

About Oral Cavity and Oropharyngeal Cancer

Overview and Types

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

• What Are Oral Cavity and Oropharyngeal Cancers?

Research and Statistics

See the latest estimates for new cases of oral cavity and oropharyngeal cancers in the US and what research is currently being done.

- Key Statistics for Oral Cavity and Oropharyngeal Cancers
- What's New in Oral Cavity and Oropharyngeal Cancer Research?

What Are Oral Cavity and Oropharyngeal Cancers?

Oral cavity cancer starts in the mouth. It might also be called oral cancer. Oropharyngeal cancer starts in the the middle part of the throat just behind the oral cavity that can be seen when the mouth is open. Cancer starts when cells in the body start to grow out of control. To learn more about how cancers start and spread, see <u>What Is Cancer?</u>¹

The oral cavity (mouth) and oropharynx (throat)

The **oral cavity** includes the lips, the inside lining of the lips and cheeks (buccal mucosa), the teeth, the gums, the front two-thirds of the tongue, the floor of the mouth below the tongue, the bony roof of the mouth (hard palate) and the area behind the wisdom teeth (called the retromolar trigone).

The **oropharynx** is the middle part of the throat just behind the oral cavity. It can be seen when your mouth is wide open. It includes the base of the tongue (the back third of the tongue), the soft palate (the back part of the roof of the mouth), the tonsils, and the side and back walls of the throat.

The oral cavity and oropharynx help you breathe, talk, eat, chew, and swallow. Minor salivary glands all over the oral cavity and oropharynx make saliva (spit) that keeps your mouth and throat moist and helps you digest food.

Ask your doctor to explain or show you where your cancer is. Explore the 3D interactive model here to learn more.

Types of oral cavity (mouth) and oropharynx (throat) cancers

The different parts of the oral cavity and oropharynx are made up of many types of cells. Different cancers can start in each type of cell. These differences are important, because they can determine a person's treatment options and prognosis (outlook).

Squamous cell carcinoma of the oral cavity and oropharynx

Almost all of the cancers in the oral cavity and oropharynx are squamous cell carcinomas, also called squamous cell cancers. These cancers start in squamous cells, which are flat, thin cells that form the lining of the mouth and throat.

The earliest form of squamous cell cancer is called **carcinoma in situ**. Thismeans that the cancer cells are only in the layer of cells called the **epithelium**(the top layer of cells lining the oral cavity and oropharynx). This is different from invasive squamous cell cancer, where the cancer cells have grown past the epithelium, into the deeper layers of the oral cavity or oropharynx.

HPV-related cancers: Infection with certain high-risk types of the human papillomavirus

(HPV)² causes most of the squamous cell cancers of the oropharynx (called **HPV-positive cancer**). HPV is rarely associated with oral cavity cancer. HPV-positive cancers are seen more often in young people with no history of tobacco or alcohol use. These cancers tend to have a better outcome (prognosis) than squamous cell cancers not related to an HPV infection (**HPV-negative cancer**). This is most likely because HPV-positive cancers shrink when treated with chemotherapy and radiation. See <u>Risk Factors for Oral Cavity and Oropharyngeal Cancers</u>³.

Verrucous carcinoma is a rare type of squamous cell cancer that is most often found in the gums and cheeks. It's a low-grade (slow growing) cancer that hardly ever spreads to other parts of the body.

Other types of oral cavity and oropharynx cancers

Minor salivary gland cancers: These cancers can start in the glands in the lining of the mouth and throat. There are many types of minor salivary gland cancers, including adenoid cystic carcinoma, mucoepidermoid carcinoma, and polymorphous low-grade adenocarcinoma. To learn more about these cancers, as well as benign salivary gland tumors, see <u>Salivary Gland Cancer</u>⁴.

Lymphomas: The tonsils and base of the tongue contain immune system (lymphoid) tissue, where cancers called **lymphomas** can start. For more information about these cancers, see <u>Non-Hodgkin Lymphoma</u>⁵ and <u>Non-Hodgkin Lymphoma in Children</u>⁶.

Leukoplakia and erythroplakia (possible pre-cancer conditions)

Leukoplakia and erythroplakia are terms used to describe certain types of tissue changes that can be seen in the mouth or throat:

- Leukoplakia is a white or gray area that does not come off when scraped.
- Erythroplakia is a flat or slightly raised, red area that often bleeds easily if it's scraped.
- Erythroleukoplakia is a patch with both red and white areas.

Your dentist or dental hygienist may be the first person to find these white or red patches. They might be cancer, they might be a pre-cancer condition called **dysplasia**, or they could be a harmless change.

The most common causes of leukoplakia and erythroplakia are smoking and chewing tobacco. Poorly fitting dentures that rub against the tongue or the inside of the cheeks

can also cause these changes. But sometimes, there's no clear cause.

Most cases of leukoplakia do not turn into cancer. But some leukoplakias are either cancer when first found or have pre-cancer changes that can turn into cancer if not properly treated. Erythroplakia and erythroleukoplakia are less common, but are usually more serious. More of these red lesions (compared to white lesions or leukoplakia) turn out to be cancer when they are biopsied or will develop into cancer later.

Dysplasia is a term that might be used to describe leukoplakia or erythroplakia. Dysplasia can be called mild, moderate, or severe, based on how abnormal the cells look in the lab. Knowing the degree of dysplasia helps predict how likely a lesion is to turn into cancer or go away on its own. For example, severe dysplasia is more likely than mild dysplasia to become cancer. Dysplasia may sometimes go away if the cause (such as poorly fitting dentures) is removed.

A biopsy is the only way to know for certain if an area of leukoplakia or erythroplakia has dysplastic (pre-cancer) cells or cancer cells. (See <u>Tests for Oral Cavity and</u> <u>Oropharyngeal Cancers</u>⁷.) But other tests might be used first to help determine if a biopsy is needed or to choose the best area to sample for a biopsy. These tests are described in <u>Can Oral Cavity and Oropharyngeal Cancers Be Found Early?</u>⁸

Still, it's important to note that most oral cancers do not develop from pre-existing lesions (either leukoplakia or erythroplakia).

Benign (not cancer) tumors

Many types of benign tumors and tumor-like changes can start in the mouth or throat, such as these:

- Peripheral giant cell granuloma
- Fibroma
- Granular cell tumor
- Schwannoma
- Neurofibroma
- Pyogenic granuloma
- Oral hemangioma

These non-cancer tumors start from different kinds of cells and have many causes. Some of them may cause problems, but they're not likely to be life-threatening. The usual treatment for these types of tumors is surgery to remove them completely since they are unlikely to recur (come back).

Hyperlinks

- 1. <u>www.cancer.org/cancer/cancer-basics/what-is-cancer.html</u>
- 2. <u>www.cancer.org/cancer/cancer-causes/infectious-agents/hpv/hpv-and-cancer-info.html</u>
- 3. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/causes-risks-prevention/risk-factors.html</u>
- 4. <u>www.cancer.org/cancer/salivary-gland-cancer.html</u>
- 5. www.cancer.org/cancer/non-hodgkin-lymphoma.html
- 6. www.cancer.org/cancer/childhood-non-hodgkin-lymphoma.html
- 7. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/detection-diagnosis-</u> <u>staging/how-diagnosed.html</u>
- 8. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/detection-diagnosis-</u> staging/detection.html

References

American Joint Committee on Cancer. Lip and Oral Cavity. In: *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017:79.

American Joint Committee on Cancer. Oropharynx (p16-) and Hypopharynx. In: *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017:123.

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, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa. Elsevier; 2020.

Maymone MBC, Greer RO, Burdine LK, Dao-Cheng A, Venkatesh S, Sahitya PC, Maymone AC, Kesecker J, Vashi NA. Benign oral mucosal lesions: Clinical and pathological findings. *J Am Acad Dermatol.* 2019 Jul;81(1):43-56. doi: 10.1016/j.jaad.2018.09.061. Epub 2018 Nov 14. PMID: 30447312.

Mendenhall WM, Dziegielewski PT, Pfister DG. Chapter 45- Cancer of the Head and Neck. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

National Cancer Institute. Physician Data Query (PDQ). Lip and Oral Cavity Cancer Treatment. September 05, 2019. Accessed at https://www.cancer.gov/types/head-and-

neck/hp/adult/lip-mouth-treatment-pdq on September 21, 2020.

National Cancer Institute. Physician Data Query (PDQ). Lip and Oral Cavity Cancer Treatment. September 05, 2019. Accessed at https://www.cancer.gov/types/head-and-neck/patient/adult/lip-mouth-treatment-pdq on September 21, 2020.

Tian S, Switchenko JM, Jhaveri J, et al. Survival outcomes by high-risk human papillomavirus status in nonoropharyngeal head and neck squamous cell carcinomas: A propensity-scored analysis of the National Cancer Data Base. *Cancer*. 2019;125(16):2782-2793. doi:10.1002/cncr.32115.

Woo SB. Oral epithelial dysplasia and premalignancy. *Head Neck Pathol.* 2019;13(3):423-439. doi:10.1007/s12105-019-01020-6.

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Key Statistics for Oral Cavity and Oropharyngeal Cancers

The American Cancer Society's most recent estimates for oral cavity and oropharyngeal cancers in the United States for 2021 are:

- About 54,010 new cases of oral cavity or oropharyngeal cancer.
- About 10,850 deaths from oral cavity or oropharyngeal cancer.

Oral cavity and oropharyngeal cancers occur most often in the following sites:

- The tongue
- The tonsils and oropharynx
- The gums, floor of the mouth, and other parts of the mouth

The rest are found in the lips, the minor salivary glands (which often occur in the roof of the mouth), and other sites.

What is the average age of people who get oral cavity or oropharyngeal cancer?

The average age of most people diagnosed with these cancers is 63, but they can occur in young people. Just over 20% (1 in 5) of cases occur in patients younger than 55.

How common is oral cavity and oropharyngeal cancer?

These cancers are more than twice as common in men as in women. They are slightly more common in White people than Black people.

Overall, the lifetime risk of developing oral cavity and oropharyngeal cancer is: about 1 in 60 (1.7%) for men and 1 in 140 (0.71%) for women. A number of other factors (described in <u>Oral Cavity and Oropharyngeal Cancer Risk Factors</u>¹) can also affect your risk for developing mouth and throat cancer.

Death rate and new cases of oral cavity or oropharyngeal cancer

The overall rate of new cases of oral cavity and oropharyngeal cancers has risen only slightly over the past 20 years. But during this same time, there has been an increase specifically in oropharyngeal cancers associated with an <u>human papillomavirus (HPV)</u> infection² in both men and women. These HPV-positive cancers tend to act differently than HPV-negative cancers. To learn more, see <u>Risk Factors for Oral Cavity and</u> <u>Oropharyngeal Cancers³ and Causes of Oral Cavity and Oropharyngeal Cancers⁴</u>.

The overall death rate for these cancers has been decreasing over the last 30 years.

For statistics related to survival, see <u>Oral Cavity and Oropharyngeal Cancer Survival</u> <u>Rates</u>⁵.

Visit the <u>American Cancer Society's Cancer Statistics Center</u>⁶ for more key statistics.

Hyperlinks

- 1. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/causes-risks-prevention/risk-factors.html</u>
- 2. www.cancer.org/cancer/cancer-causes/infectious-agents/hpv.html
- 3. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/causes-risks-prevention/risk-factors.html</u>

- 4. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/causes-risks-prevention/what-causes.html</u>
- 5. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/detection-diagnosis-</u> <u>staging/survival-rates.html</u>
- 6. <u>cancerstatisticscenter.cancer.org/</u>

References

American Cancer Society. *Facts & Figures 2021*. American Cancer Society. Atlanta, Ga. 2021.

American Joint Committee on Cancer. HPV-Mediated (p16+) Oropharyngeal Cancer. In: *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017:113.

American Joint Committee on Cancer. Oropharynx (p16-) and Hypopharynx. In: *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017:123.

Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2017, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2017/, based on November 2019 SEER data submission, posted to the SEER web site, April 2020.

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, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa. Elsevier; 2020.

Mendenhall WM, Dziegielewski PT, Pfister DG. Chapter 45- Cancer of the Head and Neck. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

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What's New in Oral Cavity and

Oropharyngeal Cancer Research?

Research on oral and oropharyngeal cancers is being done in many university hospitals, medical centers, and other institutions worldwide . Each year, scientists find out more about what causes these diseases, how to prevent them, and how to better treat them. Most experts agree that treatment in a <u>clinical trial</u>¹ should be considered for any type or stage of cancer in the head and neck areas. This way people can get the best treatment available now and may also get the new treatments that are thought to be even better.

DNA changes in oral cavity and oropharyngeal cancers

A great deal of research is being done to learn about the DNA changes that cause the cells in the oral cavity and oropharynx to become cancer.

More than half of all head and neck cancers have mutations of the *PIK3CA* oncogene. This can cause cells to grow out of control which can lead to cancer. Drugs that target the protein, called PI3K, made by the abnormal *PIK3CA* gene are already approved for use to treat other cancers, such as breast cancer. Studies are being done to see if similar targeted therapy drugs will work in head and neck cancer, especially HPVpositive cancers because they tend to make too many copies of the *PIK3CA* oncogene.

One of the changes often found in DNA of oral cavity and oropharyngeal cancer cells, especially HPV-negative cancer cells, is a mutation of the *TP53* gene. The protein produced by this <u>gene²</u> (called p53) normally helps keep cells from growing too much and helps to destroy cells that are too damaged to be fixed. Changes in the *TP53* gene can lead to increased growth of abnormal cells and cancer.

Some studies suggest that tests to find these gene changes might help find oral and oropharyngeal cancers early. These tests may also be used to better find cancer cells that might have been left behind after <u>surgery</u>³ and to determine which tumors are most likely to respond to <u>chemo</u>⁴ or <u>radiation therapy</u>⁵. The use of p53 gene therapy as a treatment for these cancers is also being studied in <u>early</u>⁶-phase clinical trials⁷.

Discoveries about how changes in the DNA of cells in the mouth and throat cause these cells to become cancer are also being applied to experimental treatments intended to reverse these changes. <u>Another type of gene therapy</u>⁸ boosts the immune system so it can better find and kill cancer cells. These forms of treatment are still in very early stages of study, so it will be several years before we know if any of them are effective.

Screening and early detection of oral cavity and oropharyngeal cancers

Looking for HPV infection has become a part of screening tests for cervical cancer over the years. Given the rise in HPV-positive head and neck cancers, especially in the oropharynx, some studies are looking at ways to screen for HPV infection in the oral cavity and oropharynx as there is no FDA approved test right now for this. Other studies are checking to see if blood tests might identify people with the high-risk types of HPV infection and if this is something that can be used as a screening tool for HPV-positive oropharyngeal cancer. This might help prevent or catch these cancers early.

Cancers of the head and neck can be hard to find early. And almost half of all oral cavity and oropharyngeal cancers have already spread to the lymph nodes when they are first diagnosed. Given these issues, research is being done to find ways to detect it more easily and hopefully sooner. For example, one study tested the air people breathe out (exhale) for certain chemicals that seem to be linked with cancer of the head and neck area.

Treatment of oral cavity and oropharyngeal cancers

Oral cavity and oropharyngeal cancers that are linked with <u>HPV</u>⁹ tend to have a better outcome than those that are HPV-negative. Clinical trials are starting to look at these HPV-positive and HPV-negative cancers separately. For instance, studies are being done to see if HPV-positive cancers can be treated with less chemotherapy and/or radiation without reducing survival. Researchers are also working on treatments aimed at HPV infections or that target HPV-infected cancer cells. Studies are also looking for better ways to treat HPV-negative cancers, too, as well as the best ways to use the treatments we already have.

A great deal of research is focused on improving results from <u>chemotherapy</u>¹⁰ (chemo) for people with these cancers. This includes figuring out which combinations of drugs work best and determining how best to use these drugs along with other forms of treatment. Researchers also continue to develop new chemo drugs that might be more effective against advanced oral and oropharyngeal cancers. They're also looking at whether drugs approved to treat other types of cancer might work for these cancers.

Doctors are always looking at newer ways of focusing <u>radiation</u>¹¹ on tumors more precisely to help them get more radiation to the tumor while limiting side effects to nearby areas. This is especially important for head and neck tumors like oral cavity and oropharyngeal cancers, where there are often many important structures very close to the tumor. Clinical trials are studying <u>targeted drug therapies</u>¹² that might block the action of substances (such as growth factors and growth factor receptors) that cause head and neck cancers to grow and spread. Some targeted drugs are being studied that block the ability of the cancer cell to keep growing and help chemoradiation work better.

Hyperlinks

- 1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
- 2. www.cancer.org/cancer/cancer-causes/genetics/genes-and-cancer.html
- 3. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-</u> <u>cancer/treating/surgery.html</u>
- 4. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-</u> cancer/treating/chemotherapy.html
- 5. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/treating/radiation-therapy.html</u>
- 6. <u>www.cancer.org/treatment/treatments-and-side-effects/clinical-trials/what-you-need-to-know/phases-of-clinical-trials.html</u>
- 7. <u>www.cancer.org/treatment/treatments-and-side-effects/clinical-trials/what-you-need-to-know/phases-of-clinical-trials.html</u>
- 8. <u>www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html</u>
- 9. <u>www.cancer.org/cancer/cancer-causes/infectious-agents/hpv/hpv-and-cancer-info.html</u>
- 10. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-</u> <u>cancer/treating/chemotherapy.html</u>
- 11. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/treating/radiation-</u> <u>therapy.html</u>
- 12. <u>www.cancer.org/cancer/oral-cavity-and-oropharyngeal-cancer/treating/targeted-therapy.html</u>

References

Boscolo-Rizzo P, Furlan C, Lupato V, Polesel J, Fratta E. Novel insights into epigenetic drivers of oropharyngeal squamous cell carcinoma: role of HPV and lifestyle factors. *Clin Epigenetics*. 2017;9:124.

Bourhis J, Sun XS, Le Tourneau C, et al; GORTEC Investigators. 3-year follow-up results of the double-blind, randomized phase II trial comparing concurrent high-dose

cisplatin chemoradiation plus xevinapant (Debio 1143) or placebo in high-risk patients with locally advanced squamous cell carcinoma of the head and neck. Presented at: 2020 European Society for Clinical Oncology Virtual Congress; September 19-21, 2020; virtual. LBA39.

Cheraghlou S, Yu PK, Otremba MD, et al. Treatment deintensification in human papillomavirus-positive oropharynx cancer: Outcomes from the National Cancer Data Base. *Cancer*. 2018;124(4):717-726.

Dharmawardana N, Goddard T, Woods C, Watson DI, Ooi EH, Yazbeck R. Development of a non-invasive exhaled breath test for the diagnosis of head and neck cancer [published online ahead of print, 2020 Sep 9]. *Br J Cancer*. 2020;10.1038/s41416-020-01051-9. doi:10.1038/s41416-020-01051-9.

Dunn LA, Fury MG, Sherman EJ, et al. Phase I study of induction chemotherapy with afatinib, ribavirin, and weekly carboplatin and paclitaxel for stage IVA/IVB human papillomavirus-associated oropharyngeal squamous cell cancer. *Head Neck*. 2018;40(2):233-241.

García-Escudero R, Segrelles C, Dueñas M, et al. Overexpression of PIK3CA in head and neck squamous cell carcinoma is associated with poor outcome and activation of the YAP pathway. *Oral Oncol.* 2018;79:55-63. doi:10.1016/j.oraloncology.2018.02.014.

Huang SH, O'Sullivan B, Waldron J. The Current State of Biological and Clinical Implications of Human Papillomavirus-Related Oropharyngeal Cancer. *Semin Radiat Oncol.* 2018;28(1):17-26.

SEER Cancer Stat Facts: Oral Cavity and Pharynx Cancer. National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/statfacts/html/oralcav.html

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