Brain tumours in children

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Sources – uptodate and Illustrated Paediatrics

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Definition

Brain tumours

In contrast to adults, brain tumours in children are almost always primary and 60% are infratentorial. They are the most common solid tumour in children and are the leading cause of childhood cancer deaths in the UK. The types of brain tumour are:

- Astrocytoma (~40%) - varies from benign to highly malignant (*glioblastoma multiforme*)
- Medulloblastoma (~20%) - arises in the midline of the posterior fossa. May seed through the CNS via the CSF and up to 20% have spinal metastases at diagnosis
- Ependymoma (~8%) - mostly in posterior fossa where it behaves like medulloblastoma
- Brainstem glioma (6%)
- Craniopharyngioma (4%) - a developmental tumour arising from the squamous remnant of Rathke pouch. It is not truly malignant but is locally invasive and grows slowly in the suprasellar region.

Incidence

Age — The incidence of childhood CNS tumors varies with age. From the CBTRUS database, the following annual age-adjusted rates of CNS tumors per 100,000 from 2007 to 2011 were reported [3]:

- Less than 1 year of age: 6.22
- Between 1 and 4 years of age: 5.53
- Between 5 and 9 years of age: 5
- Between 10 and 14 years of age: 5

Gender — The rate is higher in males compared with females [1-3,5,6].

Race and ethnicity — The incidence of CNS tumors is greatest in white and Asian/Pacific islander children. The following age-adjusted rates per 100,000 for CNS tumors in children <15 years in different races and ethnic groups were noted in the CBTRUS (2007 to 2011) report [3]:

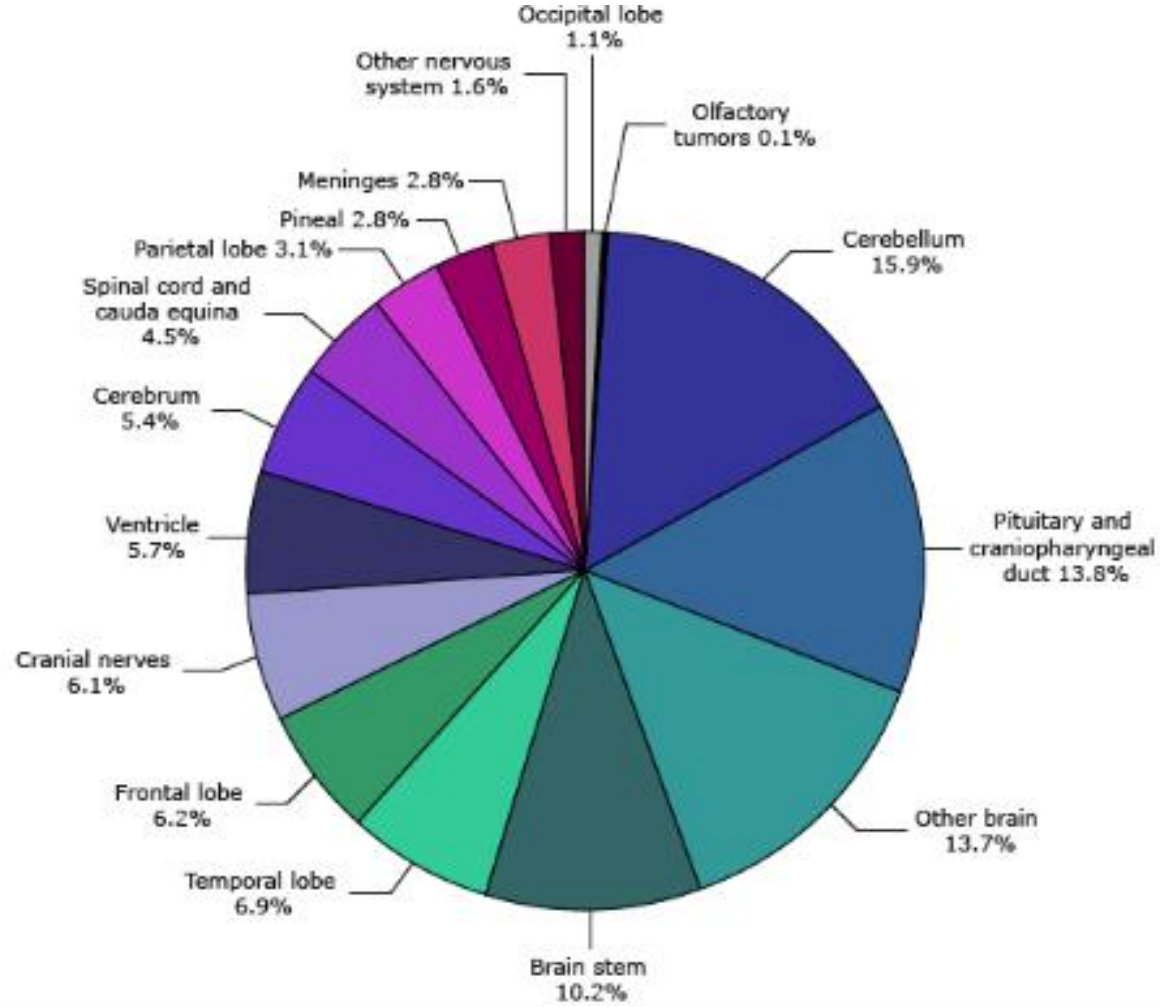
- White: 5.46
- Hispanic: 4.36
- Black: 4.12
- Asian/Pacific Islander: 6.05
- Native American: 2.46

Clinical presentation

Types of brain tumours

- Gliomas (gliomas are graded according to whether they are slow-growing (low-grade) or fast-growing (high-grade); grade 1 is the slowest-growing type and grade 4 is the fastest-growing):
  - Astrocytic tumour: low-grade astrocytoma, anaplastic astrocytoma, glioblastoma multiforme.
  - Oligodendroglioma: benign or anaplastic.
  - Ependymoma: benign or anaplastic.
  - Mixed glioma: astrocytoma and oligodendroglioma.
  - Ganglioglioma: benign or anaplastic.
  - Choroid plexus tumour: papilloma or carcinoma.

- PNETs: supratentorial primitive neuroectodermal tumours, medulloblastoma, pineoblastoma.
- Congenital: teratoma, craniopharyngioma.
- Pineal tumours: germinoma, endodermal sinus tumour, embryonal cell carcinoma, choriocarcinoma, pineocytoma or pineoblastoma.
- Very rare tumours: primary CNS lymphoma.
- Benign tumours (more common in adults): meningioma, acoustic neuroma, pituitary tumour.



CNS: central nervous system.

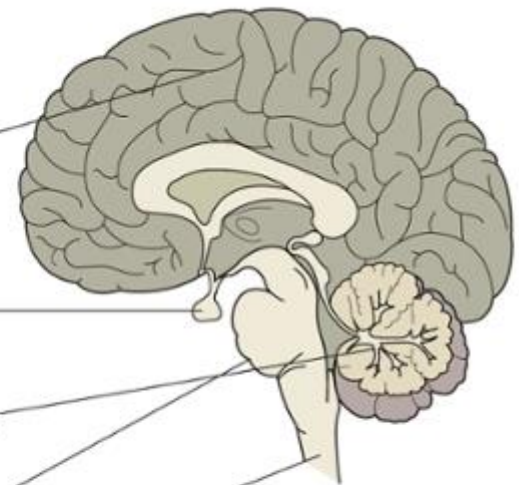
Graphic 81514 Version 3.0

Supratentorial:
- Cortex – astrocytoma

Midline:
- Craniopharyngioma

Infratentorial:
- Cerebellar – medulloblastoma, astrocytoma, ependymoma
- Brainstem – brainstem glioma

Spinal cord:
- Astrocytoma, ependymoma



(a)

Raised intracranial pressure

Children and adolescents
Headache – worse in the morning
Vomiting – especially on waking in the morning
Behaviour/personality change
Visual disturbance
Papilloedema

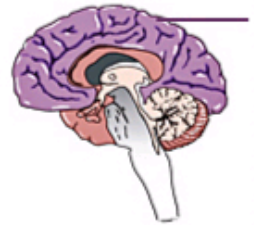
Infants
Vomiting
Separation of sutures/tense fontanelle
Increased head circumference
Head tilt/posturing
Developmental delay/regression

Signs and symptoms of pediatric central nervous system tumors based on tumor location

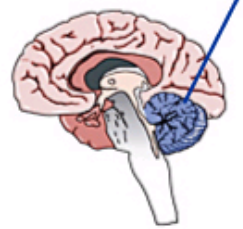
Tumor location	Presenting signs/symptoms
Cerebral cortex	Headache, seizures, hemiparesis, hyperreflexia, clonus, sensory loss, speech disturbances, memory deficits, personality changes
Posterior fossa	Nausea and vomiting, headache, abnormal gait and coordination, papilledema, abnormal eye movements
Brain stem	Cranial nerve deficits, gait and coordination disturbances, nystagmus, focal motor weakness, signs of increased ICP including headache and papilledema
Spinal cord	Radicular pain and/or weakness (symptoms correspond to level of lesion); loss of bowel/bladder control; gait abnormalities
Optic pathway	Visual disturbances; proptosis; nystagmus
Hypothalamus	Endocrine disturbances including diabetes insipidus and growth failure

ICP: intracranial pressure.

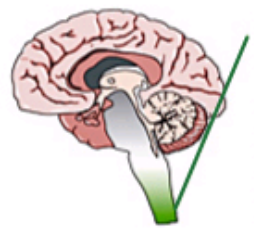
Central nervous system tumor presentation and site in children



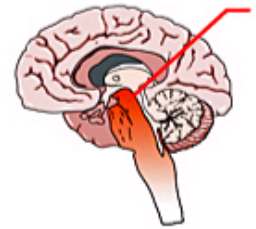
Supratentorial tumours:
- Unspecified symptoms of raised ICP* 47%
- Seizures 38%
- Papilloedema* 21%
- Focal neurological signs 17%
- Headache* 11%
- Hemiplegia 10%
- Nausea and vomiting* 8%
- Macrocephaly* 6%



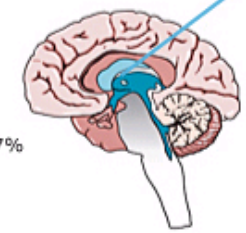
Posterior fossa tumours:
- Nausea and vomiting* 75%
- Headache* 67%
- Abnormal gait and coordination difficulties 60%
- Papilloedema* 34%
- Abnormal eye movements 20%
- Lethargy 13%
- Nausea without vomiting* 10%
- Unspecified symptoms and signs of raised ICP* 9%
- Weight loss 9%
- Focal motor weakness 9%
- Macrocephaly* 7%
- Impaired consciousness 7%
- Vertigo or auditory symptoms 7%
- Squint 6%
- Stiff neck 6%
- Head tilt
- Accidental head injury 5%



Spinal cord tumours:
- Back pain 67%
- Abnormal gait or coordination difficulties 42%
- Spinal deformity 39%
- Focal motor weakness 21%
- Sphincter disturbance 20%
- Decreased upper limb movement 17%
- Developmental delay 8%
- Head tilt 7%
- Headache* 7%

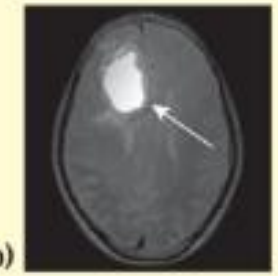
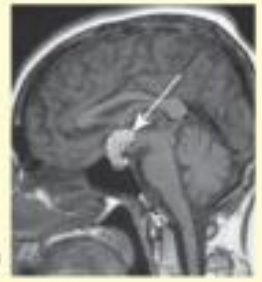
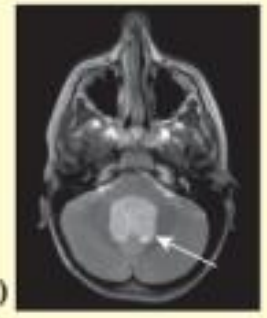
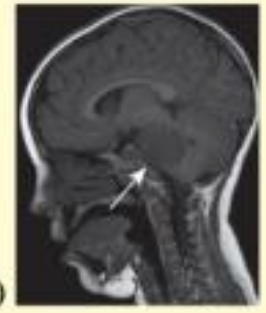


Brain stem tumours:
- Abnormal gait and coordination difficulties 78%
- Cranial nerve palsies (unspecified) 52%
- Pyramidal signs (unspecified) 33%
- Headache* 23%
- Squint 19%
- Focal motor weakness 19%
- Facial palsy 15%
- Papilloedema* 13%
- Unspecified symptoms of raised ICP* 10%
- Abnormal eye movements 6%
- Behavioural change or school difficulties 5%



Central tumours:
- Headache* 49%
- Abnormal eye movements and squint 21%
- Nausea and vomiting* 19%
- Papilloedema* 18%
- Reduced visual acuity 16%
- Unspecified symptoms and signs of raised ICP* 13%
- Diabetes insipidus 12%
- Abnormal gait and coordination difficulties 10%
- Optic atrophy 9%
- Behavioural change or school difficulties 9%
- Altered level of consciousness 9%
- Reduced visual fields 8%
- Seizures 7%
- Hemiplegia 7%
- Focal motor deficit 7%
- Developmental delay 7%
- Short stature 7%
- Weight loss 5%
- Vertigo or auditory symptoms 5%
- Visual or eye abnormalities (unspecified) 5%

%: percent.
* Symptom or sign caused by raised intracranial pressure (ICP).

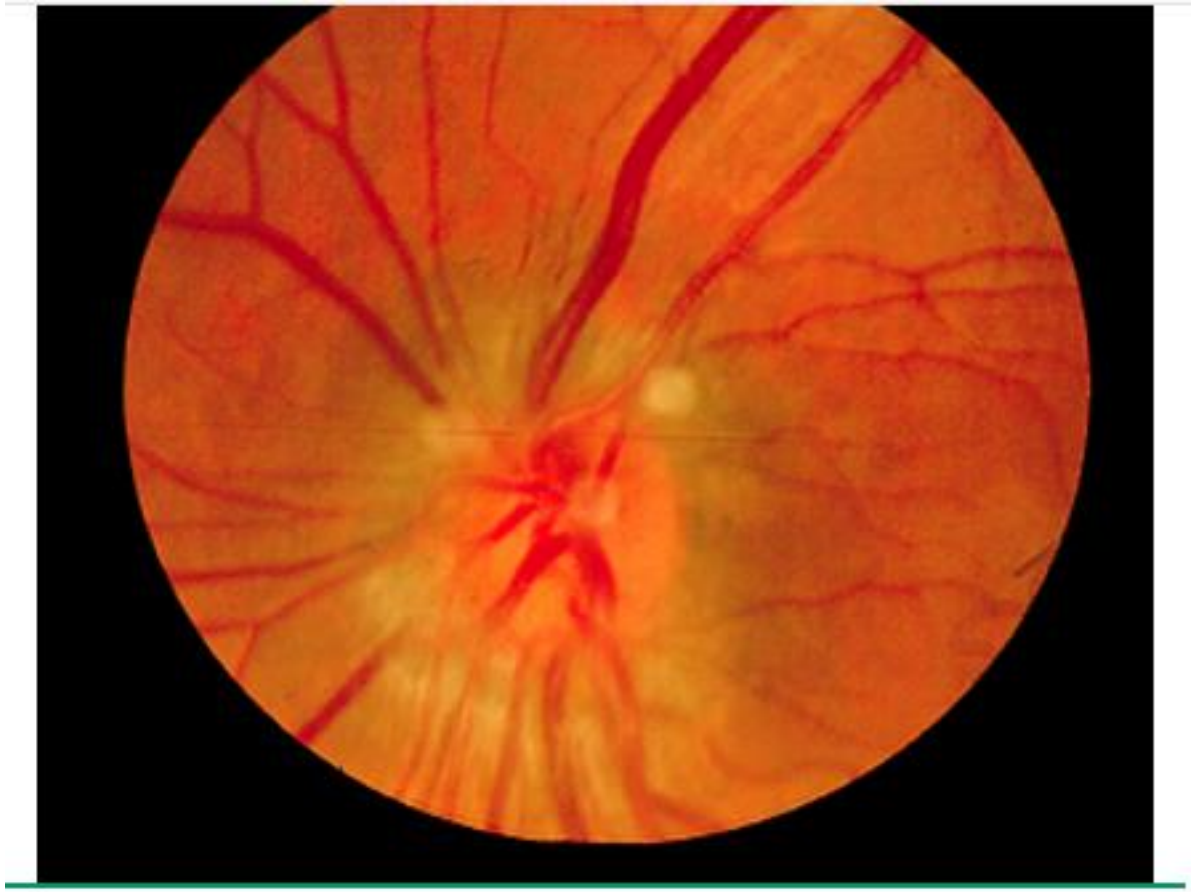
Site of tumour and clinical features specific to anatomical postition	MRI Scans	Typical case history
Supratentorial – cortex Seizures Hemiplegia Focal neurological signs	 (b)	14 year old. Aggressive behaviour at school, headaches, seizure MRI scan – **(Fig 21.8b)** Diagnosis – **astrocytoma – glioblastoma multiforme** Management – surgery, radiotherapy +/- chemotherapy, but prognosis poor (<30% survival) Astrocytomas – commonly found in the cerebral hemispheres, thalamus and hypothalamus. For posterior fossa tumours, see below.
Midline Visual field loss – bitemporal hemianopia Pituitary failure – growth failure, diabetes insipidus, weight gain	 (c)	10 year old complaining of headaches, vomiting, poor growth, struggling to see the board at school. MRI scan – **(Fig 21.8c)** Diagnosis – **craniopharyngioma** Management – surgical excision +/- radiotherapy Prognosis – good survival but risk of long-term visual Impairment and lifelong, complex pituitary insufficiency
Cerebellar and IVth ventricle Truncal ataxia Coordination difficulties Abnormal eye movements	 (d)	3 year old vomiting in the mornings, unsteady on his feet, new-onset convergent squint. MRI scan – **(Fig 21.8d)** Diagnosis – **medulloblastoma** Management – surgery, chemotherapy, radiotherapy. Prognosis – survival rates are improving with 5-year survival about 50% Other posterior fossa tumours: Astrocytoma – cystic, slow growing. Good prognosis following surgery. Ependymoma – behaves like medulloblastoma
Brainstem Cranial nerve defects Pyramidal tract signs Cerebellar signs – ataxia Often no raised intracranial pressure	 (e)	4 year old. Refuses to walk, unable to climb stairs, squint, facial asymmetry and drooling. MRI scan – **(Fig 21.8e)** Diagnosis – **brainstem glioma.** But not for biopsy as too hazardous. Management – palliative radiotherapy Prognosis – very poor (<10% survival)

Common developmental milestones

Milestone	Age at acquisition
Fixes gaze briefly, habituates to stereotyped auditory, visual, and tactile stimuli	At birth (40 weeks post conceptional age)
Smiles responsively, gurgles	2-3 months
Visual tracking of a bright object to 180 degrees	3 months
Rolls over, holds head upright when pulled from supine to sitting	3 months
Reaches out for objects	4-5 months
Maintains sitting position independently	6 months
Grasps objects using thumb and index finger pulp	8-9 months
Crawls, babbles, uses non-specific "Mama", "Dada" sounds	9-10 months
Pulls up to stand and walks with support	10-11 months
Walks independently, uses 2-3 clear words, including specific "Mama" and "Dada"	13-14 months
Can point to body parts, use simple phrases	18-19 months
Names body parts, states age, uses phrases	24 months
Pedals tricycle, speaks in sentences, asks questions, likely toilet trained, can name primary colors	36 months
Masters concepts of alphabets and numbers	4-5 years
Able to read simple words, add, subtract	5-6 years
Concepts of division, multiplication, geography, general information like cities, states, large rivers, oceans, etc.	7-8 years

Courtesy of Suresh Kotagal.

4 months	Rolls from front to back
5 months	Rolls from back to front
6 months	Sits with support
9 months	Pulls to stand
12 months	Walks independently
18 months	Runs
27 months	Walks up stairs (both feet on each step)
36 months	Walks up stairs alternating feet
	Rides tricycle
4 years	Hops
	Walks up and down stairs alternating feet
5 years	Skips
6 to 7 years	Rides bicycle without training wheels



Papilledema, characterized by blurring of the optic disc margins, loss of physiologic cupping, hyperemia, and fullness of the veins, in a 5-year-old girl with intracranial hypertension due to vitamin A intoxication.

Courtesy of Gerald Striph, MD.

Investigation

- CT or MRI, MRI is better
- MR spectroscopy, a supplementation to traditional MRI, can differentiate locally infiltrative brain tumors from other intracranial lesions by detecting the presence of specific metabolic signals (eg, N-acetylaspartate, choline, and lactate) that are present in brain tumor tissue.

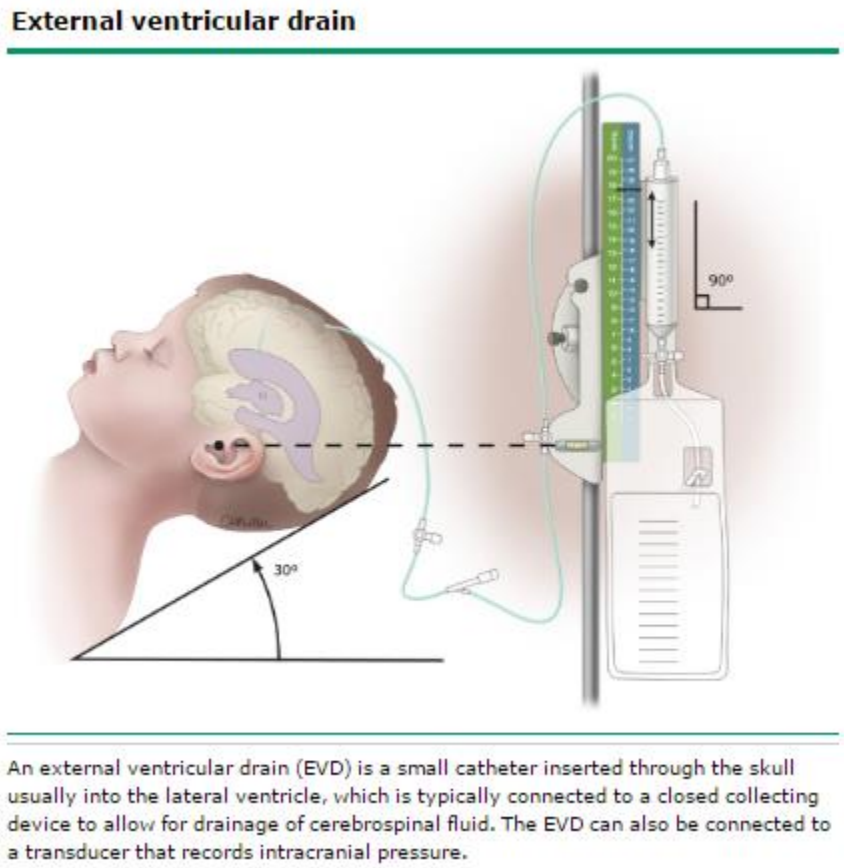
- **Positron emission tomography scans** — Positron emission tomography (PET) scans are not routinely used at all centers as part of standard workup for brain tumors, but they can provide useful information to supplement those from MRI scans. PET scans utilize a positron-emitting radionuclide isotope coupled with a sugar (eg, fluorodeoxyglucose) to differentiate malignant lesions with a high metabolic rate from more benign lesions and surrounding tissue with a lower metabolic rate.

- PET scan is useful in determining the areas of maximum glucose utilization within the tumor, which can guide the neurosurgeon to biopsy the location within the tumor with the most aggressive behavior. It is also used to differentiate recurrent tumor from changes due to radiotherapy.

- **Histology** — Children in whom neuroimaging confirms the presence of a mass should be referred to a pediatric neurosurgeon for further evaluation. The next diagnostic step is to obtain tissue to establish the histologic diagnosis, and whenever possible, reduce the tumor burden for most CNS tumors. Post-surgical therapy, which may include radiation and/or chemotherapy, is dependent upon the histological diagnosis.

Short term management

- Corticosteroid therapy (eg, dexamethasone), directed at reducing peritumor edema, is given to patients with increased ICP. Intravenous dexamethasone (**0.25 to 0.5 mg/kg administered every six hours with a maximum dose of 16 mg per day**)
- Depending on the tissue – radiotherapy and chemotherapy.



Surgical resection

- Surgical resection is very important and recent data suggest that complete total resection, especially of gliomas, should always be the aim and is associated with improved survival in children.[11]
- However, complete resection of the tumour is very rarely achievable as the margins of most tumours are indistinct. This means that during surgical resection it becomes difficult to determine whether abnormal or normal tissue is being resected. Resection also allows for a biopsy to be taken which in some types of brain tumour alters therapy.
- Biopsy may be performed beforehand and usually direct open biopsy is preferred at the time of surgery although, for basal ganglia and brainstem lesions, stereotactic biopsies are taken. Pre-operatively, children may be given phenytoin to prevent seizures and corticosteroids to reduce brain oedema.
- Hydrocephalus is common postoperatively and therefore at the time of surgery an external ventricular drain or ventriculoperitoneal shunt is inserted which will be removed a few days later once the CSF clears.
- Very young children (under the age of 2 years) require radical resection as radiotherapy is delayed until they are older, as it will damage local normal tissue which is still developing. This is usually followed by chemotherapy.

Radiotherapy

- This is provided in low doses and to very localised areas to avoid damage to surrounding normal brain tissue. There are various techniques that can be employed - eg, gamma knife (used for slow-growing lesions) and interstitial seeds which are implanted during surgery.

Chemotherapy

- There are various chemotherapy regimens in use and they usually involve vincristine. In the rare primary CNS lymphoma, chemotherapy alone has been used with good outcomes.[12]
- In low-grade gliomas, if residual disease remains after excision then chemotherapy has been used. Newer chemotherapeutic regimens are being used including vincristine, etoposide, cyclophosphamide and 5-fluorouracil.[13]

Follow-up after treatment

Children have MRI scans every six months for the first two years and then annually (although this varies according to the centre and may become less frequent after the first few years).

Complications

- Intellectual decline - a recent study of 120 young patients with primary brain tumours showed a decline in sustained attention span and reaction times. This appeared to be caused by multiple factors including local tumour effects, surgery and radiotherapy. More recently, guidance on detecting and monitoring cognitive decline has been proposed.[14]
- Growth hormone deficiency is common (thyroid hormone deficiency is less common).
- Neurological handicap may occur and be permanent.
- Increased risk of a second brain tumour 10-20 years down the line due to irradiation (eg, developing meningioma or sarcoma) - risk is increased if the brain is irradiated at a very young age.[15, 16]
- Reduced bone mineral density of multifactorial origin.[17]
- Cavernomas presenting as haemorrhagic lesions are increasingly being associated with CNS irradiation.[18]

Prognosis

- **Survival** — Five- and 10-year survival rates for children with central nervous system (CNS) tumors are 73 and 70 percent, respectively,

  (In the United States)