may be due to hypothyroidism or a blood dyscrasia. The problem of late effects must not overshadow the huge advances that have been made in the treatment of children's cancer. More, having been recognised as a significant problem, they should spur on doctors and researchers in the field to develop strategies to achieve the goal of cure with minimal long-term adverse outcomes.

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