THE JOURNAL OF FAMILY PRACTICE

ONLINE EXCLUSIVE

Head & neck cancers: What you'll see, how to proceed

What physical findings should raise your suspicion? How are tumors treated and what follow-up care can you provide? Here's what you need to know.

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The authors reported no potential conflict of interest relevant to this article.

PRACTICE RECOMMENDATIONS

› *Do not treat a neck mass with antibiotics unless it has features consistent with infection.* (C)

› *Order laryngoscopy for all patients with hoarseness that does not resolve after 3 months—or sooner, if malignancy is suspected.* (C)

› *Order ultrasonography-guided fine-needle aspiration for diagnostic evaluation of salivary gland masses.* (B)

› *Manage a thyroid nodule based on its sonographic features, including size, consistency, and the presence of concerning features.* (B)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

The statistics reveal a serious problem: This year, an estimated 63,030 Americans will be given a diagnosis of head and neck cancer (which includes laryngeal, oropharyngeal, sinonasal, nasopharyngeal, and salivary gland cancer[1]); approximately 13,360 of them will die. Furthermore, thyroid cancer is the most rapidly increasing cancer diagnosis in the United States, with an estimated 56,870 cases in 2017.[1,2] Major risk factors for head and neck cancer are tobacco and alcohol exposure and infection with Epstein-Barr virus and human papillomavirus (HPV).[3]

In this article, we review the background for each of the principal types of head and neck cancer with which you should be familiar. We also discuss how to evaluate signs and symptoms that raise suspicion of these neoplasms; outline the diagnostic strategy in the face of such suspicion; and summarize accepted therapeutic approaches. Last, we describe the important role that you, the family physician, play in providing posttreatment care for these patients, especially prevention and management of late adverse effects of radiation therapy.

General characterizations of these cancers

Approximately one-half of patients with head and neck cancer present initially with a nonspecific, persistent neck mass that should be deemed malignant until proven otherwise, because a delay in diagnosis is associated with a worse outcome.[4] In a series of 100 patients with head and neck cancer, for example, delay in diagnosis occurred in nearly 25%—most often because of time spent providing inappropriate antibiotic treatment.[5] Guidelines for management of neck masses recommend against the use of antibiotics in patients who do not have evidence of infection.[6]

Patients with a neck mass that has been present for longer than 2 weeks or that is ulcerated, fixed to underlying tissues,

of firm consistency, or > 1.5 cm should have a physical examination that includes visualization of the base of tongue, pharynx, and larynx. The mass should be evaluated with fine-needle aspiration (FNA) biopsy, which has a positive predictive value of 96% and negative predictive value of 90% for the diagnosis of a head and neck mass. (Note: Anticoagulation therapy is not an absolute contraindication to FNA, which is not associated with an increased risk of bleeding.[6])

One-half of head and neck cancers present with a neck mass that warrants appropriate initial assessment, so as not to delay diagnosis.

Laryngeal cancer

What you need to know. More than 90% of laryngeal cancers are squamous cell carcinoma (SCC). Smoking or heavy drinking (> 8 drinks/d), compared to neither behavior, is associated with an increased risk of laryngeal cancer (odds ratio, 9.4 and 2.5, respectively).[7] The risk of cancer is directly proportional to the degree of tobacco exposure.

Laryngeal cancer occurs in the supraglottic region in one-third of patients; in the glottic region in one-half; and in the subglottic region in a very few.[8] Glottic cancer presents earlier than supraglottic cancer with hoarseness, whereas supraglottic cancer presents with more advanced disease, causing stridor, dysphagia, and throat pain. (Note: Guidelines recommend against prescribing acid suppressants in patients with hoarseness who do not have symptoms of reflux.[9])

Stage 1 and Stage 2 laryngeal cancers are localized; Stages 3-4B are locally advanced or involve lymph nodes, or both; Stage 4C is metastatic disease. Overall, 60% of patients have Stage 3 or Stage 4 disease at diagnosis.[10]

What is the diagnostic strategy? Laryngoscopy should be performed before computed tomography (CT) or magnetic resonance imaging is considered in a patient with hoarseness that does not resolve after 3 months—or sooner, if there is suspicion of malignancy.

How is it treated? Most patients presenting with Stage 1 or Stage 2 cancer can be treated with local radiation or, less commonly, larynx-preserving surgery. Patients with Stage 3 or Stage 4 disease can be treated with a combination of radiation and chemotherapy, which, compared to radiation alone, confers a decreased risk of local recurrence and increased laryngectomy-free survival.[11] Patients whose vocal cords are destroyed or who have recurrence following radiation and chemotherapy might need total laryngectomy and formation of a tracheostomy and prosthetic for voice creation.

Five-year overall survival for Stage 1 and Stage 2 supraglottic and glottic cancers is 80%—lower, however, for later-presenting subglottic cancers.[12]

Oropharyngeal cancer

What you need to know. The lifetime risk for cancer of the oropharynx is approximately 1%.[13] SCC is responsible for approximately 90% of these cancers. Early detection is important: The 5-year survival rate is more than twice as high for localized disease (83%) than it is for metastatic disease (39%) at detection.[13]

At any given time, 7% of the US population has HPV infection of the oropharynx. Most of these cases clear spontaneously, but persistent high-risk HPV infection led to a 225% increase in HPV-positive oropharyngeal SCC from 1988 to 2004.[14] The representative case of HPV-positive oropharyngeal SCC is a middle-aged (40- to 59-year-old) white male with a history of multiple sexual partners and with little or no tobacco exposure and low alcohol consumption.

What is the diagnostic strategy? Oral cancers present with a lesion, often ulcerative, that should be examined by palpation with a gloved finger to describe the presence, color, and number of lesions; any tenderness; tissue consistency (soft, firm, hard); and fixation to underlying structures.[15] The oropharynx should be examined without protrusion of the tongue, which obscures the oropharynx and can make it harder to depress the posterior part of the tongue.

A finding of leukoplakia (white plaques) and erythroplakia (red plaques) of the oropharynx might reflect benign hyperkeratosis or premalignant lesions; the plaques do not wipe off on examination. Referral to a dentist or otorhinolaryngologist for biopsy is indicated for all erythroplakia and leukoplakia, and for ulcers that persist longer than 2 weeks.[16]

(Note: Evidence is insufficient to support

TABLE

Managing a thyroid nodule based on US features[30]

Suspicion level	US features	Risk of malignancy (estimated)	Nodule size cutoff for FNA
High	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule, with ≥ 1 concerning features[a]	70%-90%	FNA at ≥ 1 cm is recommended
Intermediate	Hypoechoic solid nodule with smooth margins, without other concerning features[a]	10%-20%	FNA at ≥ 1 cm is recommended
Low	Isoechoic or hyperechoic solid nodule, or partially cystic nodule containing solid areas, without other concerning features[a]	5%-10%	FNA at ≥ 1.5 cm is recommended
Very low	Spongiform or partially cystic nodules, without US features of higher-risk patterns	< 3%	FNA at ≥ 2 cm should be considered; however, observation without FNA is reasonable
No suspicion (benign)	Purely cystic nodules, without solid components	< 1%	Biopsy is not recommended

FNA, fine-needle aspiration; US, ultrasonographic.

[a]"Concerning features" of a solid nodule are irregular margins; microcalcifications; taller-than-wide shape; rim calcifications with a small, extrusive soft-tissue component; and evidence of extrathyroidal extension.

Adapted from: Haugen BR et al, 2016.[30]

screening asymptomatic patients for oral and oropharyngeal cancers by physical examination. There is no US Food and Drug Administration-approved screening test for oral HPV infection.[17])

How is it treated? A diagnosis of moderate dysplasia or carcinoma in situ should be treated with surgical excision to clear margins followed by routine monitoring every 3 to 6 months, for life.[18] Topical medication, electrocautery, laser ablation, and cryosurgery are management options for less severe dysplasia.

Sinonasal cancer

What you need to know. Worldwide, sinonasal cancer accounts for approximately 0.7% of all new cancers but demonstrates strong genetic and regional associations, particularly among the Cantonese population of southern China.[19] One-half of new sinonasal malignancies are SCC; the rest are adenocarcinoma, lymphoepithelial carcinoma, and rare subtypes.[20]

What is the diagnostic strategy? Presentation tends to mimic common, nonmalignant conditions, such as sinusitis, until invasion into adjacent structures. When sinonasal passages are involved, the history might include epistaxis or nasal discharge; facial or dental pain; unilateral nasal obstruction with unexplained onset later in life; and failure to respond to treatment of presumed rhinosinusitis. Physical examination should include assessment of cranial nerves, palpation of the sinuses, and anterior rhinoscopy.

Thin-cut CT of the paranasal sinuses is the first-line imaging study. Sinonasal endoscopy, with targeted biopsy of suspicious lesions, is the evaluation of choice when malignancy is suspected.

How is it treated? Surgery is the treatment of choice, with postoperative radiation for patients at higher risk of recurrence because of more extensive disase.[12] Five-year survival for advanced disease is poor (35%); only 15% of cases are diagnosed at a localized stage because presenting symptoms are nonspecific.[21]

Nasopharyngeal cancer

What you need to know. Nasopharyngeal cancer is rare in the United States and Europe, compared with China, where it is endemic

(and where a variety of risk factors, including intake of salt-preserved fish, have been proposed[22]). Epstein-Barr virus infection and a history of smoking increase the risk.

Patients with nasopharyngeal cancer can present with epistaxis, nasal obstruction, and auditory symptoms, such as serous otitis media. Direct extension of the tumor can lead to cranial-nerve palsy, most commonly III, V, VI, and XII.[23]

What is the diagnostic strategy? Three-quarters of patients present with a neck mass from lymph-node metastases. Patients with the risk factors for nasopharyngeal cancer noted above who present with concerning symptoms should have nasoendoscopy with biopsy.

How is it treated? Radiation is the primary treatment, which is combined with chemotherapy for more advanced disease.[23] Screening high-risk populations for antibodies to Epstein-Barr virus and performing nasopharyngeal endoscopy on patients who screen positive increases the detection rate of nasopharyngeal cancer; however, this strategy has not been shown to improve survival.[9]

In a series of 100 patients with head and neck cancer, a delay in diagnosis occurred in nearly 25%—most often because of time spent providing inappropriate antibiotic treatment.

Salivary gland tumors

What you need to know. Salivary gland neoplasms are a rare and heterogeneous entity, comprising 6% to 8% of head and neck cancers.[24] More than 70% of these tumors are located in the parotid gland; 8%, in the submandibular glands; 1%, in the sublingual glands; and the rest, in the minor salivary glands. Most salivary gland tumors are benign; the most prevalent malignant tumors are mucoepidermoid carcinoma (30%) and adenoid cystic carcinoma (10%).[25] Additional identified risk factors for a salivary gland tumor include irradiation, prior head and neck cancer, and environmental exposures, including hairdressing, rubber manufacturing, and exposure to nickel compounds.[26]

What is the diagnostic strategy? The history and physical exam are essential to distinguish a salivary gland tumor from an infectious cause and sialolithiasis. Parotid tumors most commonly present as asymptomatic parotid swelling, although pain can be present in as many as 40% of malignant parotid tumors.[25] Facial nerve weakness is found in 25% of parotid tumors; although the differential diagnosis of facial nerve palsy is broad, suspicion of malignancy should be raised in the presence of a parotid mass, progressive unilateral symptoms, hemifacial spasm progressing to weakness, and a history of skin cancer on the face or scalp. Additional characteristics that favor a neoplastic cause are trismus and nontender lymphadenopathy.[25]

In contrast, sialolithiasis is associated with intermittent pain caused by eating and is more common in the settings of dehydration and poor dental hygiene. Sialadenitis should be suspected when the presentation is fever, increased pain and swelling, erythema, and expression of pus from the salivary gland.

If malignancy is suspected, the initial diagnostic evaluation should include ultrasonography (US); concurrent FNA biopsy should be performed if a mass is detected.[27] US-guided FNA has a sensitivity of 73% to 86% for salivary neoplasm.[7] CT and magnetic resonance imaging are useful for further characterization of tumors and can be advantageous for surgical planning.

How is it treated? Treatment of a salivary gland tumor involves surgical resection, followed by radiotherapy for patients in whom disease is more extensive or who exhibit high-risk pathology. Primary radiotherapy can be used in patients with an unresectable tumor. Typically, chemotherapy is used only for palliative purposes in relapsing disease, when a tumor is not amenable to radiotherapy, and in metastatic disease.[25]

Prognosis varies by histotype but is generally favorable. The survival rates for a malignant salivary gland tumor are 83% at 1 year, 69% at 3 years, and 65% at 5 years.[28] Distant metastases are the most common cause of death, occurring primarily in the lungs (80%), bone (15%), and liver.[27] Factors that indicate poor prognosis include facial nerve involvement, trismus, a tumor > 4 cm, bone involvement, nodal spread, and recurrence.[25]

Thyroid cancer

What you need to know. Thyroid cancer is the most rapidly increasing cancer diagnosis in the United States, with an annual

incidence of 4.5%.[1] In the United States, most thyroid cancers are differentiated thyroid cancer (DTC), which includes papillary and follicular cancers. Less-differentiated medullary thyroid cancer (MTC), typically associated with multiple endocrine neoplasia (MEN) 2A or 2B, and undifferentiated or anaplastic thyroid cancer are less common. The increasing incidence of thyroid cancer is primarily the result of an increase in nonclinically relevant DTC.

What is the diagnostic strategy? Thyroid cancer usually presents as a thyroid nodule found by the patient or incidentally on physical examination or imaging. Other presenting signs and symptoms include hoarseness, voice changes, and dysphagia.

Thyroid US is the study of choice for initial evaluation of the size and features of a nodule; findings are used to make recommendations for further workup. If further evaluation is indicated, FNA biopsy is the test of choice.[29]

In 2016, the American Thyroid Association released updated guidelines for evaluating thyroid nodules (TABLE).[30] The US Preventive Services Task Force recommends against screening for thyroid cancer by neck palpation or US in asymptomatic patients because evidence of significant mortality benefit is lacking.[31]

How is it treated? Treatment of thyroid cancer focuses on local excision of the nodule by partial or total thyroidectomy (depending on the size and type of cancer) and surgical removal of involved lymph nodes. Differentiated thyroid cancer is categorized as high-, medium-, or low-risk, depending on tumor extension, incomplete tumor resection, size of lymph nodes > 3 cm, and distant metastases. Adjuvant treatment with radioactive iodine can be considered for intermediate-risk DTC and is recommended for high-risk DTC.[32]

Following surgical treatment, thyroid-stimulating hormone suppression is recommended using levothyroxine.[33] Patients at higher risk of recurrence should have longer and more intense suppression of thyroid-stimulating hormone.[30] Levels of serum thyroglobulin and anti-thyroglobulin antibody should be followed postoperatively; rising values can indicate recurrent disease. The calcitonin level should be followed in patients with a history of MTC. Thyroid US should be performed 6 to 12 months postoperatively, then periodically, depending on determination of recurrence risk and any change in the thyroglobulin level.[30]

(Note: Glucagon-like peptide-1 [GLP-1]

Follow-up care after treatment of head and neck cancer[35-39]

Challenge: After radiation to the head and neck, as many as 53% of patients develop subclinical hypothyroidism and 33% develop clinical hypothyroidism.[35] **Strategy:** Measure the thyroid-stimulating hormone level within 1 year of the completion of radiotherapy and every 6 to 12 months thereafter.[36]

Challenge: Radiation to the head and neck can decrease the function of salivary glands, causing xerostomia in as many as 40% of patients. This condition can lead to problems with oral hygiene and difficulty with speech, eating, and swallowing.[37] **Strategy:**

- Treat xerostomia with artificial saliva, sugar-free candy and gum, or muscarinic cholinergic agonists, such as pilocarpine and cevimeline.
- Consider treatment with pilocarpine or cevimeline. Pilocarpine alleviates xerostomia in approximately 50% of patients who develop the condition, although its use can be limited by adverse cholinergic effects.[3,7] Cevimeline causes fewer and less pronounced adverse effects than pilocarpine because it acts more specifically on receptors in the salivary glands.[38]
- Mention the possibility of acupuncture to your patients. There is evidence that it can stimulate salivary flow.[39]

Challenge: Patients who have had radiation to the head and neck have an increased risk of dental caries from xerostomia and the direct effect of radiation, which causes demineralization of teeth. **Strategy:** Following radiation, instruct the patient about appropriate oral hygiene:

- regular flossing
- brushing and application of daily fluoride
- regular visits for dental care.[39]

Challenge: Trismus occurs in 5% to 25% of patients, depending on the type of radiation.[36] **Strategy:** Recommend exercise-based treatment, the treatment of choice. Surgery is indicated for severe cases.

Challenge: Dysphagia occurs in approximately 25% of patients treated with radiation.[36] **Strategy:** Provide a referral for swallowing exercises, which might be helpful. Some cases are severe enough to warrant placement of a feeding tube.[37]

Last, counsel all patients who have been treated for cancer of the head or neck, with any modality, about cessation of smoking and alcohol.

receptor agonists, used to treat type 2 diabetes mellitus, carry a black-box warning for their risk of MTC and are contraindicated in patients who have a personal or family history of MTC, MEN2A, or MEN2B.[34])

Anaplastic thyroid cancer, a rare form of thyroid cancer, carries a high mortality rate, with a median survival of 5 months from diagnosis and 1-year survival of 20%. Patients require expeditious total thyroidectomy and neck dissection, followed by external-beam radiation with or without chemotherapy. If this strategy is not feasible, tracheostomy might be necessary to maintain a patent airway.[2] Family physicians treating a patient who has anaplastic thyroid cancer can fulfill a crucial role by ensuring that an advance directive is established, a surrogate decision-maker is appointed, and goals of care are well defined.

Human papillomavirus is associated with an increasing number of cases of head and neck cancer.

Follow-up care for head and neck Ca

The risk of adverse effects after radiation therapy for head and neck cancer calls for close monitoring, appropriate treatment, and referral and counseling as needed. See "Follow-up care after treatment of head and neck cancer," page E5.[35-39] JFP

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