

# **About Salivary Gland Cancer**

**Overview and Types** 

If you have been diagnosed with salivary gland cancer or are worried about it, you likely

The salivary glands are organs on each side of the face. They make saliva (spit), the lubricating fluid found in the mouth and throat. Saliva has enzymes that begin the process of digesting (breaking down) food. It also has antibodies and other substances that help prevent infections of the mouth and throat.

The 2 main types of salivary glands are: major and minor.

#### Major salivary glands

- The **parotid glands**. These are the largest salivary glands and are just in front of the ears. Most salivary gland tumors start here. Most of these tumors are benign (not cancer), but the parotid glands are still where most malignant (cancer) salivary gland tumors start.
- The **submandibular glands.** These major salivary glands are smaller than the parotid glands and sit below the jaw. They make saliva which comes out under the tongue.
- The **sublingual glands**. These salivary glands are the smallest of the major salivary glands and sit under the floor of the mouth and below either side of the tongue.



Minor salivary glands

There are also several hundred minor salivary glands that are too small to see without special lab equipment. These glands are under the lining of the lips and tongue; in the roof of the mouth; and inside the cheeks, nose, sinuses, and larynx (voice box). Tumors in these glands are uncommon, but they are more often malignant than benign. Cancers of the minor salivary glands most often start in the roof of the mouth.

# Types of salivary gland cancers

There are many types of salivary gland cancers. Normal salivary glands are made up of different kinds of cells, and cancers can start in any of these cell types. Salivary gland cancers are named according to which cell types they most look like.

Based on how normal the cells look, salivary gland cancers are also often **graded** (from 1 to 3, or from low to high), The grade of the cancer gives an idea of how quickly it is likely to grow and spread. Also, people with low-grade cancers tend to have better outcomes than those with high grade cancers.

- Grade 1 (also called low grade or well differentiated) means the cancer cells look very much like normal salivary gland cells. They tend to grow slowly and have a good outcome (prognosis).
- Grade 2 (also called intermediate grade or moderately differentiated) means the cancer cells look like those between grade 1 and grade 3 cancers. The outcomes are also between a grade 1 and grade 3 cancer.
- Grade 3 (also called high grade or poorly differentiated) means the cancer cells look very different from normal cells and often grow and spread quickly. The outlook for these cancers is usually not as good as for lower grade cancers.

#### Mucoepidermoid carcinoma

**Mucoepidermoid carcinomas are the most common type of salivary gland cancer.** Most start in the parotid glands. They develop less often in the submandibular glands or in minor salivary glands inside the mouth. These cancers are usually low grade, but can sometimes be intermediate or high grade.

#### Adenoid cystic carcinoma

Adenoid cystic carcinoma is the second most common type of salivary gland cancer, is usually slow growing, and often appears to be low grade when looked at in the lab. Still, it's very hard to get rid of completely because it tends to spread along nerves. These tumors tend to come back after treatment (usually surgery and radiation), sometimes many years later. The outlook is better if the tumor is smaller.

#### Acinic cell carcinoma

Most acinic cell carcinomas start in the parotid gland. They tend to grow slower and

tend to develop in younger people than most other salivary gland cancers. They are usually low grade, but how far they have grown into nearby tissue is probably a better predictor of a person's outlook.

#### Polymorphous adenocarcinoma

These tumors tend to start in the minor salivary glands. They usually (but not always) grow slowly and are mostly curable. They are more common in women than men.

#### Adenocarcinoma, not otherwise specified (NOS)

When seen in the lab, these cancers have enough features to show that they are adenocarcinomas, but not enough detail to classify them further. They are most commonly found in the parotid glands and the minor salivary glands. These tumors can be any grade. They are often seen in people older than 60 years of age.

#### Secretory carcinoma (Mammary analogue secretory carcinoma)

These cancers are more often found in minor salivary glands. They tend to be low grade and grow slowly. They can be found equally in men and women.

#### Rare adenocarcinomas

Several types of adenocarcinoma are quite rare.

Some of these tend to be low grade and people who have them usually have a very good outcome:

- Basal cell adenocarcinoma
- Clear cell carcinoma
- Cystadenocarcinoma
- Sebaceous adenocarcinoma
- Sebaceous lymphadenocarcinoma
- Mucinous adenocarcinoma

Other rare adenocarcinomas are more likely to be high grade and may have a less favorable outcome:

- Oncocytic carcinoma
- Salivary gland duct carcinoma

#### Malignant mixed tumors

Mixed tumors have more than one type of cancer cell. There are 3 types of malignant mixed tumors:

- Carcinoma ex pleomorphic adenoma (has benign cells and carcinoma cells)
- Carcinosarcoma (has both carcinoma and sarcoma cells)
- Metastasizing mixed tumor

Nearly all malignant mixed tumors are carcinoma ex pleomorphic adenomas. The other 2 types are very, very rare.

Carcinoma ex pleomorphic adenoma develops from a benign mixed tumor (also known as a pleomorphic adenoma). This tumor is found mainly in the major salivary glands. Both the grade of the cancer and how far it has spread (its <u>stage</u><sup>1</sup>) are important in predicting outcome.

#### Other rare salivary gland cancers

Several other types of cancer can develop in the salivary glands.

**Squamous cell carcinoma:** This cancer occurs mainly in older men. It can develop after radiation therapy for other cancers in the area, but most often cancer is spread from a <u>squamous cell cancer of the skin</u><sup>2</sup> that started in the head and neck area. This type of cancer tends to have a poorer outlook.

**Epithelial-myoepithelial carcinoma:** This rare tumor tends to be low grade, but it can come back after treatment and/or spread to other parts of the body.

**Anaplastic small cell carcinoma:** The cells in these tumors have neuroendocrine features. This means the cells get messages from nerves to release certain hormones. These tumors are most often found in minor salivary glands and tend to grow quickly.

**Undifferentiated carcinomas:** This group of cancers includes small-cell undifferentiated carcinoma, large-cell undifferentiated carcinoma, and lymphoepithelial carcinoma. These are high-grade cancers that often spread. Overall, the survival outlook tends to be poor. Lymphoepithelial carcinoma, which is much more common in Eskimo and Inuit people, is associated with the Epstein-Barr infection and has a slightly better outcome.

# Types of benign salivary gland tumors

Most salivary gland tumors are benign, that is, they are not cancer and will not spread to other parts of the body. These tumors are almost never life-threatening.

There are many types of benign salivary gland tumors, with names such as pleomorphic adenoma, oncocytomas, and Warthin tumors.

Benign tumors are almost always cured by surgery. Very rarely, they may become cancer if left untreated for a long time or if they are not completely removed and grow back. It's not clear exactly how benign tumors become cancers.

#### Our information about salivary gland cancers does not cover benign tumors.

# Other cancers that can affect the salivary glands

These types of cancer are typically not thought of as true salivary gland cancers, either because they start more often in other parts of the body, or because they start elsewhere and then grow into or spread to the salivary glands.

#### Non-Hodgkin lymphoma

Most non-Hodgkin lymphomas start in lymph nodes. Rarely,these cancers start in immune system cells within the salivary glands. They behave and are treated differently from other types of cancers in the salivary glands. Most lymphomas that start in the salivary glands affect people with Sjögren syndrome (a disorder that causes the immune system to attack salivary gland cells). For more information, see <u>Non-Hodgkin Lymphoma<sup>3</sup></u>.

#### Sarcoma

The salivary glands have blood vessels, muscle cells, and cells that make connective tissue. Cancers that start in these types of cells are called sarcomas. These rarely occur in the salivary gland. For more information, see <u>Soft Tissue Sarcoma<sup>4</sup></u>.

#### Cancers that spread to the salivary glands

Some cancers, like <u>squamous cell skin cancer</u><sup>5</sup> or <u>melanoma</u><sup>6</sup>, might start elsewhere but spread to the salivary glands. These cancers are treated based on where the cancer started.

# Hyperlinks

- 1. <u>www.cancer.org/cancer/salivary-gland-cancer/detection-diagnosis-</u> <u>staging/staging.html</u>
- 2. www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer.html
- 3. www.cancer.org/cancer/non-hodgkin-lymphoma.html
- 4. www.cancer.org/cancer/soft-tissue-sarcoma.html
- 5. www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer.html
- 6. www.cancer.org/cancer/melanoma-skin-cancer.html

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# Key Statistics About Salivary Gland Cancer

# How common are salivary gland cancers?

Salivary gland cancers are not very common, making up 6% to 8% of all head and neck cancers in the United States. There are about 2,000 to 2,500 cases in the US each year. They occur at a rate of about 3 cases per 100,000 people per year in the Western world.

# Who gets salivary gland cancer?

These cancers can occur in people of almost any age, but they become more common as people get older. The average age of people when they are diagnosed is 55.

# Where are most salivary gland cancers found?

Most salivary gland cancers are found in the parotid glands, followed by the submandibular, sublingual, and minor salivary glands.

#### References

Laurie SA. Salivary gland tumors: Epidemiology, diagnosis, evaluation, and staging. In: Shah S, ed. *UpToDate*. Waltham, Mass.: UpToDate, 2021. https://www.uptodate.com. Accessed April 22, 2021.

Leeman JE, Katabi N, Wong RJ, Lee NY, Romesser PB. Ch. 65 - Cancer of the Head and Neck. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE,

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# What's New in Salivary Gland Cancer Research?

A lot of research on the causes and treatment of salivary gland cancer is being done in medical centers world-wide. This is a challenging disease to study because it's quite rare and there are many types of salivary gland cancer. But each year, scientists find out more about the disease and how to better treat it.

# Gene changes in salivary gland cancers

Studies have found certain gene changes in various types of salivary gland cancers. Researchers are learning more about how these changes can cause salivary gland cells to become cancer. They are also finding out that some of these gene changes can be targeted by specific drugs for treatment.

For example, in adenoid cystic cancers, a mutation in the *NOTCH1* gene appears to make this cancer more aggressive and have a higher chance of cancer spread. But this also means that salivary gland cancers with this *NOTCH1* mutation might respond to a category of drugs called *NOTCH1* inhibitors. Some secretory cancers have an *ETV6-NTRK3* fusion gene that makes <u>TRK inhibitors</u><sup>1</sup> a possible treatment option. More research is being done to test targeted drugs against gene changes in different types of salivary gland cancers.

As scientists learn more about these gene changes in salivary gland cancer cells, they hope to develop new targeted treatments that work better and cause fewer side effects. Someday these cell changes may also be used to diagnose salivary cancers, predict outcomes, and make treatment choices.

# Treatment of salivary gland cancers

#### Surgery

With advances in surgical techniques, teams of head and neck surgeons and neurosurgeons can now remove small tumors and tumors near key structures, such as cancers that have spread near the base of the skull. These operations are becoming more common and successful.

Reconstructive surgery is becoming more sophisticated and successful, too. This lets surgeons do more extensive surgery to remove the cancer and improves patients' quality of life after treatment.

#### **Radiation therapy**

New ways of giving radiation therapy now allow more precise targeting of radiation.

Chemo drugs, often given along with radiation, continue to be studied in clinical trials.

#### **Targeted therapy**

As researchers have learned more about the gene changes in cells that cause cancer, they have been able to develop drugs that specifically target these changes. These targeted drugs work differently from standard chemotherapy drugs. They sometimes work when chemo drugs don't, and they often have different (and sometimes less severe) side effects.

Studies have identified gene changes in some salivary gland cancer cells that help the cancer grow and spread. Some of these changes affect proteins that can be blocked by targeted drugs that are already used to treat other types of cancer. So far these drugs are used in cases of advanced salivary gland cancer and the tumor must be tested for specific proteins or genes before the drug can be tried. See <u>Targeted Drug Therapy</u><sup>2</sup>

#### Hormone therapy

Early research has found that some salivary gland tumors have too many receptors (proteins) for male hormones called androgens. Drugs that block these receptors or lower hormone levels, such as <u>bicalutamide or leuprolide</u><sup>3</sup>, appear to be helpful in treating these tumors.

# Treating side effects of salivary gland cancer treatment

Even with better radiation and surgical techniques, some people still have long-term side effects, like dry mouth, from treatment for their salivary gland cancer. Photobiomodulation therapy (PBMT) has been investigated to help with this common side effect of salivary gland cancer treatment. It is a low-level laser therapy that is applied to the salivary glands and initial studies have shown some success in people with dry mouth. More studies are needed to show that this therapy is helpful for this side effect.

Other studies are looking at different types of prevention and treatment of dry mouth including new medicines, acupuncture, hyperbaric oxygen, submandibular gland transfer, and increasing saliva production through stimulation of the taste buds and by chewing.

# **Hyperlinks**

- 1. www.cancer.org/cancer/salivary-gland-cancer/treating/targeted-therapy.html
- 2. www.cancer.org/cancer/salivary-gland-cancer/treating/targeted-therapy.html
- 3. www.cancer.org/cancer/salivary-gland-cancer/treating/targeted-therapy.html

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