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About Testicular Cancer

Overview and Types

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

What Is Testicular Cancer?

Research and Statistics

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

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

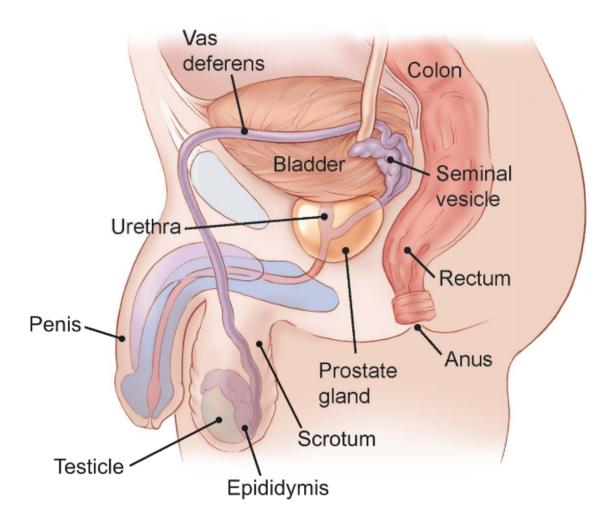
What Is Testicular Cancer?

Cancer starts when cells begin to grow out of control. Cells in nearly any part of the body can become cancer and spread to other parts of the body. To learn more about how cancers start and spread, see What Is Cancer?¹

Cancer that starts in the testicles is called testicular cancer. To understand this cancer, it helps to know about the normal structure and function of the testicles.

What are testicles?

Testicles (also called **testes**; a single testicle is called a **testis**) are part of the male reproductive system. The 2 organs are each normally a little smaller than a golf ball in adult males. They're held within a sac of skin called the **scrotum**. The scrotum hangs under the base of the penis.



Testicles have 2 main functions:

- They make male hormones (androgens) such as testosterone.
- They make sperm, the male cells needed to fertilize a female egg cell to start a pregnancy.

Sperm cells are made in long, thread-like tubes inside the testicles called seminiferous tubules. They're then stored in a small coiled tube behind each testicle called the epididymis. This is where they mature.

During ejaculation, sperm cells are carried from the epididymis through the vas deferens to the seminal vesicles. There, they mix with fluids made by the vesicles, prostate gland, and other glands to form semen. This fluid then enters the urethra, the tube in the center of the penis through which both urine and semen leave the body.

Types of testicular cancer

The testicles are made up of many types of cells, each of which can develop into one or more types of cancer. It's important to know the type of cell the cancer started in and what kind of cancer it is because they differ in how they're treated and in their prognosis (outlook).

Doctors can tell what type of testicular cancer you have by looking at the cells under a microscope.

Germ cell tumors

More than 90% of cancers of the testicle start in cells known as germ cells. These are the cells that make sperm. The main types of germ cell tumors (GCTs) in the testicles are **seminomas** and **non-seminomas**.

These types occur about equally. Many testicular cancers contain both seminoma and non-seminoma cells. These **mixed germ cell tumors are treated as non-seminomas** because they grow and spread like non-seminomas.

Seminomas

Seminomas tend to grow and spread more slowly than non-seminomas. The 2 main sub-types of these tumors are classical (or typical) seminomas and spermatocytic seminomas.

- Classical seminoma: More than 95% of seminomas are classical. These usually occur in men between 25 and 45.
- **Spermatocytic seminoma:** This rare type of seminoma tends to occur in older men. (The average age is about 65.) Spermatocytic tumors tend to grow more slowly and are less likely to spread to other parts of the body than classical

seminomas.

Some seminomas can increase blood levels of a protein called human chorionic gonadotropin (HCG). HCG can be checked with a simple blood test and is considered a tumor marker for certain types of testicular cancer. It can be used for diagnosis and to check how the patient is responding to treatment.

Non-seminomas

These types of germ cell tumors usually occur in men between their late teens and early 30s. The 4 main types of non-seminoma tumors are embryonal carcinoma, yolk sac carcinoma, choriocarcinoma, and teratoma. Most tumors are a mix of different types (sometimes with seminoma cells too), but this doesn't change the treatment of most non-seminoma cancers.

Embryonal carcinoma: These cells are found in about 40% of testicular tumors, but pure embryonal carcinomas occur only 3% to 4% of the time. When seen under a microscope, these tumors can look like tissues of very early embryos. This type of non-seminoma tends to grow rapidly and spread outside the testicle.

Embryonal carcinoma can increase blood levels of a tumor marker protein called **alphafetoprotein** (AFP), as well as **human chorionic gonadotropin** (HCG).

Yolk sac carcinoma: These tumors are so named because their cells look like the yolk sac of an early human embryo. Other names for this cancer include yolk sac tumor, endodermal sinus tumor, infantile embryonal carcinoma, or orchidoblastoma.

This is the most common form of testicular cancer in children (especially in infants), but pure yolk sac carcinomas (tumors that do not have other types of non-seminoma cells in them) are rare in adults. When they occur in children, these tumors usually are treated successfully. But they're of more concern when they occur in adults, especially if they are pure. Yolk sac carcinomas respond very well to chemotherapy, even if they have spread.

This type of tumor almost always increases blood levels of AFP (alpha-fetoprotein).

Choriocarcinoma: This is a very rare and fast-growing type of testicular cancer in adults. Pure choriocarcinoma is likely to spread rapidly to other parts of the body, including the lungs, bones, and brain. More often, choriocarcinoma cells are seen with other types of non-seminoma cells in a mixed germ cell tumor. These mixed tumors tend to have a somewhat better outlook than pure choriocarcinomas, although the

presence of choriocarcinoma is always a worrisome finding.

This type of tumor increases blood levels of HCG (human chorionic gonadotropin).

Teratoma: Teratomas are germ cell tumors with areas that, under a microscope, look like each of the 3 layers of a developing embryo: the endoderm (innermost layer), mesoderm (middle layer), and ectoderm (outer layer). Pure teratomas of the testicles are rare and do not increase AFP (alpha-fetoprotein) or HCG (human chorionic gonadotropin) levels. Most often, teratomas are seen as parts of mixed germ cell tumors.

There are 3 main types of teratomas:

- Mature teratomas are tumors formed by cells a lot like the cells of adult tissues.
 They rarely spread. They can usually be cured with surgery, but some come back² (recur) after treatment.
- Immature teratomas are less well-developed cancers with cells that look like those of an early embryo. This type is more likely than a mature teratoma to grow into (invade) nearby tissues, spread (metastasize) outside the testicle, and come back (recur) years after treatment.
- Teratomas with somatic type malignancy are very rare. These cancers have some areas that look like mature teratomas but have other areas where the cells have become a type of cancer that normally develops outside the testicle (such as a sarcoma, adenocarcinoma, or even leukemia).

Carcinoma in situ of the testicle

Testicular germ cell cancers can start as a non-invasive form of the disease called carcinoma in situ (CIS) or intratubular germ cell neoplasia. In testicular CIS, the cells look abnormal under the microscope, but they have not yet spread outside the walls of the seminiferous tubules (where sperm cells are formed). Carcinoma in situ doesn't always progress to invasive cancer.

It's hard to find CIS before it becomes an invasive cancer because it generally doesn't cause symptoms or form a lump that you or the doctor can feel. The only way to diagnose ³testicular CIS is to have a biopsy. (This is a procedure to take out a tiny bit of tissue so it can be checked under a microscope.) Sometimes CIS is found incidentally (by accident) when a testicular biopsy is done for another reason, such as infertility.

Experts don't agree about the best treatment for CIS. Since CIS doesn't always become an invasive cancer, many doctors in the United States consider observation (watchful waiting) to be the best treatment option.

When CIS of the testicle becomes invasive, its cells are no longer just in the seminiferous tubules, they've grown into other structures of the testicle. These cancer cells can then spread either to the lymph nodes (small, bean-shaped collections of white blood cells) through lymphatic vessels (tiny fluid-filled tubes that connect the lymph nodes), or through the blood to other parts of the body.

Stromal tumors

Tumors can also start in the supportive and hormone-producing tissues, or stroma, of the testicles. These tumors are known as **gonadal stromal tumors**. They make up less than 5% of adult testicular tumors, but up to 20% of childhood testicular tumors. The main types are **Leydig cell tumors** and **Sertoli cell tumors**.

Leydig cell tumors

These tumors start in the Leydig cells in the testicle that normally make male sex hormones (androgens like testosterone). Leydig cell tumors can develop in both adults and children. These tumors often make androgens (male hormones), but sometimes they make estrogens (female sex hormones).

Most Leydig cell tumors are not cancer (benign). They seldom spread beyond the testicle and can often be cured with surgery. Still, a small number of Leydig cell tumors do spread to other parts of the body. These tend to have a poor outlook because they usually don't respond well to chemo or radiation therapy.

Sertoli cell tumors

These tumors start in normal Sertoli cells, which support and nourish the sperm-making germ cells. Like the Leydig cell tumors, these tumors are usually benign. But if they spread, they usually don't respond well to chemo or radiation therapy.

Secondary testicular cancers

Cancers that start in another organ and then spread (metastasize) to the testicle are called secondary testicular cancers. These are not true testicular cancers – they don't start in the testicles. They're named and treated based on where they started.

<u>Lymphoma</u>⁴ is the most common secondary testicular cancer. Testicular lymphoma is more common in men older than 50 than primary testicular tumors. The outlook depends on the type and stage of lymphoma. The usual treatment is surgical removal, followed by radiation and/or chemotherapy.

In boys with acute <u>leukemia</u>⁵, the leukemia cells can sometimes form a tumor in the testicle. Along with chemotherapy to treat the leukemia, this might require treatment with radiation or surgery to remove the testicle.

Cancers of the prostate, lung, skin (melanoma), kidney, and other organs also can spread to the testicles. The prognosis for these cancers tends to be poor because these cancers have usually spread widely to other organs as well. Treatment depends on the specific type of cancer.

Hyperlinks

- 1. www.cancer.org/treatment/understanding-your-diagnosis/what-is-cancer.html
- 2. <u>www.cancer.org/treatment/survivorship-during-and-after-treatment/long-term-health-concerns/recurrence.html</u>
- 3. <u>www.cancer.org/cancer/testicular-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. www.cancer.org/cancer/non-hodgkin-lymphoma.html
- 5. www.cancer.org/cancer/leukemia-in-children.html

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See all references for Testicular Cancer_(www.cancer.org/cancer/testicular-cancer/references.html)

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2018.

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Key Statistics for Testicular Cancer

The American Cancer Society's estimates for testicular cancer in the United States for 2023 are:

- About 9,190 new cases of testicular cancer diagnosed
- About 470 deaths from testicular cancer

The incidence rate of testicular cancer has been increasing in the US and many other countries for several decades. The increase is mostly in seminomas. Experts have not been able to find reasons for this. Lately, the rate of increase has slowed.

Testicular cancer is not common: about 1 of every 250 males will develop testicular cancer at some point during their lifetime.

The average age of males when first dignosed with testicular cancer is about 33. This is largely a disease of young and middle-aged men, but about 6% of cases occur in children and teens, and about 8% occur in men older than 55.

Because testicular cancer usually can be treated successfully, a man's lifetime risk of dying from this cancer is very low: about 1 in 5,000. If you would like to know more about survival statistics, see <u>Testicular cancer survival rates</u>¹.

Visit the American Cancer Society's <u>Cancer Statistics Center</u>² for more key statistics.

Hyperlinks

- 1. <u>www.cancer.org/cancer/testicular-cancer/detection-diagnosis-staging/survival-rates.html</u>
- 2. cancerstatisticscenter.cancer.org/

References

American Cancer Society. *Cancer Facts & Figures 2023*. Atlanta, Ga: American Cancer Society; 2023.

Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2014, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2014/, based on November 2016 SEER data submission, posted to the SEER web site, April 2017.

SEER Cancer Stat Facts: Testicular cancer . National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/statfacts/html/testis.html. Accessed January 5, 2018.

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What's New in Testicular Cancer Research?

Important research into testicular cancer is being done in many university hospitals, medical centers, and other institutions around the world. Each year, scientists find out more about what causes the disease, how to prevent it, and how to improve treatment.

Genetics

In recent years, researchers have found that changes in certain genes, such as PLAP, NANOG, SOX2, and REX1, appear to be linked to testicular cancer. These findings could someday help identify men at higher risk, but they need to be studied more.

Scientists are also studying changes in the genes of testicular cancer cells to learn more about the causes of this disease. Their hope is that improved understanding will lead to better treatment. Certain gene mutations found in the testicular cancer cells have been linked to resistance to chemotherapy and predict poor outcomes. These

findings may help personalize treatment. They could also help find new drugs to treat testicular cancer, drugs that can target these gene mutations. A better understanding of the genetic changes will also help doctors decide which patients need further treatment and which ones can be safely treated with surgery alone.

Treatment

Clinical trials have refined doctors' approaches to treating these cancers. For example, studies have found factors that help predict which patients have a particularly good prognosis and may not need lymph node surgery or radiation therapy. Studies also have found unfavorable prognostic factors that suggest certain patients may benefit from more intense treatment.

New drugs and new drug combinations are being tested for patients with testicular cancer that comes back or doesn't respond to treatment. And high-dose chemotherapy followed by a <u>stem cell transplant</u>¹ is being studied for men who have tumors with a poor prognosis.

Sentinel lymph node biopsy is used for other types of cancer to help limit the number of nodes that are removed, which can decrease the risk of long-term side effects. Researchers are looking at how this procedure might be used with testicular cancer.

Other studies are using robotic-assisted surgery to remove lymph nodes after chemotherapy. It appears to be a safe option instead of standard "open" surgery, but more research is needed to show this and to see if there are other benefits.

Long-term treatment side effects

A large amount of work is being done to try to better understand, limit, and prevent the long-term toxicities of treatment while maintaining the high cure rate. Chemo combinations are being refined to see if eliminating certain drugs, replacing them with others, or lowering doses can reduce side effects for some men without reducing the effectiveness of treatment.

Doctors also want to be able to predict whose cancer is more likely to <u>come back</u> <u>later</u>²(recur) and then base treatment on this. This way they couldn't under- or over-treat anyone. For instance, one study reported good results by individualizing treatment in men with metastatic cancer based on the decline of tumor marker (AFP and HCG) levels after chemo, giving more intense treatment to those with a slower decline.

Hyperlinks

- 1. www.cancer.org/cancer/testicular-cancer/treating/high-dose-chemo-stem-cell.html
- 2. <u>www.cancer.org/treatment/survivorship-during-and-after-treatment/long-term-health-concerns/recurrence.html</u>

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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)

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