Improving care for central nervous system tumours: a mood for change

Central nervous system (CNS) tumours are both numerically and clinically important. They share a similar incidence with acute leukaemia, making them the commonest group of solid tumours. However, such a statement masks the histological and clinical diversity of this group of tumours. Included within the category are both classically described ‘benign’ and ‘malignant’ tumour types. Outside the brain, these terms confer a meaningful prediction of the risk of tumour spread, tumour recurrence, sensitivity to treatment, and subsequent prognosis. The application of these terms within the brain is less clear cut, as additional factors such as the age of the patient and the anatomical site of the tumour are also critical factors which dictate life expectancy. Furthermore, the histological grading of tumours can underestimate malignant potential either because of sampling error in heterogenous tumours or because tumours evolve into a more malignant phenotype.

The commonest tumour type is the astrocytic tumour that can be classified as either high grade (malignant) or low grade (benign). High grade astrocytic tumours are rare but are associated with a very poor prognosis because of their propensity to recur locally, and spread within the CNS. Low grade astrocytic tumours include a wide variety of discrete histological entities that tend to grow slowly and recur many years after primary diagnosis. The commonest malignant tumours are in the embryonic tumour group, which includes medulloblastomas and primitive neuroectodermal tumours (MB/PNET). Many of the tumours carry an abysmal prognosis for survival: diffuse intrinsic brainstem gliomas 0–15%, glioblastoma multiforme 0%, and anaplastic astrocytoma 30%. Even an embryonal tumour such as MB/PNET carries a five year survival of only 6% and a lower 10 year survival. One unifying theme in all these tumours is their occurrence in a developing CNS that is vulnerable to local effects of the tumour, the effects of raised intracranial pressure, and the toxic effects of chemotherapy and radiotherapy.

Radiotherapy in particular, has been shown to have a detrimental effect upon growth and neuropsychological outcome with the magnitude of the effect being inversely related to age at treatment. Such issues pose clinical and ethical questions. How do we improve survival rate while minimising subsequent brain damage? Is it acceptable to change our treatment and risk current cure rates in the hope that the survivors will have a higher health related quality of life.

Achieving a balance between improved survival and quality of life is of course a major preoccupation of all paediatric oncologists whether they treat brain tumours or not. Why should this be a special concern for paediatric neuro-oncologists? For the majority of childhood tumours, the greatest gains in terms of survival came from the introduction of effective chemotherapy during the 1950s and 1960s. This was true even for rare tumours such as rhabdomyosarcoma and was initially achieved by the centralisation of expertise (in the UK through the United Kingdom Children’s Cancer Study Group, UKCCSG) and subsequently the setting up of national and international clinical studies or trials. Childhood acute lymphoblastic leukaemia and Wilms’ tumour were the first diseases to be tackled by a coordinated national approach and this model has been extended to all of the major childhood tumours with the notable exception of many CNS tumours. The result is that 87% of haematological malignancies and between 60–92% of paediatric extracranial solid malignancies are managed in accredited UK (UKCCSG) centres by a paediatric oncologist. The conduct of each trial has been associated with sequential improvement in survival and there is a significant survival benefit linked to treatment in a specialist centre. Through assiduous long term follow up of treated patients important questions have been answered including the rate of late relapse, incidence of second tumours, and the influence of treatment on normal organ development. It is a sign of the maturity of these studies that current clinical trials are able
to look at the issue of maintaining excellent survival while attempting to reduce late morbidity.

The story for CNS malignancy lags far behind other tumours. In the UK any improvement in survival has largely been attributable to improvements in perioperative care, the introduction of radiotherapy, and most recently the startling developments in neuroimaging. While there may be good biological explanations for lack of progress, some operational issues also need to be explored. It is certainly true that with the exception of medulloblastoma there has been no commitment to sequential clinical trials. Not surprisingly there has been a low referral rate of most CNS malignancies to paediatric oncologists. These two facts are probably related, as the sequential trials in medulloblastoma that have been running since the late 1970s have resulted in 80% of children with medulloblastoma being registered by UKCCSG centres. Opening a trial is therefore likely to be a powerful tool in directing referral to specialist teams. The lack of trials means that we have much poorer information about the natural history, optimal treatments, and outcome of many CNS malignancies. It is sad to say that in 1996 we still do not really know the true place of even our most established adjuvant therapy, radiotherapy, in tumours such as ependymoma and low grade astrocytoma.

Over the past five years there have been signs of change. This has been driven by three main forces: the research based professional groups, the parents and the Department of Health, through their drive to identify standards of care with which to guide purchasers. The UKCCSG in close cooperation with the International Society for Paediatric Oncologists (SIOP), has made a commitment to open a portfolio of clinical studies and trials for all brain tumour types. The studies that are developing are designed both to evaluate multimodality strategies of care, as well as to investigate the role of adjuvant chemotherapy. In order to investigate multimodality strategies of care, a consensus among clinical specialists must be reached regarding standard clinical practice before novel adjustments can be proposed and tested. In addition, the studies are asking important questions about the role of adjuvant chemotherapy. Can it be used to delay radiotherapy in young children so that normal brain maturation can occur? Will novel scheduling of drugs as well as novel agents, selected for their good CNS penetration, improve our ability to shrink tumours or eradicate residual disease? Studies have opened for high grade and low grade astrocytic tumours, malignant tumours in young children (<3 years),

intracranial germ cell tumours, as well as the ongoing studies in medulloblastoma. More studies will open during this year including ones for brain stem glioma and ependymomas. A number of phase 1 and 2 trials of novel agents have been developed by the UKCCSG New Agents Group with CNS tumours particularly in mind.

The second force comes from the parent body. A better informed public looks for evidence both within the UK and abroad. Information on novel treatment is widely published both in popular literature and through computer networks. Data from single institutions is freely available and is very powerful in raising expectation of cure and quality of survival. Failure to provide information to parents on investigational treatments and to assist them in understanding their meaning, leads families to seek care overseas where hope is on offer, even if a cure is not. A recent survey performed through the UKCCSG revealed that families being seen in the NHS were known to have sought treatment abroad. This treatment has largely been provided in the context of research programmes, and therefore not proved treatment. There is no doubt that similar treatments could have been given within the UKCCSG research framework, closer to home and with less monetary and emotional cost.

The third force has evolved from the first two. The Department of Health has responded to the concerns of physicians, neurosurgeons, and parents by promoting the development of national guidelines for provision of brain tumour services for children and young people. These guidelines have been accepted by a wide variety of relevant specialist royal colleges and professional associations. They are to be launched this year and form the basis of recommendations to purchasers.

We are at a point therefore where there is a mood of change. The opening of new studies and discussion of neuro-oncology teams has lead to increased referral to UKCCSG centres. In 1996, 60% of UK children with brain tumours were registered by a cancer centre. This has risen from 40% in the mid 1980s, yet compares with 90% of children treated for acute lymphoblastic leukaemia. This is a big improvement but masks substantial regional variations (4–70%) and does not identify when the referral was made in the evolution of the child’s illness, that is referral at diagnosis or at time of tumour recurrence.

Where are the current challenges? The first must be to establish clear patterns of referral to specialist units where individual specialists declare their intention to take a major interest in the management of children with brain and spinal tumours. The first line of referral is most commonly to a neurosurgeon. There has been an historical reluctance on the part of neurosurgeons to accept that this sort of subspecialisation is necessary. While it seems intuitively right that a better clinical outcome might be expected if expertise was built up among a limited number of surgeons, this is actually difficult to prove. However the process of establishing a multidisciplinary management team would undoubtedly be easier with a smaller number of neurosurgeons contributing more intensively to discussion of individual cases and research protocols, and would be in line with principles established in other surgical disciplines.13–12 The second challenge is to establish robust mechanisms and funding for successive national and international trials of novel treatments. The third is to optimise the arrangements within community paediatric services for rehabilitation of these children who may have substantial acquired neurological handicap as well as the personal experience of complex treatment and the knowledge that they have a life threatening disease.

The general paediatrician has a very important role to support this mood of change. Most children present to their local paediatrician or paediatric neurologist. Children’s services should identify which neurosurgical unit is to provide an integrated neuro-oncology service. Moreover it should be possible to identify a neurosurgeon within that unit who will take the lead in the management of children and liaise with the oncologists and radiotherapists to provide integrated care. Once the patients are included in a standardised clinical environment, treated according to standardised and research orientated treatment programmes, we might begin to determine whether there are biological reasons as to why we have made only modest progress.

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School refusal and truancy

School refusal

DEFINITION
School refusal is a condition characterised by reluctance and often outright refusal to go to school in a child who: (1) seeks the comfort and security of home, preferring to stay home excessively and avoiding contact with other children or friends; and/or (2) displays evidence of emotional upset when faced with the prospect of having to attend school, although this may only take the form of unexplained physical symptoms; (3) manifests severe antisocial tendencies, apart from possible aggressiveness when attempts are made to force school attendance; and (4) does not attempt to conceal the problem from parents.  

FEATURES
Boys and girls are equally affected and there is no relationship to social class. Neither is there any relationship with intellectual or academic ability. The youngest in a family of several children is more likely to be affected and parents are often older than would otherwise be expected. It can affect a school child of any age, but young teenagers at about the time of transition from primary to secondary school are more likely to develop school refusal. Although uncommon in the general population, it forms a not inconsiderable proportion of referrals to child mental health services. Onset tends to be gradual, with increasing problems in facing up to leaving home to go to school, but it may occur suddenly after time away from school because of illness or holidays, it may occur after some upsetting event, or just come on without any obvious reason. There may be no associated social impairment, but there often is, including staying home excessively and avoiding contact with other children. The problem has been called 'home-bound school absence'.

PSYCHIATRIC DISORDER
School refusal can sometimes occur without any accompanying disorder classifiable on currently used systems of classification. On the International Classification of Diseases, 10th revision (ICD-10), a frequent disorder linked to school refusal is separation anxiety disorder (F93.0), although one of the criteria for saying that this disorder exists is school refusal, but there are several other disorders mostly involving anxiety and depression that may be present: for example, phobic disorder of childhood (F93.1), social anxiety disorder of childhood (F93.2), agoraphobia without panic disorder (F40.0), mild depressive episode (F32.0), and adjustment disorder (F41). More than one of these may coexist, a situation described as comorbidity.

DIAGNOSIS
The problem is clearly one of school refusal when the criteria in the definition above are present and symptoms of anxiety and depression are very evident. Physical symptoms that are clearly manifestations of emotional upset when they are limited to school mornings include tummy ache, frequency of micturition, anorexia, diarrhoea, pallor, and headache. Less clear cut vague physical symptoms, without a cause being found, sometimes occur not so obviously related to having to go to school, but the fact of excessive school absence and the child’s unwillingness to make an effort to attend school suggest the diagnosis. The name ‘masquerade syndrome’ has been given to the situation where school refusal masquerades as physical illness. The condition may be thought to be ME.

MANAGEMENT
It is important to convince child and parents that the problem is a pathological emotional reaction to leaving home and/or going to school and not some undiagnosed physical disorder. It is also important to convince them that, despite any anxiety/mood disorder, return to school will substantially improve matters. Early return to school is the treatment of choice. To accomplish this, the child needs a great deal of help in the form of coordinated action on the part of family, school, community workers, and the medical profession. Any physical investigations required to exclude a physical cause for symptoms should be speedily completed and the family encouraged not to pursue the search for physical illness as an explanation for the problem. Referral to mental health services for children will be required if return to normal school attendance cannot be achieved in a reasonable period of time or if psychiatric symptoms persist when it is. Medication has no part to play in the treatment of school refusal.

OUTCOME
The long term outcome is very good, in so far as school refusers in later life only tend to suffer from minor problems of anxiety and/or depression, and possibly some reluctance to leave home and set up their own families. However, if it not satisfactorily managed, it can persist for months or even years. In the short term the main problem of school refusal is the loss of education.