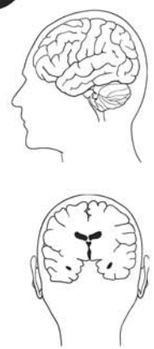
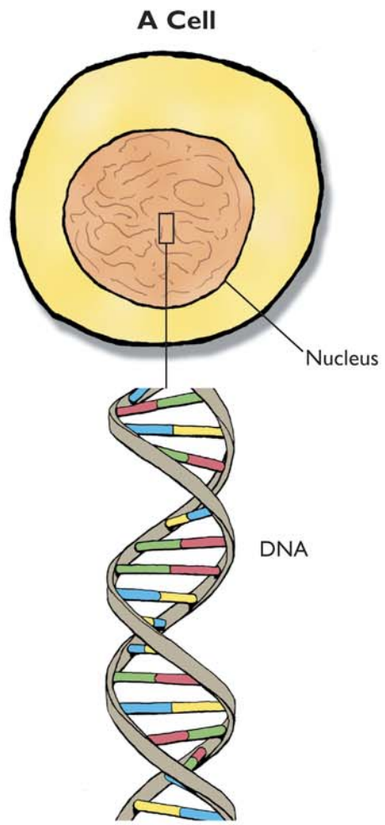
gliomas

diagnosis & management



what is a glioma?

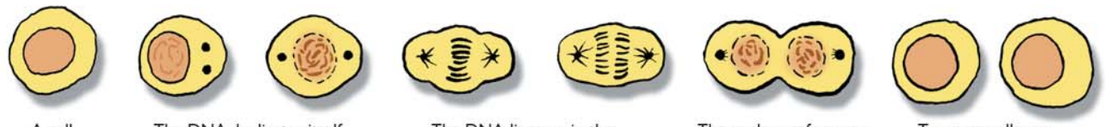


The brain tumor has already been found, and surgery has been performed to establish a diagnosis and/or to remove the tumor. The doctor says the brain tumor is a kind of **glioma** *[glee-OH-mah]*, but what does that mean? This booklet will tell you how these tumors form in the brain, what the different kinds are, and how they are commonly managed.

Our human body contains about thirty trillion cells. Each cell contains a blueprint for the design of the entire body. This blueprint is coded in microscopic form by long, threadlike molecules of deoxyribonucleic acid (DNA). Every time a single cell divides to become two cells, a process known as **mitosis** *[my-TOE-sis]*, the DNA duplicates before the cell divides. This way each new cell gets a complete copy of the DNA. Mitosis (cell division) occurs repeatedly in every part of a baby or child's body. In the adult brain, the majority of cells are no longer capable of dividing, except for a few precursor cells. The precursor cells are able to divide and are believed to be the origin of most gliomas *[glee-OH-mahs]*.

Gliomas are a family of brain cancers. When the DNA in our cells changes or mutates in a certain way, the cells become cancerous. Then the mutated cells multiply beyond normal limits, forming a tumor. In the brain, a tumor can be **primary** *[PRY-may-ree]* or **metastatic** *[meh-tuh-STA-tick]*. Metastatic brain tumors happen when a cancerous cell from another source in the body gets into the brain via the bloodstream. **Gliomas are the most common primary brain tumors.**

Mitosis



A cell. The DNA duplicates itself as the nucleus dissolves. The DNA lines up in the middle, and a copy goes to each half. The nucleus reforms as the rest of the cell pinches in half. Two new cells are formed.

normal brain cells

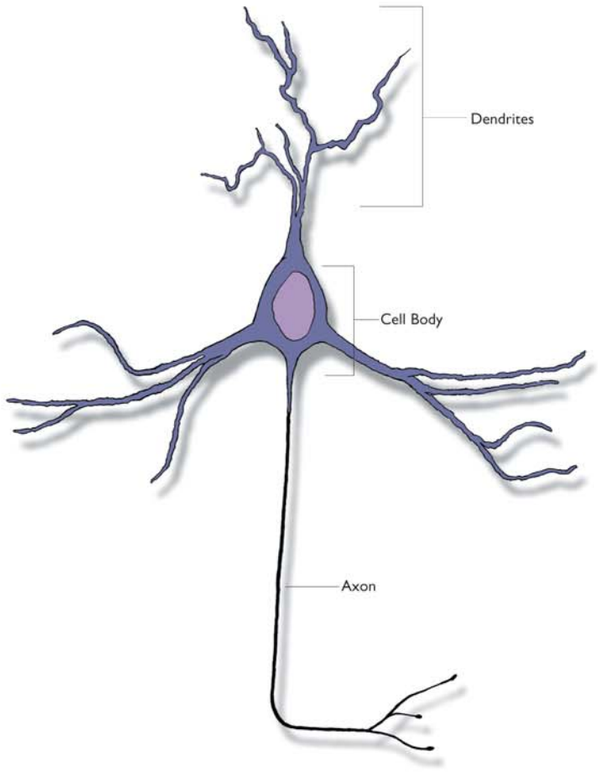
The adult brain is made up of two types of cells—**nerve cells** and **glial cells.** Nerve cells, or neurons, make up the thinking and acting part of the brain. Glial cells provide protection and support for the neurons. By weight, glial cells make up half the brain, and nerve cells make up the other half.

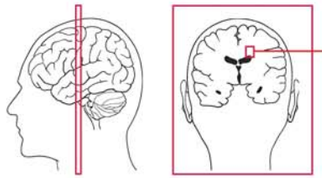
Nerve Cells

Neurons

[NUR-ons]

These are the cells that do our thinking. Neurons use electrical impulses combined with chemical transmitters to communicate with one another. Each neuron has three parts: a cell body, an axon, and dendrites. Neurons are so specialized for their task of communication that they need other cells to help them survive.





Glial Cells

'Glial' means glue, and these cells are the glue supporting the neurons.

Astrocytes

[AS-tro-sites]

Atrocyte means 'star cell', which is what these cells look like. An astrocyte's many arms support the nerve cells and blood vessels in the brain like scaffolding. Astrocytes bring oxygen and nutrients from the blood to the neurons. They also clean up after our neurons by removing waste.

Oligodendrocytes

[OLLY-go-DEN-dro-sites]

Their name means 'few arms'. These cells send out arms like the astrocytes, but their arms wrap around the neuron in sheets to make insulation. As electric signals travel from neuron to neuron, the insulation provided by oligodendrocytes makes the signals travel faster. Oligodendrocyte insulation also keeps the neuron-to-neuron communication from becoming confused.

Glioblasts:

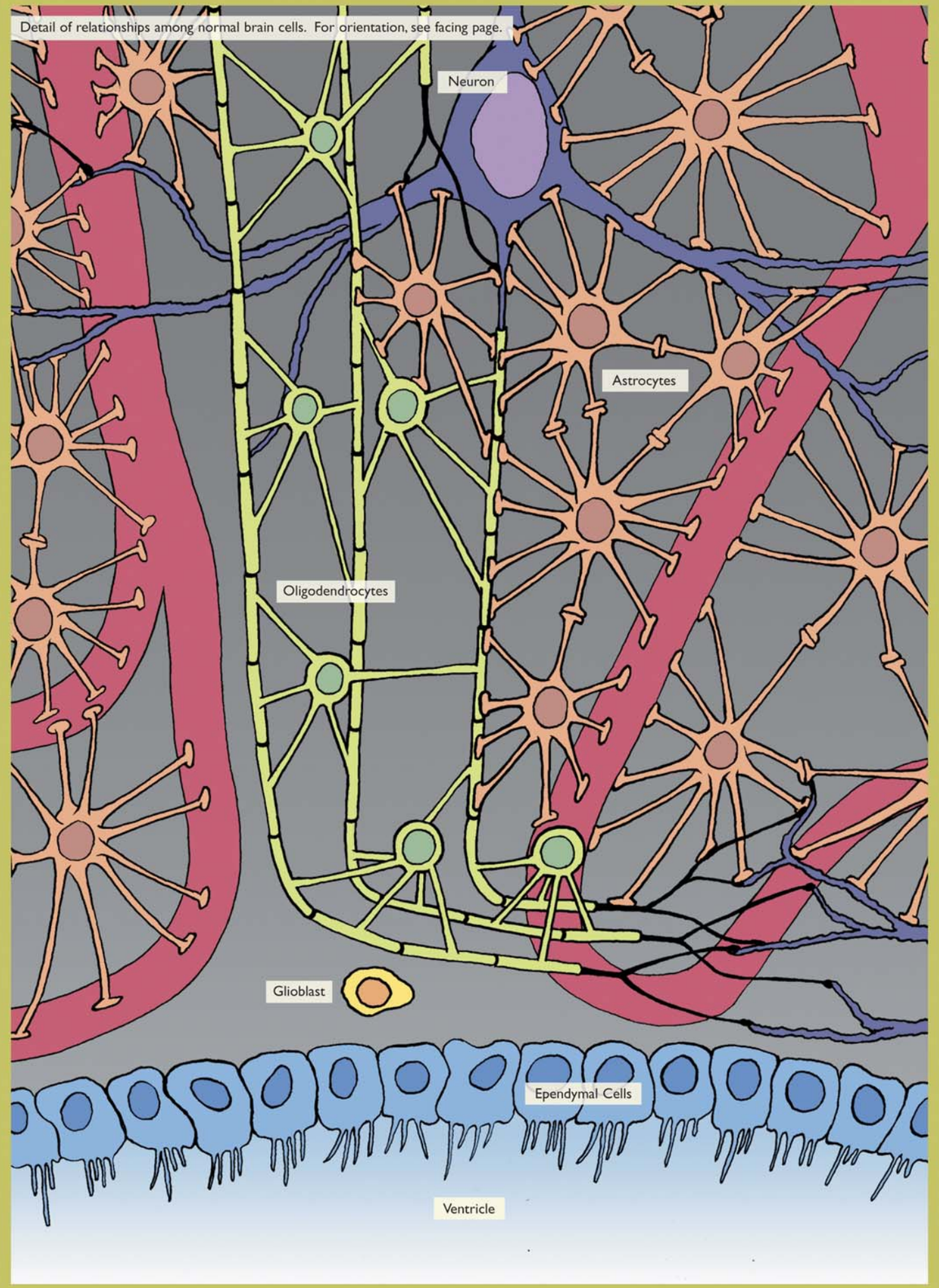
[GLEE-oh-blasts]

A glioblast is a precursor cell that does no work, but has the potential to divide and produce many mature functioning cells. A glioblast can become either an astrocyte or an oligodendrocyte. The adult brain has a few glioblasts waiting to become astrocytes or oligodendrocytes if needed.

Ependymal Cells:

[eh-PEN-deh-mul]

Ependymal cells line the ventricles (fluid chambers) of the brain. Fluid is produced continually in these chambers to help cushion the brain. The ependymal cells have hair-like cilia on the surface facing the inside of the ventricle.

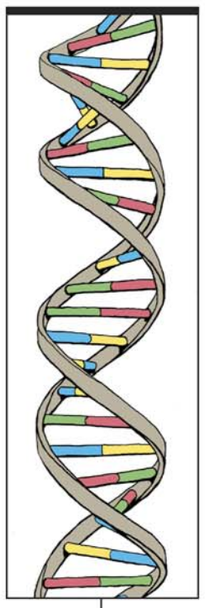


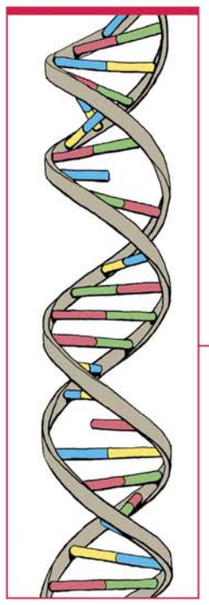
how a glioma begins

Scientists once believed that a glioma began when a mature astrocyte or oligodendrocyte changed and regressed to become a tumor cell—a cell that divides without control. Research has now shown that **a glioma occurs when the DNA inside a glioblast changes, or mutates**. A glioblast with mutated DNA produces non-functional cells that continue to divide and overrun cellular boundaries until a tumor is formed. Although these tumor cells share characteristics with normal astrocytes and oligodendrocytes, they were never—and can never be—functional cells.

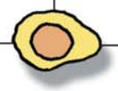
The DNA within tumor cells often continues to mutate, and these mutations may cause the glioma to become more malignant in time. Becoming more malignant means the glioma cells grow faster and have greater mobility. This mobility makes gliomas especially difficult to treat. Cells from the main tumor mass often migrate into nearby healthy brain tissue, making it impossible to catch and treat every cancerous cell.

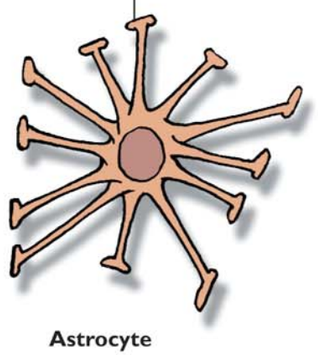
In mutated DNA, parts of the blueprint are missing, switched, or moved. Each change is called a **mutation.**

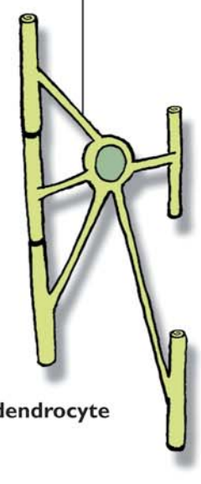




A **normal glioblast** becomes an astrocyte or an oligodendrocyte if those working cells are needed in the brain.



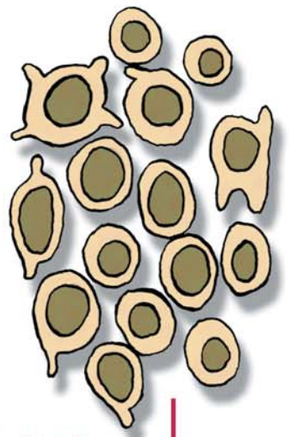




A **mutated glioblast** can become different gliomas, depending on the location and number of changes in its DNA.

Well-Differentiated Gliomas

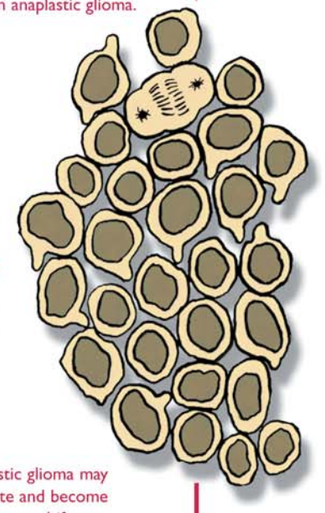
Astrocytoma
Oligodendroglioma
Mixed Glioma



A well-differentiated glioma may continue to mutate and become an anaplastic glioma.

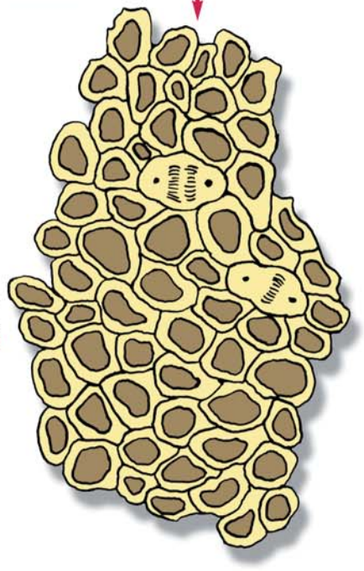
Anaplastic Gliomas

Anaplastic Astrocytoma
Anaplastic Oligodendroglioma
Anaplastic Mixed Glioma



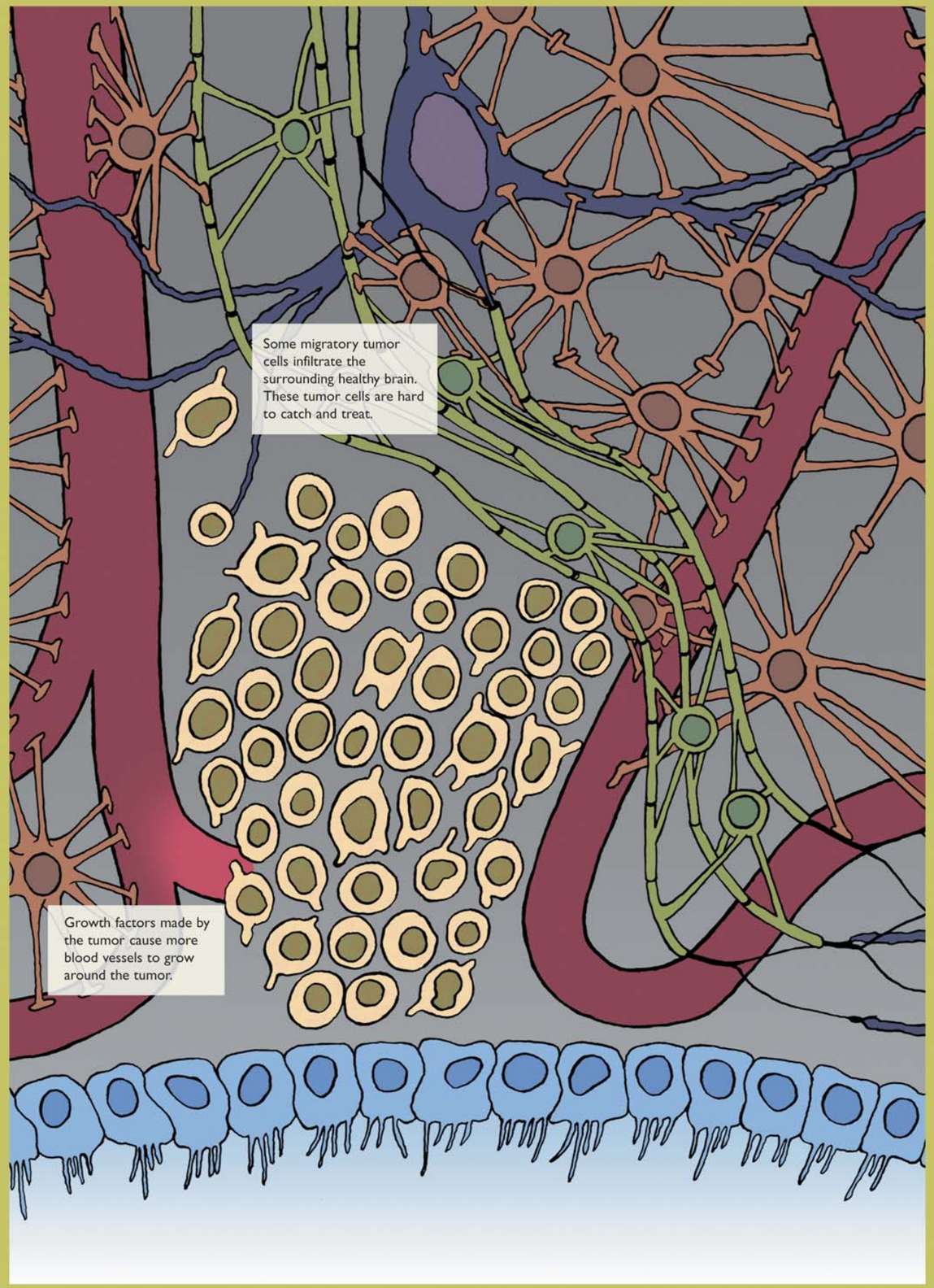
An anaplastic glioma may continue to mutate and become a glioblastoma multiforme.

Glioblastoma Multiforme



A Note About "Grading"

The terms "high grade" and "low grade" are used to describe different degrees of malignancy in gliomas. This is because tumors were once graded for malignancy based on their microscopic appearance, beginning in 1920. Since then, standards of pathology have changed, and it is now customary to apply specific names to gliomas. However, the terms "low grade" and "high grade" are still in use. "Low grade" refers to well-differentiated gliomas; "high grade" refers to anaplastic gliomas and glioblastoma multiforme.



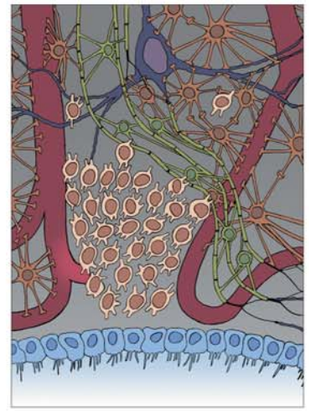
well-differentiated gliomas

Astrocytoma, oligodendroglioma, and mixed glioma are the three **well-differentiated gliomas**. Differentiated means that these tumor cells still resemble the normal cells they should have become. Although the tumor cells are organized similarly and with equal sizes, they do not function as normal cells. These gliomas grow relatively slowly.

Astrocytoma

[AS-tro-sigh-toh-ma]

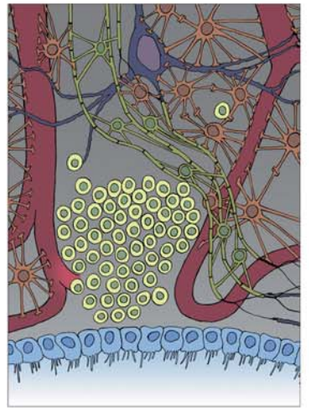
The cells of an astrocytoma still look like normal astrocytes, except that their shorter, fewer arms serve no purpose. The nuclei of the astrocytoma cells are slightly irregular in shape. Mitotic figures are rarely seen, because astrocytomas grow slowly. The tumor cells can grow around healthy nerve cells and blood vessels, but are generally distinct from the healthy cells. Still, a few cells can infiltrate into the surrounding, healthy cells. An astrocytoma may develop anywhere in the brain and spinal cord, but most are located in the cerebrum, especially in the frontal or temporal lobes. The tumor may cause seizures, headaches, or subtle changes such as difficulty in speaking or moving. It can also cause changes in sensation, vision, and behavior.



Oligodendroglioma

[OLLY-go-DEN-dro-glee-OH-ma]

Oligodendrogliomas are composed of cells with uniform, round or oval nuclei and no arms. Since oligodendrogliomas grow slowly, there are few blood vessels to the tumor and mitotic figures are seldom seen. A few tumor cells will infiltrate the surrounding healthy cells. Oligodendrogliomas most commonly occur in the white matter of the cerebrum, especially in the frontal lobe, although they may arise anywhere in the brain or spine. This tumor commonly causes seizures and headaches, and patients may have a long history of these symptoms before being diagnosed with an oligodendroglioma.



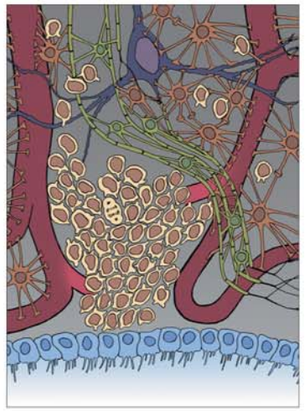
Mixed Glioma

[mixed glee-OH-mah]

This kind of low-grade glioma is called of a mixed glioma because some of the tumor cells look like oligodendroglioma, while some tumor cells resemble astrocytoma. There are small, armless tumor cells with round nuclei next to larger tumor cells with small arms and irregular nuclei. These tumors grow slowly, so there is little growth in the surrounding blood vessels, and mitotic figures are rarely seen. A few cells of the tumor mass will migrate into the surrounding healthy cells. Mixed gliomas usually occur in the cerebral hemispheres, commonly in the frontal or temporal lobes. They cause the same symptoms as astrocytomas and oligodendrogliomas. The most common symptoms are seizures, headaches, and difficulty in motor control.

anaplastic gliomas

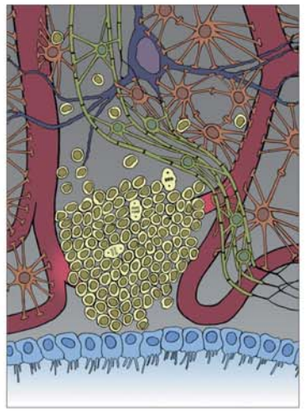
Anaplastic *[AN-uh-plaz-tick]* means the cells in a tumor look more like a glioblast and less like a mature cell. This occurs because the DNA of anaplastic tumor cells has more mutations which cause these tumors to be more malignant. Researchers believe that anaplastic gliomas were once low-grade gliomas in which the tumor DNA mutated further. Anaplastic gliomas are treated more vigorously than low-grade gliomas.



Anaplastic Astrocytoma

[AN-uh-plaz-tick AS-tro-sigh-toh-ma]

The cells of an anaplastic astrocytoma have short, nearly absent arms and come in various sizes. Unlike astrocytoma cells, the anaplastic astrocytoma cells are disorganized and dense with atypical nuclei. Mitotic figures are always found in the biopsies of these tumors. This means the tumor cells are reproducing faster than a low-grade astrocytoma. The reproducing tumor cells stimulate more blood vessels to branch out into the area. The new blood vessels feed the tumor, allowing new growth. These tumor cells migrate into our surrounding tissues with greater ease, making them harder to treat. Anaplastic astrocytomas occur in the same places as astrocytomas and have the same symptoms. Anaplastic astrocytoma may be a patient's initial diagnosis, or it may become the diagnosis after a recurring low-grade astrocytoma has become more malignant.



Anaplastic Oligodendroglioma

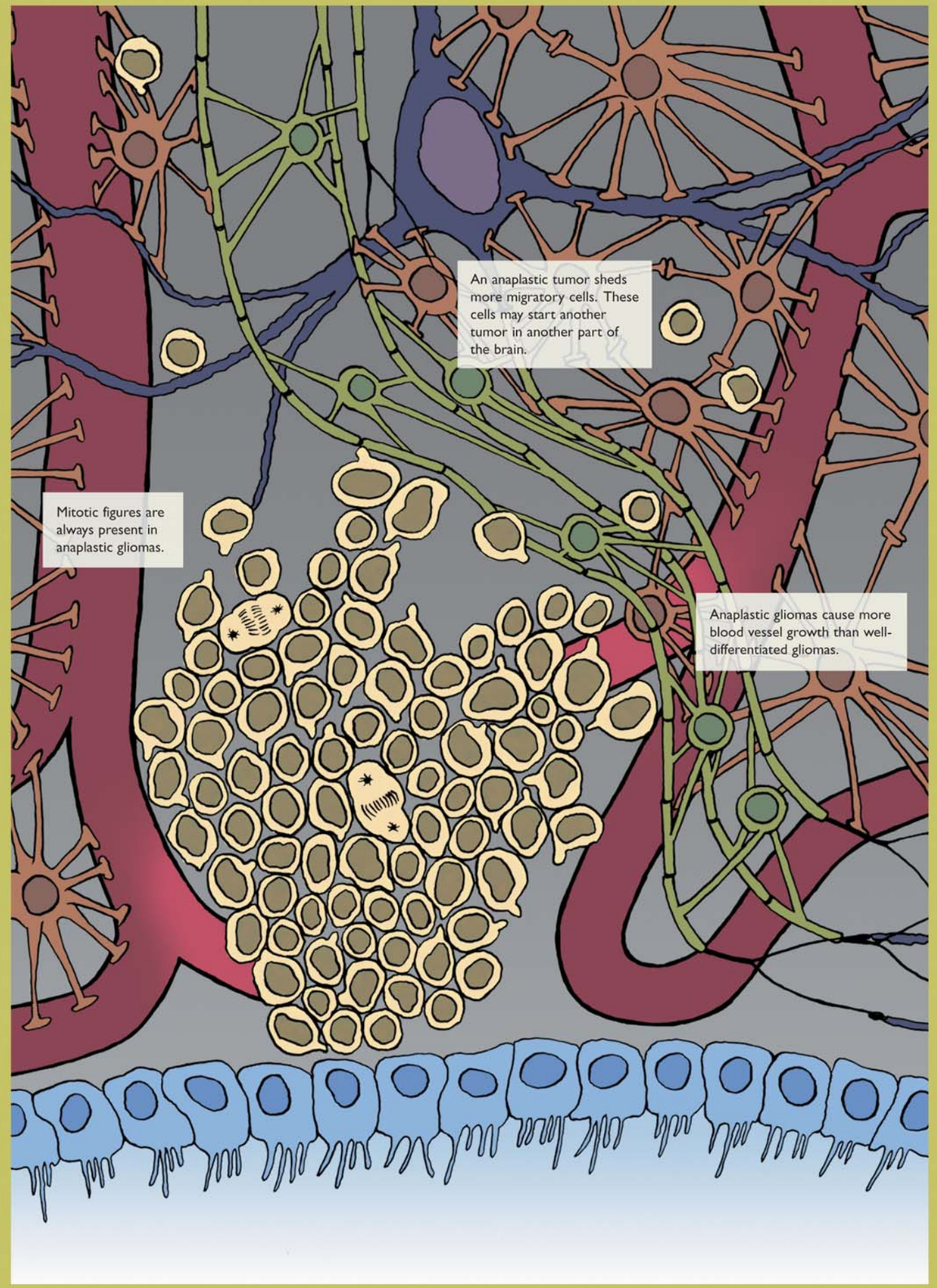
[AN-uh-plaz-tick OLLY-go-DEN-dro-glee-OH-ma]

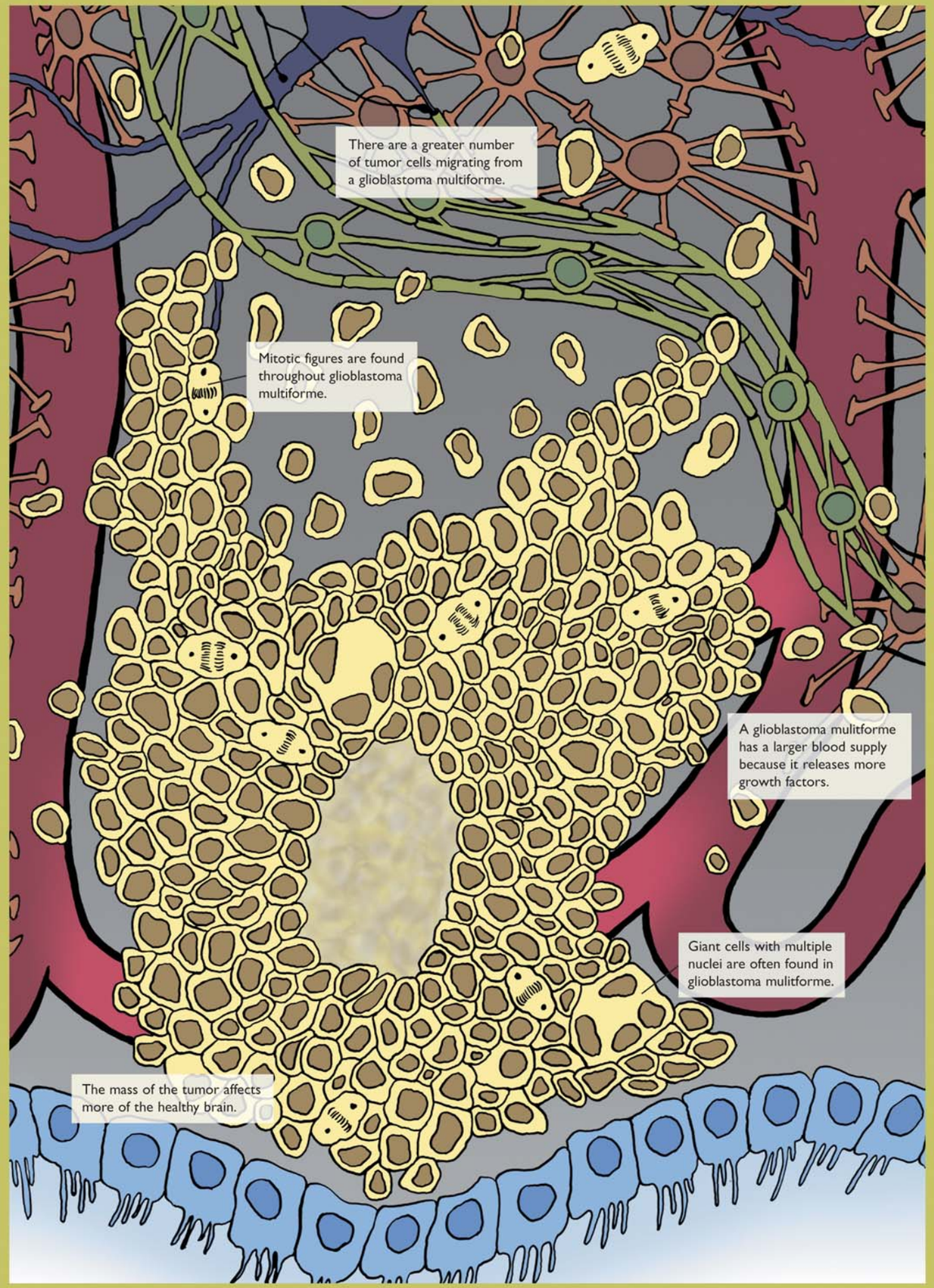
Anaplastic oligodendroglioma cells have oddly shaped nuclei. Compared to a low-grade oligodendroglioma, there are more tumor cells packed into a small space. The cells show less organization than an oligodendroglioma and slightly varying sizes. These tumors grow faster than low-grade oligodendrogliomas, and there are more blood vessels supplying the anaplastic oligodendroglioma. Mitotic figures are always present. More of the tumor cells migrate into the healthy tissue than in a low-grade oligodendroglioma. Anaplastic oligodendrogliomas have the same symptoms and occur in the same places as oligodendroglioma. Anaplastic oligodendroglioma may be a patient's initial diagnosis, or it may become the diagnosis after a recurring low-grade oligodendroglioma has become more malignant.

Anaplastic Mixed Glioma

[AN-uh-plaz-tick mixed glee-OH-mah]

Anaplastic mixed gliomas have traits of both anaplastic astrocytoma and anaplastic oligodendroglioma. These tumor cells come in various sizes, with more irregularly shaped nuclei than a low-grade mixed glioma. Anaplastic mixed gliomas are dense and always show mitotic figures because they are growing faster than a low-grade tumor. There are more blood vessels growing to the tumor site. These tumor cells migrate into the surrounding healthy brain in greater numbers than the low-grade mixed glioma. Anaplastic mixed gliomas have the same symptoms and occur in the same places as low-grade mixed gliomas. Anaplastic mixed glioma may be a patient's initial diagnosis, or it may become the diagnosis after a recurring low-grade mixed glioma has become more malignant.





glioblastoma multiforme

Glioblastoma Multiforme

[glee-oh-blast-OH-mah mul-tee-FOR-may]

Glioblastoma multiforme is the most commonly diagnosed glioma. Unfortunately, it is also the most malignant, due to the greatest number of DNA mutations. It is believed that any of the anaplastic gliomas can and will become glioblastoma multiforme given enough time for the tumor DNA to accumulate mutations. Most of the cells in a glioblastoma multiforme appear similar to a glioblast (therefore the 'glioblastoma' part of the name) but some of the tumor cells have features like other cells in the body (therefore the 'multiforme' part of the name). There are often giant cells with multiple nuclei. Because these tumor cells spend less time differentiating, they reproduce quickly and show several mitotic figures. These tumors are very dense, so dense they often outgrow their blood supply and have areas of necrosis (dead cells), even though blood vessels proliferate around the site. Glioblastoma multiforme tumors don't have defined borders. Instead, islands of tumor cells spread between healthy cells. There can also be migratory tumor cells far away from the main tumor masses. These tumors require the most aggressive treatment plan.

treatment

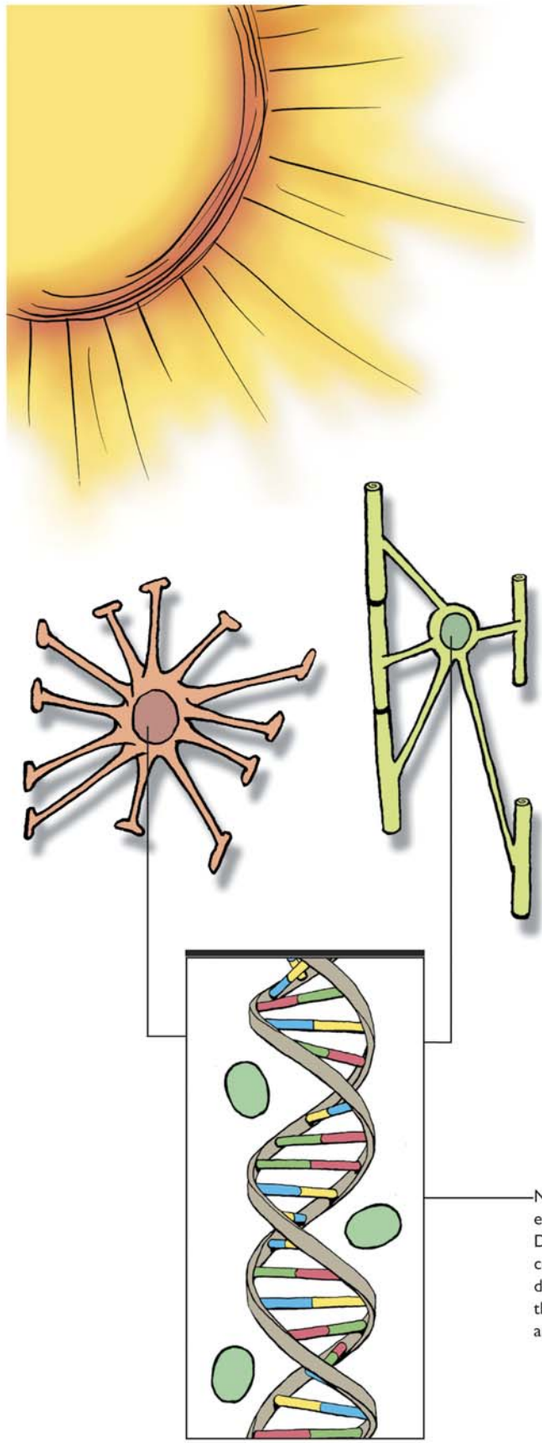
There are many treatments available to glioma patients. These treatments are designed to remove or kill as much of the tumor as possible and prolong the life of the patient. A doctor creates a treatment plan that takes into account the patient's age and health, the location of the tumor, and the type of glioma. **The treatment plan is usually some combination of surgery, observation, radiation, and chemotherapy**. It is important to communicate any questions or fears you may have about your treatment to your doctor. Being honest and open about how you feel physically and mentally helps the doctor create the right treatment plan for you.

Surgery

The role of surgery in the management of a glioma is first to provide an accurate diagnosis and second, if the tumor is favorably located, to remove it as completely as possible. The diagnosis, or classification, of the glioma is used to make recommendations about its future management.

Observation

Observation of the tumor occurs throughout the tumor's management. Periodically, MRIs and CTs will be taken of the tumor site to document any changes in the tumor or surrounding tissue. At the same time, your physical condition, symptoms, and medication will be reviewed. New or additional treatments may be recommended.



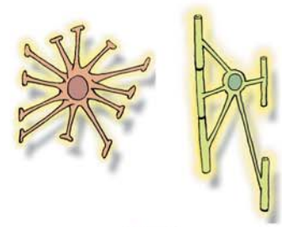
Radiation

The goal of radiation therapy is to kill tumor cells and to halt their reproduction. Some gliomas are more responsive to radiation than others.

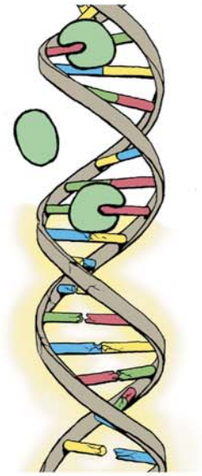
How Radiation Works

Radiation breaks DNA. We experience radiation from the sun everyday. Our cells have adapted to it, and normal cells easily repair the damage caused by the sun. Normal cells can even repair radiation damage in higher doses. Tumor cells, however, can't make repairs quickly. Their DNA repair mechanisms are usually shut down or slowed by the mutations required for cells to become tumor cells. In radiation therapy, measured doses of radiation are beamed on the tumor, usually multiple times with rests in between doses. The radiation breaks the DNA in the tumor cells and any normal cells also exposed. In the rest between doses, normal cells are able to repair the damage. The tumor cells have a much harder time recovering, and are treated with radiation again and again until their DNA is useless for growth. Then, the tumor cells die.

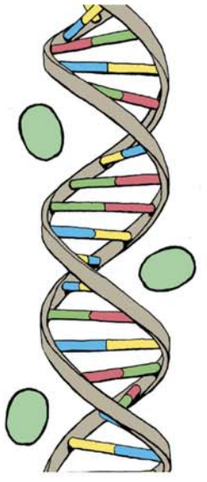
Normal cells have enzymes that check our DNA constantly and correct errors or repair damage. In tumor cells, these helpful enzymes are broken.



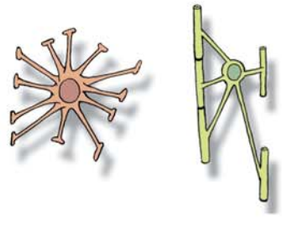
Normal cells during radiation therapy.



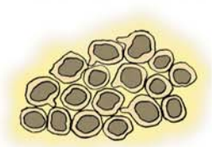
The bonds in the DNA of the normal cells are affected by radiation.



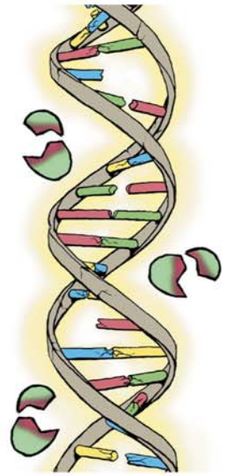
Enzymes repair the DNA in the normal cells.



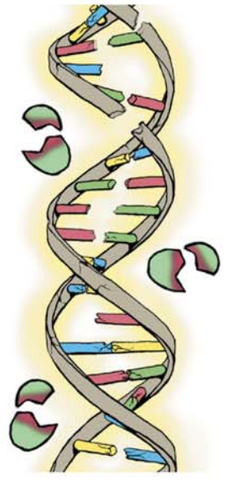
The normal cells continue to be healthy.



Tumor cells during radiation therapy.



The bonds in the mutated DNA of the tumor cell are broken down by radiation.



The broken enzymes of the tumor cell cannot repir the damage to the mutated DNA.

The tumor cells die.

Chemotherapy

The goal of chemotherapy is to kill tumor cells by using drugs that target rapidly reproducing cells to stop cell division. Chemotherapy also affects healthy cells elsewhere in the body that naturally divide at a higher rate, stopping their reproduction and causing the temporary side effects of treatment. Healthy cells will fight off the effects of chemotherapy, but tumor cells can't. Tumor cells lose the ability to fix damage quickly because that's one of the mutations necessary for cells to become cancerous—repair mechanisms are turned off. Chemotherapy is less toxic to healthy cells now than even a few years ago, but this treatment continues to have side effects and risks.

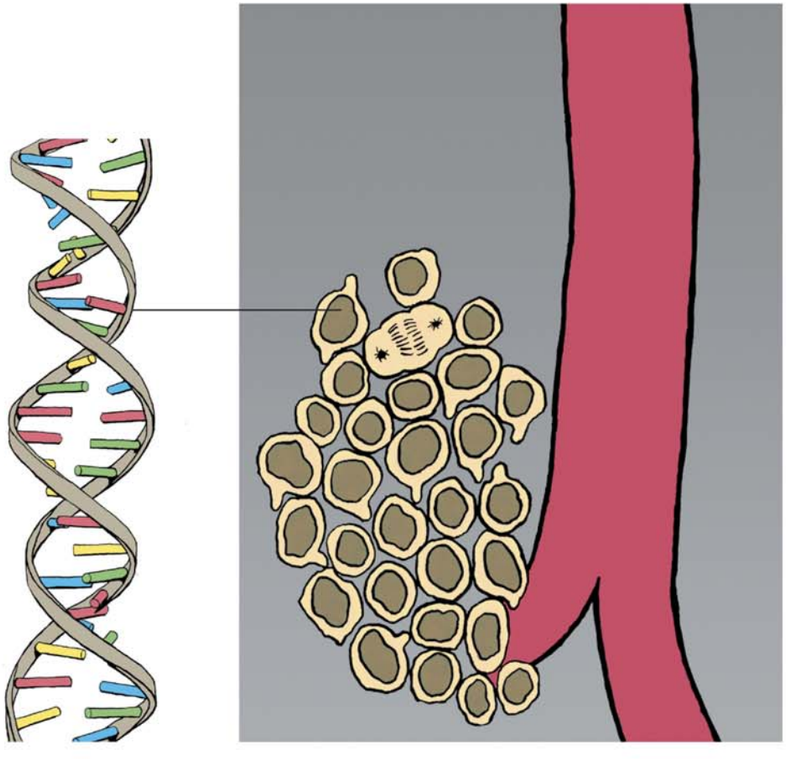
Chemotherapy drugs can be given orally or injected into a blood vessel. Doses are usually given in increments to gradually kill tumor cells and allow healthy cells to recover. Dosage amount and length of treatment depend on the chemotherapy drug chosen and your overall health. If chemotherapy is or may become part of your treatment plan, your doctor will go over possible drugs and their specific side effects with you.

During Chemotherapy

While chemotherapy targets tumor cells, it also affects dividing healthy cells. Areas in the body that are sites of regular cell division are: bone marrow (it manufactures blood cells), lining of the mouth, esophagus, stomach, intestines, skin, and hair. The effect of chemotherapy on these areas is temporary and ends with treatment. Chemotherapy also affects the testicles and ovaries. The effects of chemotherapy on fertility may be permanent. Your doctor will speak with you and answer any questions you have about the side effects of the chemotherapy drug before you undergo treatment. If you experience any discomfort while undergoing chemotherapy, call your doctor. Your doctor can prescribe medications or adjust your dosage to make you more comfortable.

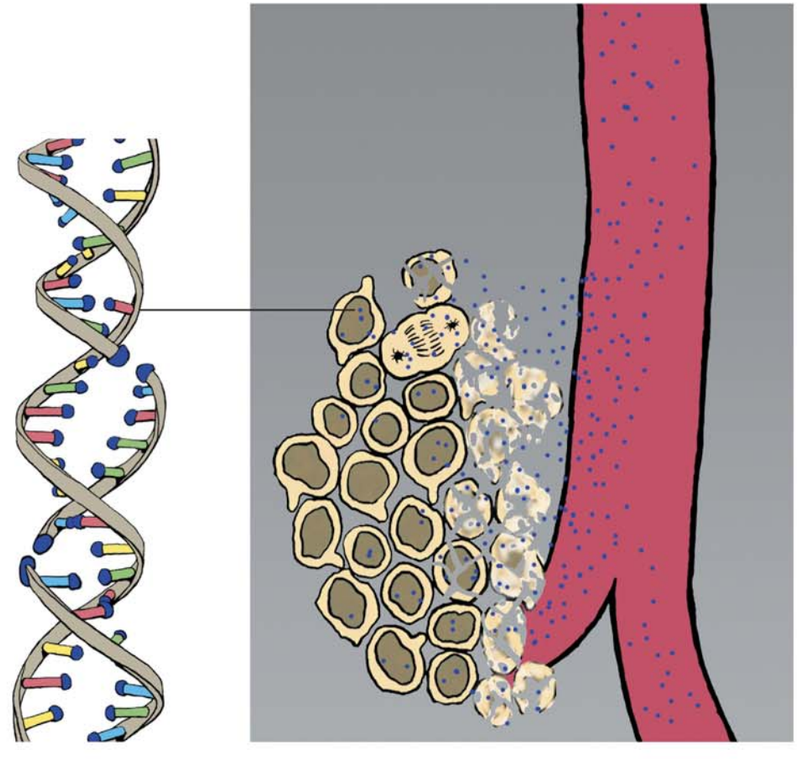
Tumor Cell DNA Preparing to Divide

In tumor cells preparing to undergo mitosis, the two strands of DNA separate to allow for their duplication prior to division.



Tumor Cell Division Blocked By Chemotherapy

The chemotherapy drugs travel to sites of dividing cells. The drugs cross into the brain from blood vessels to target the dividing cells. While some drugs work differently, most chemotherapy drugs interfere with DNA so that it cannot duplicate. This kills the cells as they attempt to divide.



for further research

Additional Resources

Websites

Clinical Trials and Noteworthy Treatments for Brain Tumors. Maintained by the Musella Foundation For Brain Tumor Research and Information.
Website:
http://www.virtualtrials.com/

Glioblastoma Multiforme and Anaplastic Astrocytoma,
Anaplastic Oligodendroglioma: A Guide For Patients.
By John W. Henson, M.D., at the Massachusetts General Hospital Brain Tumor Center.
Website:
http://brain.mgh.harvard.edu/glioblastoma.htm

Brain Cancer at cancerpage.com
Website:
http://www.cancerpage.com/cancers/default.asp?channel=Brain_Cancer

Online Brain Tumor Support Group.
Website:
http://www.med.nyu.edu/neurosurgery/obtsg.html

Books

Local Therapies for Glioma: Present Status and Future Developments
by Manfred Westphal (Editor), Christian Tonn (Editor), Zvi Ram. Published by Springer Verlag; (October 2003).

The Gliomas
by Mitchel S., Md. Berger (Editor), Charles B., Md. Wilson, Richard Zorab (Editor). Published by W B Saunders; 1st edition (January 15, 1999).

Brain Tumors: An Encyclopedic Approach
by Andrew H. Kaye (Editor), Edward R., Jr. Laws (Editor). Published by Churchill Livingstone; 1st edition (January 15, 1995).

Cancer Information Contacts

American Cancer Society
1.800.ACS.2345
Website: www.cancer.org

Cancer Information Line
1.800.4.CANCER
Website: www.cancercare.org

National Institutes of Health
1.800.352.9494
Website: cancernet.nci.nih.gov

Glioma Information Contacts

American Brain Tumor Association
2720 River Road, Suite 146
Des Plaines, IL 60018-4110
Patient Info: 1.800.886.2282
Tel: 847.827.9910
Fax: (847) 827-9918
Website: www.abta.org
E-mail: info@abta.org

The Brain Tumor Society
84 Seattle Street
Boston, MA 02134
Patient Info: 1.800.770.8287
Tel: 617.924.9997
Fax: 617.924.9998
Website: www.tbts.org
Email: info@tbts.org

National Brain Tumor Foundation
414 Thirteenth Street,
Suite 700
Oakland, CA 94612-2603
Patient Info: 1.800.934.2873
Tel: 510.839.9777
Fax: 510.839.9779
Website: www.braintumor.org

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