

Astrocytoma

Astrocytomas are tumours that grow from a type of cell in the brain called an astrocyte.

They are the most common type of a group of brain tumours called gliomas and account for about one third of all brain tumours.

There are various types of astrocytomas, each of which affect both adults and children.

The information in this fact sheet gives an overview of astrocytomas and answers some of the questions you may have about this type of tumour.

This fact sheet does not deal in detail with grade 4 astrocytoma (glioblastoma/GBM) as this is explained in a separate fact sheet.

In this fact sheet:

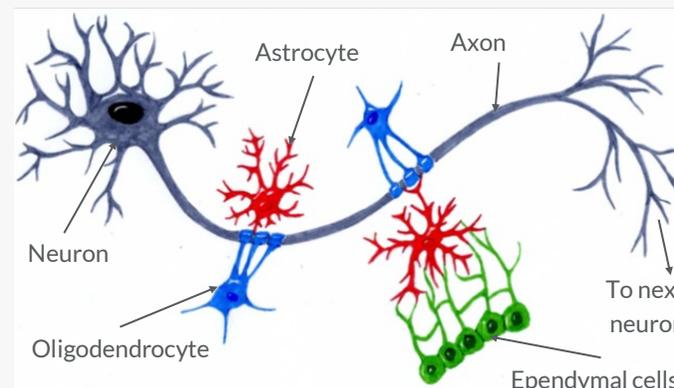
- What is an astrocytoma?
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What is an astrocytoma?

Astrocytomas are tumours that grow from a type of cell in the brain called an astrocyte.

Throughout the brain and spinal cord we all have nerve cells called 'neurons', which transmit messages (electrical and chemical signals) to, from and within the brain. Surrounding the neurons are cells called 'glial cells', that support and protect the neurons by providing them with oxygen and nutrients and removing dead cells.

An astrocyte is a type of glial cell. (There are three main types of glial cells - astrocytes, oligodendrocytes and ependymal cells.)



Astrocytes are the most abundant cells in the brain, and as well as supporting and protecting neurons, they also help to pass messages between the neurons and, therefore, are vital in processing information in the brain.

Like all cells, astrocytes normally grow in an orderly, controlled manner. However, if this process is upset or disrupted for some reason, they can continue to grow and divide when they shouldn't, causing a lump (a tumour) to form. (Tumours are an abnormal growth caused by cells dividing in an uncontrolled way.)

Brain tumours are usually named according to the type of cell they grow from and/or the part of the brain they grow in. So when astrocytes form a tumour it is known as an astrocytoma.

You may also hear it referred to as a type of 'glioma'. Tumours that grow from any glial cell are collectively called 'gliomas'. A tumour that grows from the astrocytes is therefore a glioma, but is more accurately described as an astrocytoma.

Types of astrocytoma

Brain tumours are graded by the World Health Organisation (WHO) from 1 - 4, according to how they behave i.e. how fast they grow and how likely they are to spread within the brain.

Tumours graded 1 and 2 are slow-growing, and are sometimes referred to as 'benign' or low grade. This term is used less often nowadays as it is not thought to be helpful in describing the tumour, as these low grade tumours are still serious.

Tumours graded 3 and 4 are fast-growing, more aggressive tumours, sometimes referred to as 'malignant' or 'cancerous', meaning they are more likely to get bigger more quickly and sometimes spread to other parts of the brain or spinal cord.

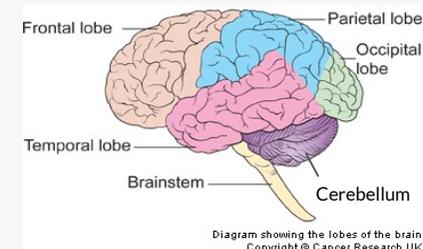
Astrocytomas can be any grade, from 1 - 4.

Grade 1 astrocytoma ('pilocytic astrocytoma')

Grade 1 astrocytomas are called 'pilocytic astrocytomas'. (Pilocytic means the cells are elongated and look hair-like.) These are slow growing, relatively contained and unlikely to spread to other parts of the brain. They are also unlikely to return after being surgically removed.

They are most often found in children and young adults under the age of 20 and are equally common in males and females. They are very rare in adults over 50 years.

They tend to occur in the cerebellum - the part of the brain at the back that controls balance, but they can also occur in the optic pathways. These are the pathways from the eyes to the 'visual cortex' in the occipital lobe at the back of the brain, which is responsible for sight.



Pilocytic astrocytomas also occur in around 10% of people who have 'neurofibromatosis type 1' (NF1). This is a genetic condition you are born with that causes tumours to grow along your nerves.

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Grade 2 astrocytoma ('diffuse astrocytoma')

The most common grade 2 astrocytoma is called a 'diffuse astrocytoma'. (Diffuse means it does not have well-defined edges.) These are slow-growing, but they can sometimes return, following initial treatment, as a higher, grade 3 astrocytoma.

They occur most often in adults between the ages of 20 and 45. They are more common in males than females.

Grade 3 astrocytoma ('anaplastic astrocytoma')

A grade 3 astrocytoma is called an 'anaplastic astrocytoma'. (Anaplastic means the cells divide rapidly and do not resemble normal cells in structure or function.) They are fast-growing and often referred to as malignant or cancerous. They often recur following initial treatment in a more advanced form i.e. grade 4 astrocytoma (glioblastoma). *(Please see the Glioblastoma fact sheet for more information).*

They are more common in adults between the ages of 30 and 70 and are more common in males.

Grade 4 astrocytoma ('glioblastoma')

Grade 4 astrocytomas are usually referred to by the term glioblastoma. You may sometimes hear them called glioblastoma multiforme, or GBM for short, though these terms are less used nowadays. *(Please see the separate Glioblastoma fact sheet for more information).*

What causes astrocytomas?

The first things to stress is that there is nothing you could have done, or avoided doing, that would have prevented you from developing a brain tumour.

As with most brain tumours, the cause is not known. However, much research is being carried out into possible causes, focussing round our genes.

Genes

Astrocytomas, like all brain tumours, are the result of the uncontrolled growth of cells in the brain.

Normal cells grow, divide and die in a controlled way, in response to signals from your genes, which are present in all your cells. These signals use a particular 'pathway' within the cell to tell the cell when to grow and when to stop growing.

Even if these signals are absent in the right combination, our bodies also have 'checkpoints' to limit the ability of cells to divide in an uncontrolled way.

Mutations (changes) in specific genes in the DNA (genetic material) of a cell can lead to tumour growth by altering the pathway and causing the cell to behave as if it is receiving a growth signal, even if it is not.

Alternatively, the mutations can inactivate the checkpoints that would normally stop the cell from dividing. As a result, any cells affected will continue to divide and can develop into a tumour.

Different grades of astrocytoma have mutations in different genes and research funded by The Brain Tumour Charity has played a large part in identifying some of these:

- grade 1 pilocytic astrocytomas often have a mutation in genes called NF1 and BRAF
- grade 2 diffuse astrocytomas and grade 3 anaplastic astrocytomas often have mutations in genes called TP53 and PDGFR
- a mutation in the IDH-1 gene has also been found in a large number of astrocytomas (as well as other types of glioma) across all grades,

It is hoped that this information will help in the development of more personalised treatments. *(Please see Biomarkers and future treatments section later in this fact sheet).*

Cells

Other research has found that that grade 1 pilocytic and grade 2 diffuse astrocytomas may come from astrocytes known as 'reactive astrocytes'.

These are astrocytes that 'react' rapidly when the brain or spinal cord is injured by infection, injury or other diseases. They react by filling the space created by neurons that have died as a result of the injury (sometimes referred to as an 'insult'). Tumour cells of pilocytic and diffuse astrocytomas show many similarities under the microscope to normal reactive astrocytes that are found in areas of injury, so it could be that astrocytomas may develop from these reactive cells that have not received the signal to stop dividing and growing.

Grade 3 anaplastic astrocytomas often develop from grade 2 diffuse astrocytomas that have become more advanced and

malignant. However, it is not clear whether this is the case for all, or just most, anaplastic astrocytomas, as there are a number of cases of grade 3 anaplastic astrocytomas that have 'grown from new'. You may hear this referred to as 'de novo'.

How is an astrocytoma diagnosed?

If your doctor (GP or A&E doctor) suspects you have a brain tumour, they will refer you to a specialist - a neurologist or neurosurgeon (specialists in brain and nerve disorders). If it is your child that they suspect has a tumour, they will refer them to a paediatrician.

Neurological examination

The specialist will ask questions about your health and give you a physical examination. They will also test your nervous system (called a neurological examination). This involves looking at your vision, hearing, alertness, muscle strength, co-ordination, and reflexes.

They may also look at the back of your eyes to see if there is any swelling of the optic disc. (The optic disc is where the optic nerve from the brain enters the eye). Any swelling is a sign of raised pressure inside the skull, which could be a sign of a brain tumour.

Scans

You will then have one or more further tests, such as an MRI (magnetic resonance imaging) or CT (computerised tomography) scan to establish whether a brain tumour is present. *(For information about these scans, please see the Scans fact sheet).*

For some people, their first symptom may be a seizure, so they are seen as an emergency. In this case they may be given a scan as their first test, after which their case will be referred to a neuro-oncology 'MDT' (multi-disciplinary team) followed by a consultation with the neurologist/neurosurgeon. *(Please see 'The Multi-Disciplinary Team (MDT)' fact sheet for more information).*

Some GPs can refer you for a scan directly, or you may have been admitted to hospital with a problem and a brain scan was arranged to investigate this further.

If, following the scan, a tumour is found, you may be given a body scan to establish if your tumour is a primary brain tumour (one

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which started in the brain) or a secondary tumour and there is a primary tumour elsewhere in the body.

Biopsy

If the tumour is a primary tumour and is in an area of the brain which can be operated on, a biopsy (small sample of the tumour) may be taken from your tumour to aid diagnosis of the tumour type. It is important to realise that a biopsy is an operation that takes several hours. Any risks will be explained to you by your surgical team.

Surgery

Alternatively to a biopsy, and if possible, the resection (surgical removal) of the whole tumour, or as much as possible, will be undertaken at the same time. If only part of the tumour can be removed, this is known as 'debulking'.

Biobanking

In both cases of biopsy or surgery, you may like to ask, before your operation, about the possibility of 'biobanking' some of the tissue from your tumour.

A key to accelerating research towards improving survival and quality of life for people with brain tumours, is for researchers to have access to centralised tissue banks containing patients' tumour samples so they can carry out more research.

Currently there is no centralised tissue bank and not all centres are able to take and store samples, as they need to be licenced under the Human Tissue Act, with ethical approvals in place. As a result, routine collection of tissue for research is not yet a reality.

The Brain Tumour Charity is committed to establishing a centralised tissue bank with simpler access arrangements. As there are many types of brain tumour, some of which are very rare, we need to ensure that we learn from every patient. This will require systems and cultural changes in the approach to collecting samples. By asking about biobanking some of your tumour, you may help with the move towards this.

Speak to us and to your health team if this is something you are interested in doing. (The Brain Tumour Charity Support & Info Line - 0808 800 0004 or support@thebraintumourcharity.org)

Laboratory analysis

Following biopsy or surgery, cells from the tumour will be

analysed in a laboratory by a neuropathologist. (Please see *The Multi-Disciplinary Team (MDT) fact sheet*.)

The neuropathologist will examine the cells, looking for particular cell patterns that are characteristic of the different grades of astrocytoma.

Confirming the diagnosis of the different grades of astrocytoma can be difficult as low grade and high grade astrocytoma cells can look very similar, but detection of the various gene mutations, previously mentioned in this fact sheet, are now being used to aid accurate diagnosis - for example, the BRAF fusion gene is used for diagnosing pilocytic astrocytomas,

Accurate diagnosis is important as it allows your medical team to give you information about how the tumour could behave in the future, and also to recommend treatment options. This could include a clinical trial.

Biomarker testing

As part of this analysis, you may like to ask about 'biomarker testing'. This is where the doctors look for markers (changes) in certain genes in the tumour cells that may indicate how well you will respond to certain treatments. (Please see the 'Biomarker tests and future treatment' section later in this fact sheet.)

How are astrocytomas treated?

The treatment for astrocytomas depends on the grade of the tumour, as well as its size and location.

Grade 1 pilocytic astrocytoma

Surgery - complete tumour removal

Where possible, treatment for grade 1 pilocytic astrocytomas in adults is normally surgery. The aim is to remove as much of the tumour as possible. How much can be removed will depend on where the tumour is in the brain.

If the tumour is in the cerebrum or cerebellum (please see previous diagram or *The human brain fact sheet*) they can often be removed completely. You may hear this referred to as 'complete or total resection'.

If the tumour is completely removed, more treatment may not be needed. Your hospital will continue to monitor you with regular MRI scans (See *the Scans or Scans for children fact sheets*), with

no treatment given, unless you develop symptoms, any symptoms you have worsen or your scan changes. This is often called 'watch and wait'. (Please see *the Watch and wait fact sheet for more information*.)

With tumour locations other than the cerebrum or cerebellum, complete removal may still be possible, but the benefits need to be weighed up against various possible after-effects. For example, if the tumour is in the optic nerve, complete removal may be achieved, but it can result in blindness in the affected eye. Or if the tumour is in one of the 'midline structures' (e.g. hypothalamus, brain stem, spinal cord), surgery can affect the functions these areas control, such as breathing, sleep, body temperature, particularly in children younger than 2 years old. (Please see *diagram below or The human brain fact sheet*).

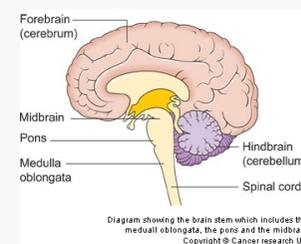


Diagram showing the brain stem, which includes the medulla oblongata, the pons and the midbrain

Surgery - partial tumour removal

In some cases, complete removal of the tumour may not be possible. It may be located in a difficult area of the brain to operate, or near important parts of the brain where surgery could do more harm than good. In this case, the surgeon will remove as much of the tumour as they can. This is known as 'debulking' or 'partial resection'.

Depending on how much of the tumour is removed, you may be put on a 'watch and wait' approach after surgery. (Please see the sections further on in this fact sheet and also the *Watch and wait fact sheet*).

Alternatively you may be given radiotherapy after your surgery, though doctors try to avoid this in people with the genetic condition NF1 and also in children under three years old.

Occasionally chemotherapy may also be given. (Please see the *Chemotherapy, Radiotherapy, Chemotherapy for children, or Radiotherapy for children fact sheets*).

Further surgery may be needed later to remove the rest of the tumour that was left, or if it starts to regrow. You may also need further surgery if the tumour is blocking the flow of the cerebro-spinal fluid (a condition called 'hydrocephalus'), to insert a shunt to remove the excess fluid from the brain.

Chemotherapy

For children, chemotherapy is often the first line of treatment. *(Please see Chemotherapy for children fact sheet.)*

Watch & wait

In some cases, your medical team may decide not to use surgery initially, but to use the 'watch & wait' approach. This approach may also be used after surgery,

This may be used if the tumour:

- is growing very slowly
- is not causing any symptoms
- is causing only a few symptoms that are being well-controlled or which are not badly affecting your quality of life,

The reason for adopting this approach may be that it is felt that surgery carries more risks than giving no initial treatment. This may feel like they are 'doing nothing'. However, they will monitor your tumour and, where necessary, treat any symptoms.

In this situation, treatment may not be needed for many months or even years. Some people may never need any further treatment.

Some tumours have also been known to reduce in size with no apparent cause. This is known as 'spontaneous regression'.

If your symptoms worsen, or the tumour changes or starts to grow, your medical team will then look at other treatment options, such as surgery.

Grade 2 diffuse astrocytoma

As with pilocytic astrocytomas, surgery is usually the first treatment for diffuse astrocytomas in adults. If they can be completely removed or almost completely removed, then treatment is the same as pilocytic astrocytomas.

However, as these tumours are more diffuse (the edges are less well-defined), complete removal is often not possible and

more of the tumour is often left behind. These tumours are more likely to regrow.

Surgery, therefore, is more often followed up with radiotherapy. This is particularly the case if you have symptoms such as weakness in an area of your body.

For children, particularly young children, chemotherapy, rather than surgery, is usually the first treatment given.

Grade 3 anaplastic astrocytoma

As these tumours are faster growing and more aggressive, the usual course of treatment is surgery followed by radiotherapy and sometimes chemotherapy. If you are relatively fit, a long course of radiotherapy over several weeks may be suggested - if not, a shorter course may be more suitable. Radiotherapy is very rarely used in children under 3 years.

Where chemotherapy is suggested, chemotherapy drugs are sometimes put inside a polymer wafer and inserted into the brain during surgery. The polymer gradually dissolves over 2-3 weeks, releasing the chemotherapy drug (usually carmustine) directly into the brain.

Wafers are used to target cells which couldn't be removed by surgery. You may also hear these implants referred to as Gliadel® wafers.

They are only licensed for use in adults with high grade gliomas (such as anaplastic astrocytomas) and recurrent glioblastoma (GBM), so their use in children is extremely rare.

NICE guidelines also mean that these can only be used when the surgeon is confident that at least 90% of the tumour has been removed. (NICE is the National Institute for Health and Care Excellence). *(For more information, please see the Chemotherapy and the Chemotherapy for children factsheets).*

Your oncologist may also recommend a drug called temozolomide (Temadol®). Both carmustine and temozolomide stop the tumour cells copying their DNA (genes), which needs to happen before the cells can divide. This in turn stops the tumour cells dividing.

Grade 4 astrocytoma (glioblastoma)

(Please see the separate Glioblastoma fact sheet for more information).

Biomarker tests and future treatment

A biomarker is a biological marker or indicator, such as a change in a gene in a tumour's DNA, that can indicate how likely the tumour is to respond to treatment or how it is likely to progress. *(Please see the Biomarkers fact sheet for more information.)*

MGMT methylation test

This test involves looking at how much of a particular protein involved in DNA repair (MGMT) is present in the tumour cells.

MGMT can disrupt the action of some chemotherapy drugs, such as temozolomide, so high levels of MGMT means that chemotherapy is likely to be less effective. This information helps to plan suitable, individualised treatment.

The test is only suitable for certain types of tumour, of which anaplastic astrocytoma is one.

The MGMT methylation test is now routinely carried out in many neuro-oncology centres.

IDH-1 test

This test looks for a mutation in a gene known as IDH-1.

For people with high grade types of certain gliomas, including astrocytomas, mutations of the IDH-1 gene are often linked with longer-term survival rates.

It is not yet clear how mutations of the IDH-1 gene link to outcomes for people with low-grade brain tumours.

In addition to long-term survival rates, scientists have looked at whether the IDH-1 gene mutation predicts treatment outcomes.

Further research needs to be carried out before clear conclusions can be drawn, but it looks possible that chemoradiotherapy (a combination of chemotherapy and radiotherapy) may be more effective for people who have the IDH-1 mutation, than those who do not (particularly in grade 2 gliomas).

You may be suitable for IDH-1 testing - please speak to your neuro-oncologist for information and advice.

Future treatment

As we gain greater understanding of the role played by genes and signalling pathways within cells in the development of astrocytomas (see previous sections of this fact sheet), possible drug treatments which target these processes may be developed that don't affect surrounding healthy tissue.

For example, work funded by The Brain Tumour Charity on the BRAF fusion gene and its pathway called MAP kinase, has led directly to clinical trials with drugs that target this pathway, in inoperable and recurrent pilocytic astrocytoma.

These drugs were chosen to investigate as it follows the successful use of similar drugs to treat malignant melanoma (a type of skin cancer), which also has defects in the MAP kinase pathway.

What if I have further questions?

If you require further information, any clarification of information, or wish to discuss any concerns, please contact our Support and Information Team:

Call: 0808 800 0004

(free from landlines and most mobiles:
3, O2, Orange, T-mobile, EE, Virgin and Vodafone)

Email: support@thebraintumourcharity.org

Join our closed Facebook group:
bit.ly/supportonfacebook

About us

The Brain Tumour Charity makes every effort to ensure that we provide accurate, up-to-date and unbiased facts about brain tumours. We hope that these will add to the medical advice you have already been given. Please do continue to talk to your health team if you are worried about any medical issues.

The Brain Tumour Charity is at the forefront of the fight to defeat brain tumours and is the only national charity making a difference every day to the lives of people with a brain tumour and their families. We fund pioneering research to increase survival, raise awareness of the symptoms and effects of brain tumours and provide support for everyone affected to improve quality of life.

We rely 100% on charitable donations to fund our vital work. If you would like to make a donation, or want to find out about other ways to support us including fundraising, leaving a gift in your will or giving in memory, please visit us at thebraintumourcharity.org, call us on **01252 749043** or email fundraising@thebraintumourcharity.org

About this fact sheet

This fact sheet has been written by Peter Hill, PhD. and written and edited by The Brain Tumour Charity's Support and Information Team. The accuracy of medical information has been verified by leading health professionals specialising in neuro-oncology. Our fact sheets have been produced with the assistance of patient and carer representatives and up-to-date, reliable sources of evidence. If you would like a list of references for any of the fact sheets, or would like more information about how we produce them, please contact us.



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Your notes

**Saving lives through research,
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