



ORAL CAVITY AND OROPHARYNGEAL CANCER

What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person's DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

What Are Oral Cavity and Oropharyngeal Cancers?

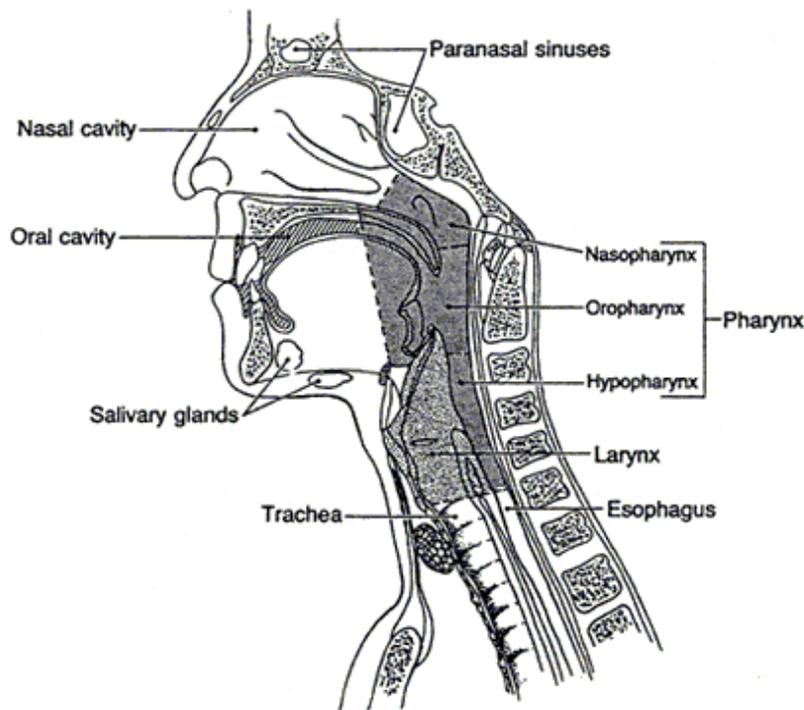
Oral cancer starts in the mouth, also called the oral cavity. The oral cavity includes the lips, the inside lining of the lips and cheeks (buccal mucosa), the teeth, the gums, the front two-thirds of the tongue, the floor of the mouth below the tongue, the bony roof of the mouth (hard palate), and the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

Oropharyngeal cancer develops in the part of the throat just behind the mouth, called the oropharynx. Sometimes this is called throat cancer. The oropharynx begins where the oral cavity stops. It includes the base of 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 wall of the throat.

The oral cavity and oropharynx help you breathe, talk, eat, chew, and swallow. Minor salivary glands located throughout the oral cavity and oropharynx make saliva that keeps your mouth moist and helps you digest food.

The oral cavity and oropharynx have several types of body tissues, and each of these tissues is made up of several types of cells. Different cancers can develop from each type of cell. The differences are important, because they can influence a person's treatment options and *prognosis* (outlook for survival).

There are cancers that start in other parts of the throat that aren't discussed in this document. Cancers of the nasopharynx (the part of the throat above the oropharynx) are discussed in the separate American Cancer Society document, *Nasopharyngeal Cancer*. Cancers that start in the hypopharynx (the part of the throat below the oropharynx) or the larynx (voice box) are discussed in the separate American Cancer Society document, *Laryngeal & Hypopharyngeal Cancer*.



Many types of tumors (abnormal growths of cells) can develop in the oral cavity and oropharynx. Some of them are benign, or non-cancerous, which means they do not invade other tissues and do not spread to other parts of the body. Other tumors are cancerous. They can grow into surrounding tissues and spread to other parts of the body. Some growths start off harmless but can later develop into cancer. These are known as pre-cancerous conditions.

Benign (Non-cancerous) Oral Cavity and Oropharyngeal Tumors

Many types of benign tumors and tumor-like conditions can start in the mouth or throat:

- eosinophilic granuloma
- fibroma
- granular cell tumor
- keratoacanthoma
- leiomyoma
- osteochondroma
- lipoma
- schwannoma
- neurofibroma
- papilloma
- condyloma acuminatum
- verruciform xanthoma
- pyogenic granuloma

- rhabdomyoma
- odontogenic tumors (tumors that start in tooth-forming tissues)

These non-cancerous tumors start from different kinds of cells and have a variety of causes, but the usual treatment is to surgically remove them since they are unlikely to recur (come back).

Leukoplakia and Erythroplakia (Possible Pre-cancerous Conditions)

Leukoplakia and erythroplakia are terms used to describe an abnormal area in the mouth or throat. Leukoplakia is a white area. Erythroplakia is a slightly raised, red area that bleeds easily if scraped. Often, your dentist or dental hygienist may be the first person to spot these problems.

These white or red areas may be a cancer, they may be a pre-cancerous condition called *dysplasia*, or, they could also be a relatively harmless condition. There are mild, moderate, and severe forms of dysplasia, which are distinguished from one another based on how abnormal the tissue looks under the microscope. Knowing the degree of dysplasia helps predict how likely it is to progress to cancer or to go away on its own or after treatment.

The most frequent causes of leukoplakia, and erythroplakia, are smoking or chewing tobacco. Poorly fitting dentures rubbing against the tongue or the inside of the cheeks can also cause them. Often dysplasia will go away if what is causing it is removed.

The seriousness of leukoplakia or erythroplakia can be accurately determined only by a biopsy, looking at a sample of tissue under the microscope. But other tests may be used first to help determine if they might be cancers (and therefore will need a biopsy).

- One method uses a dye called *toluidine blue*. The dye is spread over the abnormal area and if there is cancer, it will stain the malignant tissues blue.
- Another method uses *laser light*. When the light is reflected off cancerous tissue, it looks different from the light reflected off normal tissue.
- Another system uses a special light to view the area after the mouth has been rinsed with a solution of acetic acid (the acid in vinegar).
- Sometimes the abnormal area can be evaluated by *exfoliative cytology*. In this technique, the lesion is scraped with a stiff brush (brush biopsy), and the cells from the scraping can be looked at under the microscope.

Most of the time, leukoplakia is very unlikely to develop into cancer. But about 1 out of 4 leukoplakias are either cancerous when first found or have pre-cancerous changes that eventually progress to cancer if not properly treated. Erythroplakia is usually more serious. As many as 7 out of 10 of these red lesions turn out to be cancer when they are biopsied or will develop into cancer later.

Cancerous Oral Cavity and Oropharyngeal Tumors

Several types of cancers can start in the mouth or throat.

Squamous Cell Carcinomas

More than 90% of cancers of the oral cavity and oropharynx are squamous cell carcinomas, also called squamous cell cancers. Squamous cells are flat, scale-like cells that normally form the lining of the mouth and throat. Squamous cell cancer begins as a collection of abnormal squamous cells.

The earliest form of squamous cell cancer is called *carcinoma in situ*, meaning that the cancer cells are present only in the outer layer of cells called the epithelium. This is different from invasive squamous cell carcinoma, where the cancer cells have spread into deeper layers of the oral cavity or oropharynx.

Verrucous Carcinoma

Verrucous carcinoma is a type of squamous cell carcinoma that makes up less than 5% of all oral cavity tumors. It is a low-grade cancer that rarely spreads to other parts of the body but can deeply spread into surrounding tissue. Therefore, it is important to surgically remove the tumor and a wide margin of surrounding tissue.

Minor Salivary Gland Carcinomas

Minor salivary gland cancers can develop in the glands that are found throughout the lining of the mouth and throat. There are several types of minor salivary gland cancers, including adenoid cystic carcinoma, mucoepidermoid carcinoma, and polymorphous low-grade adenocarcinoma. For more information about these cancers and benign salivary gland tumors, see the American Cancer Society document, *Salivary Gland Cancer*.

Lymphomas

The tonsils and base of the tongue contain immune system (lymphoid) tissue that can develop into a cancer called a lymphoma. For more information about these cancers refer to the American Cancer Society documents, *Non-Hodgkin Lymphoma*, *Non-Hodgkin Lymphoma in Children*, and *Hodgkin Disease*.

The information in the rest of this document about oral cavity and oropharyngeal cancer refers only to squamous cell carcinoma.

What Are the Key Statistics About Oral Cavity and Oropharyngeal Cancers?

The American Cancer Society estimates about 35,310 new cases (25,310 in men and 10,000 in women) of oral cavity and oropharyngeal cancer will be diagnosed in the United States in 2008. An estimated 7,590 people (5,210 men and 2,380 women) will die of these cancers in 2008.

These cancers are about twice as common in men as in women, and are slightly more common in blacks than in whites. The rate of new cases of this disease has been dropping during the past 30 years. Along with this, the death rate for these cancers has been decreasing since the late 1970s.

Oral cavity cancers occur most commonly in the following sites:

- the tongue (about 20% to 25%)
- the floor of the mouth (about 15%)
- the lip (about 10% to 15%)
- the minor salivary glands (about 10% to 15%)

The rest are found in the gums, tonsils, and other sites.

The average age of most people diagnosed with these cancers is 62, but they can occur in young people. Although they occur rarely in children, about one-third of the cancers occur in patients younger than 55.

The rates of these cancers vary among countries. For example, they are much more common in Hungary and France than in the United States and much less common in Mexico and Japan. Scientists think these differences are probably caused by environmental risk factors. (See the section, [What Are the Risk Factors for Oral Cavity and Oropharyngeal Cancers?](#))

When patients newly diagnosed with oral and oropharyngeal cancers are carefully examined, about 15% will have another cancer in a nearby area such as the voice box (larynx), the tube leading from the throat to the stomach (esophagus), or lung. Of those who are cured of the oral or oropharyngeal cancer, 10% to 40% later will develop cancer in one of these organs or a second cancer of the oral cavity or oropharynx. For this reason, it is important for patients with oral and oropharyngeal cancer to have follow-up exams for the rest of their lives and to avoid habits like using tobacco and alcohol, which increase the risk for these second cancers.

For statistics related to survival, see the section, [How Is Oral Cavity and Oropharyngeal Cancer Staged?](#)

What Are the Risk Factors for Oral Cavity and Oropharyngeal Cancers?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer.

But just because you have a risk factor or more than one risk factor for a disease does not mean you will get it. Some people who have oral cavity or oropharyngeal cancer do not have any known risk factors, and others who have several risk factors never develop the disease. Even if someone does have one or more risk factors, it is impossible to know for sure how much they contributed to causing the cancer.

Using Tobacco

About 9 out of 10 people with oral cavity and oropharyngeal cancers use tobacco, and the risk of developing these cancers is related to how much and how long they smoked or chewed.

Smokers are many times more likely than nonsmokers to develop these cancers. Tobacco smoke from cigarettes, cigars, or pipes can cause cancers anywhere in the mouth or throat, as well as causing cancers of the larynx (voice box), lungs, esophagus, kidneys, bladder, and several other organs. Pipe smoking has a particularly significant risk for cancers in the area of the lips that touch the pipe stem. What's more, about 1 out of 3 people who continue to smoke after their cancer seems to be cured will develop a second cancer of the oral cavity, oropharynx, or larynx (voice box), compared with less than 1 in 10 of those who stop smoking.

Oral tobacco products (snuff or chewing tobacco) are associated with cancers of the cheek, gums, and inner surface of the lips. Using snuff for a long time poses an especially high risk. These products also cause gum disease, destruction of the bone sockets around teeth, and tooth loss.

Heavy Drinking

Drinking alcohol strongly increases a smoker's risk of developing oral cavity and oropharyngeal cancers. About 7 out of 10 patients with oral cancer are heavy drinkers. People who are particularly heavy alcohol drinkers but don't smoke have a high risk of these cancers, but it is the combination of the drinking and smoking that is the most dangerous. According to some studies, heavy drinkers and smokers may have as much as a 100-fold increase in the risk of developing these cancers compared with people who don't smoke or drink.

Gender

Oral and oropharyngeal cancers are about twice as common in men as in women. This may be because men are more likely to use tobacco and alcohol. This difference is decreasing as more women are now using tobacco and drinking.

Ultraviolet Light

Sunlight is the main source of ultraviolet (UV) light for most people. Cancers of the lip are more common in people who have outdoor jobs that involve prolonged exposure to sunlight.

Poor Nutrition

Several studies have found that a diet low in fruits and vegetables is linked with an increased risk of cancers of the oral cavity and oropharynx.

Human Papilloma Virus Infection

Human papilloma viruses (HPV) are a group of more than 100 related viruses. Most HPV types cause warts on various parts of the body, but a few HPV types seem to be involved in some cancers. For example, nearly all cancers of the cervix are related to infection with certain HPV types. These same HPV types (especially HPV 16) are found in some oral and oropharyngeal cancers. The current view is that HPV may be a factor in the development of around 20% to 30% of oral and oropharyngeal cancers. People with oral cancer linked with HPV infection are less likely to be smokers and drinkers, and in general seem to have a better outlook than those without HPV.

Immune System Suppression

People taking drugs that suppress the immune system to prevent rejection of transplanted organs or to treat certain immune system diseases may be at increased risk for cancers of the oral cavity and oropharynx.

Lichen Planus

This is a disease that occurs mainly in middle-aged people. Most often it affects the skin (usually as an itchy rash), but it sometimes affects the lining of the mouth and throat, appearing as small white lines or spots. A severe case may slightly increase the risk of oral cancer.

Uncertain, Unproven or Controversial Risk Factors

Mouthwash

Some studies have suggested that mouthwash with a high alcohol content might be linked to a higher risk of oral and oropharyngeal cancers. But recent research has questioned these results. Studying this possible link is complicated by the fact that smokers and frequent drinkers (who are already at increased risk of these cancers) are more likely to use mouthwash than people who neither smoke nor drink.

Irritation From Dentures

It has been suggested that long-term irritation of the lining of the mouth caused by poorly fitting dentures is a risk factor for oral cancer. But many studies have found no increased risk in denture wearers. Since poorly fitting dentures can tend to trap agents that have been proven to cause oral cancer, such as alcohol and tobacco particles, denture wearers should have them checked by a dentist regularly to ensure a good fit. All denture wearers should remove their dentures at night and clean and rinse them thoroughly every day.

Do We Know What Causes Oral Cavity and Oropharyngeal Cancers?

Doctors and scientists can't say for sure what causes each case of oral cavity or oropharyngeal cancer. But they do know many of the risk factors and how some of them cause cells to become cancerous.

Cancers develop when the DNA of cells are damaged. DNA contains genes -- the instructions for how the cells in our bodies function. Some of these genes help cells grow at a proper rate. If these genes are altered, the cells may grow out of control and form a tumor.

Tobacco and alcohol can damage cells in the lining of the oral cavity and oropharynx. The cells in this layer must grow more rapidly to repair this damage. The more often cells need to divide, the more chances there are for them to make mistakes when copying their DNA which may increase their chances of becoming cancerous.

Many of the chemicals found in tobacco can damage DNA directly. Scientists are not sure whether alcohol directly damages DNA, but they have shown that alcohol helps many DNA-damaging chemicals get into cells more easily. This may be why the combination of tobacco and alcohol damages DNA far more than tobacco alone.

This damage can cause certain genes (for example, those in charge of starting or stopping cell growth) to malfunction. Abnormal cells can begin to build up, forming a tumor. With additional damage, the cells may begin to spread into nearby tissue and to distant organs.

In cases where human papilloma virus (HPV) infection may be involved, scientists think the virus causes cells to make 2 proteins known as E6 and E7. When these are made, they turn off some genes responsible for keeping cell growth in check. Uncontrolled cell growth may in some cases lead to cancer.

Can Oral Cavity and Oropharyngeal Cancers Be Prevented?

It is possible that most oral cavity and oropharyngeal cancers could be prevented if people avoided known risk factors.

Limiting Tobacco and Alcohol Exposure

Tobacco and alcohol are the most important risk factors for these cancers. Not starting to smoke is the best approach and quitting tobacco greatly lowers your risk of developing these cancers, even after many years of use. The same is true of heavy drinking.. Limit how much alcohol you drink, if you drink at all.

Limiting Exposure to Ultraviolet (UV) Light

Ultraviolet radiation is an important and avoidable risk factor for cancer of the lips, as well as for skin cancer. If possible, limit the time you spend outdoors during the middle of the day, when the sun's UV rays are strongest. If you are out in the sun, wear a wide-brimmed hat and use sunscreen and lip balm with a Sun Protection Factor (SPF) of at least 15.

Wearing Properly Fitted Dentures

Avoiding sources of oral irritation (such as dentures that do not fit properly) may also lower your risk for oral cancer.

Eating a Healthy Diet

A poor diet has been related to oral cavity and oropharyngeal cancers, although it's not exactly clear what substances in healthy foods might be responsible for reducing the risk of these cancers. In general, eating a healthy diet is much better than adding vitamin supplements to an otherwise unhealthy diet. The American Cancer Society recommends eating a healthy diet, with an emphasis on foods from plant sources. Eat at least 5 servings of

a variety of vegetables and fruits every day, as well as servings of whole grain foods, such as breads, cereals, rice, and pasta. Eat fewer processed meats and red meats; consider fish, poultry, or beans as alternatives.

Treating Pre-cancerous Growths

At one time it was thought that because leukoplakia or erythroplakia often preceded the development of cancer, removing these areas would prevent cancer from developing. But studies have found that even when these areas are completely removed, people with certain types of erythroplakia and leukoplakia still have a higher chance of developing a cancer in some other area of their mouth. This risk is particularly high if the tissue looks abnormal under the microscope (dysplasia).

One reason surgery for these conditions doesn't help prevent cancer is that the whole lining of the mouth can be considered pre-cancerous. This is called field cancerization, which may be related to the fact that the entire lining has probably been exposed to carcinogens (such as tobacco and alcohol).

Chemoprevention

In recent years, doctors have been testing medicines to help prevent these cancers. This approach, called chemoprevention, is particularly needed for people who have a higher risk of these cancers, such as those with leukoplakia or erythroplakia. For example, isotretinoin (13-cis-retinoic acid) is a drug chemically related to vitamin A (a retinoid). When used by patients with oral cavity or oropharyngeal cancer, it may reduce the risk of developing a second cancer in the head and neck region. Unfortunately, side effects of this medicine limit its use.

Vitamin A supplements are not recommended unless prescribed by a doctor for a specific health problem. High doses of vitamin A do not decrease cancer risk, and may, in fact, raise the risk of some cancers. This is why researchers are studying synthetic (man-made) retinoids, which may be more effective than natural vitamin A for preventing cancer.

Research into other anti-cancer compounds that may be given as oral rinses is now under way. This is discussed further in the section, What's New in Oral Cavity and Oropharyngeal Cancer Research and Treatment?

Can Oral Cavity and Oropharyngeal Cancers Be Found Early?

Many pre-cancers and cancers of the oral cavity and oropharynx can be found early, during routine screening exams by a doctor, dentist, dental hygienist, or by self-exam.

Some early cancers have symptoms that cause patients to seek medical or dental attention (see [How Are Oral Cavity and Oropharyngeal Cancers Diagnosed?](#)). Many doctors and dentists recommend that you look at your mouth in a mirror every month to check for any abnormal areas. Unfortunately, some cancers may not cause symptoms until they've reached an advanced stage or may cause symptoms similar to those caused by a disease other than cancer, such as a toothache.

Regular dental checkups that include an exam of the entire mouth are important in finding oral and oropharyngeal cancers (and precancers) early. The American Cancer Society also recommends that doctors examine the mouth and throat as part of a routine cancer-related checkup.

Along with a normal exam of the mouth and throat, some dentists and doctors may use special dyes and/or lights to look for abnormal areas, especially if you are at higher risk for these cancers. The usefulness of these newer techniques is still being studied.

How Are Oral Cavity and Oropharyngeal Cancers Diagnosed?

Signs and Symptoms of Oral Cavity or Oropharyngeal Cancer

Possible signs and symptoms of these cancers can include:

- a sore in the mouth that does not heal (most common symptom)
- pain in the mouth that doesn't go away (also very common)
- a persistent lump or thickening in the cheek
- a persistent white or red patch on the gums, tongue, tonsil, or lining of the mouth
- a sore throat or a feeling that something is caught in the throat that doesn't go away
- trouble chewing or swallowing
- trouble moving the jaw or tongue
- numbness of the tongue or other area of the mouth
- swelling of the jaw that causes dentures to fit poorly or become uncomfortable
- loosening of the teeth or pain around the teeth or jaw
- voice changes
- a lump or mass in the neck
- weight loss
- persistent bad breath

Many of these signs and symptoms can also be caused by less serious, benign problems, or even by other cancers. It is important to see a doctor or dentist if any of these conditions lasts more than 2 weeks. Remember, the sooner you receive a correct diagnosis, the sooner you can start treatment and the more effective your treatment will be.

If you have any of the signs or symptoms that suggest cancer may be present, your doctor may recommend additional tests.

Tests Used to Find Oral Cavity or Oropharyngeal Cancer

Complete Medical History

As a first step, your doctor will probably ask you questions about symptoms, possible risk factors, and any other medical conditions you may have.

Physical Exam

Your doctor will do a physical exam to look for possible signs of an oral or oropharyngeal cancer (or pre-cancer). These could be bumps or other abnormal areas on your head, face or neck, or problems with the nerves of the face and mouth. The doctor will look at the entire inside of your mouth, and may feel around in it with a gloved finger.

Consultation With a Specialist

If there is a reason to think you might have cancer, your doctor will refer you to a doctor who specializes in these cancers, such as an oral and maxillofacial surgeon or a head and neck surgeon (also known as an ear, nose, and throat (ENT) doctor or an otolaryngologist). This specialist will probably do additional tests.

Complete Head and Neck Exam Including Nasopharyngoscopy, Pharyngoscopy, and Laryngoscopy

The doctor will pay special attention to the head and neck area, being sure to look and feel for any abnormal areas. This will include the lymph nodes of the neck, which will be felt carefully for any signs of cancer.

Because the oropharynx is deep inside the neck and some parts are not easily seen, the doctor may use mirrors or special fiber optic scopes (flexible, lighted, narrow tubes inserted through the mouth or nose) to examine these areas.

Indirect pharyngoscopy and laryngoscopy is the use of small mirrors placed at the back of the mouth to look at the throat, base of the tongue, and part of the larynx (voice box).

Direct laryngoscopy and nasopharyngoscopy uses a fiber optic scope (called an endoscope) to look at areas that can't easily be seen with mirrors, such as the region behind the nose (nasopharynx) and the larynx.

Panendoscopy (Including Laryngoscopy, Esophagoscopy, and Possible Bronchoscopy)

If the chances that a head or neck cancer are present are high, the entire area may be examined more thoroughly, including the oral cavity, oropharynx, larynx, esophagus (tube leading to the stomach), and the trachea and bronchi (breathing passageways that lead to the lungs). This exam, called a panendoscopy, is done in the operating room, while you are under general anesthesia (in a deep sleep). This allows these areas to be looked at more closely.

During this exam, the doctor will use endoscopes to look at the throat, larynx, and esophagus, and possibly the windpipe (trachea) and bronchi. If any tumors are found, the doctor will remove samples to look at under a microscope.

Types of Specimens Used to Diagnose Oral Cavity and Oropharyngeal Cancer

The actual diagnosis of oral and oropharyngeal cancers can only be made by biopsy. A sample of tissue or cells is always needed to confirm that cancer is really present before starting treatment. Several sample procedures may be used, depending on each individual case.

Exfoliative Cytology

In this technique, the doctor scrapes a suspicious area and smears the collected tissue onto a glass slide. The sample is then stained with a dye so the cells can be seen under the microscope. Then, if any of the cells look abnormal, the area can be biopsied. The advantage of this technique is that it is easy, and even minimally abnormal-looking areas can be examined. This can make for an earlier diagnosis and a greater chance of cure if there is cancer. But this method does not detect all cancers. Sometimes it's not possible to tell the difference between cancerous cells and abnormal but non-cancerous cells (dysplasia) with this approach, so a biopsy would still be needed.

Incisional Biopsy

This can be done either in the doctor's office or in the operating room, depending on the location of the tumor and how easy it is to get a good tissue sample. If it can be done in the doctor's office, the area around the tumor will be numbed before the biopsy is taken. When the biopsy can't be done in the doctor's office because the tumor is deep inside the mouth or

throat, it is done in the operating room with the patient under general anesthesia (in a deep sleep). The surgeon uses special instruments through an endoscope to remove small tissue samples.

Fine Needle Aspiration Biopsy

If a patient has a neck mass (or lump) that can be felt, the doctor uses a very thin needle attached to a syringe to withdraw (aspirate) a small amount of tissue from the mass, which is then looked at under a microscope. Fine needle aspiration (FNA) biopsy can be used in several different situations.

Determining the cause of a new neck mass: An FNA biopsy is sometimes used as the first test for someone with a newly found neck mass. The FNA may show that the neck mass is a benign lymph node that has grown in reaction to a nearby infection, such as a sinus or tooth infection. In this case, treatment of the infection is all that is needed.

The FNA may find a benign (non-cancerous) fluid-filled cyst that can be cured by surgery. Even when the FNA results are benign, if the patient has symptoms suggesting cancer, more tests (such as pharyngoscopy and panendoscopy) are needed.

If the FNA finds cancer, the doctor looking at the sample can usually tell what type of cancer it is. If the type of cells seen look like cancers that start in the oral cavity or oropharynx, more exams will be done to search for a source in the oral cavity and oropharynx. If the cancer is a lymphoma (a type of cancer that starts in the lymph nodes), or if it is a cancer that has spread to a lymph node in the neck from a source in the thyroid, lungs, or other distant organs, more tests will be done, and specific treatment for that type of cancer will be given.

Determining the extent of a known cancer: FNA is often done in patients known to have oral or oropharyngeal cancer to find out whether or not the cancer has metastasized, or spread, to lymph nodes in the neck. This information will help the doctor decide if more treatment (such as a neck dissection or radiotherapy) is needed.

Determining if cancer has come back after treatment: FNA may be used in patients whose cancer has been treated by surgery and/or radiation therapy, to find out if a new neck mass in the treated area is scar tissue or a cancer that has come back.

Imaging Tests

Imaging tests may help a doctor make a diagnosis if there is some question about whether a person has cancer, but they are often used to help determine the stage (extent) of the cancer once it has already been found.

Chest X-ray

An x-ray of your chest may be done to see if cancer has spread to your lungs. Unless your cancer is far advanced, it is very unlikely that the cancer will have spread. This x-ray can be done in an outpatient setting. If the results are normal, you probably don't have cancer in your lungs.

Computed Tomography Scan

The computed tomography (CT) scan is a special kind of x-ray that gives detailed, cross-sectional images of your body. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures of the part of your body being studied as it rotates around you. A computer then combines these pictures into images of slices of the part of your body being studied.

After the first set of pictures is taken you may receive an intravenous (IV) injection of a contrast dye. You may also be asked to drink a contrast solution. These help better outline structures in your body. A second set of pictures is then taken.

The solution you drink and the injection may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lie in while the pictures are being taken.

The CT scan provides information about the size, shape, and position of any tumors, and can help find enlarged lymph nodes that might contain cancer.

Magnetic Resonance Imaging Scan

Magnetic resonance imaging (MRI) scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. This produces cross-sectional slices of the body like a CT scanner, but it can also show slices (views) from several angles. As with CT scans, a contrast material might be injected, but this is done less often.

MRI scans take longer than CT scans -- often up to an hour. During the scan, you need to lie still inside a narrow tube, which is confining and can upset people who don't like enclosed spaces. The machine also makes clicking and buzzing noises. Some places provide headphones with music to block this out.

Although MRI scans are very useful for some kinds of cancer, they are rarely used for oral and oropharyngeal cancer.

Positron Emission Tomography Scan

Positron emission tomography (PET) scans involve injecting glucose (a form of sugar) that contains a radioactive atom into the blood. Because cancer cells in the body are growing rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information.

This test is useful to see whether the cancer has spread to lymph nodes. PET scans are also useful when your doctor thinks the cancer may have spread, but doesn't know where. Newer devices combine a CT scan and a PET scan to pinpoint the tumor even better.

Barium Swallow

A barium swallow (also known as an upper GI series) can be used to examine the lining of the upper part of the digestive system, especially the esophagus (the tube connecting the throat to the stomach). Patients getting this test first drink a solution of barium, a chalk-like drink with the consistency of a milk shake. A series of x-ray pictures are then taken.

Because patients with oral and oropharyngeal cancers are at risk for second cancers of the digestive tract, your doctor may order this test to see if there is a cancer in the esophagus. It is also a useful test to see if the cancer may be interfering with normal swallowing.

Other Tests

Blood Tests

There are no blood tests that can diagnose tumors of the oral cavity or oropharynx. However, your doctor may order routine blood tests to help determine your overall health, especially before treatments such as surgery. Such tests can help diagnose malnutrition, low red blood counts (anemia), liver disease, and kidney disease. They may also suggest the possibility of liver metastasis or bone metastasis from an oral cavity or oropharyngeal cancer, which will mean more testing.

Dental Consultation

When radiation therapy will be used as part of the treatment, it is likely you will be asked to see a dentist, who will help with preventive dental care and removing teeth, if necessary, before radiation treatment is started.

If the cancer is located in the jaw or roof of the mouth, then a dentist with special training (a prosthodontist) may be asked to evaluate you. This dentist can make replacements for missing teeth or other structures of the oral cavity to restore your appearance, comfort, and ability to chew, swallow, and speak after treatment. If part of the jaw or roof of the mouth (palate) will be removed with the tumor, the prosthodontist will work to ensure that the replacement artificial teeth and the remaining natural teeth fit together correctly. This can be done with dentures, other types of prostheses, or dental implants.

How Are Oral Cavity and Oropharyngeal Cancers Staged?

Staging is the process of finding out how far a cancer has spread. The outlook for chances of survival (prognosis) for people with cancer depends, to a large extent, on the cancer's stage. The stage of oral cavity and oropharyngeal cancers is one of the most important factors in choosing treatment.

Staging information is based on the results of the physical exam, endoscopy, and imaging tests (CT scan, MRI, chest x-ray, and/or PET scans), which are described in the section How Are Oral Cavity and Oropharyngeal Cancers Diagnosed?.

The TNM Staging System

A staging system is a standard way for doctors to describe and summarize how far a patient's cancer has spread. The most common system used to describe the extent of oral cavity and oropharyngeal cancers is the TNM system of the American Joint Committee on Cancer (AJCC). The TNM system for staging describes 3 key pieces of information:

- **T** indicates the size of the main (primary) **tumor** and which, if any, tissues of the oral cavity or oropharynx it has spread to.
- **N** describes the extent of spread to nearby (regional) lymph **nodes**. Lymph nodes are small bean-shaped collections of immune system cells that are important in fighting infections. Cells from oral cavity or oropharyngeal cancers can travel to lymph nodes in the neck area.

- **M** indicates whether the cancer has spread (**metastasized**) to other organs of the body. (The most common site of spread is to the lungs. The next most common sites are the liver and bones.)

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

- The numbers 0 through 4 indicate increasing severity.
- The letter X means "cannot be assessed" because the information is not available.

T categories for cancers of the lip, oral cavity, and oropharynx:

- **TX:** primary tumor cannot be assessed; information not known
- **T0:** no evidence of primary tumor
- **Tis:** carcinoma in situ. This means the cancer is still within the epithelium (layer of cells lining the oral cavity and oropharynx) and has not yet penetrated to a deeper layer of oral or oropharyngeal tissue
- **T1:** tumor is 2 cm (about $\frac{3}{4}$ inch) across or smaller
- **T2:** tumor is larger than 2 cm across, but smaller than 4 cm (about $1\frac{1}{2}$ inch)
- **T3:** tumor is larger than 4 cm across
- **T4 (for oral cavity and oropharyngeal cancers):** tumor invades nearby structures (such as bone, connective or muscle tissue of the neck, deep muscle of the tongue, skin, sinuses, or the larynx)
- **T4 (for lip cancer):** tumor invades nearby structures (such as bones, floor of mouth, or skin of face)

N categories:

- **NX:** nearby lymph nodes cannot be assessed; information not known
- **N0:** no spread to nearby lymph nodes
- **N1:** the cancer has spread to one lymph node on the same side of the head or neck as the primary tumor, which is smaller than 3 cm (about $1\frac{1}{4}$ inch) across
- **N2** includes 3 subgroups:
 - N2a:** the cancer has spread to one lymph node on the same side as the primary tumor, which is larger than 3 cm across but smaller than 6 cm (about $2\frac{1}{2}$ inches)
 - N2b:** the cancer has spread to multiple lymph nodes on the same side as the primary tumor, but none are larger than 6 cm across
 - N2c:** the cancer has spread to one or more lymph nodes on both sides of the neck or on the side opposite the primary tumor, but none are larger than 6 cm across
- **N3:** the cancer has spread to a lymph node that is larger than 6 cm across

M categories:

- **MX:** presence of distant spread cannot be assessed; information not known
- **M0:** no distant spread
- **M1:** the cancer has spread to distant sites outside the head and neck region (for example, the lungs)

Stage Grouping

Once the T, N, and M categories have been assigned, this information is combined by a process called stage grouping to assign an overall stage of 0, I, II, III, or IV. Stage IV is further divided into A, B, and C.

Stage 0

Tis, N0, M0: The cancer is "in situ". It is still confined to the outer layer of oral or oropharyngeal tissue; it has not yet invaded into a deeper layer and has not spread to nearby structures, lymph nodes, or distant sites.

Stage I

T1, N0, M0: The tumor is 2 cm (about ¾ inch) across or smaller and has not spread to nearby structures, lymph nodes, or distant sites.

Stage II

T2, N0, M0: The tumor is larger than 2 cm across but smaller than 4 cm and has not spread to nearby structures, lymph nodes, or distant sites.

Stage III

One of the following applies:

T3, N0, M0: The tumor is larger than 4 cm across, but it hasn't invaded nearby structures or spread to the lymph nodes or distant sites

T1, N1, M0 or T2, N1, M0 or T3, N1, M0: The tumor is any size and hasn't invaded nearby structures. It has spread to one lymph node on the same side of the head or neck, which is smaller than 3 cm across. The cancer hasn't spread to distant sites.

Stage IVA

One of the following applies:

T4, N0, M0 or T4, N1, M0: The tumor is any size but invades nearby structures. It has either not spread to the lymph nodes or has spread to one lymph node, on the same side of the head or neck, which is smaller than 3 cm across. The cancer hasn't spread to distant sites.

Any T, N2, M0: The tumor is any size and may or may not invade nearby structures. It has spread to one of the following:

- one lymph node on the same side of the head and neck (between 3 and 6 cm across)
- one lymph node on the opposite side of the head and neck (less than 6 cm across)
- more than one lymph node (on either side, and all smaller than 6 cm across)

The cancer hasn't spread to distant sites.

Stage IVB

Any T, N3, M0: The tumor is any size and may or may not invade nearby structures. It has spread to one or more lymph nodes larger than 6 cm across, but it hasn't spread to distant sites.

Stage IVC

Any T, Any N, M1: The tumor is any size, and it may or may not have spread to lymph nodes. It has spread to distant sites, most commonly the lungs.

Recurrent (Relapsed) Cancer

This is not an actual stage in the TNM system. Recurrent (relapsed) disease means that the cancer has come back (recurred) after treatment. Recurrent oral cavity or oropharyngeal cancer may return in the mouth or throat (local recurrence), in the lymph nodes (regional relapse) or in another part of the body (distant recurrence, usually in the lungs).

Talk with your doctor, if you have any questions about the stage of your cancer or how it affects your treatment.

Relative 5-year Survival Rates by Stage

The following survival statistics come from the AJCC Cancer Staging Manual (6th Ed).

There are some important points to note about these numbers:

- The *5-year survival rate* refers to the percentage of patients who live *at least 5 years* after being diagnosed. Many of these patients live much longer than 5 years after diagnosis. Five-year *relative* survival rates assume that some people will die of other causes and compares the observed survival of people with cancer with that expected for people without cancer. That means that relative survival only includes deaths from the cancer. They are considered to be a more accurate way to describe the outlook for patients with a particular type and stage of cancer.
- These numbers were derived from patients treated between 1985 and 1991. While they are among the most current numbers we have available, they represent people who were first diagnosed and treated at least 15 to 20 years ago. Improvements in

- treatment since then mean that the survival rates for people now being diagnosed with these cancers are likely to be higher.
- While survival statistics can sometimes be useful as a general guide, they may not accurately represent any one person's prognosis. A number of other factors, including other tumor characteristics and a person's age and general health, can also affect outlook. Your doctor is likely to be a good source as to whether these numbers may apply to you, as he or she is familiar with the aspects of your particular situation.

Lip

Stage	5-Year Relative Survival Rate
I	83%
II	73%
III	62%
IV	47%

Oral Cavity

Stage	5-Year Relative Survival Rate
I	68%
II	53%
III	41%
IV	27%

Oropharynx

Stage	5-Year Relative Survival Rate
I	57%
II	54%
III	43%
IV	30%

How Are Oral Cavity and Oropharyngeal Cancers 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.

The first part of this section describes the various types of treatments used for oral cavity and oropharyngeal cancers. This is followed by a description of the most common approaches used for these cancers based on their stage and where they started.

Making Treatment Decisions

The main treatment options for people with oral and oropharyngeal cancers are surgery, radiation therapy, chemotherapy, and newer targeted therapies. These may be used either alone or in combination, depending on the stage and location of the tumor.

After the cancer is found and staged, your doctor will discuss treatment choices with you. It is important to take time and think about all of your choices. When you choose a treatment plan, consider your overall health, the type and stage of the cancer, the chances of curing the disease, and the impact of the treatment on functions like speech, chewing, and swallowing.

It is often a good idea to seek a second opinion. A second opinion can provide more information and help you feel more confident about the treatment plan you choose.

Surgery

Several operations are commonly used to treat oral cavity and oropharyngeal cancers. Depending on where the cancer is and its stage, one or more of the following procedures may be used to remove the cancer, and to help restore the appearance and function of the tissues affected by the cancer or its treatment.

Primary Tumor Resection

This operation removes (resects) the entire tumor and an area of normal-appearing tissue surrounding it. Removing some normal tissue decreases the chance of leaving any cancer behind. The primary tumor can be removed in several different ways -- through the mouth, for instance, if it is small and easy to reach. Sometimes with larger tumors, especially those involving the oropharynx, the cancer is removed through an incision in the neck or by cutting the jaw bone with a saw to provide access to the tumor (mandibulotomy).

Full or Partial Mandible (Jaw Bone) Resection

If the doctor can easily move a tumor in the mouth when feeling it and there is no suggestion that it has invaded the jaw bone, a simple primary tumor resection, without removing any bone tissue, is recommended. If there is limited tumor movement, presumably because it has grown into the jaw bone, but no evidence of jaw bone invasion on x-ray, then a partial-

thickness mandibular resection is done (where a piece of jaw bone is removed, but overall the bone stays intact). If the x-ray, shows the tumor has grown into the jaw bone, a whole portion of the mandible will need to be removed

Maxillectomy

If a cancer involves the hard palate (front part of the roof of the mouth), all or part of the involved bone (maxilla) will need to be removed. This operation is called a maxillectomy or partial maxillectomy. The defect in the roof of the mouth resulting from this operation can be filled with a special denture called a prosthesis. This is created by a prosthodontist, a dentist with special training.

Mohs Micrographic Surgery (For Some Cancers of the Lip)

Some cancers that involve the lip may be removed by Mohs surgery, also known as micrographic surgery. In this method, the tumor is removed in very thin slices. Each slice is looked at right away under the microscope to see if there are cancer cells. The surgeon continues to remove more slices until there are no cancer cells seen. This method can reduce the amount of normal tissue removed with the tumor, which limits the change in appearance the surgery causes.

Laryngectomy (Removal of the Voice Box)

Very rarely, surgery to remove large tumors of the tongue or oropharynx may also require removing tissue that a person needs to swallow normally. As a result, food may enter the windpipe (trachea) and reach the lungs, where it can cause serious pneumonia. When this is a significant risk, sometimes the voice box (larynx) is removed together with the primary tumor. With removal of the voice box, the windpipe is attached to the skin of the neck as a hole (stoma), which the patient will breathe through (instead of breathing through the mouth or nose). Losing one's voice box does not necessarily mean that one loses the ability to talk. There are several ways to restore one's voice. See the American Cancer Society document *Laryngeal and Hypopharyngeal Cancer* to find out more about voice restoration.

Neck Dissection

Cancers of the oral cavity and oropharynx often spread to the lymph nodes in the neck. Depending on the stage and exact location of the cancer, it may be necessary to remove these lymph nodes by an operation called a neck dissection. The goal is to remove lymph nodes proven or likely to contain cancer.

There are several types of neck dissection procedures, and they differ in how much tissue is removed from the neck. The amount of tissue removed depends on the primary cancer's size and extent of spread to lymph nodes.

- In a *partial or selective neck dissection* only a few lymph nodes are removed.
- For a *modified radical neck dissection* most lymph nodes on one side of the neck between the jaw bone and collarbone, as well as some muscle and nerve tissue are removed.
- In a *radical neck dissection* nearly all nodes on one side, as well as even more muscles, nerves, and veins are removed.

The most common side effects of any neck dissection are numbness of the ear, weakness in raising the arm above the head, and weakness of the lower lip. These side effects are caused by injury during the operation to certain nerves that supply these areas. After a selective neck dissection, the weakness of the arm and lower lip usually resolve after a few months. But if either nerve is removed as part of a radical neck dissection or because of involvement with tumor, then the weakness will be permanent. After any neck dissection procedure, physical therapists can teach the patient exercises to improve neck and shoulder movement.

Pedicle or Free Flap Reconstruction

The narrow zone of normal tissue removed along with small tumors usually does not need reconstruction. But removing larger tumors may cause defects in the mouth, throat, or neck that will need to be repaired. Sometimes a thin slice of skin, taken from the thigh, can be used to resurface a small defect.

To repair a larger defect, a piece of muscle with or without skin may be rotated from an area close by, such as the chest (pectoralis major pedicle flap) or upper part of the back (trapezius pedicle flap). Thanks to advances in microvascular surgery (sewing together small blood vessels under a microscope), surgeons have many more options for reconstructing the oral cavity and oropharynx. Tissue from other areas of the body, such as the intestine, arm muscle, abdominal muscle, or lower leg bone, may be used to replace parts of the mouth, throat, or jaw bone. Before you have extensive head and neck surgery, it is a good idea to ask the surgeon about your options for reconstructive surgery.

Tracheostomy

If the cancer is blocking the throat and is too large to remove completely, a hole (tracheostomy) may be opened in the windpipe and in the front of the neck to bypass the tumor and allow the person to breathe more comfortably. If a lot of swelling is expected after the tumor is removed, the doctor may want to do a temporary tracheotomy (incision of the trachea) to allow the person to breathe more easily until the swelling goes down.

Gastrostomy Tube

Cancers in the oral cavity and oropharynx may prevent a person from swallowing enough food for adequate nutrition. It is sometimes necessary to place a feeding (gastrostomy) tube through the skin and muscle of the abdomen directly into the stomach. Gastrostomy is a minor surgical procedure. It can be placed by a radiologist, who can put the tube directly into the stomach. Another way is for a doctor to put the tube into the stomach through the mouth and then it is "snared" by a device that goes into the stomach. Usually this is aided by a doctor who is looking into the stomach through the mouth with a device called a gastroscope. The tube can be used to feed a patient indefinitely. The feeding is done with special liquid nutrients that are dripped through the tube.

If the swallowing problem is thought to be temporary, then a nasogastric feeding tube (an "NG tube") may be placed through the nose, down the esophagus into the stomach. Again, feeding is done with special liquid nutrients that are dripped through the tube.

In either case, the patient and family are taught how to use the tube. After the patient goes home, home health nurses usually visit to make sure that the patient is comfortable with tube feedings.

Dental Extraction and Implants

When radiation treatment is planned, a dental evaluation is mandatory. Depending on the radiation plan and condition of the patient's teeth, it may be necessary to remove some or even all of the teeth, as they are very likely to cause major problems (such as serious infections) if left in and exposed to radiation. The teeth may be removed either by the head and neck surgeon or an oral surgeon.

When part of the jaw bone is removed and reconstructed with bone from another part of the body, the surgeon may place dental implants (hardware to which prosthetic teeth can be attached) in the bone. This can be done either at the same time the mandible is reconstructed or at a later date.

Radiation Therapy

Radiation therapy uses high-energy x-rays or particles to destroy cancer cells or slow their rate of growth. Radiation therapy can be used in several situations for oral and oropharyngeal cancers:

- It can be used as the main treatment for small cancers.
- Patients with larger cancers may need both surgery and radiation therapy or a combination of radiation therapy and chemotherapy or a "targeted" agent (see below).

- After surgery, radiation therapy can be used, either alone or with chemotherapy, as an additional (adjuvant) treatment to kill very small deposits of cancer that cannot be seen and removed during surgery.
- Radiation therapy can also be used to relieve symptoms of the cancer, such as pain, bleeding, trouble swallowing, and problems caused by metastases to bones.

External Beam Radiation Therapy

The most common way to give radiation for these cancers is to carefully focus a beam of radiation from a machine outside the body. This is known as external beam radiation therapy. To reduce the risk of side effects, doctors carefully figure out the exact dose needed and aim the beam as accurately as they can to hit the carefully outlined target. External beam radiation therapy usually means having treatments 5 days a week for 6 to 7 weeks.

Newer radiation approaches, such as giving radiation twice a day (accelerated fractionation or hyperfractionation) or using more focused techniques like three-dimensional conformal radiation therapy (3D-CRT) or intensity modulated radiation therapy (IMRT), are now being studied as well. These are discussed in more detail in the section, *What's New in Oral Cavity and Oropharyngeal Cancer Research and Treatment?*.

Brachytherapy

Another way radiation treatment is given is by placing radioactive materials directly into or near the cancer. This method is called internal radiation, interstitial radiation, or brachytherapy. Different types of brachytherapy may be used.

High-dose rate (HDR) brachytherapy: For this technique, hollow catheters (thin tubes) are placed into or around the tumor in the operating room. This may require general anesthesia (where the patient is in a deep sleep). They are left in place for several days while the patient stays in the hospital. The catheters themselves are not radioactive. The actual radiation treatment takes place each day in a special room in the hospital. The catheters are hooked up to a machine that inserts radioactive materials into them for a short time and then removes them. Patients are not radioactive in between or after treatments. The catheters are removed before the patient goes home.

Low-dose rate (LDR) brachytherapy: This type of brachytherapy may be done in one of two ways.

In the *temporary* approach, the doctor implants thin, hollow, plastic tubes into and around the tumor. These tubes are loaded with tiny radioactive pellets (called "seeds") that remain in place for a few days to kill the cancer. The patient stays in the hospital during treatment.

Although the radiation travels a very short distance, the length of time that visitors, nurses, and other caregivers can spend with the patient will be limited as a precaution. The seeds and the tubes are removed before the patient goes home. The patient is not radioactive after treatment.

Permanent brachytherapy is rarely used to treat these cancers any more. This technique implants small radioactive pellets (about the size and shape of a grain of rice) directly into the tumor. The pellets give off low levels of radioactivity for several weeks and eventually lose their strength. The pellets themselves are left in place permanently and rarely cause any problems.

Sometimes, both internal and external beam radiation therapy are used together.

Chemotherapy

Chemotherapy is the use of anti-cancer drugs that are given into a vein or taken by mouth. These drugs enter the bloodstream and can reach cancer that has spread to organs beyond the head and neck. It may be used in several different situations:

- Chemotherapy may be combined with radiation therapy instead of using surgery to control larger cancers that are confined to the head and neck region. Several recent studies have found this resulted in local control rates close to those of surgery plus radiation.
- Chemotherapy is sometimes given to shrink the cancer before surgery or radiation treatment. This is called neoadjuvant or induction chemotherapy. In some cases this makes it possible to use less radical surgery and resect (remove) less tissue. However, most studies have shown that neoadjuvant chemotherapy has little effect on the cancer cure rate.
- Chemotherapy (often together with radiation) has also been used to reduce the severity of symptoms of cancers of the head and neck that are too large to be completely removed and which radiation treatment alone has not been able to control.

The chemotherapy drugs used most often for cancers of the oral cavity and oropharynx are:

- cisplatin
- 5-fluorouracil (5-FU)
- carboplatin
- paclitaxel
- docetaxel
- methotrexate
- ifosfamide
- bleomycin

These drugs may be used by themselves or in combination to have a stronger effect. The most commonly used combination is cisplatin and 5-FU. It is more effective than either drug alone in temporarily shrinking cancers of the oral cavity and oropharynx. However, cancers become resistant to these drugs over time, and no improvement in overall survival has been shown.

Several studies have shown that chemoradiotherapy (chemotherapy given at the same time as radiation) helps shrink tumors in some patients with head and neck cancer. Some doctors prefer to give the radiation and chemotherapy before surgery. However, the side effects can be substantial and may be unacceptable for some patients.

Several recent studies of patients with cancers too advanced for surgery, but not widespread, showed chemotherapy and radiation given together yielded a better outcome than radiation alone. The cancer was less likely to come back and patients lived longer. But this combined approach to treatment is hard for people who are in poor health to tolerate. Their history of smoking, drinking, and poor nutrition may cause them to die of other problems such as pneumonia, emphysema, or heart disease.

Targeted Therapy

In recent years, new drugs that target specific parts of cancer cells have been developed. Their side effects are different (and generally less severe) than those seen with standard chemotherapy drugs.

One target on oral and oropharyngeal cancer cells is called epidermal growth factor receptor (EGFR). Many oral and oropharyngeal cancer cells have too many copies of EGFR, which helps them grow faster and become more resistant to radiation or chemotherapy.

A drug called *cetuximab* (*Erbix*), which blocks EGFR, has been shown to help keep tumors under control longer. It can be used with radiation in people with advanced oral and oropharyngeal cancers. Most doctors have used chemotherapy with the radiation; it isn't yet clear whether using cetuximab with radiation is better. Cetuximab is also used in people with widespread cancer that can't be treated with radiation and that no longer responds to chemotherapy.

This drug is given by infusion into a vein (IV). It can cause allergic reactions while being given, which in rare cases can be serious. The other main side effect is an acne-like rash on the face, upper chest, and back, which usually occurs within a few weeks of starting treatment.

Several other drugs that target EGFR are now being studied as well, some of which are already being used to treat other cancers (see [What's New in Oral and Oropharyngeal Cancer Research and Treatment?](#)).

Coping With the Side Effects and Complications of Treatment

Treatment of oral cavity and oropharyngeal cancers can lead to side effects, depending on the type and intensity of therapy being used.

Radiation Side Effects

Radiation can cause several short-term side effects. These include skin changes like a sunburn or suntan that slowly fades away, hoarseness, and redness and soreness of the mouth and throat. The latter may make it hard to eat during the treatment, which might require supplemental liquid feeding through a tube placed into the stomach (gastrostomy; see the surgery section). Taste buds are affected, and the sense of taste is often lost, sometimes partially and sometimes completely, for a few months.

Radiotherapy may also cause long-term or permanent side effects. The mouth may become permanently dry because the salivary glands are damaged. A dry mouth promotes tooth cavities. Careful oral hygiene and treatment with fluoride, however, may help prevent this problem. Newer radiotherapy techniques such as intensity modulated radiation therapy (IMRT) make it possible to aim radiation more precisely at the tumor or nodes and thereby spare normal tissues like the salivary glands, which may help reduce this side effect. (See *What's New in Oral Cavity and Oropharyngeal Cancer Research and Treatment?*) Recent research also suggests that the drug amifostine can help reduce this side effect by limiting radiation damage to salivary glands. The drug is given into a vein a few minutes before each radiation treatment.

Jaw bone damage called *osteoradionecrosis* may also occur, particularly after tooth infection or trauma and be hard to treat. Its main symptom is bone pain but the bone may also break. Sometimes the fractured bone heals by itself, but in some cases the damaged bone will have to be treated surgically.

Radiation side effects are likely to be more severe in people who are getting chemotherapy at the same time. These people also have to contend with the side effects of the chemotherapy itself (see below), which can make this treatment hard to tolerate. For this reason, it's important that people getting both chemotherapy and radiation are in relatively good health before starting treatment, that they understand the potential for serious side effects, and that they are treated at a medical center with a lot of experience with this approach.

Surgery Side Effects

If the surgery is not too involved, the only symptom may be some pain afterward, which will go away. In some cases surgery may be very complicated, in which case side effects may include infection, wound breakdown, problems with eating and speaking, or on very rare

occasions even death during or shortly after the procedure. It also can be disfiguring. The surgeon's skill is very important in minimizing these problems, while removing all of the cancer.

Impact of laryngectomy: Laryngectomy, the surgery that removes the voice box, leaves a person without the normal means of speech. There are several ways to restore one's voice. See the American Cancer Society document *Laryngeal and Hypopharyngeal Cancer* to find out more about voice restoration.

After a laryngectomy, breathing is done through a stoma, or opening, placed in the front of the lower neck. Your health care team will teach you how to care for and adjust to your stoma. Since the air can't be purified by the nose's natural filter, a stoma cover is needed. Besides catching dust and particles, the stoma cover hides the mucus that the stoma secretes.

Impact of facial bone removal: Some cancers of the head and neck are treated by operations that remove part of the facial bone structure. Because the changes that result are so visible, they can be devastating. Surgery on the jaw, roof of the mouth, or tongue can also affect speech.

Recent advances in facial prostheses and in plastic (reconstructive) surgery now give many people a more normal look and clearer speech. Ears and noses can be made out of plastic, tinted to match the skin, and attached to the face. All of these things can be a great help to a person's self-esteem.

Chemotherapy Side Effects

Chemotherapy drugs work by attacking 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, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are taken. These side effects can include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- increased chance of infections (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelet counts)
- fatigue (due to low red blood cell counts)

These side effects are usually short-term and go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. A few side effects that are specific to certain drugs, such as some loss of kidney function or hearing, may persist.

Impact of Side Effects on Quality of Life

Everyday life can be very disturbed by treatment of these cancers. Many studies have found that the patient's quality of life tends to get worse in the first few months after treatment. After that, however, if the patient has given up smoking and drinking alcohol, things tend to get better. Within a year, many patients are feeling reasonably well and happy.

Clinical Trials

You have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is deciding which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you. Clinical trials are one way to get state-of-the-art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

What Are Clinical Trials?

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

The Purpose of Clinical Trials

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)

- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Phases of Clinical Trials

There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

Phase II clinical trials: These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III clinical trials: Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) will get the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

Phase IV clinical trials: Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

What It Will Be Like to Be in a Clinical Trial

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were treated outside of a clinical trial. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

Deciding to Enter a Clinical Trial

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason.

Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

How Can I Find Out More About Clinical Trials That Might Be Right for Me?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at <http://clinicaltrials.cancer.org>.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know*. You can read this on the Web site, www.cancer.org, or have it sent to you by calling 1-800-ACS-2345.

Complementary and Alternative Therapies

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These methods can include vitamins, herbs, and special diets, or methods such as acupuncture or massage—among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if a non-standard treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- What does my doctor know/think about these methods? Should I tell the doctor that I'm thinking about trying them?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" methods?
- Where can I find out more about these treatments?

The Terms Can Be Confusing

Not everyone uses these terms the same way, so it can be confusing. The American Cancer Society uses *complementary* to refer to medicines or methods that are used *along with* your regular medical care. *Alternative* medicine is a treatment used *instead of* standard medical treatment.

Complementary Methods

Complementary methods, for the most part, are not presented as cures for cancer. Most often they are used to help you feel better. Some methods that can be used in a complementary way are meditation to reduce stress, acupuncture to relieve pain or aromatherapy or peppermint tea to relieve nausea. There are many others. Some of these methods are known to help, while others have not been tested. Some have been proven not to be helpful. A few have even been found harmful. However, some of these methods may add to your comfort and well-being.

There are many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

Alternative Methods

Alternative methods are those that are used instead of standard medical care. These treatments have not been proven safe and effective in clinical trials. Some of these methods may even be dangerous and some have life-threatening side effects. The main danger with trying any of these is that you may lose the chance to benefit from standard treatment. Delays or interruptions in your standard medical treatment may give the cancer more time to grow. Most of these methods are not covered by insurance.

Deciding What to Do

It is easy to see why people with cancer may consider alternative methods. You want to do all you can to fight the cancer. Sometimes mainstream treatments such as chemotherapy can be hard to take, or they may no longer be working.

Sometimes people suggest that their method can cure your cancer without having serious side effects, and it's normal to want to believe them. But the truth is that most non-standard methods of treatment have not been tested and proven to be effective for treating cancer. As you consider your options, here are 3 important steps you can take:

- Talk to your doctor or nurse about any method you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative methods in general and to learn more about the specific methods you are thinking about.

Red Flags

You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

The Decision Is Yours

Decisions about how to treat or manage your cancer are always yours to make. If you are thinking about using a complementary or alternative method, be sure to learn about the method and talk to your doctor about it. With reliable information and input from your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment Options by Stage

The type of treatment your doctor will recommend depends on the tumor site and how far the cancer has spread. This section summarizes options usually considered for each stage of oral cavity or oropharyngeal cancer. These are general comments about the treatment, because the approach to each site may be different.

Stage 0 (Carcinoma In Situ)

Although cancer in this stage has not become invasive, it does have the potential to do so. The usual treatment is surgical stripping or thin resection (removing the top layers of tissue along with a small margin of normal tissue). Close follow-up for recurrence is important. Recurrent carcinoma in situ that cannot be controlled with resection may require radiation therapy. About 95% to 100% of patients at this stage survive long-term without the need for significant surgery of their oral cavity or oropharynx. It is important for these patients to realize that continuing to smoke increases the risk that a new cancer will develop.

Stages I and II

Most patients with stage I or II oral cavity and oropharyngeal cancer can be successfully treated with either surgery or radiation therapy. Both approaches work equally well in treating these cancers. The choice of treatment is influenced by the expected side effects.

Lip: Lip cancer is generally treated with surgery, including Mohs surgery. Radiation therapy or more extensive surgery may be used if the tumor turns out to be larger than expected. If needed, special reconstructive surgery can help correct the defect in the lip.

Radiation alone may also be used as the first treatment. This can be either external beam or brachytherapy (or sometimes a combination of the two). Surgery may be used if radiation doesn't completely get rid of the tumor.

If the tumor is thick, the surgeon may remove and examine lymph nodes in the neck.

Floor of the mouth: Surgery is preferred if it can be done because of possible bone damage from radiation. If the cancer does not appear to have been completely removed by surgery, radiation may be added. This cancer readily spreads to neck lymph nodes. Surgery (neck dissection) may be recommended to remove these. Usually, the surgeon will remove lymph nodes from the side of the neck nearest the tumor. But if the tumor is in the middle, then lymph nodes on both sides of the neck will need to be removed.

Front of tongue: Surgery is preferred for small tumors and radiation for larger ones, especially if cutting these out would impair speech or swallowing. If surgery could not remove all the cancer, radiation may be added. For larger tumors, surgery or radiation to treat neck lymph nodes will likely be recommended.

Buccal mucosa (cheek): These cancers are usually treated with surgery. Radiation may be recommended instead. If surgery is used, radiation may be added. If the tumor is large, the neck lymph nodes will be removed as well.

Lower gums: Cancer in the lower gums is usually treated with surgery, which may include removing part of the mandible (jaw bone). Radiation may be added if all of the cancer could not be removed. Radiation may be used as the main treatment, but it carries a risk of damage to the jaw bone. Surgery to remove the neck nodes is often recommended.

Upper gums and hard palate: Cancers in the upper gum or hard palate (the front of the roof of the mouth) are also usually managed with surgery. Radiation may be added as well if needed. Lymph nodes in the neck may be removed.

Back of tongue: Radiation is generally preferred because surgery would cause more problems with speech and swallowing, although surgery is used in some cases. The lymph nodes in the neck generally need to be treated as well.

Soft palate (back of the roof of the mouth): Because surgery would probably interfere with speech and swallowing, radiation is often the preferred treatment. Radiation may also be given to the neck. If surgery is used as the first treatment, then the neck nodes also might be removed.

Tonsils: Although either surgery or radiation may be used with equal benefit, radiation is generally preferred because there are fewer side effects. The neck lymph nodes may also

need the same kind of treatment: surgical removal for patients treated with surgery or radiation to the neck for those treated with radiation.

Stages III and IV

More advanced oral cavity and oropharyngeal cancers generally require combined therapy of either surgery and radiation, or radiation and either chemotherapy or cetuximab. The effect of combining radiation with both chemotherapy and cetuximab is also being studied. The choice of treatment is influenced by the expected side effects and the patient's current health status.

Surgery usually includes a neck dissection because of the high risk of lymph node metastasis. Radiation therapy often is required after surgery, particularly if the tumor has spread to the lymph nodes. The amount of tissue removed depends on the extent of cancer, and the method of reconstruction depends on the surgical defect created.

Primary tumors that are too large to be completely removed by surgery are often treated with radiation, either alone or with chemotherapy. Another option may be to use cetuximab along with the radiation.

Cancers that have already spread to other parts of the body are usually treated with either single-drug or combined chemotherapy. Other treatments such as radiation may also be used to help relieve symptoms from the cancer or to help prevent problems from occurring.

Clinical trials are looking at different ways of combining radiation and chemotherapy with or without cetuximab or other new agents to improve survival and quality of life, and reduce the need for radical resection of advanced oral cavity and oropharyngeal cancers.

Recurrent Oral Cavity or Oropharyngeal Cancer

For cancers that come back after treatment, the options will depend on the location and size of the cancer, what treatments have already been used, and on the person's general health.

If the cancer comes back in the same area and radiation therapy was used as the first treatment, surgery is often the preferred option if possible. Usually, external beam radiation therapy cannot be repeated in the same site except in selected cases. However, brachytherapy can often be used to control the cancer if it has come back where it started. If surgery was used first, surgery, radiation therapy, or a combination of these may be considered.

If the cancer comes back in a distant area, chemotherapy is the preferred form of treatment. Although chemotherapy can shrink some cancers for a time, the response often does not last long. Chemotherapy has not been shown to improve survival rates, but the temporary tumor response may help relieve some symptoms.

Clinical trials are also testing new combinations of treatments in people whose cancer recurs, and may be a good option.

More Treatment Information

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

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What Should You Ask Your Doctor About Oral Cavity and Oropharyngeal Cancers?

As you cope with cancer and cancer treatment, we encourage you to have honest, open discussions with your doctor. Feel free to ask any question that's on your mind, no matter how small it might seem. Here are some questions you might want to ask. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions.

- What kind of oral cavity or oropharyngeal cancer do I have?
- Has my cancer spread beyond the main (primary) site?
- What is the stage of my cancer? What does the stage mean in my case?
- What treatment choices do I have? Which do you recommend? Why?
- Based on what you've learned about my cancer, what are my chances for long-term survival?
- What side effects can I expect from my treatment?
- What are the other risks of treatment?
- How long will it take me to recover from treatment?
- When can I go back to work after treatment?
- Will I need reconstructive surgery or a prosthesis after treatment?
- What are the chances that my cancer will recur?
- Does one type of treatment reduce the risk of recurrence more than another does?
- What should I do to be ready for treatment?
- Should I get a second opinion?

In addition to these sample questions, be sure to write down some of your own. For instance, you may want to ask about clinical trials for which you may qualify.

What Happens After Treatment for Oral Cavity and Oropharyngeal Cancers?

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. You can learn more about what to look for and how to learn to live with the possibility of cancer coming back in the American Cancer Society document, *Living with Uncertainty: The Fear of Cancer Recurrence*, available at 1-800-ACS-2345.

Follow-up Care

After your treatment is over, it is very important to keep all follow-up appointments. This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Patients with cancer of the oral cavity or oropharynx may develop recurrences or new cancers in the head and neck area or lungs. Therefore, they must be followed closely after treatment. Recurrences happen most often in the first 2 years after treatment, so patients are usually examined about every other month during the first year after treatment, every few months during the second year, and then once or twice a year after that. Chest x-rays and other imaging tests may be used to watch for a recurrence or for a new cancer.

With improvements in surgery and radiation therapy, the ability to control a patient's main cancer mass has greatly improved. However, development of second cancers in the head and neck remains an important risk. Drugs called chemopreventive agents are being tested to see if they can reduce the risk of second cancers.

About 1 out of 3 patients who have had radiation in the neck area will have damage to the thyroid gland that results in low thyroid hormone levels (hypothyroidism). This may cause chronic tiredness, which can be treated by taking a pill containing thyroid hormone each day. Blood tests to check thyroid function may be part of the post-treatment follow-up.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. 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.

Speech and Swallowing Therapy

After surgery or other treatment for oral cavity or oropharyngeal cancer, a speech pathologist may help if you have problems speaking or swallowing. These experts are knowledgeable about speech and swallowing problems.

A dietitian may help in choosing foods that are more palatable if the mouth is dry and taste is lost. The doctor may recommend a saliva substitute as well.

Seeing a New Doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

It is also important to keep medical insurance. Even though no one wants to think of their cancer coming back, it is always a possibility. If it happens, the last thing you want is to have to worry about paying for treatment. Should your cancer come back the American Cancer Society document, *When Your Cancer Comes Back: Cancer Recurrence* gives you information on how to manage and cope with this phase of your treatment. You can get this document by calling 1-800-ACS-2345.

Lifestyle Changes to Consider During and After Treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also 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 begin this process during cancer treatment.

Make Healthier Choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes *today* that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than *now* to take advantage of the

motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. 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's Quitline[®] tobacco cessation program at 1-800-ACS-2345.

Diet and Nutrition

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

Rest, Fatigue, Work, and Exercise

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any program of physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that you're not doing it alone. Having family or friends involved when starting a new exercise 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, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the publication, "Cancer Related Fatigue and Anemia Treatment Guidelines for Patients.")

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 1 physical activity for 30 minutes or more on 5 days or more of the week.

How About Your Emotional Health?

Once your treatment ends, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for

instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. 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 is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not to 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-ACS-2345 and we can put you in touch with an appropriate group or resource.

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally.

What Happens if Treatment Is No Longer Working?

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can

estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called "palliative" treatment.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this can be given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. 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. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This 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.

What's New in Oral Cavity and Oropharyngeal Cancer Research and Treatment?

Important research into oral and oropharyngeal cancers is taking place in many university hospitals, medical centers, and other institutions around the country. Each year, scientists find out more about what causes the disease, how to prevent it, and how to improve treatment.

DNA Changes

A great deal of research is being done to learn what DNA changes are responsible for causing cells of the oral cavity and oropharynx to become cancerous.

One of the changes often found in DNA of oral cancer cells is a mutation of the p53 gene. The protein produced by this gene normally works to prevent cells from growing too much and helps to destroy cells with too much damage for the cells to repair. Changes in the p53 gene can lead to increased growth of abnormal cells and formation of cancers. Recent studies suggest that tests to detect these p53 gene changes may allow oral and oropharyngeal tumors to be found early. These tests may also be used to better define surgical margins (area of normal cells after the tumor is removed) and to determine which tumors are most likely to respond to surgery or radiation therapy.

Another DNA change found in some oral cancer cells is the presence of DNA from a human papilloma virus (HPV). Some parts of the HPV DNA instruct the cells to make proteins that inactivate the p53 protein, which may allow the cancer cells to grow and divide. Studies are looking at whether tests to detect HPV DNA may help in diagnosing these cancers.

Chemoprevention

As mentioned in the section, *Can Oral Cavity and Oropharyngeal Cancers Be Prevented?*, doctors are looking for medicines to help prevent these cancers, particularly in people at increased risk, such as those with leukoplakia or erythroplakia. Isotretinoin (13-cis-retinoic acid), a drug related to vitamin A (a retinoid), may reduce the risk of developing a second cancer in the head and neck region, but side effects of this medicine limit its use.

Several other compounds are now being tested to help prevent these cancers.

Nonsteroidal anti-inflammatory drugs (NSAIDs), such as sulindac and celecoxib are being tested as chemopreventive drugs. Some early research has found that certain extracts of black raspberries may help prevent these cancers. Another compound showing some promise is known as Bowman-Birk inhibitor (BBI), a protein derived from soybeans.

All of these drugs and compounds would need further study before they could be recommended.

Treatment

Sentinel Lymph Node Mapping and Biopsy

In many oral cancers, the nearby lymph nodes are routinely removed during surgery (known as a lymph node dissection). The sentinel node procedure can help the doctor determine whether the cancer has spread to these nodes beforehand, which may allow the patient to avoid this surgery if the cancer has not spread. Sentinel node mapping and biopsy allows the doctor to identify and examine the "sentinel node(s)" - the one(s) that the cancer would have

spread to first before it went to other nodes. If this node doesn't contain cancer, it's very unlikely that any other nodes would contain cancer either.

In this procedure, the surgeon injects a radioactive material around the tumor, usually the day before surgery. The material will travel the same route that any cancer cells would likely have taken if they went to the lymph nodes. On the day of surgery a blue dye is injected into the tumor site, which will also travel to the nearby lymph nodes.

During surgery, the surgeon can use a radiation detector to find the lymph node region that the radioactivity (and presumably the cancer) may have spread to. The surgeon then cuts into the area to look for radioactive or blue stained lymph nodes. These are removed and examined by a pathologist. If there is no cancer, then no further surgery is needed. If there is cancer, then all the lymph nodes in the area will be removed.

This procedure is still experimental, and more work is needed to tell if this can replace routine lymph node removals.

New Chemotherapy Approaches

A great deal of research is focusing on improving results from chemotherapy in people with these cancers. This includes finding the best time to give these drugs, figuring out which combinations of drugs work best, and determining how best to use these drugs with other forms of treatment.

Researchers also continue to develop new chemotherapy drugs that might be more effective against advanced oral and oropharyngeal cancers. The combination of docetaxel, cisplatin, and 5-fluorouracil (TPF) given before radiotherapy has shown promising results in early clinical trials. Its role in combination with radiation and other chemotherapeutic agents is now being tested in larger studies.

One newer approach to treating head and neck cancers involves injecting the drug directly into the tumor (intralesional chemotherapy). Success with this approach has been limited in the past because the drug tended to spread out of the tumors and to nearby tissues and the rest of the body quite quickly. Recent advances in preparing the drug solution so that it remains in the tumor (such as suspending it in a gel) have renewed interest in this treatment.

New Radiotherapy Methods

Accelerated and hyperfractionated radiation therapy: Many clinical trials have found that better tumor control rates can be obtained by delivering radiation twice a day (as opposed to once a day) during some or all of the treatment days, although it may cause more side effects. Studies are ongoing to determine whether chemotherapy combined with twice-a-day

radiation gives better results. Trials of radiation and chemotherapy with or without cetuximab are also in progress.

Newer radiation techniques allow doctors to be more accurate in treating the head and neck area while reducing the radiation exposure to nearby healthy tissues. These techniques appear to offer better chances of increasing the success rate and reducing side effects, particularly dry mouth.

Three-dimensional conformal radiation therapy (3D-CRT): 3D-CRT uses special computer programs to precisely map the location of the cancer. Radiation beams are then shaped and aimed at the tumor from several directions, which makes it less likely to damage normal tissues. In theory, by aiming the radiation more accurately, doctors can reduce radiation damage to important normal tissues in the area (such as nerves, blood vessels, and other organs) and may be able to cure more cancers by increasing the radiation dose to the tumor itself. Long-term study results are still needed to confirm this.

Intensity modulated radiation therapy (IMRT): IMRT is an advanced form of 3D therapy. It uses a computer-driven machine that actually moves around the patient as it delivers radiation. In addition to shaping the beams and aiming them at the tumor from several angles, the intensity (strength) of the beams can be adjusted to minimize the dose reaching the most sensitive normal tissues. This allows doctors to deliver an even higher dose to the cancer areas. Many major hospitals and cancer centers are now able to provide IMRT, although its use in treating these cancers is still being studied.

Targeted Therapy

Several drugs that target the epidermal growth factor receptor (EGFR) may help treat oral and oropharyngeal cancers. Cetuximab (Erbix) is already approved for use against these cancers. Other drugs now being studied include erlotinib (Tarceva), panitumumab (Vectibix), lapatinib (Tykerb), and gefitinib (Iressa).

Drugs that block the growth of blood vessels tumors need to survive, such as bevacizumab (Avastin) and sunitinib (Sutent), are now being studied for use against these cancers as well.

Vaccines

Most people think of vaccines as a way to prevent infectious diseases such as polio or measles. Vaccines against human papilloma virus (HPV) infection are already being used to help prevent cervical cancer. They may have the added benefit of preventing some oral cancers as well, although they won't help treat the disease.

However, there are some early forms of vaccines that are being studied as a way to treat people with cancer by helping their immune system to recognize and attack the cancer cells. Many of these vaccines involve dendritic cells (cells of the immune system), which are removed from the patient's blood and exposed in the lab to something that causes them to attack tumor cells. The dendritic cells are then injected back into the body, where they should induce other immune system cells to attack the patient's cancer.

Gene Therapy

New discoveries about how changes in the DNA of cells in the oral cavity and oropharynx cause these cells to become cancerous are being applied to experimental treatments intended to reverse these changes. For example, clinical trials are testing whether it is possible to replace abnormal tumor suppressor genes (such as the p53 gene) of oral cancer cells with a normal copy, to restore normal growth control. Gene therapies that interfere with the growth-stimulating effect of certain human papilloma viruses are also being developed. Another type of gene therapy adds new genes to the cancer cells to make them more susceptible to being killed by certain drugs. These forms of treatment are still in the earliest stages of study, so it will probably be several years before we know if any of them are effective.

Additional Resources

More Information from Your American Cancer Society

The following related information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-ACS-2345.

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

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

Questions About Smoking, Tobacco, and Health (also available in Spanish)

Understanding Chemotherapy (also available in Spanish)

Understanding Radiation Therapy (also available in Spanish)

The following book is available from the American Cancer Society. Call us at 1-800-ACS-2345 to ask about cost or to place your order.

National Organizations and Web Sites*

In addition to the American Cancer Society, other sources of patient information and support include:

National Cancer Institute
Telephone: 1-800-4-CANCER
Internet Addresses: www.cancer.gov

National Coalition for Cancer Survivorship
Telephone: 1-888-650-9127
Internet Address: www.canceradvocacy.org

Let's Face It
Internet Address: www.faceit.org

SPOHNC (Support for People with Oral, Head, and Neck Cancer)
Telephone 1-800-377-0928
Internet Address: www.spohnc.org

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

The American Cancer Society is happy to address almost any cancer-related topic. If you have any more questions, please call us at 1-800-ACS-2345 at any time, 24 hours a day.

References

American Cancer Society. *Cancer Facts and Figures 2008*. Atlanta, Ga: American Cancer Society; 2008.

American Joint Committee on Cancer. *AJCC Cancer Staging Manual*, 6th ed. New York, Springer: 2002; 23-42.

Bsoui SA, Huber MA, Terezhalmay GT. Squamous cell carcinoma of the oral tissues: A comprehensive review for oral healthcare providers. *J Contemp Dent Pract*. 2005;4:1-16.

Cogliano V, Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F. Smokeless tobacco and tobacco-related nitrosamines. *Lancet Oncol*. 2004;5:708.

D'Souza G, Kreimer AR, Viscidi R, et al. Case-control study of human papillomavirus and oropharyngeal cancer. *N Engl J Med*. 2007;356:1944-1956.

Henley SJ, Thun MJ, Connell C, Calle EE. Two large prospective studies of mortality among men who use snuff or chewing tobacco (United States). *Cancer Causes Control* 2005;16:347-358.

Kreimer AR, Clifford GM, Boyle P, Franceschi S. Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. *Cancer Epidemiol Biomarkers Prev*. 2005;14:467-475.

Menedenhall WM, Riggs CE, Cassisi NJ. Treatment of head and neck cancers. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 7th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2005:662-732.

National Cancer Institute. Surveillance Epidemiology and End Results (SEER) Cancer Statistics Review, 1975-2004. 2007. Available at: http://seer.cancer.gov/csr/1975_2004/sections.html. Accessed June 14, 2007.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Head and Neck Cancers. Version 1.2007. Available at: www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf. Accessed June 21, 2007.

Paleri V, Rees G, Arullendran P, et al. Sentinel node biopsy in squamous cell cancer of the oral cavity and oral pharynx: A diagnostic meta-analysis. *Head Neck*. 2005;27:739-747.

Quon H, Hershock D, Feldman M, et al. Cancer of the head and neck. In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE, Kastan MB, McKenna WG, eds. *Clinical Oncology*. 3rd ed. Philadelphia, Pa. Elsevier; 2004: 1497-1560.

Shiboski CH, Shiboski SC, Silverman S. Trends in oral cancer rates in the United States 1973-1996. *Community Dent Oral Epidemiol*. 2000;28:249-256.

Last Medical Review: 9/26/2007

Last Revised: 3/22/2008

2007 Copyright American Cancer Society

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