Episode 78 – Oral Cancer: Part 3 February 20, 2023

Introduction

Squamous cell carcinoma (SCC) is the most common malignant tumour occurring in the head and neck region, accounting for >90% of all head and neck cancers. Skin SCC is most common in high sun exposed areas (e.g., scalp, face, ears, lips), with ~38% of all oral squamous cell carcinoma (OSCC) occurring on the lower lip. Skin SCC is usually cured with local therapy. More serious, debilitating, and potentially life-threatening SCC can affect mucosal linings of the head and neck, with the most common sites being the oral cavity, oropharynx, and larynx. About 40% of OSCCs begin on the floor of the mouth or on the lateral and ventral surfaces of the tongue. [1] [2] [3]

Over 95% of individuals with OSCC have a history of alcohol use, tobacco use, or both. Heavy long-term tobacco and alcohol use is estimated to raise OSCC risk 100-fold in females and 38-fold in males. All types of alcohol beverages increase cancer risk. Human papillomavirus (HPV) infection[1] is another risk factor, which is associated with oropharyngeal cancer. HPV-positive cancer incidence continues to increase, often affecting younger individuals with no history of tobacco or alcohol use. [3] [4]

A study by Seidenberg et al. (2023) showed there is low accurate public awareness of cancer harms associated with alcohol use, including wine, beer, and liquor consumption. The “health halo” surrounding alcohol use related to reduced heart disease has led many to overgeneralize alcohol’s health benefits to other diseases, including cancer. Research shows drinking a little alcohol neither decreases nor increases ischemic heart disease risk. However, alcohol use is a risk factor for many types of cardiovascular disease, including hypertension, heart failure, atrial fibrillation, and hemorrhagic stroke. The fact alcohol is a carcinogen that can cause at least seven types of cancer, including oral cancer, is often overlooked. [5] [6] [7]

The average lifetime risk for Canadians to develop oral cancer is one in 68, with one in 206 dying from the disease. Oral cancer is the ninth most diagnosed cancer in males, and fourteenth for females. Cancers that form deep in the body (e.g., lung, pancreas, stomach) are more likely to present at a late stage. However, despite their superficial location, most oral cancers are diagnosed at stage IV. Screening for oral cancer[2] promotes earlier referral, diagnosis, and treatment, which increases the potential for better prognosis and quality of life. [8]

[1] Refer to Episodes 7, 12, 53, 61, 76, and 77 for additional information on HPV.
[2] Refer to Episodes 76 and 77 for additional information on oral cancer.

Diagnosis

Certain tests and procedures are used to diagnose and stage cancer (e.g., biopsy, imaging). Other tests are necessary prior to cancer therapy. [9]

Diagnostic tests [10] [11] [12] [13] [14] [15] [16] [17] [18]

Test	Description
Comprehensive head and neck exam	If oral cancer is suspected or detected through initial biopsy, a referral to a specialist is required. The specialist (e.g., radiation oncologist, medical oncologist, otolaryngologist) will complete a head and neck exam and order additional tests (e.g., endoscopy, biopsy, imaging). To help view the oropharynx, a long handled small mouth mirror and/or an endoscope[3] may be used during the comprehensive exam.
Endoscopy	A fibre-optic scope with a light and lens or video camera on the end. The procedure and endoscope used are named for the structure they examine or treat, such as: Nasopharyngoscopy for nasopharynx and hypopharynx, uses a nasopharyngoscope. Laryngoscopy for larynx and vocal cords, uses a laryngoscope. Bronchoscopy for the trachea, bronchi, and lungs, uses a bronchoscope. Esophagoscopy for the esophagus, uses an esophagoscope.
Indirect pharyngoscopy and laryngoscopy	Small mirror on long, thin handle used to look at throat, base of tongue, and part of larynx. Topical anesthetic spray may be used to make the procedure more comfortable.
Direct (flexible) pharyngoscopy and laryngoscopy	Endoscope is passed through oral or nasal cavity to view areas not easily seen with mirrors (e.g., nasopharynx and larynx). Topical anesthetic spray may be used to make the procedure more comfortable.
Panendoscopy	Different types of endoscopes are passed down the oral or nasal cavity to do a nasopharyngoscopy, laryngoscopy, pharyngoscopy, esophagoscopy, or bronchoscopy to examine the oral cavity, pharynx, larynx, esophagus, trachea, or bronchi. Usually done under general anesthesia. Also used to: • Biopsy tissue, • Remove polyps or tumours, • Stage a head or neck cancer, • Look for recurrence, or • Find a primary tumour when cancer is found in another part of the body. Since tobacco and alcohol use are risk factors for oral and oropharyngeal cancers, as well as cancers of the esophagus and lung, there is up to a 10% chance of finding more than one cancer at the same time. To help ensure there are no

[3] An endoscope can be flexible or rigid and may have a tool to biopsy tissue for histological examination. [11]

Test	Description
	other cancers in the esophagus or lung, a panendoscopy might be done. This procedure is also helpful if it is unclear where the cancer started or if neck lymph nodes seem abnormal.
Biopsy[4]	Removal of cells or tissues for histological assessment by a pathologist. Several types of biopsies may be used depending on the case.
Incisional biopsy	Sample of the lesion is removed and examined. It is done when the differential diagnosis includes malignancy. Its' accuracy is relative, since the entire lesion is not histologically examined. Most common type of biopsy used to check for changes in the oral cavity or throat. Done with local anesthetic. Sedation is used if tumour is deep in oral cavity or oropharynx.
Excisional biopsy	Entire tumour is removed using local or general anesthesia depending on its location. For example, excisional biopsy is done to remove a sentinel node.
Endoscopic biopsy	Tissue samples taken out through an endoscope.
Fine needle aspiration (FNA) biopsy	Very thin needle used to aspirate cells or fluid from a tumour. Local anesthetic maybe used. If tumour is near the surface of the body the needle is aimed while the specialist palpates the tumour. If tumour is deeper inside the body and cannot be felt, the needle is guided by an ultrasound or CT scan. Advantages of FNA biopsy are the tissue does not have to be cut and it may be possible to make a diagnosis the same day. Disadvantage is sometimes the needle cannot remove enough tissue for a definite diagnosis and FNA must be repeated or different biopsy done. FNA biopsy is not used to sample abnormal areas in the oral cavity or throat, but sometimes used for a neck mass that can be felt, or seen on a CT scan. Also used to collect samples from the thyroid or lymph nodes. FNA might be done after oral or oropharyngeal cancer has been diagnosed to determine if the cancer has spread to lymph nodes in the neck.
Core needle biopsy (core biopsy)	Needles used in core biopsy are slightly larger than those used in FNA, as a result they remove a small cylinder of tissue. Local anesthetic is used. Core biopsy can sample tumours that can be palpated as well as smaller tumours that must be located using imaging tests (e.g., ultrasound or CT scan). Processing core biopsy samples usually takes longer than FNA biopsies, so results may take longer.
Sentinel lymph node mapping and biopsy	Sentinel lymph node is the first lymph node to which cancer is likely to spread from the primary tumour before spreading to other lymph nodes. Sentinel lymph node mapping and biopsy is a common way to determine whether a cancer has spread to lymph nodes. The procedure finds the lymph nodes that drain lymph fluid from the primary tumour site. To find the sentinel lymph node(s), a small amount of slightly radioactive material is injected into the cancer area. Various lymph node chains are checked for radioactivity. A small amount of a harmless blue dye is then injected into the cancer site. Sometimes the dye and radioactive material are combined and injected together. After about an hour, a small

[4] Refer to Episode 77 for additional information on biopsies, including incisional and excisional biopsies.

Test	Description
	incision is made in the skin to view the lymph node area found with the radioactive test. Those lymph nodes are then checked for blue dye or radioactivity. When the sentinel node is found, it is removed (i.e., excisional biopsy) and histologically examined. If the sentinel node does not contain cancer cells, no further lymph nodes are removed as it is unlikely the cancer would have spread beyond this point. If cancer cells are found in the sentinel node, the rest of the lymph nodes in this area are removed and examined (i.e., via lymph node dissection).
Skin biopsy	There are several ways to biopsy skin depending on the suspected type of skin tumour. Shave biopsies remove outer layers of skin and are used for some basal cell or squamous cell skin cancers, but usually are not used for suspected melanomas. Punch biopsies[5] or excisional biopsies remove deeper layers of the skin, and can be used to determine how deep a melanoma has progressed into the skin, which is important in determining melanoma treatment.
HPV (p16) testing	For oropharyngeal cancers, biopsy samples are often tested for the p16 protein to see if HPV infection is present. This is a key part of staging and is considered when making treatment decisions. Test results can help predict the probable course of the cancer, since p16-positive cancers have better prognosis than p16-negative oropharyngeal cancers. A meta-analysis by O'Rorke et al. (2012) found both progression-free survival and disease-free survival were significantly improved in HPV-positive head and neck squamous cell cancers (HNSCCs). Those with HPV-positive HNSCCs and oropharyngeal SCCs had a significantly lower disease specific mortality and were less likely to experience progression or recurrence than those with HPV-negative cancer. [19]
Imaging tests	Imaging tests are not used to diagnose oral or oropharyngeal cancers, but may be done for various reasons before and after a cancer diagnosis, including to: • Look at a suspicious area that might be cancer, • Learn how far the cancer has spread, • Determine if treatment is working, and • Look for signs the cancer recurred after treatment.
Chest x-ray	Chest x-ray might be done after oral or oropharyngeal cancer has been diagnosed to see if the cancer has spread to the lungs. More often though, a CT scan or PET/CT scan of the lungs is done since they tend to give more detailed images.
Computed tomography (CT or CAT scan)	CT scan uses x-rays to make detailed cross-sectional images to help determine: • Size and location of a tumour, • If it is growing into nearby tissues, and • Metastasis to lymph nodes in the neck, lungs, or other distant organs. Sometimes a dye or other contrast material is used (e.g., intravenously) to improve imaging.

[5] Refer to Episode 77 for additional information on punch biopsies.

Test	Description
Magnetic resonance imaging (MRI)	Displays detailed images of soft tissues using radio waves and strong magnets instead of x-rays. A contrast material (e.g., gadolinium) may be injected intravenously before the scan to improve imaging. May be done for oral cancer if there are many metal restorations that might distort CT images, or to determine if the cancer is growing into the bone marrow.
Positron emission tomography (PET)	Type of nuclear scan that makes detailed 3-D images of areas where glucose is taken up. A slightly radioactive form of sugar (known as FDG) is injected intravenously and collects mainly in cancer cells. Images are used to find cancer as cancer cells often take up more glucose than healthy cells. Often a PET scan is combined with a CT scan using a machine that does both scans simultaneously (i.e., PET/CT scan). This allows areas of higher radioactivity on the PET scan to be compared with the more detailed image on the CT scan. PET/CT scans are useful: • If it is believed the cancer has metastasized but it is not known to where it has spread. PET/CT scans can show cancer metastasis to the liver, bones, and some other organs. • After oral or oropharyngeal cancer treatment as follow up.
Bone scan (bone scintigraphy)	Type of nuclear scan where a small amount of low-level radioactive material is injected intravenously. The material collects mainly in abnormal areas of bone and is detected by a scanner. These areas are called “hot spots.” Bone scans help show if cancer has metastasized to the bones. However, this test is seldom needed because PET scans usually show if cancer has metastasized to the bones.
Barium swallow	Used to image the lining of the upper part of the digestive system, especially esophagus. In this test, the individual drinks a chalky liquid containing barium which coats the walls of the throat and esophagus. A series of x-rays is taken as the individual swallows. The test may be ordered because individuals with oral and oropharyngeal cancers are at risk for cancer of the esophagus. It is also useful to see if the cancer is causing swallowing problems.
Ultrasound	Neck ultrasound is used to determine if lymph nodes are enlarged or look abnormal. Ultrasound can also help guide a needle into the abnormal lymph node for an FNA biopsy. It might also be used after treatment to look for signs of cancer recurrence.
Blood tests	Blood tests do not diagnose oral or oropharyngeal cancer. However, routine blood tests may be ordered to help determine overall health, especially before cancer treatment.
Blood chemistry test	Measures the amount of certain substances in the body, such as electrolytes (e.g., sodium, potassium, chloride), fats, proteins, glucose, and enzymes. Helps to determine how kidneys, liver, and other organs are functioning. An abnormal amount of a substance in the blood can be a sign of disease or treatment side effect. Also used to help diagnose and monitor many conditions before, during, and after cancer treatment. If the thyroid or pituitary gland are in the radiation treatment area, there is an increased risk of hypothyroidism. Thyroid hormone levels should be checked before and after treatment.

Test	Description
Complete blood count (CBC)	Measures the number of erythrocytes (red blood cells [RBCs]), leukocytes (white blood cells),[6] and thrombocytes (platelets). Also measures amount of hemoglobin, hematocrit level, and size of the RBCs. Often part of a routine health check-up. Can help diagnose some cancers, especially leukemias. Also used to monitor health during and after cancer treatment.
Functional tests	If surgery is planned, an electrocardiogram (EKG) and pulmonary function tests may be necessary.
Oral health exam	If radiation therapy is part of treatment, an oral health exam including any necessary treatment should be completed to help eliminate existing oral health problems.
Hearing test	Cisplatin, a chemotherapy drug used in treating oral and oropharyngeal cancer, may cause hearing loss. Hearing may be checked with an audiogram by an audiologist prior to treatment in case hearing problems develop from chemotherapy.
Nutrition test	Dietician may evaluate nutrition status before, during, and after treatment to help ensure weight and protein stores are maintained.
Speech / swallow test	Speech-language pathologist may test ability to swallow and speak and assign exercises during cancer treatment to help strengthen head and neck muscles to enable the individual to eat and talk easily after treatment.

Pathology report

A pathology report is written by a pathologist and describes the characteristics of a tissue specimen. It is also used for staging (describing the extent of cancer within the body, especially whether it has spread) and planning treatment.

Sections of a pathology report [15] [20] [21]

Section	Details
Identifying information	Person's name, birthdate, age, gender Date of biopsy
Contact information	Clinical provider of the sample, pathologist, lab where the sample was tested
Biopsy specimen	Site where tissue was removed, number of samples taken, and number of lymph nodes removed (if applicable).
Gross description	Describes the tissue sample as seen by the naked eye (e.g., colour, weight, size, consistency, texture). May also include shape of the tissue sample and any visible abnormalities.
Microscopic description	Appearance of cells after stained with routine stains hematoxylin and eosin (H&E) and viewed under a microscope. H&E staining helps identify the types of tissue and cells. Provides important information about the number, pattern, shape, and

[6] Refer to Episodes 44 and 45 for information on leukocytes and the immune system.

Section	Details
	structure of cells in a tissue sample. There are several factors in this section that affect diagnosis and treatment, including grade and lymph node involvement.
Grade	Describes how abnormal the cells look compared with healthy cells, such as differences in size, shape, and staining features. Low-grade (well-differentiated) cancer cells look more like normal cells and tend to grow and spread more slowly. High-grade (poorly differentiated, undifferentiated) cancer cells look less like healthy cells. Grading systems are different for each type of cancer and are used to help plan treatment and determine prognosis. Grade 1 to 4 is used for oral cancer. In general, lower the grade, the better the prognosis.
Invasive or noninvasive	Noninvasive or in situ cancers stay in one specific part of the body. Invasive: cancer has grown into nearby healthy tissue. Metastatic: cancer has spread to another part of the body.
Margin status	Describes whether abnormal cells are found in the margins of the sample. A margin is described as negative or clean when no cancer cells are found at the edge of the tissue, suggesting all the cancer was removed. A margin is described as positive or involved when cancer cells are found at the edge of the tissue, suggesting all the cancer was not removed.
Lymph nodes	Indicates whether lymph nodes are positive or negative for cancer.
Mitotic rate	A measure of how quickly cancer cells are dividing. The report usually indicates how many cells are dividing. Tumours with fewer dividing cells are usually low grade.
Stage	A stage is assigned usually using the TNM system: T for tumour, N for lymph nodes involved; M for metastasis.
Other test results	Pathologist may perform additional tests to identify specific genes, proteins, and other factors unique to the tumour (e.g., HPV p16 testing). Additional tests are important for diagnosis as best treatment option may depend on these results.
Diagnosis	If cancer is the definitive diagnosis, the report will state cancer type, tumour grade, lymph node status, margin status, and stage.
Additional comments	Pathologist may provide comments to offer further explanation or recommend additional tests.

Common pathology report terms [4] [9] [15] [22] [23] [24]

Term	Description
Atypical	Cells that are not normal but are not cancerous. Atypical cells could become a cancer over time or may increase the risk of cancer.
Invasive	Cancer that has spread beyond the layer of tissue in which it developed and is growing into surrounding healthy tissues. Also called infiltrating cancer.
Noninvasive	Cancer that has not spread outside the tissue in which it began.
In situ	Abnormal cells are present but have not spread to nearby tissue.

Term	Description
Adenocarcinoma	Cancer that forms in glandular tissue. Glandular tissue lines certain internal organs and makes and releases substances (e.g., mucus, digestive juices). Most cancers of the breast, lung, esophagus, stomach, colon, rectum, pancreas, prostate, and uterus are adenocarcinomas.
Carcinoma	Cancer arising in the epithelial tissue of the skin or lining of the internal organs. Most oral and oropharyngeal cancers are squamous cell carcinomas. Basal cell carcinoma is the most common type of skin cancer.
Leukemia	Cancer cells that started in the blood or bone marrow.
Lymphoma	Cancer cells that started in the lymphatic system.
Sarcoma	Cancer arising in bones and soft tissues.
Dysplasia	An increase in the number of abnormal or atypical cells in an organ. Dysplasia is a response to infection or is a state in between normal cells and cancer cells.
Hyperplasia	An abnormal increase of cells in a tissue or organ. Hyperplasia may increase the risk of developing some types of cancer. May also be the body's response to various diseases.
Neoplasia	Uncontrolled cell growth. The cells can be benign or malignant.
Neoplasm (tumour)	An abnormal mass of tissue that forms by uncontrolled, abnormal growth of cells or by cells that do not die when they should (i.e., apoptosis). If apoptosis is prevented, it can lead to uncontrolled cell division and the subsequent development of a tumour. Neoplasms may be benign or malignant.
Benign (nonmalignant)	Not cancer. Benign neoplasms may grow large but do not spread into, or invade, nearby tissues or other parts of the body.
Malignant	Cancer cells grow in an uncontrolled way and can invade nearby tissues and spread to other parts of the body through the blood and lymph systems.
Margin	Refers to the edge or border of the tissue removed in cancer surgery. A margin is negative or clean when no cancer cells are found at the edge of the tissue, suggesting all the cancer was removed. A margin is positive or involved when cancer cells are found at the edge of the tissue, suggesting all the cancer was not removed.
Infiltrating	Cancer that has spread beyond the layer of tissue in which it developed and is growing into surrounding healthy tissues. Also called invasive cancer.
Undifferentiated (high-grade, poorly differentiated)	Differentiation means how developed or mature a cell is. Undifferentiated cancer cells often grow and spread quickly.
Well-differentiated (low-grade)	Well-differentiated cancer cells look more like normal cells under a microscope and tend to grow and spread more slowly than poorly differentiated or undifferentiated cancer cells.

Cancer staging
Stage refers to the extent and spread of a cancer. Staging is usually based on:
- Location of the primary (original) tumour.
- Tumour size and extent.
- Lymph node involvement.
- Presence or absence of distant metastasis.

Various tests are used to collect data to determine the stage of cancer, such as:
- Physical examinations help determine tumour location and size, lymph node involvement.
- Imaging tests (e.g., CT and MRI scans) show tumour location, size, and metastasis.
- Laboratory tests (e.g., blood tests).
- Pathology reports describe tumour size, type, grade (i.e., how closely cancer cells resemble normal tissue), and growth into other tissues.
- Surgical reports describe tumour size and appearance, and lymph node and organ involvement.

Stage of cancer is used to:
- Determine the prognosis,
- Treatment plan and predict how well treatment will work,
- Effectively communicate and collaborate with the oncology team,
- Study participants in clinical trials, and
- Identify clinical trials that may be a treatment option. [9] [16] [25]

TNM staging system
Different staging systems are used for different types of cancer. The most common staging system used in Canada is the American Joint Committee on Cancer (AJCC) TNM system. T describes the size of the tumour and any spread of cancer into nearby tissue; N describes spread of cancer to nearby lymph nodes; and M describes metastasis. [26] [27]

TNM system uses numbers after each letter to give more details about the cancer (e.g., T1N0MX). Sometimes the lowercase letter a, b, or c is used to subdivide the tumour, lymph nodes, or metastasis categories to provide more detail (e.g., T1a). Lowercase “is” is added after T (Tis) to describe a carcinoma in situ.

<u>Regional lymph nodes (N)</u>
Node (N) refers to the number of nearby lymph nodes positive for cancer.
- NX: Cancer in nearby lymph nodes cannot be measured.
- N0: No cancer in nearby lymph nodes.
- N1, N2, N3: Refers to the number and location of lymph nodes that contain cancer. Higher the number after the N, the more lymph nodes contain cancer.

Distant metastasis (M)
Metastasis (M) refers to whether the cancer has metastasized through the blood or lymphatic system.

- MX: Metastasis cannot be measured.
- M0: Cancer has not spread to other parts of the body.
- M1: Cancer has spread to other parts of the body. [9] [26]

Types of TNM staging
Clinical staging determines how much cancer there is based on physical examination, imaging tests, and biopsies of affected areas. Clinical stage is given before surgery, and treatment is often based on the clinical stage. The clinical stage is shown by a lowercase "c" before the letters TNM on medical reports (i.e., cTNM).

Pathological staging is determined when surgery is performed to remove a tumour and lymph nodes (if applicable). Pathological staging combines the results of both the clinical staging with the surgical results. Pathologic stage gives more information about the cancer than the clinical stage. The pathologic stage is shown by a lowercase "p" before the letters TNM on a pathology report (i.e., pTNM).

The clinical and pathologic stages of a cancer can be different. For example, during surgery cancer may be found in an area that did not show up in imaging tests so the pathologic stage may result in a higher stage. [25] [26]

Stage grouping
Once T, N, and M are determined, they are combined and an overall stage of 0, I, II, III, or IV is assigned. Stage I cancers are the least advanced and often have a better prognosis. Higher stage cancers are more advanced.

Stages of cancer [16] [28] [29]

Stage	Oral cancer	Oropharyngeal cancer	HPV-related oropharyngeal cancer*
Stage 0 (carcinoma in situ)	Cancer only in lining of oral cavity or lips.	Tumour is only in lining of oropharynx.	Tumour is only in lining of oropharynx.
Stage I	Tumour is ≤2 cm.	Tumour is ≤2 cm.	Tumour is <4 cm. Cancer may have spread to one lymph node in the neck on same side as tumour. Lymph node is <6 cm.
Stage II	Tumour is >2 cm but <4 cm.	Tumour is >2 cm but <4 cm.	Tumour is <4 cm and cancer has spread to one or more lymph nodes on opposite side of neck as the tumour or to lymph nodes on both sides of neck. Lymph nodes are <6 cm. **OR** Tumour is >4 cm or has grown to epiglottis. Cancer may have spread to lymph nodes in neck and are <6 cm.
Stage III	Tumour is >4 cm or cancer has spread to one lymph node in neck on same side as tumour and lymph node is ≤3 cm.	Tumour is >4 cm or has grown to epiglottis. **OR** Cancer has spread to one lymph node in neck on same side as tumour. Lymph node is <3 cm.	Cancer has spread to one or more lymph nodes in neck that are >6 cm. **OR** Tumour has grown around a carotid artery or has grown into any of the following: • Larynx • Muscles of the tongue • Nearby bones of the skull • Hard palate • Mandible • Nasopharynx.

Stage	Oral cancer	Oropharyngeal cancer	HPV-related oropharyngeal cancer*
Stage IV	**Stage IVA** Tumour is any size and has grown into any of the following: • Bone in palate or mandible • Inferior alveolar nerve • Floor of the mouth • Skin of the face Cancer may also have spread to one or more lymph nodes in neck, and are ≤6 cm.	Stage IV can be divided into stages IVA, IVB, or IVC depending on: • Which nearby areas tumour has grown into (e.g., larynx, muscles of tongue, mandible, skull) • Number and size of lymph nodes with cancer • If the cancer has grown outside of lymph nodes (i.e., extranodal extension) • Whether affected lymph nodes are on same or opposite side of neck as the tumour, or on both sides of neck • Distant metastasis: cancer has spread farther from pharynx (e.g., lungs, liver).	Distant metastasis: cancer has spread to other parts of body (e.g., lungs, liver, other bones).
	Stage IVB Tumour has grown into soft tissues of cheek (e.g., muscles, nerves, blood vessels), or into base of the skull, or tumour is wrapped around internal carotid artery. **OR** Cancer has spread to lymph nodes in neck and one is >6 cm or cancer in a lymph node has grown into surrounding tissue.		
	Stage IVC Distant metastasis: cancer has spread to other parts of body (e.g., lungs, liver, bone). Also called metastatic oral cancer.		

*Since oropharyngeal cancers that contain HPV DNA (p16-positive) have a better prognosis than p16-negative oropharyngeal cancers, a separate staging system is used.

Recurrence or retreatment staging
The formal stage of a cancer does not change over time, even if the cancer progresses. A cancer that recurs or spreads is still referred to by the stage it was given during initial diagnosis. For example, it does not mean a stage I cancer changes to a stage III cancer. However, a tumour initially staged as a T2 may be described as a T3 or T4 if the cancer has enlarged or grown into nearby tissues.

Recurrence or retreatment staging is used to determine the extent of the disease if a cancer recurs after treatment and is determined by exams, imaging tests, biopsies, and possibly surgery. It helps determine best treatment options for recurring cancer and is shown with a lowercase "r" before the letters TNM on a medical report.

Recurrent oral or oropharyngeal cancer may return in the oral cavity or throat (local recurrence), in nearby lymph nodes (regional recurrence), or in another part of the body, such as the lungs (distant recurrence). [16] [25] [26]

Discussing diagnosis
Decision-making in oncology is complex as both the attending oncologist and the individual must weigh risks of treatment with their potential benefit for survival and impact on quality of life. Treatment of head and neck squamous cell carcinoma (HNSCC) is often disfiguring and affects some of the most basic functions (e.g., speech, eating, breathing). Thus, informing and actively involving individuals in the decision-making process is important to reduce decisional conflict (DC). DC is an individual's uncertainty in choosing treatment options when choice of options involves risk, regret, or challenge to their life values. It is influenced by inadequate knowledge and support, unclear values, and the perception that an ineffective decision has been made. Individuals who experience less DC are more engaged in treatment and less prone to decisional regret, nervousness, and fretting.

A prospective cohort study by Hoesseini et al. (2022) assessed DC before treatment in two groups of participants diagnosed with HNSCC: small laryngeal SCC and other HNSCC (e.g., cancer of oropharyngeal, oral cavity, parotid gland, etc.). The study found almost half of participants (48%) diagnosed with HNSCC experienced clinically significant DC. Participants in the other HNSCC group experienced significant DC related to not knowing which options were available to them, as well as the benefits, risks, and adverse effects of each option. These results suggest there is room for improvement to reduce decision delay and decision-related distress related to DC. It stresses the importance of effectively informing individuals of their cancer diagnosis so they can fully engage with the decision-making process and the choices of management and treatment. [30] [31]

Prognosis for squamous cell carcinoma
In general, the 5-year survival rate is:
- >75% if carcinoma of the tongue is localized (i.e., no lymph node involvement).
- 75% for localized carcinoma of the floor of the mouth. Lymph node metastasis decreases survival rate by about half.
- 90% for lower lip lesions (metastases are rare). Carcinoma of the upper lip tends to be more aggressive and metastatic.
- 60% overall for oropharyngeal cancer

- >75% (and a 3-year survival of almost 90%) for HPV-positive oropharyngeal cancer.
- <50% for HPV-negative oropharyngeal cancer.

Higher survival with HPV-positive cancer is due to a favourable tumour biology and usually a younger, healthier population. High expression of p16 appears to improve prognosis for both HPV-positive and HPV-negative oropharyngeal tumours. Note: p16 is an intracellular protein present in most HPV-positive cancers but also in a few HPV-negative cancers. [3] [32]

Treatment

Oral and oropharyngeal cancers can often be successfully treated, especially if detected, diagnosed, and treated early. Although curing cancer is the primary goal of treatment, preserving the function of nearby nerves, organs, and tissues and the individual's quality of life are also important.

Individuals diagnosed with head and neck cancer are cared for by a multidisciplinary oncology team due to the complexity and associated morbidities of the illness. Members of the team often include: medical oncologist, radiation oncologist, surgical oncologist, pathologist, nurse practitioner, registered nurse, otolaryngologist, prosthodontist, plastic surgeon, dentist, dental hygienist, physiotherapist, speech-language pathologist, audiologist, dietician, social worker, and psychologist or psychiatrist.

There are three main treatment options for oral and oropharyngeal cancer: surgery, radiation therapy, and therapies using medication. Treatment options depend on several factors, including type and stage of cancer, possible side effects, and the individual's preferences and overall health. A single therapy or a combination may be used. [33] [34]

Surgery

An important goal of surgery is complete removal of the tumour with negative margins. Surgeons are often able to determine during surgery if all the tumour was removed with assistance of a pathologist. Surgery may be followed by radiation therapy, therapies using medication, or both. Depending on the location, stage, grade, and other features of the tumour, some individuals may need more than one surgery to remove the cancer and help restore the function and appearance of affected tissues. [34]

Common surgical procedures for oral and oropharyngeal cancer [34] [35]

Surgical procedure	Description
Primary tumour surgery	Tumour and a margin of healthy surrounding tissue are removed to decrease chance of cancer cells remaining. Tumour may be removed through the oral cavity or an incision in the neck. A mandibulotomy, where the mandible is split to allow access, may be required.
Glossectomy	Partial or total removal of the tongue.
Maxillectomy	Partial or total removal of the hard palate. Prostheses or flaps of soft tissue with and without bone can be placed to fill tissue defects created during surgery.
Mandibulectomy	Partial or total removal of the mandible.
Neck dissection	Removal of lymph nodes and surrounding tissue in the neck. Main types of neck dissection surgery include:

Surgical procedure	Description
	• Radical neck dissection: All tissue on the side of the neck from mandible to collarbone is removed, including lymph nodes, muscle, nerve, salivary glands, and major blood vessels in the area. • Modified radical neck dissection: Most common type of neck dissection. Less neck tissue is removed than radical dissection. All lymph nodes are removed. May spare nerves in the neck and, sometimes, blood vessels or muscle. • Selective neck dissection: If cancer has not spread far, fewer lymph nodes are removed. May spare muscles, nerves, and blood vessels in the neck. A neck dissection may be followed by radiation therapy or chemoradiation, to help ensure no cancer is remaining in the lymph nodes. For oropharyngeal cancer, sometimes a neck dissection will be recommended after radiation therapy or chemoradiation. If neck dissection is not possible, radiation therapy may be used instead.
Laryngectomy	Complete or partial removal of the larynx. Laryngectomy is rarely needed to treat oral or oropharyngeal cancer. However, when there is a large tumour of the tongue or oropharynx, the larynx may need to be removed to protect the airway during swallowing. If the larynx is removed, the trachea is reattached to the skin of the neck where a hole (i.e., stoma or tracheostomy) is made. Rehabilitation is needed to learn a new way of speaking.
Transoral robotic surgery (TORS) and transoral laser microsurgery (TLM)	TORS and TLM are minimally invasive surgical procedures. In TORS, an endoscope is used to view the tumour in the throat, base of the tongue, and tonsils, while two small robotic instruments are used to remove the tumour. In TLM, an endoscope connected to a laser is inserted through the oral cavity and the laser is used to remove the tumour in the oropharynx.
Micrographic surgery	Frequently used to treat skin cancer. Often used with cancer of the lip. Sometimes used for oral cavity tumours. It involves removing the visible tumour in addition to small fragments of tissue surrounding the tumour. Each small fragment is examined under a microscope until all the cancer has been removed. Helps to reduce amount of healthy tissue removed.
Tracheostomy	If cancer is blocking the airway or is too large to completely remove, a hole is made in the neck called a tracheostomy. A tracheostomy tube is then placed for the individual to breathe through. Tracheostomy can be temporary or permanent.
Gastrostomy tube	If cancer prevents an individual from swallowing, a gastrostomy (feeding) tube is placed. The tube goes through the skin and muscle of the abdomen and directly into the stomach. These tubes may be used as a temporary method for maintaining nutrition until the individual can safely and adequately swallow food taken in through the mouth. For temporary swallowing problems, a nasogastric (NG) tube may be used instead. An NG tube is inserted through the nose, down the esophagus, and into the stomach.
Reconstruction	Reconstructive surgery may be necessary to help the individual swallow and speak again if treatment required the removal of large areas of tissue. Healthy bone or tissue are taken from other parts of the body to fill tissue defects left by the tumour removal or to replace part of the lip, tongue, palate, or jaw.

Radiation therapy

Radiation therapy (radiotherapy) uses high-energy x-rays or other particles to destroy cancer cells. A radiation therapy schedule usually consists of a specific number of treatments given over a set time period. Before beginning radiation treatment for any head and neck cancer, individuals should receive a thorough oral health exam so existing problems can be treated.

External-beam radiation therapy

- External-beam radiation therapy (EBRT) is the most common type of radiation treatment for oral or oropharyngeal cancer. EBRT uses a machine outside the body to aim high-energy radiation at the cancer. The machine can rotate around the individual, delivering radiation from many different angles to provide highly conformal treatment. A mesh mask helps keep the individual's head and neck from moving during treatment. Small ink marks are put on the mask to line up the machine in the same position before each treatment. Generally done as an outpatient procedure.
- Proton therapy is a type of EBRT that uses protons rather than x-rays. At high energy, protons can destroy cancer cells.
- Intensity modulated radiation therapy (IMRT)[7] is a type of 3-dimensional EBRT that uses a computer to make pictures of the size and shape of the tumour. Thin beams of radiation of different intensities are aimed at the tumour from many angles. IMRT allows more effective doses of radiation to be delivered to the tumour while reducing damage to healthy cells. [18]

Internal radiation therapy

- Internal radiation therapy or brachytherapy is radiation treatment using a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The implant is left in place for several days while the individual stays in the hospital. [36]

Radiation therapy may be the main treatment for oral cancer, or used after surgery to destroy small areas of cancer that could not be removed. Radiation therapy can also be used to treat lymph nodes. Combining radiation therapy with cisplatin (i.e., chemoradiation) may be used for this purpose in some cases. [34]

[7] Refer to Episode 68 for discussion on research by Dr. Glogauer and colleagues on the effect of IMRT on the oral innate immune response and oral microbiome. Findings included:

- Radiation may, directly and indirectly, influence oral neutrophil counts and activation states with a shift in oral polymicrobial communities.
- Oral samples collected during and after radiotherapy showed a significant reduction in abundance of Gram-negative bacteria and an increase in the genera *Streptococcus*, *Lactobacillus*, *Treponema*, and *Prevotella*. While this may be seen as a desired outcome, disturbing normal flora may result in disease-inducing microbial communities, including aciduric microbes.
- Changes in the oral microbiome and oral neutrophils did not return to baseline preradiotherapy levels at 6-months postradiotherapy. [66]

Therapies using medication
Medications may be given systemically (e.g., intravenously or orally) or locally (e.g., applied directly to the cancer or localized to an area of the body). An individual may receive one drug at a time or a combination are given at the same time. Medications can also be given as part of a treatment plan that includes surgery and/or radiation therapy.

Individuals should disclose to their oncologist if they are taking any prescription or over the counter (OTC) medications, herbs, or supplements since they may interact with cancer medications, causing unwanted side effects or reduced effectiveness.

Types of medications used for oral and oropharyngeal cancer include chemotherapy, immunotherapy, and targeted therapy. [34]

Chemotherapy
Chemotherapy is the use of drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

A chemotherapy schedule usually consists of a specific number of cycles given over a set time period. An individual may receive one drug at a time or a combination of drugs are given at the same time.

The use of chemotherapy in combination with radiation therapy, called chemoradiation, is often recommended. This combined treatment, using cisplatin, may be an option for oral or oropharyngeal cancer that may have spread to the lymph nodes. Sometimes, chemoradiation for oropharyngeal cancer will be followed with neck dissection.

Chemotherapy may be used as initial treatment before surgery, radiation therapy, or both (i.e., neoadjuvant chemotherapy). Or it can be given after surgery, radiation therapy, or both (i.e., adjuvant chemotherapy). Chemotherapy for oral cancer is most often given as part of a clinical trial.

Each drug or combination of drugs can cause specific side effects. While some side effects can be permanent, most are temporary and can typically be controlled. In general, chemotherapy may cause fatigue, nausea, vomiting, hair loss, dry mouth, hearing loss, appetite loss (often due to a change in sense of taste), difficulty eating, weakened immune system, diarrhea, constipation, or oral mucositis. [34]

Immunotherapy
Immunotherapy or the use of biologics is designed to boost the body's natural defenses to fight the cancer. It uses materials made either by the body or in a laboratory to improve, target, or restore immune system function. Pembrolizumab (Keytruda) and nivolumab (Opdivo) are two immunotherapy drugs approved by Health Canada for the treatment of adults with recurrent or metastatic HNSCC that has not been stopped by platinum-based chemotherapy. Both are also approved for the treatment of some individuals with advanced lung cancer or melanoma. [34] [37] [38]

Immunotherapy in combination with chemotherapy and radiation therapy may also be used in clinical trials.

Different types of immunotherapy can cause different side effects. Common side effects include skin reactions, flu-like symptoms, diarrhea, and weight changes. [34]

Targeted therapy

Targeted therapy is a treatment that targets cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This treatment blocks the growth and spread of cancer cells and limits damage to healthy cells. Monoclonal antibodies[8] are a type of targeted therapy being used to treat head and neck cancer.

Monoclonal antibodies are immune system proteins made in the laboratory to treat many diseases, including cancer. As a cancer treatment, these antibodies attach to a specific target on cancer cells or other cells that may help cancer cells grow. The antibodies then kill the cancer cells, block their growth, or keep them from spreading. Monoclonal antibodies are given by infusion.

Currently, monoclonal antibodies directed against a cellular receptor called the epidermal growth factor receptor (EGFR) are being used in combination with radiation therapy for head and neck cancers. Cetuximab (Erbitux) is Health Canada approved for use in combination with radiation therapy for the initial treatment of locally or regionally advanced HNSCC. Cetuximab binds to the EGFR, an antigen on the surface of certain tumour cells. As a result of this binding, the tumour cells can no longer receive the messages it needs for growth, progression, and metastasis. [34] [39]

Oral management before radiation therapy or chemotherapy

A complete oral health exam is important prior to cancer therapy. Ideally, this exam should be performed at least one month before the start of cancer treatment to permit adequate healing from any required invasive procedures. The exam may include a radiographic survey of existing teeth, periodontal assessment, and evaluation of any worn prosthesis. The aim is to maximize the individual's quality of life following cancer therapy by retaining teeth for function, esthetics, and speech when possible. Teeth scaling and restorations should be completed prior to starting therapy. Extractions may be necessary to help avoid osteoradionecrosis (ORN) from developing as a result of extracting teeth postradiotherapy.

Prevention of oral complications includes a healthy diet, good oral care, and oral health checkups. Good oral hygiene reduces the risk of developing many oral problems in individuals undergoing cancer therapy.

Radiation therapy and chemotherapy make soft tissues very susceptible to trauma. Thus, it is important to smooth all irregular teeth and sharp areas on restorations and to adjust dentures to avoid irritation. Clients should be instructed to clean dentures daily and remove overnight.

[8] Refer to Episodes 52 and 57 for information on monoclonal antibodies and COVID-19 treatment.

Measuring the maximum mouth opening before radiation therapy is started (i.e., inter-arch or inter-incisal distance) is important. The client and/or clinician should measure this distance frequently thereafter to ensure it is maintained. [40] [41] [42]

Dr. Glogauer and colleagues developed 'Clinical practice guidelines for dental management prior to radiation for head and neck cancer' (2021). The guidelines were developed based on expert consensus from dental oncologists. Some of the recommendations include:

- Referring all clients, both dentate and edentulous, to a dental oncology clinic.
- Allowing at least 7-14 days of healing between extraction or other surgical procedures before radiotherapy commencement.
- Considering risk factors, such as risk of infection, oral health status, cancer type and prognosis, and client compliance and motivation when deciding to extract or restore teeth with dental caries.
- Extracting teeth with moderate-severe periodontal involvement that will receive a dose at or above the critical radiation threshold (70 Grays [Gy] in the maxilla and 60 Gy in the mandible). Research has shown 33% of individuals develop ORN when moderate-severely periodontally involved teeth were not extracted. [43]

Smoking cessation

Smoking cessation is important before cancer treatment. If an individual used to smoke before being diagnosed, it is important they do not start during treatment. Smoking can increase the risk that the cancer will recur or a second cancer will form.

Smoking during treatment can cause:

- Poor wound healing, especially after surgery
- More side effects from chemotherapy
- Radiation to not work as well
- Higher chance of infection
- Longer hospital stays
- Increased risk of mortality [10] [44]

Side effects of radiation therapy

Therapeutic radiation to the head and neck can cause both acute sequelae (e.g., mucositis, dysphagia, dysgeusia, weight loss, fatigue, hair loss, pain) and chronic sequelae (e.g., rampant caries, trismus, xerostomia, osteoradionecrosis). The effects are dose-related and are significant above an absorbed dose of 60 Gy. IMRT can help to reduce side-effects of radiation since the radiation is tailored to maximize the dose to the tumour while minimizing the dose to adjacent normal tissues. [42] [45]

Side effects [40] [41] [42] [43] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55] [56] [57] [58] [59]

Side effect	Description	Management strategies
Mucositis	Inflammation of oral mucosa resulting from chemotherapeutic agents or ionizing radiation. Presents as widespread oral erythema, pain, bleeding, and ulceration due to damage to oral mucosal lining. Symptoms may occur during the second or third week of radiation therapy. Symptoms are common, temporary, and gradually subside within two or three weeks of completing treatment. Oral mucositis increases the risk of local and systemic infection.	Recommendations for minimizing oral mucositis include: • Good oral hygiene. • Avoiding spicy, salty, acidic, hard, and hot foods; hot beverages and alcoholic drinks. Choose foods that are soft, wet, and easy to swallow. Soften dry foods with gravy, sauce, or other liquids. Use a blender to blend food to make it easier to swallow. • Use mild-flavored toothpaste. • Avoid smoking and tobacco products. • Use a bland rinse (one teaspoon salt, one teaspoon baking soda, four cups of water) after meals, every one to two hours while awake, and every four hours through the night, if awake. • More advanced interventions may be implemented by the oncology team, e.g., palifermin therapy, oral cryotherapy at time of chemotherapy administration, photobiomodulation (also called low level laser therapy), and mouthwashes containing morphine or benzydamine, but only in certain groups of individuals.
Xerostomia	Dry mouth due to reduced or absent saliva flow caused by damage to saliva glands. Most common long-standing problem following orofacial radiotherapy. Salivary flow is reduced from first week of radiation therapy and may result in permanently dry mouth. Particularly severe if both parotid glands are in radiotherapy field.	Management of xerostomia may include: • Staying hydrated by drinking/sipping water throughout the day. • Sucking on ice chips. • Limiting alcoholic beverages and beverages high in sugar or caffeine (e.g., juices, sodas, teas, coffee, especially sweetened). • Smoking cessation. • OTC commercial saliva substitutes, moisturizers, and lubricants. • Sugarless gums, mints, lozenges to stimulate saliva flow (e.g., xylitol-sweetened); self-adhering xylitol discs. • Using lip lubricants frequently. • Low sugar diet to help prevent dental caries. • Daily use of high-fluoride toothpaste. • Nighttime use of bedside humidifier. • Thorough denture hygiene and removal of dentures to sleep. • Topical fluoride applications (e.g., fluoride varnish).

Side effect	Description	Management strategies
Radiation-associated caries	Can start within three months of completing radiation therapy. High risk of developing caries is due to combination of permanent reduced saliva flow, high sugar consumption, and high level of cariogenic flora. Also, high-sugar containing food supplements are often prescribed to aid calorie intake.	To prevent post-radiation caries: • Comprehensive oral health assessment. • Home care instruction and diet counselling. • Daily fluoride applications (e.g., fluoride trays). • Regular dental and dental hygiene appointments. • Fluoride varnish applications. • Xerostomia management. • Smoking cessation. • Good home care including gentle tooth brushing morning and night with soft bristled brush and mild flavoured high fluoride-containing toothpaste. • Daily gentle interdental cleaning using dental floss, dental tape, or interdental brushes. • Daily use of mild flavoured sodium fluoride (0.05%) alcohol-free mouthrinse for individuals with xerostomia to help arrest any initial carious lesions. Mouthrinse should be used at a time separate from tooth brushing (e.g., lunch time each day). Rinsing should be done for one minute.
Periodontal disease	Radiation to periodontal tissues makes them more susceptible to disease since vascularity is reduced and capacity of the supporting bone to remodel and repair is impaired. Reduced saliva flow encourages plaque accumulation. Uncontrolled periodontal disease, especially in furcation areas, can predispose to osteoradionecrosis (ORN), making it vital to treat any evidence of periodontal disease prior to cancer therapy.	Strategies to prevent further tooth loss and ORN in individuals with periodontal disease include: • Oral hygiene instruction and excellent home care. • Frequent follow-up and regular scaling every three months. • Xerostomia management. • Smoking cessation. • Chlorhexidine mouthrinse can be used to complement oral hygiene, especially for those with limited access due to trismus.
Oral candidal infections[9]	Radiation induced xerostomia can result in increased oral candida counts. Xerostomia often persists for several months or permanently after treatment	Optimum denture care and oral hygiene are first line measures. Persistent infection should be treated with antifungals, including dentures. Use of nystatin and chlorhexidine simultaneously should be avoided as some evidence suggests both drugs inhibit each

[9] Refer to Episode 61 and 62 for additional information on oral candidiasis.

Side effect	Description	Management strategies
	increasing susceptibility to candidiasis, particularly when dentures are worn.	other's action; it is preferable to separate administration of these agents by at least one hour.
Ageusia, hypogeusia, dysgeusia	Resulting from direct effect of radiation on taste buds and due to changes in the saliva. Can range from ageusia (inability to taste), hypogeusia (decreased ability to taste), or dysgeusia (distorted taste), which may cause change in sweet, sour, bitter, and salty tastes. Taste acuity is partially restored in 20-60 days after completion of radiation and is usually restored almost completely within four months. Some may experience life-long alteration or loss of taste.	Marinate foods or add spices/herbs to improve flavour. Switch to other high-protein foods (e.g., chicken, eggs, fish, peanut butter, turkey, beans, dairy products), if certain meats taste bland. Switch to plastic utensils and non-metal cooking dishes if food tastes metallic. Try sugar-free drops, gum, or mints if experiencing bad taste.
Dysphagia	Problems with swallowing either due to surgery (e.g., to tongue or pharynx) or fibrosis and scarring secondary to radiotherapy. Dysphagia and inability to take adequate nutrition and hydration by mouth are considered high nutritional risk factors. Untreated or poorly managed dysphagia adversely affects quality of life, interferes with cancer treatment, and may lead to life threatening conditions (e.g., aspiration pneumonia).	Speech-language pathologist involvement is crucial for planning appropriate swallowing rehabilitation. Dysphagia may be short- and long-term meaning long-term use of enteral feed or nutritional supplements is required. Nutritional supplements (e.g., Ensure drinks) contain sucrose and/or glucose and are often consumed in frequent small sips. This combined with poor oral hygiene and compliance with fluoride toothpastes and mouthrinses increases caries risk. Close liaison with the dietician and dental hygienist at this stage are essential.
Weight loss	Only being able to eat certain foods (e.g., fluids or pureed foods) leads to difficultly acquiring adequate nutrition. Dysgeusia or ageusia generally causes loss of interest in food, which can lead to weight loss and compromised nutritional status.	As post-treatment symptoms lessen, some individuals are able to consume more food and drink orally. Small frequent meals are encouraged because appetite can be poor at this stage. A high calorie sweet diet may be encouraged for weight maintenance, which needs close surveillance to ensure oral health is not adversely affected.
Trismus	Side effect of radiotherapy especially when the tumour invades the muscles of mastication and when surgical intervention is required. Surgery may induce scar tissue reducing mouth opening due to scar contraction in the muscles of mastication. Radiotherapy may induce fibrosis in these muscles as a late effect. Most decisive	Prevention of trismus, rather than its treatment, is the most desirable objective. Home exercises to maintain maximum opening and jaw mobility should begin at the start of radiotherapy. A simple wedge made by stacking and taping together tongue depressors can be used by the individual, both as a guide to improved opening and as a target for exercises at least three to four times daily.

Side effect	Description	Management strategies
	factor in trismus development is the inclusion of the medial pterygoid muscles in the treatment field.	
Osteoradionecrosis (ORN)	An area of exposed devitalized irradiated bone that fails to heal over a period of three to six months in the absence of local neoplastic disease. Radiation treatment destroys normal cells leading to damaged arteries, reduced circulation, and reduced healing ability of the bone. Occasionally it can develop spontaneously in post-radiation, but it is more common when irradiated bone sustains an injury because of a tooth extraction, surgery, or denture irritation. Initially, ORN is completely asymptomatic. Pain severity may range from mild to severe, depending on extent of involvement. Early presentation of ORN, within two years, is thought to be related to high doses of radiotherapy (>70 Gy). Late presentation is usually secondary to trauma and delayed wound healing within compromised tissue. Tooth extraction has been considered one of the main risk factors of ORN. Other risk factors include: • Total radiation dose exceeded 60 Gy. • Local trauma (e.g., due to tooth extraction, uncontrolled periodontal disease, ill-fitting prosthesis). • Immunodeficiency or malnutrition. • Poor oral hygiene. • Posterior mandible more commonly affected possibly due to its compact and dense nature and it is more often in the radiation field than the maxilla.	Efforts should be made to avoid ORN by preradiotherapy oral health assessment. Careful oral health maintenance, timely dental treatment, and dealing promptly with oral trauma are essential in preventing ORN. Treatment is variable depending on the severity (stage) and clinical symptoms. It may range from simple sequestrectomy, irrigation and antibiotics, to hyperbaric oxygen therapy with surgical debridement of sequestra to resection.
Fatigue	A common side effect of many cancer treatments, including radiation therapy, chemotherapy, immunotherapy, and surgery. Conditions such	Balancing rest, activity, and nutrition to decrease fatigue. Relaxing activities may include listening to music, reading, meditating, practicing guided imagery, or spending time with friends/family.

Side effect	Description	Management strategies
	as anemia, pain, medications, and stress can cause or worsen fatigue.	Relaxing can lower stress. Light exercise may be advised to increase energy and promote health. Short naps (i.e., less than one hour) may help. Staying hydrated and eating a balanced diet.
Hair loss	Hair loss on the area being treated. Chemotherapy can cause hair loss from the head. Hair often grows back in three to six months after radiation treatment and in two to three months after chemotherapy.	Use a hairbrush with soft bristles or a wide-tooth comb. Do not use hair dryers, irons, or products such as gels or clips that may hurt the scalp. Wash hair very gently with a mild shampoo and wash less often. Pat dry with a soft towel. Some individuals choose to cut their hair short to make it easier to deal with hair loss. Others choose to shave their head (with an electric shaver to avoid cuts). Protect scalp with sunscreen or a hat.
Skin changes	May cause the skin on area receiving radiation to become dry, peel, itch, and turn red or darker. Skin may look sunburned, swollen, or puffy.	Use mild gentle soaps and skin products as recommended by oncology team. Use sunscreen and sun-protective lip balm.

Follow up

Follow up after cancer therapy is essential to identify the presence of residual or recurrent cancer early, detect a new cancer, or identify treatment side effects. Note some side effects do not show up until years after therapy has finished.

Early in the follow-up pathway, appointments are more frequent (e.g., 1-2 months apart), as the risk of cancer recurrence is higher. Later, appointment intervals become longer due to reducing risk of recurrent disease and the reduction in morbidity. [60] [61]

Follow-up visits may include:

- Discussion on treatment side effects and how the individual is coping. Some individuals experience depression. Diagnosing and treating depression is an important part of cancer care. Screening for depression at the time of cancer diagnosis, and during and after treatment is recommended, with referral for treatment as required.[10]
- Head and neck exam including an oral cancer screening, palpating lymph nodes, and examining teeth for decay. Regular oral healthcare appointments are recommended due to xerostomia or other effects of cancer therapy.
- Endoscopy of the nasal cavity.
- Imaging tests (e.g., chest x-ray, CT scan, MRI, PET scan) to look for signs of disease, cancer recurrence, or a new tumour.
- Blood tests to check thyroid-stimulating hormone (TSH) levels and monitor thyroid function after radiation therapy to the neck.
- Assessment of speech and hearing.
- Tests to assess swallowing, such as a fibre optic endoscopic evaluation of swallowing (FEES) using an endoscope with a fibre optic camera to view the pharynx and larynx while the individual swallows; or a modified barium swallow (MBS) which uses x-rays and a contrast medium (barium) to record swallowing movements.
- Swallowing, speech, and hearing rehabilitation. Radiation, surgery, and certain chemotherapy drugs can lead to problems with swallowing, speech, and hearing. A multidisciplinary team may be involved with rehabilitation, such as a speech-language pathologist to help manage speech and swallowing problems; an audiologist for hearing aids to improve hearing; a registered dietician to improve nutrition.
- Oral and dental rehabilitation. Lifelong dental follow-up care and rehabilitation is important after cancer therapy. Dental extractions after radiation therapy to the oral cavity should be referred to a dental oncologist or oral surgeon for appropriate management. Appointments with a prosthodontist who specializes in management of head and neck cancers for individuals who have lost teeth and tissues. [61] [62] [63]

Follow-up visits for oral cancer are usually scheduled every:

- 1 to 3 months for the first year
- 2 to 6 months for the second year

[10] Canadian Cancer Society offers CancerConnection.ca, an online community to help individuals with cancer and cancer survivors, as well as their loved ones and caregivers, connect with others who know what they are going through.

- 4 to 8 months for the third to fifth year
- 12 months from the sixth year onward [63]

Individuals who have had oral or oropharyngeal cancer can still develop other cancers. Survivors of these cancers can develop any type of second cancer, but they have an increased risk of developing certain second cancers. Many of these cancers are also linked to smoking and alcohol use, which are also risk factors for oral and oropharyngeal cancers. [61]

Increased risk of second cancer [61]

Type of second cancer	Survivor of oropharyngeal cancer	Survivor of oral cancer
Lung cancer	✓	✓
Esophageal cancer	✓	✓
Cancer of larynx & hypopharynx	✓	✓
Oral cancer	✓	Different than primary cancer
Oropharyngeal cancer	Different than primary cancer	✓
Pancreas cancer	✓	
Bile duct cancer	✓	
Anal cancer	✓	
Cervical cancer	✓	✓
Colon cancer	✓	✓
Rectal cancer	✓	✓
Stomach cancer	✓	✓
Chronic myeloid leukemia	✓	
Hodgkin lymphoma	✓	
Thyroid cancer	✓	
Liver cancer		✓

Lowering risk of a second cancer

- Smoking cessation, including all tobacco products (e.g., cigarettes, pipes, cigars, chewing tobacco, snuff, betel quid, etc.). Individuals who quit smoking have a lower risk of lung, esophagus, larynx, hypopharynx, oral, and oropharyngeal cancer than those who continue to smoke.
- Keep follow-up appointments after completing cancer treatment. Follow-up tests look for signs that the cancer has recurred or spread are also useful in finding some second cancers, particularly a new lung cancer or cancer in the oral cavity or throat.
- Maintain a healthy weight and keep physically active, limiting time spent sitting or lying down.
- Follow a healthy eating pattern that includes plenty of fruits, vegetables, and whole grains, and limits or avoids processed meats, sugary drinks, and highly processed foods.
- Avoid drinking alcohol. If you drink, follow *Canada's Guidance on Alcohol and Health*.

- Use proper sun protection (e.g., lip balm with SPF, sunscreen, wide brimmed hat), avoid tanning beds.
- Undergo routine oral cancer screening and perform oral cancer self-examination on a regular basis.
- Reduce risk for HPV infection by practicing safe sex and getting the HPV vaccine.
- Maintain good oral health. [7] [61] [64] [65]

Take home messages

- Oral health professionals should routinely conduct oral cancer screenings, including visual inspection and tissue palpation, for all clients and refer any suspicious findings to the appropriate medical or dental provider.
- Given how common cancer is, it is likely oral healthcare providers will encounter individuals either with a history of cancer or who are currently embarking on or undergoing cancer treatment. It is vital clinicians understand cancer treatment, side effects, and management strategies in order to support clients in their cancer journey.
- More frequent preventive periodontal and follow-up appointments may be required, and administration of oral probiotics[11] may be recommended to counteract the radiotherapy changes in the oral microbiome to improve oral health outcomes of individuals post-radiotherapy.[12]
- Targeted oral health treatments and preventive measures need to be included in the standard of care for individuals undergoing radiotherapy and chemotherapy to help maintain good oral health and function.

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Client resources

Multinational Association of Supportive Care in Cancer (MASCC) has produced several information sheets and short videos to educate clients on cancer therapy side effects and oral care before, during, and after cancer therapy.
https://mascc.org/resources/patient-education/

CancerConnection.ca is an online community to help individuals with cancer and cancer survivors, as well as their loved ones and caregivers, connect with others who know what they are going through.
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