Eye Cancer (Melanoma and Lymphoma)

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide to make new cells, and die in an orderly way. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. In most cases the cancer cells form a tumor. Cancer cells can also invade (grow into) other tissues, something that normal cells can't do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA is damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first abnormal cell does.

People can inherit damaged DNA, but most often the DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called *metastasis*. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is named (and treated) based on where it started. For example, prostate cancer that has spread to the bones is still prostate cancer, not bone cancer.

Different types of cancer can behave very differently. They grow at different rates and respond to different treatments. This is why people with cancer need treatment that is aimed at their particular kind of cancer.

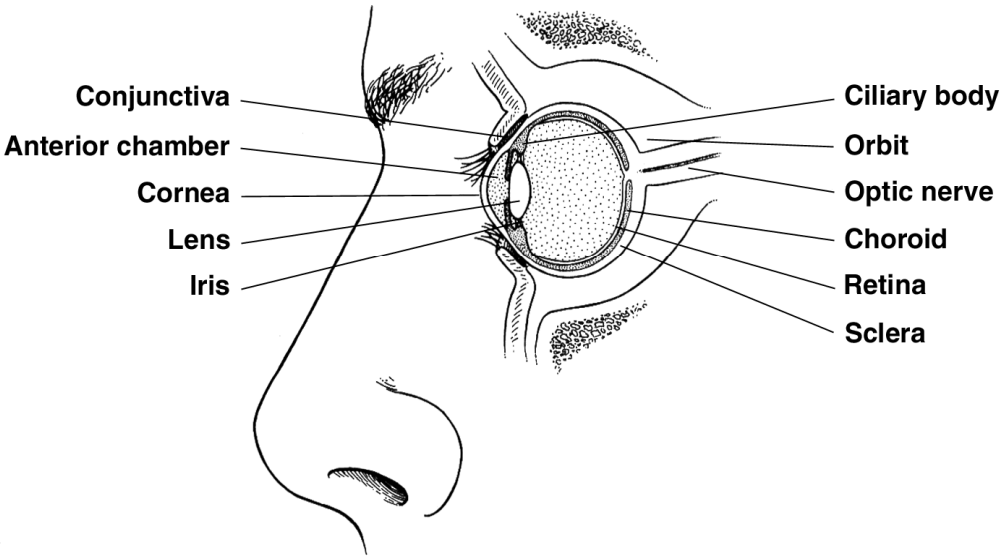
Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems — they can grow very large and press on healthy organs and tissues. But they can't grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are rarely life threatening.

What is eye cancer?

An eye cancer starts in the eye. There are different types of eye cancers. To understand eye cancers, it helps to know something about the parts of the eye and what they do.

Parts of the eye

The eye has 3 major parts: the eyeball (globe), the orbit, and the adnexal structures.



Eyeball

The main part of the eye is the eyeball (also known as the *globe*), which is mostly filled with a jelly-like material called *vitreous humor*. The eyeball has 3 main layers: the sclera, the uvea, and the retina.

Sclera: The sclera is the tough, white covering over most of the outside of the eyeball. In the front of the eye it is continuous with the cornea, which is clear to let light through.

Uvea: The uvea is the middle layer of the eyeball. It is where most melanomas of the eye develop. The uvea has 3 main parts:

- The **iris** is the colored part of the eye (most often blue or brown). It surrounds the pupil, the small opening that lets light enter the eyeball.
- The **choroid** is a thin, pigmented layer lining the eyeball that nourishes the retina and the front of the eye with blood.
- The **ciliary body** contains the muscles inside the eye that change the shape of the lens so that the eye can focus on near or distant objects. It also has cells that make aqueous humor, the clear fluid in the front of the eye between the cornea and the lens.

Retina: The retina is the inner layer of cells in the back of the eye. It is made up of specialized nerve cells that are sensitive to light. These light-sensing cells are connected to the brain by the optic nerve. When light enters the eye it passes through the lens, which focuses it on the retina. The pattern of light (image) appearing on the retina is sent through the optic nerve to an area of the brain called the *visual cortex*, allowing us to see.

Cancers that affect the eyeball are called *intraocular* (within the eye) cancers.

Orbit

The orbit consists of the tissues surrounding the eyeball. These include muscles that move the eyeball in different directions and the nerves attached to the eye.

Cancers of these tissues are called *orbital* cancers.

Adnexal structures

Adnexal (accessory) structures include the eyelids and tear glands. Cancers that develop in these tissues are called *adnexal* cancers.

Cancers in the eye (intraocular cancers)

Two types of cancers can be found in the eye.

Primary intraocular cancers start inside the eyeball. In adults, melanoma is the most common primary intraocular cancer, followed by primary intraocular lymphoma. These 2 cancers are the focus of this document.

In children, retinoblastoma (a cancer that starts in cells in the retina) is the most common primary intraocular cancer, and medulloepithelioma is the next most common (but is still extremely rare). These childhood cancers are discussed in our document *Retinoblastoma*.

Secondary intraocular cancers start somewhere else in the body and then spread to the eye. These are not truly "eye cancers," but they are actually more common than primary intraocular cancers. The most common cancers that spread to the eye are breast and lung cancers. Most often these cancers spread to the part of the eyeball called the uvea. For more information on these types of cancers, see our documents on them.

Intraocular melanoma (melanoma of the eye)

Intraocular melanoma is the most common type of cancer that develops within the eyeball in adults, but it is still fairly rare. Melanomas of the skin are much more common than intraocular melanomas.

Melanomas develop from pigment-making cells called *melanocytes*. When melanoma develops in the eye, it is usually in the uvea, which is why these cancers are also called *uveal melanomas*.

About 9 out of 10 intraocular melanomas develop in the choroid or ciliary body (which are parts of the uvea). Choroid cells make the same kind of pigment as melanocytes in the skin, so it's not surprising that these cells sometimes form melanomas.

Most of the other intraocular melanomas start in the iris (also part of the uvea). These are the easiest for a person (or their doctor) to see because they often start in a dark spot on the iris that has been present for many years and then begins to grow. These melanomas usually are fairly slow growing, and they rarely spread to other parts of the body. For these reasons, people with iris melanomas generally have a good prognosis (outlook).

Intraocular melanomas are generally made up of 2 different kinds of cells.

- **Spindle cells:** These are long, thin cells.
- **Epithelioid cells:** These cells are almost round but with some straight edges.

Most tumors have both kinds of cells. The outlook is better if the tumors are mostly spindle cells as opposed to mostly epithelioid cells. Epithelioid tumors are more likely to spread to distant parts of the body (such as the liver). If you have intraocular melanoma, your doctor can tell you which type of cells were found.

Primary intraocular lymphoma (lymphoma of the eye)

Lymphoma is a type of cancer that starts in immune system cells called *lymphocytes*. Most lymphomas start in lymph nodes, which are bean-sized collections of immune system cells scattered throughout the body. Lymphomas can also start in internal organs such as the stomach, lungs, and rarely, in the eyes.

There are 2 main types of lymphoma: Hodgkin disease and non-Hodgkin lymphoma. Primary intraocular lymphoma is a type of non-Hodgkin lymphoma. Most people with primary intraocular lymphoma are elderly or have immune system problems such as AIDS. Primary intraocular lymphoma is often seen along with lymphoma of the brain, known as *primary central nervous system (CNS) lymphoma*.

Orbital and adnexal cancers

Cancers of the orbit and adnexa develop from tissues such as muscle, nerve, and skin around the eyeball and are like their counterparts in other parts of the body. These are described in our other documents on cancers of muscle, nerve, skin, etc. For example, cancers of the eyelid are usually skin cancers, which are described in our documents on skin cancers (*Melanoma Skin Cancer* and *Skin Cancer: Basal and Squamous Cell*). Muscle cancer is described in our document *Rhabdomyosarcoma*.

Most of the rest of this document focuses on intraocular melanomas and lymphomas.

What are the key statistics for eye cancer?

The American Cancer Society's estimates for eye cancer in the United States for 2015 are:

- 2,580 new cancers (mainly melanomas) of the eye and orbit: 1,360 in men and 1,220 in women
- 270 deaths from cancers of the eye and orbit: 140 in men and 130 in women

Primary eye cancers can occur at any age, but the risk for most types increases as people get older. The rate of eye melanomas has been fairly stable over the past few decades. Cancers that spread to the eye from another part of the body (secondary eye cancers) are actually more common than primary eye cancers.

Most cancers of the eye and orbit in adults are melanomas, with lymphomas being the next most common. Both of these cancers start more often in other parts of the body. More than 9 out of 10 melanomas start in the skin, while most lymphomas begin in lymph nodes.

For statistics on survival, see the section "Eye cancer survival rates."

What are the risk factors for eye cancer?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

But having a known risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may have few or no known risk factors.

Risk factors for eye melanoma

Race/ethnicity

The risk of intraocular melanoma is much higher in whites than in African Americans or Asian Americans.

Eye color

People with light colored eyes are somewhat more likely to develop melanoma of the eye than are people with brown eyes.

Age and gender

Eye melanomas can occur at any age, but the risk goes up as people get older. Eye melanoma is slightly more common in men than in women.

Certain inherited conditions

People with *dysplastic nevus syndrome*, who have many abnormal moles on the skin, are at increased risk of skin melanoma. They also seem to have a higher risk of developing melanoma of the eye.

People with abnormal brown spots on the uvea (known as *oculodermal melanocytosis* or *nevus of Ota*) also have an increased risk of developing eye melanoma.

BAP1 cancer syndrome is a rare inherited condition in which family members are at increased risk for eye melanoma, as well as melanoma of the skin and some other cancers. This condition is caused by an inherited mutation (change) in the *BAP1* gene.

Eye melanomas can run in some families who do not have these conditions, but this is very rare.

Unproven risk factors

Sun exposure: Too much exposure to sunlight (or sunlamps), a known risk factor for melanoma of the skin, has also been proposed as a possible risk factor for melanoma of the eye, but this has not been proven.

Certain occupations: Some studies have suggested that welders, farmers, fishermen, chemical workers, and laundry workers may have a higher risk of eye melanoma, but none of these links has been proven conclusively.

Risk factors for eye lymphoma

The only known risk factor for primary lymphoma of the eye is having a weakened immune system. Examples include people with AIDS and people who take anti-rejection drugs after organ or tissue transplants.

Do we know what causes eye cancer?

The exact cause of most eye cancers is not known. But scientists have found that the disease is linked with some other conditions, which are described in the section “What are the risk factors for eye cancer?” A great deal of research is being done to learn more about the causes.

Scientists are learning how certain changes in the DNA inside cells can cause the cells to become cancerous. DNA is the chemical in each of our cells that makes up our *genes*, the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But DNA can also influence our risk for developing certain diseases, such as some kinds of cancer.

Some genes control when our cells grow, divide into new cells, and die. Genes that help cells grow, divide, or stay alive are called *oncogenes*. Genes that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Some people with cancer have DNA changes they inherited from a parent that increase their risk for the disease. For example, some people inherit a change (mutation) in the *BAP1* tumor suppressor gene, which increases their risk of eye melanoma and some other cancers. When the *BAP1* gene is mutated, it doesn’t work normally, which can allow cells with this change to grow out of control.

Most DNA changes linked to cancer are acquired during life rather than inherited before birth. For example, recent research has shown that about 4 out of 5 eye melanomas have changes in either of 2 related genes, *GNA11* or *GNAQ*, which appear to be oncogenes. Other, as of yet unknown, gene changes are probably needed for these cancers to develop as well.

Scientists are studying these and other DNA changes to learn more about them and how they might lead to eye cancer. But it is still not exactly clear what causes these changes to occur in some people and not others.

Can eye cancer be prevented?

We do not yet know what causes most cancers of the eye, so it is not yet possible to prevent them.

Eye melanoma

We know there is a link between sunlight and melanomas of the skin, and there are things you can do that might reduce your risk of these cancers, including limiting your exposure to intense sunlight, covering up with protective hats and clothing, and using sunscreen.

The American Cancer Society also recommends wearing UV-protected sunglasses when outside in strong sunlight. Wrap-around sunglasses with 99% to 100% UVA and UVB absorption provide the best protection for the eyes and the surrounding skin. This might help reduce the risk of developing cancers of the skin around the eyes. The link between sunlight and eye melanomas is not proven, but some doctors think that sunglasses might also reduce eye melanoma risk.

Eye lymphoma

Many people with eye lymphoma have no clear risk factors for this disease. For now, the best way to limit the risk of eye lymphoma is to try to avoid infection with HIV, the virus that causes AIDS.

Can eye cancer be found early?

Eye cancer is uncommon, and there are no widely recommended screening tests for this cancer in people at average risk. (Screening is testing for a disease like cancer in people without any symptoms.) Still, some eye cancers can be found early.

Some doctors may recommend yearly eye exams for those at higher risk of eye melanoma, such as people with dysplastic nevus syndrome. Regular eye exams are an important part of everyone’s health care, even if they have no symptoms. Often melanomas of the eye are found during a routine eye exam. When the doctor looks through the pupil at the back of the eye, he or she may see a dark spot that might be an early melanoma.

Many doctors feel that most melanomas start from a *nevus* (mole), which is a benign (non-cancerous) tumor of pigment cells. If an eye nevus is present, it should be looked at regularly by an ophthalmologist (a doctor who specializes in eye diseases). People who notice a dark

spot on the colored part of their eye (the iris) should have a doctor look at it, especially if it is getting bigger.

How is melanoma of the eye diagnosed?

Certain signs and symptoms might suggest that a person could have an eye melanoma, but tests are needed to confirm the diagnosis.

Signs and symptoms of eye melanoma

Many people with eye melanoma don't have symptoms unless the cancer grows in certain parts of the eye or becomes more advanced. Signs and symptoms of eye melanomas can include:

- Problems with vision (blurry vision or sudden loss of vision)
- Floaters (spots or squiggles drifting in the field of vision) or flashes of light
- Visual field loss (losing part of your field of sight)
- A growing dark spot on the colored part of the eye (iris)
- Change in the size or shape of the pupil (the dark spot in the center of the eye)
- Change in position of the eyeball within its socket
- Bulging of the eye
- Change in the way the eye moves within the socket

Pain is rare unless the tumor has grown extensively outside the eye. In such cases, bulging or a change in the position of the eye may also be noted.

Other, less serious conditions can also cause many of these symptoms. For example, floaters can be a normal part of the aging process. Still, if you have any of these symptoms, it's important to see a doctor right away so the cause can be found and treated, if needed.

Eye exam

Examination of the eye by an ophthalmologist (a medical doctor specializing in eye diseases) is often the most important step in diagnosing melanoma of the eye. The doctor will ask if you are having any symptoms and check your vision and eye movement. The doctor will also look for enlarged blood vessels on the outside of the eye, which can be a sign of a tumor inside the eye.

The ophthalmologist may also use special instruments to get a good look inside the eye for a tumor or other abnormality. You may get drops in your eye to dilate the pupil before the doctor uses these instruments.

- An **ophthalmoscope** (also known as a *direct ophthalmoscope*) is a hand-held instrument consisting of a light and a small magnifying lens.
- An **indirect ophthalmoscope** and a slit lamp is more like a large microscope. For this exam, you sit down and rest your chin on a small platform, while the doctor looks into your eye through magnified lenses. This exam can often give a more detailed view of the inside of the eye than the direct ophthalmoscope.
- A **gonioscopy lens** is a specially mirrored lens that is placed on the cornea (the outer part of the eye) after it is numbed. This lets the doctor see the deep structures in the angle of the front of the eye near the iris. It can be used to look for tumor growth into areas of the eye that would otherwise be hard to see.

Most of the time if a person has an eye melanoma, a doctor can make the diagnosis with just an eye exam. In some cases, imaging tests such as ultrasound may be needed to confirm the diagnosis. Very rarely a biopsy will also be needed.

Some people might have a benign tumor in the eye called a *choroidal nevus*, which can sometimes be mistaken for an eye melanoma. A small number of these will eventually turn into melanomas. If your ophthalmologist spots one of these, he or she will likely advise regular eye exams to see if it grows.

Even if you recently had an eye exam, if you start to have any of the symptoms listed above, get another exam. Sometimes these tumors are missed or grow so fast that they weren’t there when you were last examined.

If an eye exam suggests you might have eye cancer, more tests will likely be needed. These might include imaging tests or other procedures.

Imaging tests

Imaging tests use sound waves, x-rays, or magnets to create pictures of the inside of your body. Imaging tests may be done for a number of reasons, including to help find a suspicious area that might be cancer, to le

arn how far cancer might have spread, or to help determine if treatment is working.

Ultrasound (echography): This is a very common test for helping to diagnose eye melanomas. Ultrasound uses high-frequency sound waves to make pictures of parts of the body. For this test, a small wand-like instrument is placed up against the eyelid or eyeball, and sound waves are sent through the eye. The instrument picks up the pattern of echoes that comes back, which is converted into an image on a computer screen.

This test is especially useful for diagnosing eye melanomas because they look a certain way on ultrasound. Using this test, doctors can confirm a diagnosis of melanoma of the eye in most cases. This test can also show the location and the size of the tumor.

Ultrasound biomicroscopy (UBM) is a special type of ultrasound that uses sound waves at even higher frequency to image the front parts of the eye.

Optical coherence tomography (OCT) is a similar type of test that uses light waves instead of sound waves to create very detailed images of the back of the eye.

If you have already been diagnosed with eye melanoma, an ultrasound may be done of your abdomen to look for tumors in the liver, which is a common site of spread of this cancer.

Fluorescein angiography: For this test, an orange fluorescent dye (fluorescein) is injected into the bloodstream through a vein in the arm. Pictures of the back of the eye are then taken using a special light that makes the dye fluoresce (glow). This lets the doctor see the blood vessels inside the eye. Although melanomas don't have a special appearance with this test, some other eye problems do. Doctors can use this method to tell if something is not a melanoma.

This test can also be done using a special green dye to look at the blood vessels. This is known as *indocyanine green (ICG) angiography*.

Chest x-ray: If you have been diagnosed with eye melanoma, an x-ray of your chest may be done to see if the cancer has spread to your lungs. This is very unlikely unless your cancer is far advanced. This x-ray can be done in any outpatient setting. If the results are normal, you probably don't have cancer in your lungs.

Computed tomography (CT) scan: A CT uses x-rays to produce detailed cross-sectional images of parts of the body. This test is sometimes used to see if a melanoma has spread outside of the eye into nearby structures. It may also be used to look for spread of the cancer to distant organs such as the liver.

A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. You need to lie still on the table while the scan is being done. CT scans take longer that regular x-rays, and you might feel a bit confined by the ring you have to lie in while the pictures are being taken. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into detailed images of part of your body.

Before the scan, you might be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline structures in the body. You may need an IV line through which the contrast dye is injected. The injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have any allergies or have ever had a reaction to any contrast material used for x-rays.

Magnetic resonance imaging (MRI) scan: MRI scans are often used to determine the tumor's growth and spread. They are particularly useful for looking at eye tumors. They are also helpful in finding cancer that has spread to the brain or spinal cord, as well as any spread of melanoma outside the eye orbit.

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. A contrast material called *gadolinium* is often injected into a vein before the scan to better see details.

MRI scans take longer than CT scans — often up to an hour – and are a little more uncomfortable. You lie on a table that slides inside a narrow tube, which can feel confining and may upset people with a fear of enclosed spaces. Newer, open MRI machines might help with this, but they might provide less detailed images and can't be used in all cases. The machine also makes loud buzzing and clicking noises that may be disturbing. Some people might need medicine to help them relax for the test.

For more information on imaging tests, see our document *Imaging (Radiology) Tests*.

Biopsy

For most types of cancer, the diagnosis is made by removing a small piece of the tumor and looking at it under a microscope for cancer cells. This is known as a *biopsy*.

A biopsy is not often needed for eye melanomas because almost all cases can be accurately diagnosed by the eye exam and imaging tests. Many doctors prefer not to do biopsies because it can be hard to get a sample of the tumor without damaging the eye. Also, there's a chance the biopsy could possibly spread the tumor within or outside of the eye.

If a biopsy is needed, it can be done either with sedation and local anesthesia (numbing medicine) or while a person is under general anesthesia (in a deep sleep). A thin, hollow needle is passed into the eye, and cells from the tumor are sucked up into a small syringe. The sample is sent to a lab, where a doctor called a *pathologist* looks at the cells under a microscope.

While most people with melanoma of the eye are treated without having a biopsy first, this may change in the future. New technology may make biopsies safer in situations where the diagnosis is uncertain. In recent years, some doctors have started using biopsies to get a sample of the tumor for gene testing. This can help tell whether the melanoma is likely to come back outside of the eye at some point. (See "What's new in eye cancer research and treatment?" for more information.)

Blood tests

Blood tests can't be used to diagnose melanoma of the eye, but they may be done once a diagnosis is made.

Liver function tests: If you have been diagnosed with eye melanoma, your doctor may order blood tests to see how well your liver is working. Abnormal test results can sometimes be a sign that the cancer has spread to the liver.

How is lymphoma of the eye diagnosed?

Certain signs and symptoms might suggest that a person could have eye lymphoma (intraocular lymphoma), but tests are needed to confirm the diagnosis.

Signs and symptoms of eye lymphoma

The possible signs and symptoms of eye lymphomas include:

- Blurred vision or loss of vision
- Seeing floaters (spots or squiggles drifting in the field of vision)
- Redness or swelling in the eye
- Sensitivity to light
- Eye pain (uncommon)

Intraocular lymphoma most often affects both eyes, but it can cause more symptoms in one eye than in the other.

Most of these symptoms are more likely to be caused by other, less serious conditions. For example, floaters can occur as a normal part of the aging process. Still, if you have any of these symptoms, it's important to see a doctor right away so the cause can be found and treated, if needed.

Many of the exams and tests mentioned below are described in more detail in the section "How is melanoma of the eye diagnosed?"

Eye exam

The doctor will ask about any symptoms you are having and may check your vision and eye movements. During the eye exam, the doctor will use an ophthalmoscope (an instrument with a light and a small magnifying lens) to get a good look inside the eye. If lymphoma is present, the doctor may see that the vitreous (the jelly-like substance that fills most of the inside of the eye) is cloudy.

Imaging tests

Imaging tests use sound waves, x-rays, or magnets to create pictures of the inside of your body.

Ultrasound: Ultrasound is usually done to determine the size, shape, and location of the mass (tumor), especially if the back of the eye can't be seen during the eye exam.

Magnetic resonance imaging (MRI) scan: An MRI of the head is often done not only to see the eye better, but also to look for lymphoma in the brain or meninges (the thin layers of tissue that cover the brain and spinal cord), which are common sites of spread of this cancer.

Computed tomography (CT) scan: CT scans are used less often than MRI scans for eye lymphoma because they do not provide as much detail.

Positron emission tomography (PET) scan: If a lymphoma has been found, a PET scan can help give the doctor a better idea of whether it has spread to lymph nodes or other parts of the body. A PET scan can also be useful if your doctor thinks the cancer might have spread but doesn't know where.

For this test, a form of radioactive sugar (known as fluorodeoxyglucose or FDG) is injected into a vein (IV). (The amount of radioactivity is very low and will pass out of the body over the next day or so.) Because cancer cells in the body are growing rapidly, they absorb more of the radioactive sugar. After about an hour, you are moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not as detailed as a CT or MRI scan, but it can provide helpful information about whether abnormal areas seen on these tests are likely to be cancer.

Many centers have special machines that can do both a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

For more information on imaging tests, see our document *Imaging (Radiology) Tests*.

Biopsy

Symptoms and the results of exams and tests might suggest you have intraocular lymphoma, but a biopsy is usually needed to confirm the diagnosis. To biopsy the eye, an ophthalmologist most often does a procedure called a *vitrectomy*. You may be sedated and get local anesthesia (numbing medicine) or you may get general anesthesia (which puts you in a deep sleep).

The doctor takes a sample of the vitreous gel from inside the eye by inserting very small instruments into the eye, cutting the vitreous, and then sucking some of it out. The cells in the biopsy sample are then sent to a lab to be looked at under a microscope and tested by other special techniques. For more information on the lab tests done on suspected lymphoma specimens, see our document *Non-Hodgkin Lymphoma*.

Lumbar puncture (spinal tap)

This test is used to look for lymphoma cells in the fluid that surrounds the brain and spinal cord (called *cerebrospinal fluid* or *CSF*). It is done in cases of known or suspected eye lymphomas because these cancers often affect the brain or spinal cord.

For this test, you lie on your side with your knees up near your chest. The doctor first numbs an area in the lower part of the back near the spine. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

The fluid is then examined under a microscope for lymphoma cells. Other tests may be done on the fluid as well.

How are eye cancers staged?

The stage of an eye cancer is a measure of the extent of the cancer in the body. It is one of the most important factors in selecting treatment options and estimating a patient's outlook (prognosis).

The cancer stage is determined from the results of eye exams, imaging tests (ultrasound, CT or MRI scan, etc.) and other tests, which are described in the sections "How is melanoma of the eye diagnosed?" and "How is lymphoma of the eye diagnosed?"

A staging system is a standard way for the cancer care team to sum up how far a cancer has spread. The most common systems used to describe the stages of eye melanomas are the American Joint Committee on Cancer (AJCC) TNM system and the system used by the Collaborative Ocular Melanoma Study (COMS) group.

AJCC TNM staging system for melanoma of the eye

The TNM system is based on 3 key pieces of information:

- **T** describes the size of the main (primary) **tumor** and/or whether it has invaded into nearby structures.
- **N** describes whether the cancer has spread to nearby (regional) lymph **nodes** (bean-sized collections of immune system cells throughout the body).
- **M** indicates whether the cancer has **metastasized** (spread) to other organs of the body. (The most common site of eye melanoma spread is the liver.)

Numbers or letters appear after T, N, and M to provide more details about each of these factors:

- The numbers 0 through 4 indicate increasing severity. Lower case letters after the numbers divide these groups further.

- The letter X means “cannot be assessed” because the information is not available.

Most eye melanomas start in the uvea, which includes the iris, ciliary body, and choroid (see “What is eye cancer?”). The T categories for iris melanomas are different from the T categories for ciliary body and choroidal melanomas. But the N and M categories are the same for melanomas in all 3 parts of the uvea.

T categories for iris melanoma

TX: The primary tumor cannot be assessed; information not known.

T0: No evidence of a primary tumor.

T1: Tumor is only in the iris.

- **T1a:** The tumor is only in the iris and touches 1/4 or less of the iris.
- **T1b:** The tumor is only in the iris and touches more than 1/4 of the iris.
- **T1c:** The tumor is only in the iris and is causing an increase in the eye pressure (glaucoma).

T2: Tumor has grown into the ciliary body or choroid (or both).

- **T2a:** Tumor has grown into the ciliary body and/or choroid and is causing glaucoma.

T3: Tumor has grown into the ciliary body and/or choroid and into the sclera.

- **T3a:** Tumor has grown into the ciliary body and/or choroid and into the sclera and is causing glaucoma.

T4: Tumor extends outside the eyeball.

- **T4a:** The part of the tumor that is outside the eyeball is 5 millimeters (mm) — about 1/5 of an inch — or less across in size.
- **T4b:** The part of the tumor that is outside the eyeball is greater than 5 mm (about 1/5 of an inch) across in size.

T categories for ciliary body and choroidal melanoma

TX: The primary tumor cannot be assessed; information not known.

T0: No evidence of a primary tumor.

T1: A T1 tumor is either:

- No more than 3 millimeters (mm) deep and no more than 12 mm across, **OR**

- From 3.1 to 6 mm deep and no more than 9 mm across

  T1a: The T1-size tumor is not growing into the ciliary body or growing outside the eyeball.

  T1b: The T1-size tumor is growing into the ciliary body.

  T1c: The T1-size tumor is not growing into the ciliary body but is growing outside of the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across.

  T1d: The T1-size tumor is growing into the ciliary body and also outside of the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across.

T2: A T2 tumor is:

- No more than 3 mm deep and from 12.1 to 18 mm across, **OR**
- From 3.1 to 6 mm deep and 9.1 to 15 mm across, **OR**
- From 6.1 to 9 mm deep and no more than 12 mm across

  T2a: The T2-size tumor is not growing into the ciliary body or growing outside the eyeball.

  T2b: The T2-size tumor is growing into the ciliary body.

  T2c: The T2-size tumor is not growing into the ciliary body but is growing outside the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across in size.

  T2d: The T2-size tumor is growing into the ciliary body and also outside the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across in size.

T3: A T3 tumor is:

- From 3.1 to 6 mm deep and between 15.1 and 18 mm across, **OR**
- From 6.1 to 9 mm deep and between 12.1 and 18 mm across, **OR**
- From 9.1 to 12 mm deep and 18 mm or less across, **OR**
- From 12.1 to 15 mm deep and 15 mm or less across

  T3a: The T3-size tumor is not growing into the ciliary body and is not growing outside the eyeball.

  T3b: The T3-size tumor is growing into the ciliary body.

T3c: The T3-size tumor is not growing into the ciliary body but is growing outside the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across in size.

T3d: The T3-size tumor is growing into the ciliary body and also outside the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across in size.

T4: A T4 tumor is:

- Greater than 15 mm deep and any width, **OR**
- Greater than 18 mm across and any depth, **OR**
- Between 12.1 and 15 mm deep and between 15.1 and 18 mm across

T4a: The T4-size tumor is not growing into the ciliary body or growing outside the eyeball.

T4b: The T4-size tumor is growing into the ciliary body.

T4c: The T4-size tumor is not growing into the ciliary body but is growing outside the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across in size.

T4d: The T4-size tumor is growing into the ciliary body and also outside the eyeball. The part of the tumor that is outside the eyeball is 5 mm (about 1/5 of an inch) or less across in size.

T4e: The tumor can be any size. It is growing outside the eyeball and the part of the tumor that is outside the eyeball is greater than 5 mm across.

N categories for iris, ciliary body, and choroidal melanomas

NX: Lymph nodes cannot be assessed.

N0: Cancer has not spread to nearby lymph nodes.

N1: Cancer has spread to nearby lymph nodes.

M categories for iris, ciliary body, and choroidal melanomas

M0: Cancer has not spread to distant parts of the body.

M1: Cancer has spread to distant parts of the body.

M1a: The largest area of cancer spread is 3 centimeters (cm) — a little over an inch — across or smaller.

M1b: The largest area of cancer spread is between 3.1 and 8 cm across (8 cm is a little over 3 inches).

M1c: The largest area of cancer spread is 8.1 cm or more across.

Stage grouping

To assign an overall stage, the T, N, and M categories are combined in a process called *stage grouping*. The stages are described by Roman numerals from I (the least advanced) to IV (the most advanced). Some stages are further divided with letters.

Stage I	T1a, N0, M0
Stage IIA	T1b to T1d, N0, M0 **OR** T2a, N0, M0
Stage IIB	T2b or T3a, N0, M0
Stage IIIA	T2c or T2d, N0, M0 **OR** T3b or T3c, N0, M0 **OR** T4a, N0, M0
Stage IIIB	T3d, N0, M0 **OR** T4b or T4c, N0, M0
Stage IIIC	T4d or T4e, N0, M0
Stage IV	Any T, N1, M0 **OR** Any T, any N, M1

Collaborative Ocular Melanoma Study (COMS) staging of melanoma of the eye

The TNM system is very detailed, but in practice many doctors use the simpler staging system devised by the COMS group, which has done most of the clinical research on how to treat intraocular melanoma. This system divides eye melanomas into small, medium, and large:

- **Small:** Between 1 mm and 3 mm in height and between 5 mm and 16 mm across

- **Medium:** Between 3.1 mm and 8 mm in height and no more than 16 mm across
- **Large:** More than 8 mm in height or more than 16 mm across

Staging of intraocular lymphoma

Intraocular lymphoma does not have its own staging system. These cancers may be staged using the system for other non-Hodgkin lymphomas, which is described in our document *Non-Hodgkin Lymphoma*.

Unlike eye melanomas, the size of the tumor is usually not a major factor in determining the treatment options for eye lymphomas. Instead, treatment options are generally based on the type of lymphoma, as well as on whether the lymphoma is limited to the eye or is also in other areas of the body.

Eye cancer survival rates

Doctors often use survival rates as a standard way of discussing a person's prognosis (outlook). Some people with cancer may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful or may even not want to know them. If you don't want to know them, stop reading here and skip to the next section.

When discussing cancer survival statistics, doctors often use a number called the *5-year survival rate*. The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured).

To get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a better outlook for people now being diagnosed with this cancer. Five-year *relative* survival rates, such as the numbers below for eye melanoma, assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a more accurate way to describe the outlook for patients with a particular type and stage of cancer.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they can't predict what will happen in any person's case. Other factors can also affect a person's outlook, such as the type of cells in the tumor, the patient's age and general health, and how well the cancer responds to treatment. Your doctor knows your situation best and can tell you how the numbers below apply to you.

Survival rates for eye melanoma

The numbers below come from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, and are based on about 1,500 patients who were diagnosed with melanoma of the eye between 1988 and 2001.

Overall, about 3 out of 4 people with eye melanoma survive for at least 5 years. Survival rates tend to be better for earlier-stage than for later-stage cancers, but accurate survival rates for eye melanomas based on a specific stage are hard to determine because these cancers are fairly rare.

When the cancer is confined to the eye, the 5-year relative survival rate is about 80%. For people with eye melanomas that have spread to distant parts of the body, the 5-year relative survival rate is about 15%.

Survival rates for lymphoma of the eye

Because eye lymphoma is rare, accurate survival statistics for this cancer are hard to find. In one study of patients without HIV whose lymphoma was confined to the eye, about half of the patients were still alive 5 years after diagnosis. In many cases the lymphoma has already reached the brain by the time it is found, in which case the outlook is not as good.

How is eye cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Making treatment decisions

After an eye cancer is found and staged, your cancer care team will discuss your treatment options with you. Depending on the type and stage of the cancer and other factors, treatment options for eye cancer can include:

- Surgery
- Radiation therapy
- Laser therapy
- Chemotherapy
- Targeted therapy

Sometimes, more than one of type of treatment is used. In choosing the best treatment plan for you, some important factors to consider include the location and stage of the cancer, your

overall health, the chances of curing the disease, and the possible effect of the treatment on vision.

You may have different types of doctors on your treatment team, depending on the stage of your cancer and your treatment options. These doctors may include:

- An ophthalmologist: a doctor who specializes in treating diseases of the eye
- An ocular oncologist: a doctor (usually an ophthalmologist) who specializes in treating cancers of the eye
- A radiation oncologist: a doctor who treats cancer with radiation therapy
- A medical oncologist: a doctor who treats cancer with medicines such as chemotherapy

Many other specialists might be part of your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, physical therapists, social workers, and other health professionals. See *Health Professionals Associated With Cancer Care* for more on this.

It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It's also very important to ask questions if you're not sure about something. (See the section "What should you ask your doctor about eye cancer?" for some questions to ask.)

Because eye melanomas and lymphomas are rare, no matter what treatment you decide on, it should be done by doctors who are experienced in treating people with these cancers. If time permits it is often a good idea to seek a second opinion from an experienced doctor as well. A second opinion can provide more information and help you feel more confident about your chosen treatment plan.

Treatments for eye cancers might affect your vision. Doctors try to preserve vision in the eye whenever possible, but this may not always be the best choice. Eye cancers can often be fatal if left untreated, and some patients must be given treatment regardless of the possible damage to the eye. On the other hand, some eye melanomas are small, grow very slowly (if at all), and can be watched carefully without treatment. This is why it is important to get the opinion of a skilled specialist in this field before deciding on treatment.

The next few sections describe the types of treatments used for eye melanomas and lymphomas. This is followed by a description of the most common approaches to treating melanomas and lymphomas, based on the situation.

Surgery for eye cancer

Surgery is used to treat some intraocular (eye) melanomas, but it is used less often than in the past as the use of radiation therapy has grown. Surgery is not used to treat intraocular lymphoma.

The type of surgery depends on the location and size of the tumor. Patients will be under general anesthesia (in a deep sleep) during these operations, and they usually will leave the hospital 1 or 2 days afterward. The operations used to treat people with eye melanoma include:

Iridectomy: Removal of part of the iris (the colored part of the eye). This may be an option for very small iris melanomas.

Iridotrabeculectomy: Removal of part of the iris, plus a small piece of the outer part of the eyeball. Small iris melanomas may be treated with this technique.

Iridocyclectomy: Removal of a portion of the iris and the ciliary body. This operation is also used for small iris melanomas.

Transscleral resection: Surgically removing just a melanoma of the ciliary body or choroid. This type of surgery should only be done by doctors in cancer centers with a lot of experience in treating eye melanomas, because it is hard to remove the tumor without damaging the rest of the eye. This could lead to severe vision problems.

Enucleation: Removal of the entire eyeball. This is used for larger melanomas, but it may also be done for some smaller melanomas if vision in the eye has already been lost or if other treatment options would destroy useful vision in the eye, anyway.

During the same operation, an orbital implant is usually put in to take the place of the eyeball. The implant is made out of silicone or hydroxyapatite (a substance similar to bone). It is attached to the muscles that moved the eye, so it should move the same way as the eye would have. Within a few weeks after surgery, you visit an ocularist (a specialist in eye prostheses) to be fitted with an artificial eye, a thin shell that fits over the orbital implant and under the eyelids. The artificial eye will match the size and color of the remaining eye. Once it is in place, it will be hard to tell it apart from the real eye.

Orbital exenteration: Removal of the eyeball and some surrounding structures such as parts of the eyelid and muscles, nerves, and other tissues inside the eye socket. This surgery is not common, but it might sometimes be used for melanomas that have grown outside the eyeball into nearby structures. As with enucleation, an artificial eye might be placed in the socket after surgery.

Possible risks and side effects of surgery

All surgery carries some risk, including the possibility of pain, bleeding, blood clots, infections, and complications from anesthesia.

Surgery on the eye can lead to the loss of some or all of the vision in that eye. Enucleation and orbital exenteration result in complete and immediate vision loss in the eye. Other surgeries can also cause problems leading to a loss of vision, which can occur later on. In some cases, vision may have already been damaged or lost because of the cancer.

Removal of the eyeball (enucleation) obviously can affect a person's appearance. As noted above, an artificial eye can be put in place to help minimize this.

Radiation therapy for eye cancer

Radiation therapy uses high-energy x-rays or other types of radiation to kill cancer cells. It is a common treatment for intraocular (eye) melanoma. Radiation therapy can often save some vision in the eye, although sometimes this might be lost anyway if the radiation damages other parts of the eye. An advantage over surgery is that the eye structure is preserved, which can result in a better appearance after treatment.

Different types of radiation therapy can be used to treat eye cancers.

Brachytherapy (episcleral plaque therapy)

In this form of radiation therapy, the doctor places small pellets (sometimes called *seeds*) of radioactive material directly into or very close to the cancer. This has become the most common radiation treatment for most eye melanomas. Studies have shown that in many cases it is as effective as surgery (enucleation).

The pellets of radioactive material are placed inside a small carrier (shaped like a very small bottle cap), which is sewn on the outside of the eyeball with tiny stitches to keep it in place. The carrier is made of gold or lead to shield nearby tissues from the radiation. The radiation from the pellets travels a very short distance, so most of it will be focused only on the tumor.

An operation is needed to put the plaque (radioactive element and carrier) in place. This surgery usually takes 1 or 2 hours and can be done with local anesthetic (numbing medicine) and sedation. The plaque is usually kept there for 4 to 7 days, depending on the size of the tumor and the strength of the radiation source. You will probably remain in the hospital during this time. Surgery to remove the plaque usually takes less than an hour, and you will probably be able to go home the same day. The full effect of the radiation on the tumor is not seen for 3 to 6 months.

This treatment cures about 9 out of 10 small tumors and can preserve vision in some patients, depending on what part of the eye the melanoma is in. The outlook for vision is not as good if the tumor is very close to the optic nerve, which carries visual images from the eye to the brain.

External beam radiation therapy

In this approach, radiation from a source outside the body is focused on the cancer. This is the type of radiation therapy used to treat eye lymphomas. For eye melanomas the use of this type of radiation therapy is generally limited to newer methods that focus narrow beams of radiation on the tumor.

Conformal proton beam radiation therapy: Instead of using x-rays as in standard radiation therapy, this approach focuses proton beams on the cancer. Unlike x-rays, which release energy both before and after they hit their target, protons cause little damage to tissues they pass through and then release their energy after traveling a certain distance. This means that proton beam radiation may be able to deliver more radiation to the tumor and do less damage to nearby normal tissues.

Getting treatment is much like getting an x-ray, but the dose of radiation is much higher. In most cases, the total dose of radiation is divided into daily fractions (usually given Monday thru Friday) over several weeks. The treatment is not painful.

The machines needed to make protons are expensive, and there are only a handful of them in use in the United States at this time.

Stereotactic radiosurgery: This type of treatment delivers a large, precise radiation dose to the tumor area in a single session. (There is no actual surgery in this treatment.) The radiation can be delivered in one of two ways.

In one approach, radiation beams are focused at the tumor from hundreds of different angles for a short period of time. The machine used to deliver this type of radiation is known as a *Gamma Knife*.

A similar approach uses a movable linear accelerator (a machine that creates radiation) that is controlled by a computer. Instead of delivering many beams at once, this machine moves around the head to deliver radiation to the tumor from many different angles. Several machines (with names such as X-Knife, CyberKnife, and Clinac) do stereotactic radiosurgery this way.

Possible side effects of radiation therapy

The main concern with radiation therapy is damage to parts of the eye, leading to problems such as cataracts, retinal detachment, glaucoma (increased pressure inside the eye), or bleeding into the eye. These can result in partial or complete loss of vision or other problems, which might not happen right away. The risk depends on the size and location of the tumor.

Because the radiation is focused only on the affected eye, it is not likely to affect vision in the other eye or to cause other side effects sometimes linked with radiation therapy, such as hair loss or nausea.

For lymphomas, radiation therapy is sometimes directed at the brain and spinal cord. This can sometimes cause side effects such as problems with thinking, learning, and memory, which might get worse over time.

To learn more about radiation therapy, see the Radiation Therapy section of our website or our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Laser therapy for eye cancer

Lasers are highly focused beams of light that can be used to destroy body tissues. Laser therapy is sometimes used to treat intraocular (eye) melanoma, but it is not used to treat intraocular lymphoma.

Transpupillary thermotherapy (TTT)

This is the most common type of laser treatment for eye melanoma. It uses infrared light to heat and kill the tumor. It works well for small choroidal melanomas because the melanin pigment in these cells absorbs the light energy from the laser.

TTT is only used to treat small choroidal melanomas because the laser might not be able to reach the deeper parts of thicker melanomas. TTT is not usually the main treatment, but it may be used as an adjuvant (additional) treatment after brachytherapy (plaque radiotherapy). Usually 1 to 3 treatments are given to kill the tumor.

Laser photocoagulation

This treatment uses a highly focused, high-energy light beam to burn tissue. This type of treatment was first tried in the 1950s, but it is rarely used now to treat eye melanoma. It can be effective for very small melanomas, but it is more often used to treat side effects from radiation. Several laser treatments are usually given 6 or 8 weeks apart to treat a tumor.

Possible side effects of laser therapy

As with radiation therapy, the main concern with laser therapy is damage to parts of the eye that could result in loss of vision. The risk depends on the size and location of the tumor.

Chemotherapy for eye cancer

Chemotherapy (chemo) is the use of drugs to treat cancer. The drugs can be injected into a certain part of the body (such as the eye), or they can be injected into a vein or taken by mouth to reach throughout the body, making this treatment very useful for cancers that have spread. Chemo can be useful for treating intraocular (eye) lymphoma, but it is used less often for intraocular melanoma.

Chemotherapy for lymphoma of the eye

Depending on the type and the stage of the lymphoma, chemo may be used alone or in combination with radiation therapy. There are several ways chemo can be given:

- **Intraocular:** Some chemo drugs can be injected directly into the eye. This concentrates the chemo at the site of the cancer, allowing higher doses to be given without causing severe side effects in other parts of the body.
- **Intrathecal:** If the lymphoma might have spread to the brain or spinal cord, chemo can be given directly into the cerebrospinal fluid (the fluid surrounding the brain and spinal cord). Often, this is done during a lumbar puncture (spinal tap). Another option is to place a special type of catheter (an Ommaya reservoir) into the fluid through a small hole in the skull. The end of the catheter, which has a dome-shaped reservoir, stays just under the scalp. Doctors and nurses can use a thin needle to give chemo drugs through the reservoir.
- **Systemic:** Chemo drugs can be injected into a vein (usually in the arm) or taken as pills, after which they will reach all areas of the body. This route is especially useful if the cancer might have spread to other parts of the body.

Methotrexate is a chemo drug often used to treat lymphoma of the eye. It can be given directly into the eye, intrathecally, or systemically. It is often given in combination with other drugs to treat lymphoma. Many other chemo drugs can be used as well.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover. Chemo cycles generally last about 3 to 4 weeks. Most chemo treatments are given on an outpatient basis (in the doctor's office or hospital outpatient department), but some require a hospital stay. Sometimes a patient may get one chemo combination for several cycles and later switch to a different one if the first combination does not seem to be working well.

High-dose chemo followed by stem cell transplant: Doctors are limited in the doses of chemo they can give because of the side effects these drugs can cause. High doses of chemo can especially damage the bone marrow (where new blood cells are made), which can be life-threatening.

If standard doses of chemo are no longer working, doctors sometimes give high doses of chemo that they know will likely destroy the bone marrow. Before giving the chemo, they take blood-forming stem cells from the patient's body. After the chemo has been given, they infuse the stem cells back into the body. These cells settle in the bone marrow, where they make new blood cells.

This technique can be useful in some situations, but it can be hard for the patient to go through and can cause serious side effects. For more detailed information on stem cell transplants, see our documents *Non-Hodgkin Lymphoma* and *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

Chemotherapy for melanoma of the eye

Melanoma usually does not respond well to standard chemo drugs. Chemo is used only when the cancer has become widespread. If chemo is used, the treatment is generally the same as for melanoma of the skin. For more information, refer to our document *Melanoma Skin Cancer*.

Newer targeted drugs, which work in different ways from chemo drugs, have shown some promise in treating skin melanomas in recent years, and are now being studied for use against eye melanomas.

Possible side effects of chemo

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are likely to be affected by chemo, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs given, how they are given, and the length of time they are taken. The side effects of systemic chemo can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

These side effects usually go away after treatment is finished. There are often ways to lessen these side effects. For example, there are drugs to help prevent or reduce nausea and vomiting. Some drugs may also have specific side effects not listed above. Be sure to ask your doctor or nurse about medicines to help reduce side effects, and let him or her know when you do have side effects so they can be managed.

For more information on chemotherapy, see the Chemotherapy section on our website or our document *A Guide to Chemotherapy*.

Targeted drugs and immune therapy for eye cancer

Medicines for eye melanoma

Melanoma that has spread outside of the eye can be hard to treat, and unfortunately standard chemotherapy drugs often are not very helpful.

In recent years, researchers have developed newer types of drugs to treat advanced melanomas. Several of these drugs are now used to treat melanomas of the skin, but it's not yet clear if they will be as helpful in treating uveal (eye) melanomas. These newer drugs generally fall into 2 groups.

Immunotherapy drugs: These drugs work by helping the body's own immune system recognize and attack cancer cells. Drugs such as pembrolizumab (Keytruda®) and ipilimumab (Yervoy®) have been shown to help some people with melanoma of the skin. These and some other immunotherapy drugs are now being studied for eye melanomas as well.

Targeted drugs: Some newer drugs target parts of melanoma cells that make them different from normal cells. For example, about half of all skin melanomas have a change (mutation) in a gene called *BRAF*, and several drugs that target this gene change are now available to treat these cancers. Unfortunately, this mutation is much less common in uveal melanomas, but in people who have it, these drugs might be helpful. Drugs targeting other gene changes are now being studied as well.

For more information on some of these newer drugs, see "What's new in eye cancer research and treatment?"

Monoclonal antibodies for eye lymphoma

Antibodies are proteins normally made by the immune system to help fight infections. Man-made versions, called *monoclonal antibodies*, can be designed to attack a specific target, such as a substance on the surface of lymphocytes (the cells in which lymphomas start).

Several monoclonal antibodies are now being used to treat lymphoma. In some cases they may be used to help treat lymphoma of the eye.

Rituximab (Rituxan®) is an antibody that attaches to a substance called CD20 that is found on the surface of many lymphoma cells. This attachment seems to make the lymphoma cell die. Rituximab may be given by intravenous (IV) infusion or injected directly into the eye. The treatments can be given in the doctor's office or clinic. Common side effects are usually mild but may include chills, fever, nausea, rashes, fatigue, and headaches. Even if these symptoms occur during the first rituximab infusion, it is very unusual for them to recur with later doses. Rituximab is often combined with chemotherapy.

The monoclonal antibody ibritumomab tiuxetan (Zevalin®) is similar to rituximab but has a radioactive molecule attached to it, which may help it work better. Because of the radiation,

this drug is somewhat harder for doctors to give than rituximab. Another limitation is that it can't be used along with chemo because it also lowers blood counts. At this time it is generally used if chemo and/or rituximab are no longer working.

Clinical trials for eye cancer

You may have had to make a lot of decisions since you've been told you have eye cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for eye cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to learn more about promising new treatments or procedures.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get access to some newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of studies that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute (NCI) at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

You must meet certain requirements to take part in any clinical trial. But if you do qualify for a clinical trial, you get to decide whether or not to enter (enroll in) it.

To learn more about clinical trials, see our document *Clinical Trials: What You Need to Know*.

Complementary and alternative therapies for eye cancer

You might hear about ways to treat eye cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to social media groups and websites might offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used

along with your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help a person feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found to be harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delaying or interrupting your medical treatments might give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It's easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for red flags that might suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 or read our document *Complementary and Alternative Methods and Cancer* to learn more. You can also find out about the specific methods you are looking at by calling us or visiting the Complementary and Alternative Medicine section of our website.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treating uveal (eye) melanoma by location and size

The main factors in determining treatment for eye melanoma include the location and size of the cancer, as well as the likelihood of saving vision in the eye. There is not much advantage in saving an eye if a small melanoma in a crucial place has already destroyed vision in the eye. On the other hand, doctors will not necessarily want to remove an eye that functions normally even if the tumor is large. Therefore, the statements below about treatment may not apply to every situation.

It's important to keep in mind that both outcomes and quality of life tend to be similar over time in people who have had enucleation (removal of the eyeball) and those who have had radiation therapy. Radiation therapy is more likely to preserve some vision in the eye, especially during the first few years after treatment, but studies have found that people who have had radiation therapy are also more likely to be more anxious about the chance of the cancer coming back. Be sure to talk with your doctor before treatment about what factors are most important to you.

Choroidal melanomas

Treating melanomas that start in the choroid depends on the size of the tumor and how well the eye functions. The smaller the tumor, the less likely surgery will be needed, unless the eye is badly damaged or vision is lost.

Small melanomas: There are often several options for treating small choroidal melanomas. Both you and your doctor should decide which option is best for you.

- Careful observation (also known as *watchful waiting*). Not all of these melanomas grow quickly and need to be treated right away. And sometimes, it's very hard for the doctor to even be sure if a spot on the choroid is truly a melanoma. If the tumor is very small, watching it closely and treating it only if it starts to grow is often a reasonable option.
- Radiation therapy, such as brachytherapy (episcleral plaque therapy), proton beam therapy, or stereotactic radiation therapy
- Laser therapy, including transpupillary thermotherapy (TTT), most often along with brachytherapy
- Surgery, which may require removing only the tumor or might need to be as extensive as enucleation (removing the entire eye). This might be necessary if the eye is severely damaged by the tumor (for example, causing severe glaucoma).

Medium-sized melanomas: These tumors can usually be treated by many of the same approaches used for small melanomas:

- Radiation therapy, such as brachytherapy (episcleral plaque therapy), proton beam therapy, or stereotactic radiation therapy

- Laser therapy, including transpupillary thermotherapy (TTT) or laser coagulation, along with brachytherapy
- Surgery, which may require removing only the tumor or might need to be as extensive as enucleation (removing the entire eye). This might be necessary if the eye is severely damaged by the tumor (for example, causing severe glaucoma).

Once again, the choice of treatment is a decision that should be made by both you and your doctor. Radiation and surgery appear to be about equally effective. Radiation offers the best chance of preserving vision in the eye, but some people who have radiation may eventually need surgery.

Large melanomas: The standard treatment for these cancers is usually surgery, which often needs to be more extensive than for smaller melanomas. Enucleation (removal of the entire eye) is the preferred surgery. In rare cases where the cancer has grown extensively outside of the eye, the doctor might recommend removing other structures in the eye socket, such as muscles or part of the eyelid, as well.

Some doctors have begun treating large melanomas with plaque radiation therapy with fairly good results. The cure rate appears to be about as high as with surgery, but it is important to have a doctor experienced with this procedure for large melanomas. This allows people to avoid the cosmetic effect of losing their eye, but most people still end up with poor vision in the eye. Other options that may be considered include proton beam radiation and stereotactic radiosurgery.

Iris melanomas

Melanomas of the iris (the colored part of the eye) are usually small, slow-growing tumors. One option for people with an early stage iris melanoma is to watch it closely to see if it grows. A series of special photographs are taken to help monitor the tumor. If it begins to grow, treatment may be surgery or radiation therapy (in certain situations).

If surgery is recommended, the amount of eye tissue to be removed depends on the extent of the cancer. Types of surgery for early iris melanomas include:

- Iridectomy (removal of part of the iris)
- Iridotrabeculectomy (removal of part of the iris, plus a small piece of the outer part of the eyeball)
- Iridocyclectomy (removal of a portion of the iris and the ciliary body)
- Enucleation (removal of the eyeball)

Ciliary body melanomas

These rare cancers can be treated with either surgical removal of the tumor, if it is small enough, or radiation therapy. In more advanced cases or if there is serious eye damage, enucleation (removal of the eyeball) may be needed.

Advanced and recurrent melanomas

Most uveal melanomas are still only within the eye when they are first diagnosed. It is rare for the cancer to have already spread outside of the eye. But unfortunately, in about half of all patients the melanoma will come back at some point after treatment.

Cancer that comes back after treatment is called *recurrent*. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or liver).Treating melanomas that come back depends on many factors, including where the cancer recurs and what type of treatment was used initially.

Cancers that recur within the eye (intraocular recurrence) are usually treated by enucleation (removal of the eyeball).

When melanoma recurs outside the eye (called *extraocular recurrence*), it most often comes back in the liver. It might also come back in other areas, like the lungs or bones. These cancers are often hard to treat.

If the cancer is only in the liver, different types of treatments might help keep the cancer under control or help relieve symptoms. These include surgery (if there is only one or a few tumors), radiation therapy, destroying (ablating) tumors by heating or freezing them, or injecting drugs or other substances into the liver to try to kill the tumors or cut off their blood supply. Tumor ablation and radiation might also be used for tumors that have spread to other parts of the body, such as the lungs.

Systemic (whole-body) treatments such as chemotherapy, immunotherapy, and targeted therapy drugs have not yet been proven to be very helpful in treating eye melanomas that have spread, but they might help keep the cancer in check for a time in some people. Because current treatments for advanced eye melanomas are limited, clinical trials of newer treatments might be a good option. (See “What’s new in eye cancer research and treatment?” for some examples of newer treatments now being studied.)

Treating intraocular (eye) lymphoma

These lymphomas are often linked with lymphomas of the brain, which are known as *primary central nervous system (CNS) lymphomas*. Because lymphomas of the eye often spread to the brain or have already spread when the cancer is first diagnosed, in many cases both the eye and the brain are treated. For more detailed information on the treatment of CNS lymphomas, see our document *Non-Hodgkin Lymphoma*.

Because these cancers are rare, they have been hard to study. A number of approaches can be used, but the best course of treatment is not known, so it is very important to go to a doctor experienced in treating eye lymphoma.

Surgery is not used to treat eye lymphomas because it is likely that the disease has already spread beyond the eye by the time it is found. Most often, doctors treat these cancers with external radiation therapy, chemotherapy (chemo), or a combination of the two.

The radiation therapy may be given only to the eye, or it may also include the brain and spinal cord. Radiation to both eyes may also be recommended, because often the lymphoma is in both eyes. Radiation therapy to the brain and spinal cord can help prevent the lymphoma from spreading there (or help destroy cancer cells that may already be there but haven't been detected). But it can also cause side effects, leading to problems with thinking, concentration, and memory.

Chemo can be given into a vein (systemic chemo) or directly into the cerebrospinal fluid (intrathecal chemo). It can also be given directly into the eye (intraocular chemo), which gets higher doses of the drug to the tumor. Methotrexate is usually the main chemo drug used. Monoclonal antibodies such as rituximab may also be given directly into the eye. The best combination and dosage of drugs is not yet known, and the choice may be influenced by the exact cell type (classification) of lymphoma. Because recurrence rates are high if chemo is given only systemically (into a vein), therapy is usually given directly to the eye with either radiation or intraocular chemo as well.

If the lymphoma does not respond to treatment or if it comes back (recurs), high-dose chemotherapy followed by a stem cell transplant may be an option for some people.

More treatment information for eye cancer

For more details on treatment options — including some that may not be addressed in this document — the National Cancer Institute (NCI) and the National Comprehensive Cancer Network (NCCN) are good sources of information.

The NCI, part of the US National Institutes of Health, provides treatment information by phone (1-800-4-CANCER) and on its website (www.cancer.gov). Detailed information intended for use by cancer care professionals is also available on www.cancer.gov.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. These are available on the NCCN website (www.nccn.org). The NCCN has treatment guidelines for melanoma of the skin and for central nervous system (CNS) lymphoma, but not specifically for cancers of the eye.

What should you ask your doctor about eye cancer?

It’s important to have honest, open discussions with your doctor. Feel free to ask any question on your mind, no matter how small it might seem. Here are some questions you might want to ask.

- What kind of eye cancer do I have?
- Has my cancer spread beyond the eye?
- What is the stage (extent) of my cancer, and what does that mean?
- Will I need any other tests before we can decide on treatment?
- Will I need to see other doctors?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion? Can you recommend someone?
- What treatment choices do I have?
- What do you recommend and why?
- What is the goal of treatment (cure, prolonging life, relieving symptoms, etc.)?
- What are the risks or side effects to the treatments you suggest? What is the risk of losing vision in the eye from the different treatments?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect my daily activities?
- What are the chances my cancer will come back (recur) after treatment?
- What would we do if the treatment doesn’t work or if the cancer recurs?
- What type of follow-up might I need after treatment?

Along with these sample questions, be sure to write down some of your own. For example, you might want more information about recovery times so you can plan your work or activity schedule. You might also want to ask about clinical trials for which you may qualify.

Keep in mind that doctors aren’t the only ones who can give you information. Other health care professionals, such as nurses and social workers, may be able to answer some of your

questions. You can find out more about speaking with your health care team in our document *Talking With Your Doctor*.

What happens after treatment for eye cancer?

For many people with eye cancer, treatment can remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer the growing or coming back. (When cancer comes back after treatment, it is called a *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to accept this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence*, has more about this.

For other people, the eye cancer may never go away completely. These people might get regular treatments with chemotherapy, radiation therapy, or other therapies to help keep the cancer in check for as long as possible. Learning to live with cancer as a more of a chronic disease can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

If you have completed treatment, your doctors will still want to watch you closely. It's very important to keep all follow-up appointments. During these visits, your doctors will ask about symptoms, examine you, and may order certain tests.

Follow-up is needed to check for cancer recurrence or spread, as well as possible side effects of certain treatments. This is a good time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Almost any cancer treatment can have side effects. Some might last for a few weeks or months, but others can last the rest of your life. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

Follow-up after treatment of uveal (eye) melanoma

Your doctor will most likely want to see you fairly often (every couple of months or so) at first. The time between visits may get longer if you are not having any problems. During these doctor visits, you might get:

- Physical exams (including careful eye exams if the eye has not been removed) to look for tumor recurrence or side effects of treatment as early as possible
- Blood tests to look for possible signs of cancer spread to the liver

- Imaging tests such as chest x-rays, ultrasound, CT scans, or MRI scans to watch for cancer recurrence or spread, especially to the liver or lungs

Most recurrences can be treated more effectively if they are found early.

If cancer does recur at some point, further treatment will depend on where the cancer is, what treatments you've had before, and your health. For more information on how recurrent cancer is treated, see the section "Treating uveal (eye) melanoma by location and size" For more general information on dealing with a recurrence, you may also want to see our document *When Your Cancer Comes Back: Cancer Recurrence*.

Treatments for eye cancers such as surgery, radiation therapy, and laser therapy can cause side effects. Your doctors will check your treated eye for complications and may recommend medicines or operations to help control side effects and help to keep your vision as clear as possible. For example, radiation therapy might cause cataracts to form or injure muscles around the eye, resulting in blurred or double vision. In either case, surgery may help with these problems.

Follow-up exams and tests are also important for people who have had an eye removed, because melanomas can still sometimes recur in the area around the eye or in distant parts of the body.

Follow-up after treatment of eye lymphoma

Physical exams are usually done about every 3 months for the first few years after treatment. Other tests might include lumbar punctures (spinal taps) to look for lymphoma cells in the cerebrospinal fluid and MRI scans of the brain to look for recurrence or metastasis.

Seeing a new doctor

At some point after your treatment, you might be seeing a new doctor who doesn't know about your medical history. It's important to be able to give the details of your diagnosis and treatment. Gathering these details during or soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy (and always keep copies for yourself):

- A copy of your pathology report(s) from any biopsies or surgeries
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored digitally on a DVD, etc.
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that the doctor wrote when you were sent home

- If you had radiation therapy, a summary of the type and dose of radiation and when and where it was given
- If you had chemotherapy or other medicines, a list of the drugs, drug doses, and when you took them
- The names and contact information of the doctors who treated your cancer

It is also very important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

Lifestyle changes after having eye cancer

You can't change the fact that you have had eye cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society for information and support at 1-800-227-2345. A tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment causes weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is start healthier eating habits. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

You can get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a bone-weary exhaustion that often doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to be active and do other things they want to do. But physical activity can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it's normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. If you haven't been active in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Involving family or friends when starting a new activity program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to learn to balance activity with rest. It's OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more on fatigue and other treatment side effects, see the Physical Side Effects section of our website or "Additional resources for eye cancer" to get a list of available information.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.

- It can make you feel happier.
- It helps you feel better about yourself.

Getting regular physical activity also plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

Can I lower my risk of the cancer progressing or coming back?

Most people want to know if there they can make certain lifestyle changes to reduce their risk of cancer progressing or coming back. Unfortunately, for most cancers there isn't much solid evidence to guide people. This doesn't mean that nothing will help — it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or preventing it from coming back.

At this time, not enough is known about eye cancer to say for sure if there are things you can do that will be helpful. Adopting healthy behaviors such as not smoking, eating well, and staying at a healthy weight might help, but no one knows for sure. However, we do know that these types of changes can have positive effects on your health that can extend beyond your risk of cancer.

So far, no dietary supplements have been shown to clearly help lower the risk of eye cancer progressing or coming back. Again, this doesn't mean that none will help, but it's important to know that none have been proven to do so.

How might having eye cancer affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

You may find yourself grieving over the change in vision in your eye, or worrying about the cancer coming back. You may also find yourself thinking about death and dying. Or you may become aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationships with those around you. Unexpected issues may also cause concern. For instance, you might be stressed by financial concerns resulting from your treatment. You might also see your health care team less often after treatment and have more time on your hands. These changes can make some people anxious.

Almost everyone who is going through or has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, religious or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease

talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It's not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you don't include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the Emotional Side Effects section of our website for more information.

If treatment for eye cancer is no longer working

If eye cancer keeps growing or comes back after one kind of treatment, it may be possible to try another treatment plan that might still cure the cancer, or at least keep it under control enough to help you live longer and feel better. Clinical trials also might offer chances to try newer treatments that could be helpful. But when a person has tried many different treatments and the cancer is still growing, even newer treatments might no longer be helpful. If this happens, it's important to weigh the possible limited benefits of trying a new treatment against the possible downsides, including treatment side effects. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer – when you have been through many treatments and nothing's working anymore. Your doctor might offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. Your doctor can estimate how likely it is the cancer will respond to treatment you're considering. For instance, the doctor may say that more treatment might have about a 1 in 100 chance of working. Some people are still tempted to try this. But it is important to have realistic expectations if you do choose this plan.

Palliative care

No matter what you decide to do, it's important that you feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but it is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose – the main goal of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your

symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve pain caused by a large tumor. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

Hospice care

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends — times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

You can learn more about the changes that occur when treatment to cure the cancer stops working, and about planning ahead for yourself and your family, in our documents *Nearing the End of Life* and *Advance Directives*.

What's new in eye cancer research and treatment?

Many medical centers around the world are doing research on the causes and treatment of eye cancers. These are challenging diseases to study because they are not common. But each year scientists find out more about what causes them and how to improve treatment.

Genetics

Learning more about the gene changes that make eye cancer cells different from normal cells will likely play an important role in treating eye melanomas, lymphomas, and other eye cancers in the future.

Using genes to help find people at higher risk

As we learn about the gene changes in these cancers, we may be able to develop tests to identify people who are more likely to get them and then carefully screen those people.

For example, in recent years, researchers have found that some families have a change (mutation) in the *BAP1* gene that makes them more likely to develop melanoma of the eye. While this gene change affects only a small portion of people with eye melanoma, researchers might be able to study it to learn more about how eye melanomas develop.

Using genes to help predict prognosis (outlook)

The genetic changes in tumors may also help predict the likelihood of them spreading. For example, in uveal melanoma, certain genetic changes, such as the loss of one copy of chromosome 3, have been linked to an increased risk of cancer spread.

Recently, researchers have found that patterns of gene expression in tumor cells appear to be an even better way to tell if an eye melanoma is likely to spread. Based on these gene patterns, a little more than half of eye melanomas are shown to be “Class 1” tumors. These cancers have a low risk of spreading. The remaining eye melanomas fall into the “Class 2” category, which have a very high risk of spreading.

Some doctors now offer a test (DecisionDx-UM) for these gene changes, and some patients may want to have them to learn if their cancer is likely to spread. If a patient is found to be at high risk, the doctor might follow them more closely to try to detect cancer spread as early as possible. But other doctors are not as keen on using the test at this time, because we don’t yet have proven ways to prevent the cancer spread or alter the outcome in people who are in the high risk group.

Using genes to help find new treatments

Identifying gene changes in eye cancer cells might also provide specific targets for newer drugs. For example, most eye melanomas have changes in either of 2 related genes, *GNAQ* or *GNA11*. The proteins made by these genes are part of the *MAPK* signaling pathway inside cells that helps them grow. It’s not yet clear if drugs will be able to target these proteins directly, but drugs that target other proteins in the *MAPK* pathway are now being studied for use against eye melanomas, and some have shown early promising results (see Targeted therapy below).

Immunotherapy

Immunotherapies are treatments that boost the body’s immune system to try to get it to attack the cancer. Cytokines, monoclonal antibodies, cancer vaccines, and other immunotherapies are among the most promising approaches for treating melanoma and lymphoma. Although

most clinical trials of these treatments include people with melanomas of the skin and lymphomas that begin in lymph nodes, results of these studies might help treat people with eye melanomas and lymphomas as well.

One example is ipilimumab (Yervoy), a type of drug called a *monoclonal antibody* that boosts the overall activity of the immune system. This has been shown to help some people with advanced melanomas of the skin live longer, although it can also have some serious side effects. Some doctors now use it to treat melanomas of the eye as well, although its benefits against this cancer are still being studied in clinical trials.

Newer drugs such as nivolumab and pembrolizumab (Keytruda), which boost the immune response against cancer cells in a slightly different way, have shown even better results against skin melanomas in early studies. These drugs might prove to be useful against eye melanomas as well.

Targeted therapy

As researchers have learned more about some of the changes in cells that cause them to become cancer, they have begun to develop drugs that target these changes. These new targeted drugs work differently from standard chemo drugs. They might work in some cases when chemo drugs don't, and they tend to have different (and often less severe) side effects.

Most eye melanomas have changes in the *GNAQ* or *GNA11* genes. Proteins made by these genes are part of the *MAPK* gene signaling pathway that helps cells grow. Selumetinib is a drug that targets the *MEK* protein, which is also part of the *MAPK* pathway. Selumetinib has been shown to slow the growth of advanced eye melanomas in a clinical trial. While it does not cure these cancers, it often shrinks them for a time. For now, this drug is only available through clinical trials.

Other drugs might also be useful in treating cancers with these gene mutations. For example, some early research suggests that sotrastaurin (AEB071), a drug that targets protein kinase C, might be effective against cells with a *GNAQ* mutation. This is now being studied in clinical trials.

Some newer drugs, such as vemurafenib (Zelboraf®), dabrafenib (Tafinlar®), and trametinib (Mekinist™), target cells with a mutation in the *BRAF* gene. This mutation is found in about half of patients with skin melanoma, but only in about 5% of patients with eye melanoma. Still, these or similar drugs might help people whose cancer cells have these mutations.

Many targeted drugs are already used to treat other types of cancer. Some of them are now being studied for use against melanoma of the eye as well, including sunitinib (Sutent®), sorafenib (Nexavar®), vorinostat (Zolinza®), and everolimus (Afinitor®).

Other drugs target the blood vessels that tumors need to grow. These are known as *anti-angiogenesis drugs*. One example is bevacizumab (Avastin®), which is already used to treat some other types of cancer. It may help prevent some radiation side effects, which might help

people retain more vision after treatment. This drug is also being studied for use along with chemotherapy in people with advanced eye melanomas.

Additional resources for eye cancer

More information from your American Cancer Society

We have some related information that may also be helpful to you. These materials can be read on our website or ordered from our toll-free number, 1-800-227-2345.

More on related cancers

Melanoma Skin Cancer

Non-Hodgkin Lymphoma

Dealing with diagnosis and treatment

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

After Diagnosis: A Guide for Patients and Families (also in Spanish)

Coping With Cancer in Everyday Life (also in Spanish)

Living with cancer

Distress in People with Cancer

Anxiety, Fear, and Depression

Guide to Controlling Cancer Pain (also in Spanish)

Nutrition for the Person With Cancer: A Guide for Patients and Families (also in Spanish)

Living With Uncertainty: The Fear of Cancer Recurrence

When Cancer Doesn't Go Away

When Your Cancer Comes Back: Cancer Recurrence

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

Helping Children When a Family Member Has Cancer: Dealing With Diagnosis (also in Spanish)

What It Takes to Be a Caregiver

Work, insurance, and financial issues

In Treatment: Financial Guidance for Cancer Survivors and Their Families (also in Spanish)

Health Insurance and Financial Assistance for the Cancer Patient (also in Spanish)

Working During Cancer Treatment

Returning to Work After Cancer Treatment

Cancer treatments

Understanding Cancer Surgery: A Guide for Patients and Families (also in Spanish)

A Guide to Chemotherapy (also in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also in Spanish)

Targeted Therapy

Clinical Trials: What You Need to Know

Cancer treatment side effects

Caring for the Patient with Cancer at Home: A Guide for Patients and Families (also in Spanish)

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

When treatment is no longer working

Nearing the End of Life

Advance Directives

Hospice Care

Books

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at www.cancer.org/bookstore to find out about costs or to place an order.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

Eye Cancer Network
Website: www.eyecancer.com

> Helps people around the world find much needed information and research on the various forms of eye tumors and related eye diseases.

Collaborative Ocular Melanoma Study
Telephone: 1-410-955-8318
Website: www.jhu.edu/wctb/coms/

> For information about ocular melanoma and this multicenter study.

Melanoma Research Foundation
Toll free number: 1-877-673-6460
Website: www.melanoma.org

> For more on melanoma and chat rooms, patient stories, and bulletin boards – all to support and educate anyone affected by melanoma.

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
TTY: 1-800-332-8615
Website: www.cancer.gov

> Offers accurate, up-to-date information about cancer to patients, their families, and the general public.

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for cancer-related information and support. Call us at 1-800-227-2345 or visit www.cancer.org.

References: Eye cancer detailed guide

Albert DM, Kulkarni AD. Intraocular melanoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 9th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2011:2090-2098.

American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta, Ga: American Cancer Society; 2015.

American Joint Committee on Cancer. Malignant melanoma of the uvea. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010:547−553.

Carbone M, Ferris LK, Baumann F, et al. BAP1 cancer syndrome: Malignant mesothelioma, uveal and cutaneous melanoma, and MBAITs. *J Transl Med*. 2012;10:179.

Carvajal RD, Sosman JA, Quevedo F, et al. Effect of selumetinib vs chemotherapy on progression-free survival in uveal melanoma: A randomized clinical trial. *JAMA*. 2014;311:2397−2405.

Grimm SA, McCannel CA, Omuro AM, et al. Primary CNS lymphoma with intraocular involvement: International PCNSL Collaborative Group Report. *Neurology*. 2008;71:1355-1360.

Grimm SA, Pulido JS, Jahnke K, et al. Primary ocular lymphoma: An International Primary Central Nervous System Lymphoma Collaborative Group report. *Ann Oncol*. 2007;18:1851-1855.

Harbour JW, Chen R. The DecisionDx-UM gene expression profile test provides risk stratification and individualized patient care in uveal melanoma. *PLoS Curr*. 2013;Apr 9;5.

Karcioglu ZA, Haik BG. Chapter 67: Eye, orbit, and adnexal structures. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Melia M, Moy CS, Reynolds SM, et al. Quality of life after iodine 125 brachytherapy vs enucleation for choroidal melanoma: 5-year results from the Collaborative Ocular Melanoma Study: COMS QOLS report no. 3. *Arch Ophthalmol*. 2006;124:226-238.

National Cancer Institute. Physician Data Query (PDQ). Intraocular (Uveal) Melanoma Treatment. 2014. Accessed at www.cancer.gov/cancertopics/pdq/treatment/intraocularmelanoma/healthprofessional on November 24, 2014.

Onken MD, Worley LA, Ehlers JP, Harbour JW. Gene expression profiling in uveal melanoma reveals two molecular classes and predicts metastatic death. *Cancer Research*. 2004;64:7205-7209.

Van Raamsdonk CD, Griewank KG, Crosby MB, et al. Mutations in *GNA11* in uveal melanoma. *N Engl J Med*. 2010;363:2191-2199.

Weis E, Shah CP, Lajous M, et al. The association between host susceptibility factors and uveal melanoma: a meta-analysis. *Arch Ophthalmol*. 2006;124:54-60.

Wu X, Li J, Zhu M, Fletcher JA, Hodi FS. Protein kinase C inhibitor AEB071 targets ocular melanoma harboring GNAQ mutations via effects on the PKC/Erk1/2 and PKC/NF-κB pathways. *Mol Cancer Ther*. 2012;11:1905-1914.

Young JL, Ward KC, Ries LAG. Cancers of rare sites. In: Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner M-J, eds. SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007. Accessed at http://seer.cancer.gov/archive/publications/survival/index.html on November 20, 2014.

Last Medical Review: 12/9/2014
Last Revised: 2/2/2015

2014 Copyright American Cancer Society

For additional assistance please contact your American Cancer Society
1-800-227-2345 or www.cancer.org