About Eye Cancer

Overview and Types

If you have been diagnosed with eye cancer or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- What Is Eye Cancer?

Research and Statistics

See the latest estimates for new cases of eye cancer and deaths in the US and what research is currently being done.

- Key Statistics for Eye Cancer
- What's New in Eye Cancer Research?

What Is Eye Cancer?

Eye cancer can refer to any cancer that starts in the eye. Cancer starts when cells begin to grow out of control. (To learn about how cancers start and spread, see What Is Cancer?[1])

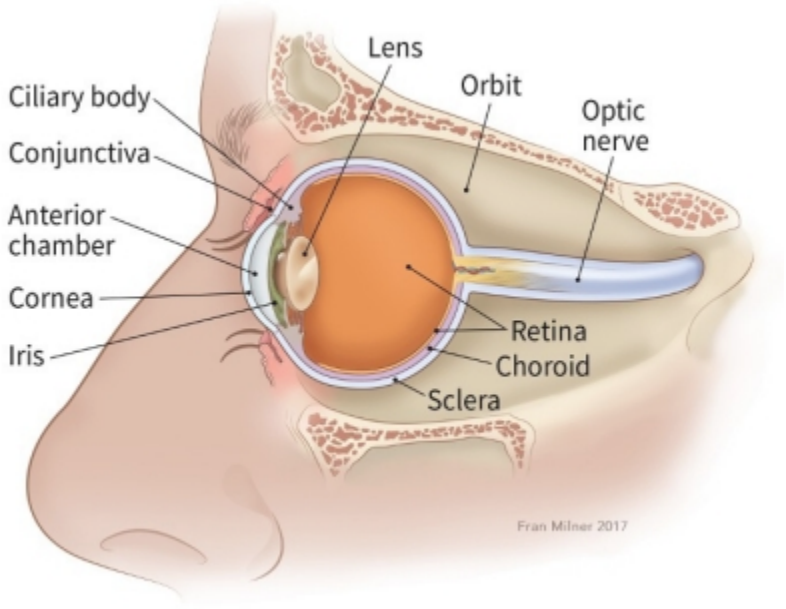
The most common type of eye cancer is melanoma. But there are other types of cancer that affect different kinds of cells in the eye.

Where eye cancers start

The eye has 3 major parts:

- the eyeball (globe) that is mostly filled with a jelly-like material called vitreous humor and has 3 main layers (the sclera, the uvea, and the retina)
- the orbit (the tissues surrounding the eyeball)
- the adnexal (accessory) structures such as the eyelids and tear glands.

Different types of cancer start in each of these areas.



Cancers in the eye (intraocular cancers)

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

Cancers that start in the eye are called *primary intraocular cancers*, and *secondary intraocular cancers* if they start somewhere else and spread to the eye.

In adults, the most common **primary intraocular cancers** are:

- Melanoma (Intraocular melanoma is the focus of our information on eye cancer)
- Non-Hodgkin lymphoma (See Non-Hodgkin Lymphoma (NHL)[2] for more information on primary intraocular lymphoma.)

In children, the most common primary intraocular cancers are:

- Retinoblastoma, a cancer that starts in cells in the retina (the light-sensing cells in the back of the eye)
- Medulloepithelioma (This is the second most common,but is still extremely rare.)

These childhood cancers are discussed in *Retinoblastoma*[3].

Secondary intraocular cancers (cancers that start somewhere else in the body and then spread to the eye) 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[4] and lung cancers[5]. Most often these cancers spread to the part of the eyeball called the *uvea*.

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 that start in the skin are much more common than melanomas that start in the eye.Melanomas develop from pigment-making cells called *melanocytes*. When melanoma develops in the eye, it is usually in the uvea (*uveal melanomas*) and rarely in the conjunctiva (*conjunctival melanomas*).

Uveal melanomas

The uvea is the middle layer of the eyeball. It has 3 main parts:

- The **iris** isthe colored part of the eye (most often blue or brown). It surrounds the pupil, the small opening where light enters the eyeball.
- The **choroid** isa 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.

About 9 out of 10 intraocular melanomas develop in the choroid or ciliary body. 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. 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 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).

Uveal melanomas can spread through the blood and commonly spread to the liver.

Conjunctival melanomas

The conjunctiva is a thin clear covering over the 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.)

These melanomas are extremely rare. They tend to be more aggressive and grow into nearby structures. Because they can spread through the blood and the lymph system, they can also spread to distant organs like the lungs, liver, or brain where the cancer can become life-threatening.

Orbital and adnexal cancers

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

Cancers of the orbit and adnexa develop from tissues such as muscle, nerve, and skin around the eyeball and are like cancers in other parts of the body. For example:

- Cancers of the eyelid are usually skin cancers. (See Melanoma Skin Cancer[6] or Skin Cancer: Basal and Squamous Cell[7].)
- For cancer affecting the eye muscles, see Rhabdomyosarcoma[8].
- Lymphomas that start in the eye are discussed in Non-Hodgkin Lymphoma[9].

Hyperlinks

1. www.cancer.org/cancer/cancer-basics/what-is-cancer.html
2. www.cancer.org/cancer/non-hodgkin-lymphoma.html

3. www.cancer.org/cancer/retinoblastoma.html
4. www.cancer.org/cancer/breast-cancer.html
5. www.cancer.org/cancer/lung-cancer.html
6. www.cancer.org/cancer/melanoma-skin-cancer.html
7. www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer.html
8. www.cancer.org/cancer/rhabdomyosarcoma.html
9. www.cancer.org/cancer/non-hodgkin-lymphoma.html

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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

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Key Statistics for Eye Cancer

The American Cancer Society's estimates for eye cancer in the United States for 2019 are:

- 3,360 new cancers (mainly melanomas) of the eye and orbit: 1,860 in men and 1,500 in women
- 370 deaths from cancers of the eye and orbit: 200 in men and 170 in women

Primary eye cancers can occur at any age, but the risk for most types increases as people get older. The rate of uveal melanomas has been fairly stable over the past few decades, but the rate of conjunctival melanomas has increased. 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, but this cancer starts more often in other parts of the body. More than 9 out of 10 melanomas start in the skin.

Melanoma of the eye is much more common in whites than blacks, and is slightly more common in men than women.

For statistics on survival, see Eye Cancer Survival Rates[1].

Visit the American Cancer Society's Cancer Statistics Center[2] for more key statistics.

Hyperlinks

1. www.cancer.org/cancer/eye-cancer/detection-diagnosis-staging/survival-rates.html
2. https://cancerstatisticscenter.cancer.org/

References

American Cancer Society. *Cancer Facts & Figures 2019*. Atlanta, Ga: American Cancer Society; 2019.

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What's New in Eye Cancer Research?

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 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.)

New tests for eye cancer

A new type of biopsy called a liquid biopsy is being looked at more often. Instead of having to make a cut or put a needle into the eye, melanoma tumor cells can be collected from a blood sample. These cancer cells can then be tested for certain traits, including genetic changes, that can help predict how likely the cancer is to spread or come back after treatment.. Liquid biopsies might help diagnose tumor spread earlier, or help the doctors know if treatment is working. This could be very helpful in people who did not have a biopsy of the tumor and want to preserve their vision. However, the equipment needed for this test is not readily available so this type of biopsy is not done routinely and is mainly done as part of a clinical trial.

Advances in treatment

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. Although most clinical trials of these treatments include people with melanomas of the skin, results of these studies might help treat people with eye melanomas 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. 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. Sometimes giving two of

these drugs together works better than just one drug alone. Initial studies of all these drugs in uveal eye melanoma have shown some benefit. More clinical trials are needed.

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 side effects than chemotherapy.

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 one clinical trial, but other studies have had disappointing results. The role of selumetinib in treating eye melanoma is not clear and for now, this drug is only available through clinical trials[1].

Some newer drugs, such as vemurafenib, dabrafenib, and trametinib, 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 conjunctival eye melanoma. Still, these or similar drugs might help people whose cancer cells have these mutations.

IMCgp100 is a new drug that attaches to two proteins at the same time to kill cancer cells. It shows promising results in people with advanced uveal melanoma. More research is being done.

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, sorafenib, vorinostat , and everolimus.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

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Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

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