Norwegian Childhood Cancer Society

Brain tumours in children and adolescents

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Our values

We give *hope* to each other and the world.

We have the *courage* to speak
out on behalf of our families.

We have the *strength* to support
children and families who are affected.

We create *joy* in daily life.

Brain tumours in children and adolescents

When a child or adolescent has a brain tumour, it's a heavy burden for both the patient and the family. It will greatly affect the daily life of both the child and the family. Countless questions come up: What exactly is a brain tumour? What treatment should be given? How will things work?

This brochure is primarily written for families with a child or adolescent who has been diagnosed with a brain tumour, but it can be useful for others, including healthcare personnel. We wish to provide some insight into the challenges ahead. A brochure like this can never answer every question, but our goal has been to provide the most important facts about each type of brain tumour in children and their treatment.

The brochure contains information that we have found that parents and the network of people around the child are looking for. It is also important to remember that no two families are alike, and that every family will have its own experiences and feelings when one of the children in the family receives a serious diagnosis.

The brochure will discuss a number of issues that are more or less common to the different brain tumours. We will describe the most common symptoms and when to react to them. You will also be able to read about treatment options and what the chances of a successful outcome are. Finally, you will be able to read about the late effects of the disease and treatment. The information in this brochure is intended to be valid over time. Therefore, some details have been omitted. We also recommend using the websites of the Norwegian Childhood Cancer Society and Barnekreftportalen (the Childhood Cancer Portal), where the information is updated at all times.

The most important information is that provided by the paediatric oncologist, neurosurgeon and other specialists treating the child, as each child has a tumour with many characteristics that are different from other cases. Only the treating physician can be fully aware of all of this.

Brain tumours are the most common group of tumours in children and adolescents, accounting for approximately 30 per cent of all patients in the Childhood Cancer Registry (Kreftregisteret). Most brain tumours in children are low grade.

The brain is the most important organ in the human body. It contains areas that are essential and vital to us. When a child is diagnosed with a brain tumour, it is therefore a special situation, different in many ways from tumours in other organs. Brain tumours are a group consisting of many different types of tumours with different biology and severity. Fortunately, in most cases, the chances of recovery are good.

If the tumour has the ability to grow into the surrounding area and spread to other areas of the brain, it is a cancerous tumour, also called a **malignant tumour.**

Tumours that do not have these characteristics are called **benign.** The largest group of brain tumours in children are however tumours with an uncertain progression called low-grade malignant, or simply **"low-grade".** As a group, they have good outcomes, but some of these tumours can have serious outcomes. We do not use the term "brain cancer" because there are seamless transitions, and there can also be severe progression in more low-grade types. We refer to the group collectively as "brain tumours".

When you hear that a child has a brain tumour without anything else being known, it is simply not possible to say anything about its progression and treatment. You need to know what type it is and where in the brain it is located. The extremes are on the one hand low-grade gliomas of the cerebellum, with an almost 100 per cent survival rate after only

Prevalence of brain tumours

Brain tumours are the most common group of tumours in children and adolescents, accounting for approximately 30 per cent of all patients in the Childhood Cancer Registry. Most tumours in children are low grade. In adults, high-grade tumours with a severe progression are more common.

Grading of brain tumours

Brain tumours are graded from 1 to 4, with grade 1 being the least aggressive and grade 4 being the most aggressive. Grades 1 and 2 are called "low grade", grades 3 and 4 are called "high grade".

Depending on the localisation in the brain, the progression can be severe even for the less aggressive tumours. The group as a whole is therefore included in cancer care and registered in cancer registries worldwide.

surgical treatment, and on the other hand diffuse intrinsic pontine gliomas (DIPG) in the brainstem, which unfortunately still has a low survival rate, despite considerable research into new treatments.

Treatment will depend on the type of tumour. For the vast majority of tumours, surgery is the first treatment. The possibility of surgery will vary with the location of the tumour in the brain. In areas in the middle of the brain, it is often impossible to remove the tumour completely because it may lead to excessive damage to the brain, while tumours towards the outer edge of the brain can often be removed in their entirety.

In addition to surgery, many patients will need chemotherapy or radiation, or both. In recent years, new "targeted drugs" have begun to be used in selected cases.

What is a brain tumour?

The cells in the body multiply by dividing in two, under careful control. A tumour is a lump of abnormal cells that has lost control of cell division. As a result, too many cells are produced, and the tumour grows. The tumour originates from originally normal cells where an error has occurred. The type of cell from which the tumour develops will determine the type of tumour that develops.

Brain and spinal cord tumours in children differ from tumours elsewhere in the body in that even benign tumours can have a "malignant progression" because they are localised in the brain. By pressing on neighbouring areas inside the brain or in the spinal cord, they can cause harmful and, in some cases, life-threatening symptoms. Because of their location, it may be difficult or impossible to surgically remove the tumours without damaging vital functions.

Most brain tumours originate from support cells, called **glial cells,** and are called gliomas. We distinguish between high-grade and low-grade gliomas. The low-grade ones are most common in children. Other tumours arise from primitive precursors of nerve cells and are called **embryonal tumours.** The most common is medulloblastoma. A smaller number of tumours may originate from other cell types.

INFO

The central nervous system (CNS) is the collective name for the brain and spinal cord. Tumours of the spinal cord account for less than ten per cent of brain tumours. When we refer to brain tumours and spinal cord tumours together in this brochure, we use the name brain tumours for simplicity, although the correct term would be "tumours of the central nervous system" (CNS tumours).

Structure and function of the brain

NERVE CELLS

An incredibly complex network of over 100 billion nerve cells makes up what we usually think of as “brain cells”. These are the cells which are used when thinking, moving and performing other complex activities controlled by the brain. Nerve cells have fibres of varying length with numerous connections between them at contact points, called synapses. Each cell can form thousands of synapses with other nerve cells.

The individual nerve fibres can be in bundles called nerve tracts. Nerve cells differ from other cells in that they stop dividing (making new ones) almost completely in the first few years of life. As a result, the brain does not grow significantly after the age of three, which means that the brain is a larger part of the body in babies and toddlers. Fortunately, we do get smarter with age because new synapses are formed throughout life.

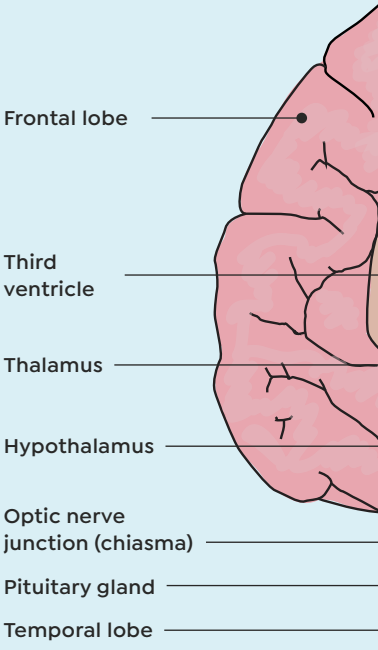
SUPPORT CELLS

Support cells (glial cells) are found in even larger amounts. Their job is to supply the nerve cells with nutrition and perform many other support tasks.

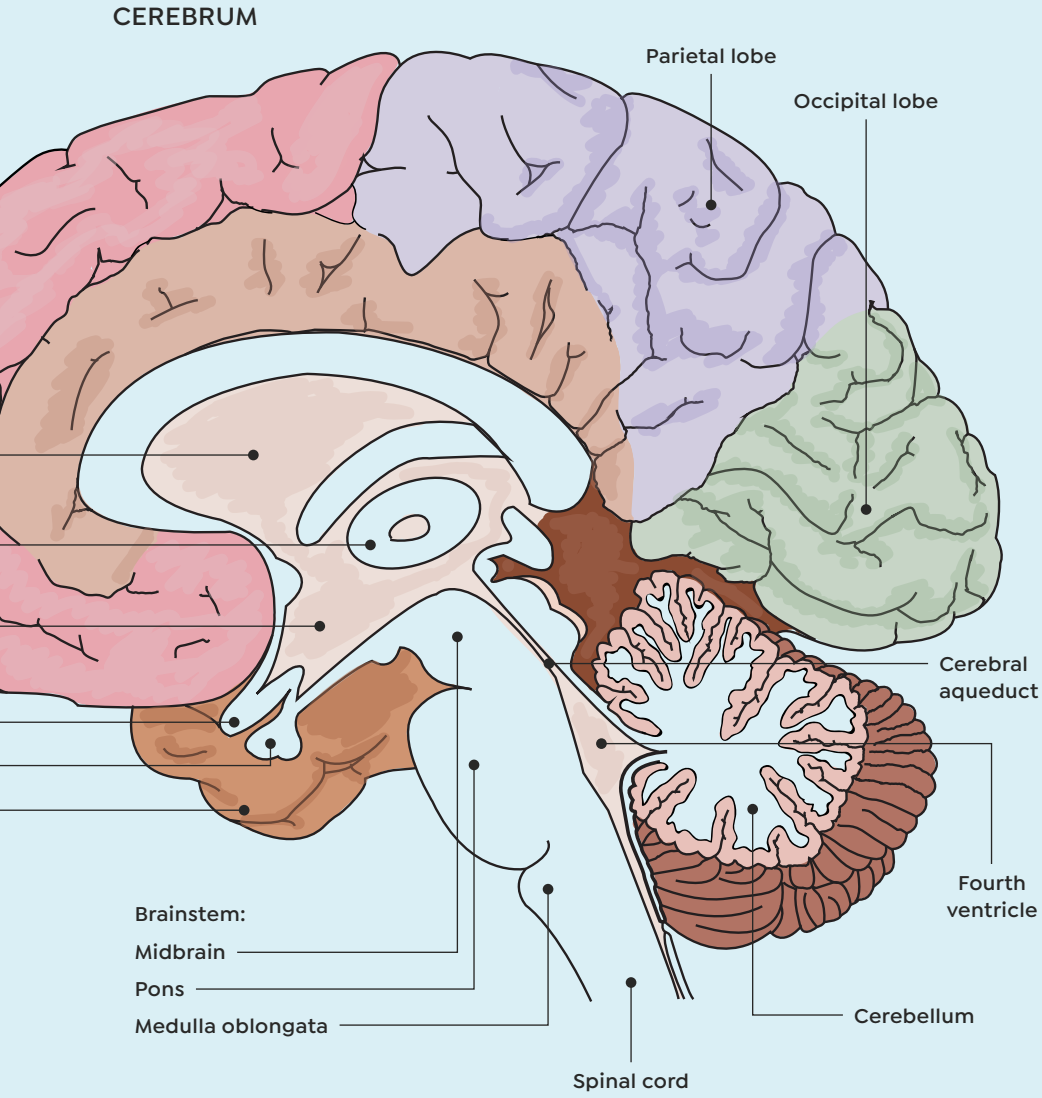
Unlike nerve cells, new glial cells are produced throughout life. As we know, cancer is caused by defects in cell division, so it’s not surprising that most brain tumours originate in glial cells. They are called gliomas. There are several subgroups of glial cells, the most common being astrocytes and the vast majority of gliomas emanate from these and are called astrocytomas.

INFO

The brain is called the cerebrum in technical language.



Midline section of the brain



Anatomy and function of the brain

The cerebrum
The largest part of the brain is the cortex. It is divided into four areas called cerebral lobes, or cerebral hemispheres. They are named for their location:

- The frontal lobe
- The parietal lobe
- The temporal lobe
- The occipital lobe

The cerebrum is divided into two distinct parts, a right and a left cerebral hemisphere. The most advanced human functions such as thinking, language, memory and emotions are controlled and processed here. Movement of the different parts of the body is controlled from here via nerves running in nerve pathways to the muscles. Different lobes have different functions. Some areas of the cerebrum are very sensitive to damage and should not be operated on, while others are more resilient.

Midline area
In the midline of the front part of the brain there are several important and sensitive areas. The **hypothalamus** has many important functions even though it is small. It is the centre for the control of many hormones via the **pituitary gland,** which extends down from the brain at the front. Hunger and weight control are performed in the hypothalamus. The area is essential in the interaction between psychological influences and physical reactions.

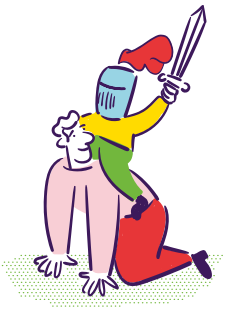
The **optic nerve junction,** the chiasm, lies directly in front of the hypothalamus and a tumour in this area often involves both structures. The **thalamus** lies just behind the hypothalamus on either side of the fluid-filled third ventricle. The thalamus processes impulses to and from the cerebrum.

The cerebellum
The cerebellum is located in the posterior fossa of the skull. The cerebellum is important for balance. Therefore, disturbances in balance may lead to the suspicion of a tumour here. The cerebellum also has other important functions, including visual function. Tumours of the cerebellum are common and if they are low grade, the prospects for recovery are excellent with surgical treatment.

Brainstem
The brainstem forms the midline of the posterior fossa of the skull. The pons is the largest part and is essential for several vital functions, such as breathing and blood circulation. Tumours that infiltrate the pons are totally impossible to remove surgically. Above the pons is the upper brainstem, called the **midbrain.** Surgery here is possible to a greater extent. The area below the pons gradually turns into the spinal cord and is called the medulla oblongata (the extended cord).

Spinal cord
The spinal cord, the medulla spinalis, is protected in a canal in the spine. The spinal cord is divided from top to bottom into cervical, thoracic, lumbar and sacral sections. In the spinal cord, nerve fibres from the brain connect to different parts of the body. Tumours here can lead to the spinal cord being pinched. This causes pain in the back and paralysis of muscles, depending on the level of the tumour.

Cerebrospinal space
The cerebrospinal space is a cavity system in the brain consisting of four cavities called **ventricles.** These are connected by small apertures and thin canals. Cerebrospinal fluid is formed in the two lateral ventricles within the cerebrum and moves "downstream" to the third ventricle in the midline, and on through a thin canal, the aqueduct, and to the fourth ventricle in the brainstem. In the case of tumours, the connections are easily pinched depending on the location of the tumour. Then the fluid is unable to pass "downstream" and there is increased pressure, and expansion of the system above the ventricle, **hydrocephalus.** This is common in brain tumours and is a major cause of typical symptoms.



Which are the most common symptoms of brain tumours?

Diagnosing brain tumours in children can be difficult, and sometimes it can take a long time from the appearance of the first symptoms until the diagnosis is made.

The main reason for this is that the symptoms of brain tumours are usually not specific, and they can therefore be interpreted as signs of other, and much more common, diseases. The symptoms of brain tumours in children can be divided into two types according to cause:

- Increased pressure in the brain.
- Local effect of the tumour.

Increased pressure in the brain

Because the brain is protected inside bone on all sides, there is no room for expansion. When something in the brain enlarges, it will press on the surrounding area and there will be increased pressure inside the "brain case".

This can have several causes. The most common is the tumour pinching off the circulation of cerebrospinal fluid and causing hydrocephalus. Increased pressure can also occur due to the size of the tumour, or the accumulation of fluid in the tissue around the tumour.

Local effect of the tumour

The tumour will disrupt the area of the brain where it is located, either by ingrowth or pressure on the cells around it. The symptoms from this are called **focal** and will vary depending on where in the brain the tumour is located. For example, a tumour in the cerebellum will cause balance problems.

SYMPTOMS DUE TO INCREASED PRESSURE IN THE BRAIN

- New-onset of severe headaches and/or nausea or vomiting, especially in the morning. These symptoms are most severe in the morning because the pressure in the head normally increases after a prolonged period of lying down. However, the daytime variation of the pain and vomiting is not always present.
- New-onset strabismus and/or double vision is often seen with increased pressure in the brain. This is due to increased pressure weakening one of the nerves responsible for the eye movement.
- Typical pressure changes in the fundus of the eye (papilloedema).

In children during the first few years of life, the bones of the skull have not grown together and can therefore be pushed apart by pressure from the inside. The circumference of the head, which can be easily measured, then becomes larger.

SYMPTOMS OF LOCAL EFFECT OF THE TUMOUR

- A tumour in the cerebellum will often cause balance problems because the area is important for the balance function.
- Tumours in the frontal and parietal lobe of the brain can cause convulsive seizures.
- Tumours in different localisations can cause paralysis of varying degrees.
- If the tumour is located in the visual pathways, this may naturally cause weakened vision and visual field narrowing, while tumours in other locations may cause disruption of eye movements.
- If the tumour is located in areas that control hormone production, the hormonal balance may be disturbed. Examples of this are growth hormone deficiency, diabetes insipidus (greatly increased urination) and disturbed puberty.
- Only the most common symptoms are included here, many more may be present.

SYMPTOMS OF SPINAL CORD TUMOURS

Impulses are sent from the brain via the spinal cord to control muscle movements in different parts of the body. Impulses are also sent in the opposite direction, transmitting pain and other sensations to the brain. There is little space for expansion in the spinal canal and a tumour could press on nearby nerve fibres in the spinal cord and cause symptoms.

- Back pain is often one of the first symptoms. Back pain in children is uncommon and must be taken seriously.
- Weakness and paralysis of the leg muscles are common symptoms.
- Crookedness in the back and neck may occur.

What symptoms in a child or adolescent should make you think about the possibility of a brain tumour?

10 symptoms that may indicate a brain tumour in a child:

- Persistent or frequently recurring headache (severe, mostly in the morning, recent onset)
- Persistent or frequent recurrent vomiting (mostly in the morning)
- Problems with balance, movement control and/or gait
- Abnormal eye movements
- Double or blurred vision
- Behavioural changes (especially lethargy, but also personality changes)
- Repeated convulsive seizures
- Abnormal head posture such as twisted neck, head tilt or neck stiffness
- Increased head circumference (only for the very young)
- Delayed onset of puberty or cessation of previously initiated pubertal development

The list was developed in England and is called “Head Smart”.

INFO

Many other more common diseases can cause some of the same symptoms. When such symptoms occur, it gives cause to investigate the condition to exclude or confirm the diagnosis of a brain tumour. The more of the listed symptoms are present, the greater the need for further examinations.

What are the reasons why a child develops a brain tumour?

No single cause

There is no common single cause that starts the tumour process. There are millions of cell divisions in the body, and it is well known that cell division errors often occur when the genetic material, DNA, divides. Only rarely can this lead to tumours and cancer. What triggers the process that leads to brain tumours in children is most often unknown. We believe that the main cause is the occurrence of random errors. Many parents feel guilty when they find out that their child has a brain tumour and wonder whether they have done something wrong that has contributed to the tumour developing. We can say with certainty that this is not the case.

There are a few hereditary diseases that more easily lead to brain tumours in children. The most common is neurofibromatosis (NF1). Patients with this congenital disorder are at high risk of developing low-grade gliomas.

In a few cases, previous radiation treatment of the brain can cause brain tumours. With modern radiation techniques, the risk can now be reduced. Proton radiation is increasingly used to protect healthy parts of the brain. We know of no other external influences that increase the risk of brain tumours.

Mechanisms of tumour development

In recent years, there has been an enormous development of knowledge about the basis of the development of cancer and other tumours. New techniques make it possible to analyse the biology of tumours down to the molecular level. The knowledge about this is called molecular biology. The details could fill thick textbooks. Changes in the DNA of tumour cells can affect cell division in different ways. The risk of increased cell division will constitute an increased risk of tumour development.

There are hundreds of molecules that affect cell growth in different ways. Changes in some of these may be linked to specific tumour types.

Many parents feel guilty when they find out that their child has a brain tumour, wondering if they have done something wrong to contribute to the tumour developing. We can say with certainty that this is not the case.

Investigations and diagnosis

The key to diagnosing brain tumours in children is that the physician considers the possibility that the patient's symptoms may be caused by such a tumour.

MRI examination

If the child has a tumour in the brain, this will almost always be found by an MRI examination of the brain, called an **MRI caput** or MRI cerebrum. The diagnosis of a brain tumour is thus simple once the possibility of this has been assessed. Further investigation is needed to find out what type of brain tumour it is. If a tumour is found, an MRI of the spinal cord will usually be performed as well, as some brain tumours can spread there. Spreading outside the central nervous system is almost never seen.

Other examinations

A sample of **cerebrospinal fluid** (CSF) is taken in cases of high-grade tumours. Some tumours give characteristic hormone disturbances, so examination of the hormone level in the blood may be indicated. If vision or eye movements may be affected, an **eye examination** is performed. In the case of increased pressure in the brain, changes in the fundus of the eye, called papilloedema, can usually be seen. In other cases, a **hearing examination** is needed.

The brain tumour itself, or the treatment, may cause late effects in the form of learning difficulties and other mental impacts. Therefore, a **neuropsychological examination** is desired before the operation, in order to have a baseline to follow the further progression. If the patient is in an urgent situation, this examination will be done later.

Biopsy

The final diagnosis is made by analysis of a tissue sample, biopsy, from the tumour. Such a biopsy requires a surgical procedure. This may be tissue taken from the tumour when it is removed. But often just a very small biopsy is taken to make the diagnosis and to do molecular biology analysis. The analyses are carried out by neuropathologists, who are highly specialised physicians. A series of advanced tests are performed on the biopsies. It will usually take a few days before the biopsy results are available.

The abbreviation MRI stands for "Magnetic Resonance Imaging" and is standard at Norwegian X-ray departments. As the technology develops, new methods are being developed for improved diagnostics.

Treatment of brain tumours

Brain tumours in children are a group of very diverse tumours and therefore the treatment will also vary.

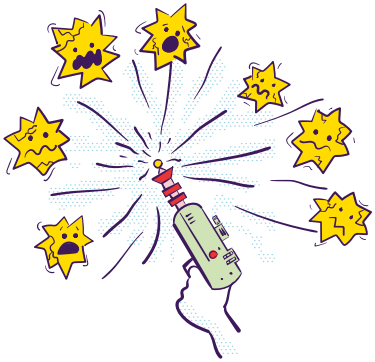
For some low-grade tumours, surgery may not be necessary, but the vast majority of tumours will be operated on. Chemotherapy is administered for some low-grade tumours and most high-grade ones. Radiation therapy is important for aggressive brain tumours and is also administered for some other tumours.

Combinations of surgery, chemotherapy and radiation are used for most high-grade malignant tumours. "Personalised treatment" is a new form of treatment used for some brain tumours in children.

International treatment protocols have been developed for many of the tumours that have a complicated and composite treatment. For these, there are written instructions called treatment protocols. These protocols are also basis for research. The Norwegian centres that treat brain tumours work closely together and participate in many international treatment protocols. New protocols are launched continuously, and Norwegian adherence is discussed in the "The Specialist Group for Tumours of The Central Nervous System in Children". There is a good international network where difficult disease cases can be discussed.

Active observation

In some patients, low-grade tumours can remain dormant for a long time without growing, some perhaps forever. If your child does not have severe symptoms, an assessment will be made to watch the progress without treatment, because surgery can lead to damage. The patient will be closely monitored with medical check-ups and MRI examinations. If the tumour grows later on, treatment will be started.



Surgery

The best treatment is to remove the entire tumour whenever possible, without causing unacceptable damage to the brain.

In sensitive areas of the brain, it will not be possible to remove the tumour in its entirety without risk of major damage. In some cases, parts of the tumour are removed, while in other cases it is not appropriate to remove anything. In such cases, it will still be desirable for the neurosurgeon to take a tissue sample of the tumour, a biopsy, to make a definite diagnosis, and to have molecular analyses done. Correct diagnosis is necessary to provide the right treatment. The decision on the size of the surgical procedure will be a balance between benefit and risk. The operations are often complicated and performed by experienced neurosurgeons at one of the hospitals with a childhood cancer centre.

Before the operation, the neurosurgeon will inform the family about the details of the surgical procedure, including the risk that is always involved in complicated brain surgery. Usually, the child will be in the intensive care unit and closely monitored in the period immediately after the operation.

INFO

There has been great progress in neurosurgical operation methods. Today, surgery is performed using microscopes and other advanced tools. For example, the brain can be navigated using MRI images taken before or during the operation. New examination and surgical methods are constantly being introduced as technology develops.

Radiation therapy

Radiation therapy works by emitting high-energy rays from a radiation machine that damage the DNA in cells. Tumour cells tolerate this less well than normal cells, and radiation doses can then be given to kill tumour cells without causing excessive damage to normal cells. The treatment is effective and is important for high-grade brain tumours in children. An area that includes the tumour and the immediate surrounding area is irradiated. This is called focal radiation. In some aggressive tumours, primarily medulloblastoma, the entire brain and spinal cord must also be irradiated to prevent spreading, which may be invisible on an MRI. A high dose is then administered to the tumour area and a lower dose to the rest of the brain.

Usually, the treatment takes place over several weeks, with a short course of radiation every day except Saturday and Sunday. Other treatments are sometimes used. The patients must lie completely still during the radiation; therefore, a mild anaesthesia is given to the youngest children.

Small children tolerate radiation poorly, so avoiding such treatment is desirable when children are under 3–4 years old. This is particularly true for whole-brain irradiation. Focal treatment is better tolerated. Radiation therapy is still necessary for some brain tumours in children.

Proton radiation is a relatively new type of radiation which administers a lower radiation dose to areas of the brain outside the tumours, and therefore the late effects after radiation can be reduced. The actual effect on the cancerous tumour is similar to that of conventional radiation. Proton radiation is not suitable for all types of tumours.

Stereotactic radiation therapy administers a very high radiation dose to a concentrated area. The **"radiation knife"** is a special form of this. This treatment method is best suited for small tumours or tumour remnants, and especially low-grade tumours.

→ **You can read more about radiation therapy in our brochure "For those who need radiation therapy".**

Chemotherapy

The brain is our most important organ and is protected from external damage in several ways. In addition to being protected inside the bony skull, the brain's blood vessels have a filtering function in the wall, which prevents many harmful substances from entering the brain via the blood. But it also means that chemotherapy, which is usually given intravenously (via the blood), is prevented to varying degrees from entering the brain. This is one of the reasons why drug treatment has been less effective for brain tumours than for other tumours in children. The biology of brain tumours also makes chemotherapy less effective than desired In some cases, chemo-therapy is administered directly into the cerebrospinal fluid. However, chemo-therapy has been used increasingly for brain tumours in children, with moderate effect on many tumours.

INFO

Chemotherapy can have many different side effects that are not described here. There is information about this on the website of the Childhood Cancer Society.

High-grade tumours have been treated with chemotherapy along with surgery and radiotherapy since the 1970s. For low-grade tumours, chemotherapy is now chosen over radiation when treatment in addition to surgery is considered necessary.

Most chemotherapy is administered in courses. This means that one or more drugs are given for a few days, followed by a break of varying duration. Then several courses are given in the same way. Before starting treatment, a central long-term catheter is inserted into a large vein. This is used to administer drugs and take blood samples from.

"Personalised treatment" and other modern treatment methods

"Personalised medicine" means finding biological changes in the tumour of the individual patient and treating them. This is a new field that builds on recent advances in understanding the biology of cells. With modern molecular research techniques, it has been found that what

Norwegian centres treating brain tumours in children work closely together and participate in many international treatment protocols.

we have considered the same disease may have a different biology from patient to patient. In cancer, different changes in the genes of the tumour cells can be found which may promote cancer development. This makes it possible to design and "tailor" drugs to counteract the consequences of this particular defect. The treatment is targeted at the molecular alterations that have been identified. Several such drugs are in use for individual tumour types, and it is expected that the number of effective drugs will increase significantly in the coming years.

Immunotherapy means treating by manipulating the immune system, so that it is strengthened in the fight against cancer cells. There are several different methods being tested.

Antiangiogenic drugs. For a tumour to grow, the body must supply it with nutrients via new blood vessels created by the tumour. This is called angiogenesis (formation of new blood vessels). Drugs have been developed to inhibit angiogenesis and thus tumour growth. Such drugs are used for a few types of brain tumours in children.

Treatment of symptoms

High pressure in the brain due to hydrocephalus can be dangerous and usually needs to be remedied surgically. Removal of the tumour may lead to normalisation of the pressure, but frequently the pressure must be relieved by creating a bypass outside the blockage. This is done either by making an opening called a ventriculostomy, from a ventricle above the blockage, to the fluid chamber around the brain, or inserting a tube from the cavity to the abdominal cavity, called a ventriculo-peritoneal shunt. The shunt is placed under the skin on the head, and has a valve that regulates the pressure.

Steroid drugs, such as dexamethasone, reduce swelling in the brain tissue and thus reduce pressure. Often such treatment is started before surgery and routinely given a few days after surgery, to prevent increased pressure.

Other complications such as epilepsy or hormone deficiency are treated if necessary.

Prognosis
– how will the course be?

Predicting the most likely course of a disease is called prognosis. For tumours and cancer, prognosis is usually used to refer to the chance of survival.

Prognosis is most often expressed by the mean percentage of patients being alive at a given time after diagnosis. Most commonly used is 5-year or 10-year survival. In long-term survival, most patients will be cured of their disease, although a few may have relapses later. We expect the prognosis to improve in the future as treatment continues to improve. We can also assess the prognosis for other factors such as quality of life and late effects.

The prospects for getting rid of the tumour and for long-term survival are variable because brain tumours are so different. Overall survival for tumours of the central nervous system in children in Norway is currently around 80 per cent, but this figure says little about the chances for the individual patient. For low-grade tumours there are good chances of survival, while some high-grade tumours have a very poor prognosis. The prognosis within each group will also vary depending on factors such as the location of the tumour, the age of the patient, the spread, treatment options and the biology of the tumour. If it is possible to remove the tumour in its entirety, this gives a better prognosis, but the risk of serious damage to the brain during surgery must be taken into consideration.

For low-grade tumours, the long-term survival is higher than 90 per cent, but even within this group there is variation depending on age, tumour type and location of the tumour. For the most common high-grade tumour, medulloblastoma, long-term survival is currently 60–70 per cent. A few types of high-grade tumours have a poor prognosis. The most serious is diffuse intrinsic pontine glioma (DIPG).

With regard to functional capacity and quality of life after treatment, there is also a wide variation. Some have almost no late effects, while others may have a significant reduction in their functional capacity. This will vary with tumour type, extent and treatment.

INFO

Patients will be monitored regularly during treatment, but also afterwards for several years. The frequency of check-ups will vary. The possibility of relapse is greatest in the initial period after completion of treatment, while late effects may occur long after treatment. MRI exams are performed during the initial period of check-ups with the doctor. New symptoms and monitoring of the onset of late effects are assessed throughout.

The different types of brain tumours

There are many different types of brain tumours in children. These have different characteristics that require different treatment.

Low-grade glioma

Low-grade glioma (LGG) is the most common type of brain tumour in children.

The tumour originates from support cells, glial cells, hence the name glioma. The vast majority come from the glial type astrocytes and are called astrocytomas. Of the many subtypes, pilocytic astrocytoma is by far the most common. LGG can occur in all parts of the brain and spinal cord, most commonly in the cerebellum and the visual pathways. They often occur in patients with the disease neurofibromatosis.

Low-grade gliomas can have variable course, but in most cases, patients have a very good outlook for survival. In some cases, the growth of the tumour may stop completely early on, in others it may stop and grow again after a shorter or longer period of time. For the group as a whole, the long-term survival is over 90 per cent. Relapses, on the other hand, are common, but can usually be treated successfully. The location of the tumour has an impact on possible treatment and therefore also on prognosis. Localisation in the cerebellum is favourable with close to 100 per cent survival, while localisation in areas in the middle of the brain does not have as good an outlook because they cannot be operated on without major damage. Patients under one year of age have a poorer prognosis.

Surgery is the primary treatment, and only a third need other treatment in addition to surgery. Today, this means drug treatment with chemotherapy, but modern targeted treatment is also tried in the most difficult cases.

LGG can in rare cases behave more like a malignant tumour. A few patients are given radiotherapy. On the other hand, some patients will manage without treatment, only with close monitoring.

→ **For more comprehensive information about the different brain tumour types, refer to our own websites and treating physicians.**

High-grade glioma

High-grade gliomas (HGG) are fortunately rare in children.

In adults, this is the most common tumour type. The vast majority require both surgery, radiation and chemotherapy. As with adults, the outlook is not good in children, but is nonetheless better in some children under the age of three.

Medulloblastoma

Medulloblastoma is the most common high-grade brain tumour in children.

It originates in the middle part of the cerebellum. Most common symptoms are balance problems and pressure symptoms. Radiation therapy of the entire brain has proven to be very effective together with surgery and chemotherapy. Because of the damage caused by such radiation to young children, especially those under three years of age, treatment options have been developed for them without radiation therapy.

Long-term survival for the whole group is now 60–70 per cent. Medulloblastoma is a tumour type for which there is much advanced molecular research, and it is hoped that this will yield even better results in the future. Medulloblastoma patients have a relatively high risk of late effects.

Ependymoma

Ependymoma originates from ependymal cells that line the inner surface of the cerebrospinal space.

The tumour is usually not very aggressive, but there are malignant forms. Chemotherapy has less effect on these tumours than on most other brain tumours. Surgery therefore becomes particularly important. The treatment approach usually consists of all three types of treatment: surgery, radiation therapy and chemotherapy. Long-term survival is high.

Diffuse intrinsic pontine glioma

Diffuse intrinsic pontine glioma (DIPG) is the most serious type of brain tumour in children.

It has been considered incurable, although a few patients have survived. Research in recent years has produced a lot of new knowledge about the biology, and this has given new hope for finding a treatment that works. A specific mutation in tumour cells (histone H3 mutation) is most often the cause of tumour development. Such an alteration is also found in some other gliomas, and the condition is called "diffuse midline glioma with Histone H3 mutation".

Today, DIPG is treated with radiation, which prolongs survival. "Experimental" treatment trials with different drugs are ongoing in many countries, but for the time being (2022) no effective treatment has been found. Supportive measures and palliative treatment are important.

It is important to be aware that there are other types of tumours (non-diffuse) in the brain stem which have a much better prognosis. Most of these are low-grade gliomas.

Craniopharyngioma

Craniopharyngioma is a biologically benign tumour originating from the area above the pituitary gland, often with ingrowth in the hypothalamus. Most tumours have areas of large or small cysts (fluid-filled cavities).

The prospects for survival are very good, but due to the location in the middle of an area with sensitive structures, the tumour has major consequences for most patients. Hormonal disturbances, major weight problems, behavioural changes and visual disturbances are most common. Hormone disorders can cause many different symptoms. For example, reduced antidiuretic hormone can lead to a sharp increase in urination. Reduced stress hormone (cortisol) can cause lethargy and dangerous situations when the body is exposed to heavy strain.

In the past, emphasis was placed on surgically removing the entire tumour. Today, more care is taken to avoid damaging the hypothalamus, which can exacerbate the severe symptoms. The neurosurgeon removes varying amounts of the part of the tumour that lies outside the hypothalamus, and then watches the progress. If there is growth, local radiation therapy will be given, most often proton radiation. Some patients are given "radiation knife" treatment. In a few cases, drugs are inserted directly into large cysts. Research on personalised drugs is in its initial stages.

Hormone deficiency is treated with hormone supplementation, weight problems

INFO **There are a number of other rare tumours that are not discussed here. For those who have such tumours, detailed information will be provided by the treating physician.**

with behavioural measures. Patients must have lifelong follow-up, particularly for monitoring visual function and hormone treatment.

Atypical teratoid/ rhabdoid tumour (AT/RT)

AT/RT was previously considered a type of medulloblastoma but has been shown to be different.

AT/RT is often seen in younger children and has a slightly poorer prognosis than medulloblastoma. With today's treatment, which is more adapted to the biology of the tumour, this has improved. Surgery, radiation and chemotherapy are given to most patients.

Germinal cell tumours

Germinal cell tumours originate from a specific type of cell and can be found in many areas of the body, including the brain.

They are most often located in the middle part of the brain. There are two main types, germinomas and non-germinomas. Some of the non-germinomas secrete specific hormones that can give the diagnosis without biopsy, while others do not. The tumours are treated with both chemotherapy and radiation. Extensive surgery is rarely necessary. The germinal cell tumours have a good prognosis, the germinomas, the best.

Spinal cord tumours

The cells in the spinal cord are of the same types as in the brain. From the brain, long nerve fibres run down and out to different parts of the body. Tumours in this area can lead to back pain and eventually paralysis, especially in the legs.

The vast majority of tumours are low grade, either gliomas or a particularly low-grade form of ependymoma. The treatment will initially be surgery. Only a small percentage of tumours can be removed in their entirety, and many regrow after surgery. This can happen many years after diagnosis. Surgery is repeated if possible, and for some, chemotherapy or radiotherapy is indicated for new tumour growth.

Some patients need to be treated several times, but the good thing is that the tumour is eventually controlled. If there is no brain tumour at the same time, long-term survival is close to 100 per cent. Permanent minor or major paralysis, and changes in the spinal column, scoliosis, can be the late damage of such tumours.

Late effects

Even if the patient is cured of the brain tumour, problems may arise later as a result of the treatment or the tumour itself.

Brain tumours cause more frequent late effects than other cancers in children. The degree of severity varies. While some patients have almost no late effects after treatment, others may have severe late damage.

Causes

Tumours located in sensitive areas can in themselves lead to permanent damage, for example hormonal disturbances in craniopharyngioma.

Surgery. Operating on sensitive parts of the brain can cause damage after the procedure. Assessing this risk is essential for deciding how extensive a procedure should be. Better equipment and methods for neurosurgery can limit the risk of damage.

Radiation therapy carries the greatest risk of late effects. Children tolerate radiotherapy less well than adults. But it is important to know that the risk varies with several factors. This is described in the section on treatment. The main risk factor for radiation damage is young age, while adolescents tolerate radiation quite well. The brain is special in that cell division of nerve cells occurs up to the age of three, while there is little cell division later.

Radiation therapy inhibits and damages cell division, therefore we try to avoid irradiation of the brain in children below this age. This is especially true for whole-brain irradiation. If the patient is under three to five years of age, other treatment is therefore given in the first instance. Local radiation of the tumour is better tolerated and can be given at a younger age. The total dose of radiation and the size of the area irradiated affect the risk of late effects. The development of new technologies and methods of radiation therapy has somewhat reduced the risk of late damage. Proton radiation therapy

strongly reduces the amount of radiation to healthy tissue near the tumour and is used today in many children who need radiation.

Chemotherapy is better tolerated by children than adults, but even this can cause late effects. For example, today's treatment of medulloblastoma carries a risk of hearing damage and kidney impact.

Combination treatment with several forms of treatment could increase the risk of late effects.

Late effects

Many children tolerate the treatment well without later symptoms, but we often see late effects of various kinds. So-called neuro-cognitive late effects are not uncommon and involve impact of varying degrees on concentration, memory, mental tempo and social skills. These are provoked in particular by radiation therapy. Fatigue is a condition of pronounced lethargy and occurs in many patients. Permanent hormonal disturbances can occur with various tumours.

Visual disturbances can be seen in tumours and operations on the optic nerves. Hearing impairment may develop.

→ **You can read more about late effects in our brochure "Late effects after cancer treatment".**

Many other conditions can be seen with different types of tumours. So-called secondary tumours can appear many years after the end of radiation therapy. Fortunately, they are rare and usually benign, but malignant ones do exist.

Most late effects can be treated and corrected to varying degrees. Neuropsychological late effects are followed up by rehabilitation departments and at school, as with several other conditions. Child neurologists, physiotherapists, occupational therapists, educators, psychologists and others are involved in the multidisciplinary collaboration that plans and carries out treatment, as well as providing support for school, home, etc. Various medical specialists are involved in following up the patients depending on the late effects that occur.

Collaboration and research

Brain tumours in children are rare. This requires close collaboration between specialists both nationally and internationally to share knowledge.

Today, patients in Norway are examined and treated at the four regional hospitals which have childhood cancer centres and advanced neurosurgical departments.

At each hospital, childhood cancer specialists, neurosurgeons, radiation oncologists, pathologists, radiologists and several other medical specialists work together. In addition, nurses, psychologists, educators and several other specialist groups participate in the treatment. At the national level, there is collaboration at the "Specialist Group for Tumours of the Central Nervous System in Children", with the participation of key persons from the four centres. Here, problems are regularly discussed between the specialists. International collaboration is formalised through the Brain Tumour Group of the International Society of Paediatric Oncology, SIOP.

There is also close collaboration with international experts, particularly in Western Europe, which enables us to discuss difficult issues concerning our patients.

The treatment, or parts of it, often follows international guidelines in so-called treatment protocols, which is simultaneously research. The investigation and treatment are recorded, and the results can be analysed. In some projects, different treatments are compared to find out which is best. Parents and adolescents must give consent before participating in such projects. Proper information is required in advance. Such international research has been essential to the progress we have seen in treatment outcomes.

All the Norwegian centres are actively involved in the collaboration. This is important for all children in Norway with brain tumours to receive the same treatment.

The Future

There has been progress in the treatment of tumours of the central nervous system in children and adolescents, but progress has been slower than what we have hoped for.

However, in recent years there has been an explosive increase of knowledge about the biology of tumours down to the molecular level. We now know how different factors contribute to the development of different tumours. The most common cause is development of errors in the DNA of the tumour cells, which leads to a loss of control of cell growth. The malformation varies with the type of tumour, but also from patient to patient. For some patients, it is now possible to provide treatment that is specifically tailored to the individual. This is also called personalised treatment or precision medicine. In the years to come, such treatment methods will be increasingly possible for more patient groups, often alongside "old" treatment methods.

There is also a continuous improvement of neurosurgery and radiotherapy. Today, specialist communities are optimistic about the potential to improve treatment.

TIPS

INFORMATION ABOUT BRAIN TUMOURS IN CHILDREN ON THE INTERNET

There is very little comprehensive information in Norwegian, and most of it is aimed at specialists. You can find some updated information via the Childhood Cancer Society's website and the Childhood Cancer Portal (Barnekreftportalen).

Internationally, there are many websites aimed at parents and patients. If you speak English, websites such as that of the National Cancer Institute in the USA is recommended. Under "Cancer types" Childhood Cancers, you will find extensive information on most cancers.

There can be an overwhelming amount of information, so the most relevant information will come from your treating physician.

About the Norwegian Childhood Cancer Society

The Norwegian Childhood Cancer Society is a voluntary and nationwide organisation.

Our office is in Oslo, and we have county associations run by families who have or have had children with cancer. The associations work for the families on a voluntary basis. Our goal is that no child should die of cancer.

The Norwegian Childhood Cancer Society exists to help children and adolescents with cancer and their families. We are there for the whole family, meaning that the sick child, siblings and parents are all included. Some of the sick children have recovered, some are living with symptoms, some are under treatment, while others we have unfortunately lost.

At the hospitals, our peer contacts organise parents' meetings with the opportunity for new families to talk to someone. When your child is diagnosed with something as serious as cancer, it can be good to have someone to talk to who has experienced what you have. We also provide positive experiences for children who have to stay in the hospital for long periods.

The Norwegian Childhood Cancer Society wants to be the largest driving force in Norway to focus on childhood cancer in the media and society. We also contribute to research and education to combat childhood cancer.

Become a member

→ Register on barnekreftforeningen.no

What does membership of the Norwegian Childhood Cancer Society mean?

As a member you have a unique ability to have an impact on conditions for children and adolescents with cancer and their families.

Membership in the Norwegian Childhood Cancer Society means access to a community of families who are, or have been, in the same situation. The association provides information, advice and support at all stages of a child who has, or has had, cancer.

TIPS

Contact your county association or the staff of the Childhood Cancer Society and tell us what is important to you.

Contact

If you have any questions about membership or the Norwegian Childhood Cancer Society, please contact us.

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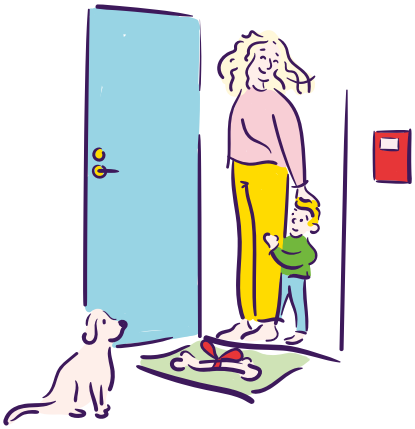

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