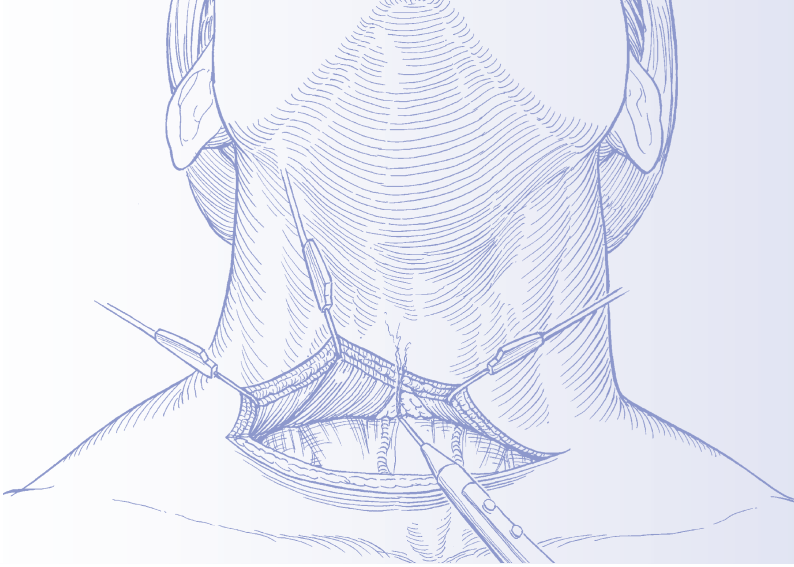
CHAPTER 35

HEAD AND NECK

Robert R. Lorenz, Marion E. Couch, and Brian B. Burkey



NORMAL HISTOLOGY

The normal histology of the upper aerodigestive tract varies in each site. A complete review of the thyroid and parathyroid glands is beyond the scope of this chapter. The nasal vestibule is considered a cutaneous structure and is lined by keratinizing squamous epithelium. The limen nasi, or mucocutaneous junction, is where the epithelium changes to a ciliated pseudostratified columnar (respiratory) epithelium to line the nasal cavities. The exception is the olfactory epithelium at the roof of the nasal cavity, which is composed of bipolar, spindle-shaped olfactory neural cells with surrounding supporting cells. The paranasal sinuses are also lined by respiratory epithelium, but it tends to be thinner and less vascular than that of the nasal cavity. The nasopharyngeal lining varies from squamous to respiratory epithelium in an inconsistent manner. The adenoidal pad is composed of lymphoid tissue containing germinal centers without capsules or sinusoids. The oral cavity is lined by nonkeratinized stratified squamous epithelium with minor salivary glands throughout the submucosa and within the muscular tissue of the tongue. Although the oropharynx is lined by squamous epithelium, Waldeyer's ring is formed by lymphoid tissues of the palatine tonsils, adenoids, lingual tonsils, and adjacent submucosal lymphatics. The tonsils contain germinal centers without capsules or sinusoids but, unlike the adenoids, the tonsils have crypts lined by stratified squamous epithelium.

The hypopharynx is lined by nonkeratinizing, stratified squamous epithelium. Seromucous glands are found throughout the submucosa of the hypopharynx, in the lower two thirds of the epiglottis, and in the potential space between the true and false vocal folds known as the ventricle. Nonkeratinizing stratified squamous epithelium lines the epiglottis and true vocal fold. Pseudostratified, ciliated respiratory epithelium lines the false vocal fold, ventricle, and subglottis. The thyroid, cricoid, and arytenoid cartilages are composed of hyaline cartilage, whereas the epiglottis, cuneiform, and corniculate cartilages are composed of elastic-type cartilage. The external ear is a cutaneous structure lined with keratinizing squamous epithelium and associated adnexal structures. The external third of the external auditory canal is unique in that it contains modified apocrine glands that produce cerumen. The middle ear is lined with respiratory epithelium.

Numerous noncancerous changes in squamous epithelium can be seen in the upper aerodigestive tract. Leukoplakia, which describes any white mucosal lesion, and erythroplasia, which describes any red mucosal lesion, are both clinical descriptions and should not be used as diagnostic terms (Fig. 35-1). Erythroplakia is more often indicative of an underlying malignant lesion. Hyperplasia refers to thickening of the epithelium secondary to an increase in the total number of cells. Parakeratosis is an abnormal presence of nuclei in the keratin layers, whereas dyskeratosis refers to any abnormal keratinization of epithelial cells and is found in dysplastic lesions. Koilocytosis is a descriptive term for the vacuolization of squamous cells and is suggestive of viral infection, especially human papillomavirus (HPV).

EPIDEMIOLOGY

The American Joint Committee on Cancer (AJCC) staging system divides sites of malignancy originating in the head and neck into six major groups: lip and oral cavity, pharynx, larynx, nasal cavity and paranasal sinuses, major salivary glands, and thyroid.[1] Of the sites arising from the aerodigestive tract, laryngeal cancer remains the most common cause of death (Table 35-1), whereas pharyngeal cancer has emerged as exhibiting the highest incidence over the past several years. Although there clearly remains a male preponderance in aerodigestive tract malignancies, the male-to-female ratio has been steadily decreasing because of the direct association between tobacco as a causative agent and the increased incidence of female smokers. Tobacco abuse increases the odds ratio for the development of laryngeal cancer by 15:1, whereas alcohol abuse carries an odds ratio of 2:1. Combined abuse of alcohol and tobacco is not additive in terms of the odds ratio but multiplicative. More recent studies have suggested that the epidemiology of head and neck cancer is shifting to mirror a change in the cause.[2] In the United States, during the period from 1973 to 2003, the incidence rate for cancer sites causally related to HPV infection significantly increased (tongue base and tonsil subsites of the oropharynx), whereas significant declines in incidence were observed for oral cancers not causally related to HPV. In

Table 35-1 Head and Neck Cancer, 2009 Statistics: Upper Aerodigestive Tract

	Estimated Incidence			Estimated Deaths		
SITE	**BOTH GENDERS**	**MALE**	**FEMALE**	**BOTH GENDERS**	**MALE**	**FEMALE**
Tongue	10,530	7470	3060	1910	1240	670
Mouth	10,750	6450	4300	1810	1110	700
Pharynx	12,610	10,020	2590	2230	1640	590
Other oral cavity	1830	1300	530	1650	1250	400
Larynx	12,290	9920	2370	3660	2900	760

From Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2009. CA Cancer J Clin 59:225–249, 2009.

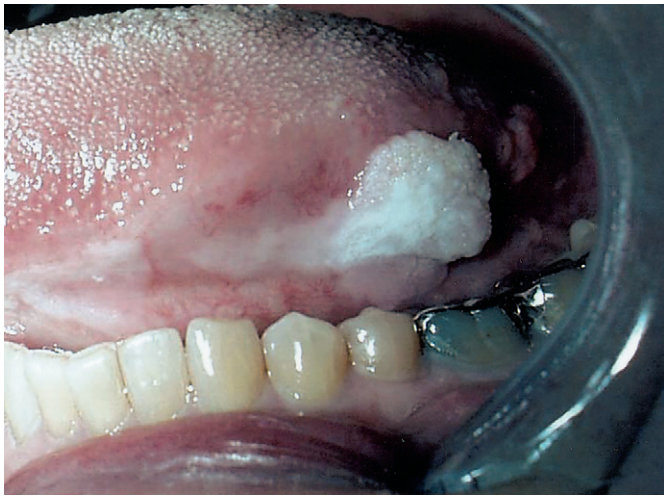


FIGURE 35-1 Leukoplakic lesion on the left mobile tongue. On biopsy, this lesion was determined to be hyperkeratosis without invasive cancer.

addition, HPV-associated cancers tended to be younger in age by 3 to 5 years and were less likely to be associated with alcohol or tobacco use. Worldwide, the highest incidence rates in males exceeded 30/100,000 in areas of France, Hong Kong, India, Spain, Italy, and Brazil, as well as in U.S. blacks, with dramatic increases in oral cancer being seen in Central and Eastern Europe, most notably Hungary, Poland, Slovakia, and Romania.[3] The highest female rates are higher than 10/100,000 and are found in India, where chewing of betel quid and tobacco is common. Although aggregate rates are slowly declining in certain areas, such as India, Hong Kong, and Brazil, as well as in U.S. whites, rates are increasing in most other regions of the world. In addition to alcohol and tobacco consumption as causative factors, other risk factors include HPV and Epstein-Barr virus infection, Plummer-Vinson syndrome, metabolic polymorphisms, malnutrition, and occupational exposure to mutagenic agents. According to the National Cancer Database, squamous cell carcinoma (SCC) is the most common head and neck tumor of the major head and neck sites (88.9%), adenocarcinoma is the most common of the major salivary glands (56.4%), SCC is the most common of the sinonasal tract (43.6%), and lymphoma is the most common of the sites classified as other (82.5%).[4]

CARCINOGENESIS

HPV infection is now recognized as a causative agent for oropharyngeal carcinoma. Based on the molecular cause, HPV-positive and HPV-negative head and neck SCCs (HNSCCs) may be considered as two distinct cancers.[5] High-risk HPV strains (subtypes 16 and 18) suppress apoptosis and activate cell growth when the HPV E6 and E7 proteins disrupt regulatory cell cycle and DNA repair pathways. Malignant transformation begins with inactivation of the p53 tumor suppressor gene by E6, whereas E7 inactivates the retinoblastoma tumor suppressor protein (Rb). E6 targets the cellular ubiquitin-protein ligase E6-AP, which then targets p53 for ubiquitination and degradation; this results in unregulated cell growth. E7 associates with Rb and p21 by blocking the interaction of Rb with E2F, which initiates uncontrolled cell proliferation.[5] Viruses such as HPV can usurp cellular processes, but often the development of carcinoma is the result of a stepwise accumulation of genetic alterations.[6] Tobacco, a well-known risk factor, was one of the first carcinogens to be linked with p53 mutations. One tobacco carcinogen, benzo[α]pyrene diol epoxide, induces genetic damage by forming covalently bound DNA adducts throughout the genome, including p53. Damage induced by benzo[α]pyrene diol epoxide and other carcinogens is repaired with the nucleotide excision repair system. Several studies have demonstrated that sequence variations in nucleotide excision repair genes contribute to HNSCC susceptibility.[7]

Many years after Slaughter proposed field cancerization, Califano and colleagues described the molecular basis for histopathologic changes in HNSCC.[8] Samples of dysplastic mucosa and benign hyperplastic lesions displayed loss of heterozygosity at specific loci (9p21, 3p21, 17p13). In particular, loss of heterozygosity at 9p21 or 3p21 is one of the earliest detectable events leading to dysplasia in this tumor progression model. From dysplasia, further genetic alteration in 11q, 13q, and 14q results in carcinoma in situ. The high rate of recurrence of HNSCC is believed to result from histopathologically benign squamous cell epithelium harboring a clonal population with genetic alterations.[8] Studies using microsatellite analysis and X chromosome inactivation have verified that metachronous and synchronous lesions from distinct anatomic sites in HNSCC often originate from a common clone. This evidence confirms that genetically altered mucosa is difficult to cure in the HNSCC patient because it is on the path to tumorigenesis, as predicted by this model. Indeed, HNSCC patients have a 3% to 7% annual incidence of secondary lesions in the upper aerodigestive

tract, esophagus, or lung. A synchronous second primary lesion is defined as a tumor detected within 6 months of the index tumor. The occurrence of a second primary lesion more than 6 months after the initial lesion is referred to as metachronous. A second primary will develop in the aerodigestive tract of 14% of patients with HNSCC over the course of their lifetime, with more than half of these lesions occurring within the first 2 years of the index tumor.

There is also evidence to suggest that changes in the programming of cells, including stem cells, may also be involved in tumorigenesis in HNSCC because of the epithelial to mesenchymal transition.[9] Abnormalities in cadherins, tight junctions, and desmosomes lead to a decrease in cell-cell adherence and loss of polarity, increasing the mobility of these cells. As epithelial cells disassemble their junctional structures, undergo extracellular matrix remodeling, and begin expressing proteins of mesenchymal origin, they become migratory. When the process of epithelial to mesenchymal transition becomes pathologic, regulatory checkpoints are deficient. Thus, in the carcinogenic process, epithelial to mesenchymal transition may cause changes that contribute to tumor invasion and metastasis, enabling cancer cell dissemination.[9]

Epidermal growth factor receptor (EGFR) signaling has been strongly implicated in tumor progression in HNSCC. The ErbB family is comprised of four structurally related receptor tyrosine kinases. EGFR mRNA and protein are preferentially expressed in HNSCC compared with surrounding normal tissues, suggesting a significant role in carcinogenesis. EGFR is overexpressed in up to 80% to 100% of HNSCC tumors, with advanced-stage and poorly differentiated carcinomas more frequently demonstrating overexpression.[10] The most common mutation, *EGFRvIII,* occurs in up to 40% of HNSCCs. This mutant receptor is only found in cancer cells and has an in-frame deletion of exons 2 to 7, which results in a constitutively active receptor. The fact that *EGFRvIII* is not found in normal tissues makes this an attractive target for therapy. The two classes of therapies are monoclonal antibodies to EGFR receptor subunits and small-molecule EGFR tyrosine kinase inhibitors (TKIs). When ligands bind to one of the ErbB receptors, a dimer forms and the receptor's intracellular tyrosine residues then undergoes ATP-dependent autophosphorylation. Once phosphorylated, the receptor has the potential to trigger many different intracellular downstream pathways. The Janus kinase–signal transducers and activators of transcription (JAK–STAT), along with the phospholipase-Cγ–protein kinase C (PLCγ–PKC) pathways are activated in association with EGFR phosphorylation.

An emerging potential target for molecular-based cancer therapy is the insulin-like growth factor-1 receptor (IGF-1R) and its ligands, insulin growth factor-1 (IGF-1) and insulin growth factor-2 (IGF-2).[11] With activation of the receptor, downstream signaling events include phosphorylation of insulin receptor substrate-1 (IRS-1), activation of mitogen-activated protein kinases (MAPKs), and stimulation of the phosphatidylinositol-3 kinase (PI3K) pathway. This activation of both the Ras-MAPK-ERK and PI3K-Akt pathways is similar to the downstream signaling seen with EGFR autophosphorylation.

With the advent of increasingly sophisticated molecular detection techniques, such as DNA microarrays, large numbers of genetic markers can now be tested with greater ease. As single molecular markers, most studied to date have failed to demonstrate sufficient predictive potential in terms of incidence or prognosis. However, although single markers may not prove to have enough clinical applicability, panels of different molecular markers may offer more promising diagnostic and prognostic value.

STAGING

Staging of head and neck cancer follows the TNM classification established by the AJCC.[1] The T classification refers to the extent of the primary tumor and is specific to each of the six sites of origin, with subclassifications within each site. The N classification refers to the pattern of lymphatic spread within the neck nodes and is the same for most head and neck sites, except thyroid, nasopharynx, mucosal melanoma, and skin (Table 35-2). In the new seventh edition of the AJCC Cancer Staging Manual,[1] a descriptor has been added as ECS+ or ECS–, depending on the presence or absence of nodal extracapsular spread (ECS). Clinical staging of the neck is based primarily on palpation, although radiographic studies, including computed tomography (CT) and magnetic resonance imaging (MRI), have been shown to be accurate in detecting positive nodes. If the CT criteria of nodes with central necrosis or size larger than 1.0 cm are used to determine positivity, only 7% of pathologically positive lymph nodes would be missed, and these smaller nodes are most often found in necks with more extensive disease. Metastatic disease is reported simply as Mx (cannot be assessed), M0 (no distant metastases are present), or M1 (metastases present). The most common sites of distant spread are the lungs and bones, whereas hepatic and brain metastases occur less frequently. The risk for distant metastases is more dependent on nodal staging than on primary tumor size.

After complete resection of the primary and nodal disease, pathologic staging may be reported. This is designated by a preceding "p," as in pTNM. It must be remembered when

Table 35-2 Metastatic Staging of Regional Lymph Nodes (N)

STAGE	DESCRIPTION
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1*	Metastasis in a single ipsilateral lymph node, ≤3 cm in greatest dimension
N2*	Metastasis in a single ipsilateral lymph node, >3 cm but not >6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension
N2a*	Metastasis in single ipsilateral lymph node >3 cm but not >6 cm in greatest dimension
N2b*	Metastasis in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension
N2c*	Metastasis in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension
N3*	Metastasis in a lymph node >6 cm in greatest dimension

From Edge SB, Byrd DR, Compton CC, et al [eds]: AJCC cancer staging manual, ed 7, New York, 2010, Springer-Verlag.

*A designation of U or L may be used for any N stage to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical or radiologic extracapsular spread (ECS) should be recorded as E– or E+, and histopathologic ECS should be designated as En (none), Em (microscopic), or Eg (gross).

measuring a pathologic mucosal specimen that tumor size may decrease up to 30% after resection. Although clinical T staging is of primary concern, pathologic N staging allows detection of occult microscopic disease and is useful in determining prognosis. Site-specific staging systems are discussed according to the primary site. The major change in the 2010 edition of the AJCC staging system for HNSCC sites, in addition to the ECS + or − descriptor, is the addition of a separate classification for mucosal melanoma of the head and neck, a very rare tumor.[1]

CLINICAL OVERVIEW

Evaluation

Proper treatment of HNSCC requires careful evaluation and accurate staging, both clinically and radiographically. Patients with HNSCC are initially evaluated in a similar manner, regardless of the site of tumor. Patient histories focus on symptomatology of the tumor, including the duration of symptoms, detection of masses, location of pain, and presence of referred pain. Special attention is paid to numbness, cranial nerve weakness, dysphagia, odynophagia, hoarseness, disarticulation, airway compromise, trismus, nasal obstruction, epistaxis, and hemoptysis. Alcohol and tobacco use histories are elicited. Office examination includes nasopharyngeal and laryngeal visualization with a mirror or fiberoptic endoscope. The examiner should be especially vigilant for second primary tumors and not be preoccupied by the obvious primary lesion. Contrast-enhanced CT and MRI of the head and neck may be performed for evaluation of the tumor and detection of occult lymphadenopathy. CT scanning is best at evaluating bony destruction, whereas MRI can determine soft tissue involvement and is excellent at evaluating parotid and parapharyngeal space tumors. Chest radiography or chest CT is performed to rule out synchronous lung lesions. Levels of serum tumor markers such as alkaline phosphatase and calcium may be determined, but such tests are not standard.

Direct laryngoscopy and examination under anesthesia are commonly performed as part of the evaluation of HNSCC. These procedures allow the physician to evaluate tumors without patient discomfort and with muscle paralysis, as well as evaluate the oropharynx, hypopharynx, and larynx and obtain biopsy samples. Pathologic confirmation of cancer is mandatory before initiating treatment. Concurrent bronchoscopy and esophagoscopy have historically been recommended for the detection of synchronous second primaries of the aerodigestive tract, which occur in 4% to 8% of patients who have one head and neck malignancy. With a normal chest radiograph or CT scan, bronchoscopy has a low yield for discovering bronchial tree second primaries. A barium esophagogram may substitute for esophagoscopy in patients at low risk for the development of esophageal tumors.

Positron Emission Tomography

^{18}F-fluorodeoxyglucose is a glucose analogue that is preferentially absorbed by neoplastic cells and can be detected by positron emission tomography (PET). The role of PET has been investigated in the initial evaluation of patients with HNSCC.[12] PET is more sensitive than CT in identifying the primary lesion, but cannot detect unknown primary tumors with more than 50% sensitivity. More than one third of patients have a change in their TNM score based on PET findings, and 14% of patients are assigned a different stage when it is added to the diagnostic workup. PET evaluates neck metastases with sensitivity equal to that of CT but with fewer false-positive results. PET can detect a higher percentage of lung metastases than chest radiography, bronchoscopy, or CT, but the specificity ranges from 50% to 80%, and how to treat a patient with a positive PET and an otherwise negative lung workup is still in question. In approximately 10% of patients, a synchronous second primary cancer is detected in various sites, including the stomach, pancreas, colon, and thyroid. Patients with tumors that demonstrate high uptake on PET have a worse prognosis than patients with less avid tumors and also have less response to radiation therapy. The exact role of PET in the initial evaluation of HNSCC is still under investigation and its use is becoming more routine, but is not within the current standard of care.

Lymphatic Spread

The cervical lymphatic nodal basins contain between 50 and 70 lymph nodes per side and are divided into seven levels (Figs. 35-2 and 35-3).

1. Level I is subdivided:
   - Level IA is bounded by the anterior belly of the digastric muscle, hyoid bone, and midline.
   - Level IB is bounded by the anterior and posterior bellies of the digastric muscle and the inferior border of the mandible. Level IB contains the submandibular gland.
2. Level II is bounded superiorly by the skull base, anteriorly by the stylohyoid muscle, inferiorly by a horizontal plane extending posteriorly from the hyoid bone, and posteriorly by the posterior edge of the sternocleidomastoid muscle. Level II is further subdivided:
   - Level IIA is anterior to the spinal accessory nerve.
   - Level IIB, or the so-called submuscular triangle, is posterior to the nerve.
3. Level III begins at the inferior edge of level II and is bounded by the laryngeal strap muscles anteriorly, by

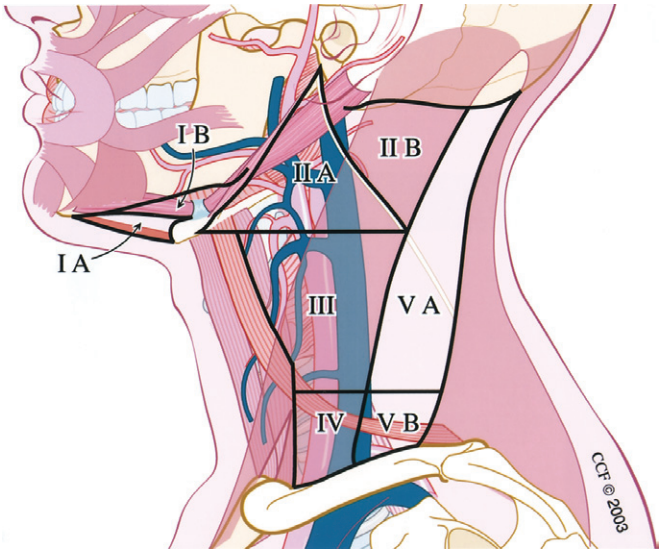


FIGURE 35-2 Diagram of cervical lymph node levels I through V. Level II is divided into regions A and B by the spinal accessory nerve. (Courtesy Cleveland Clinic Foundation, 2003.)

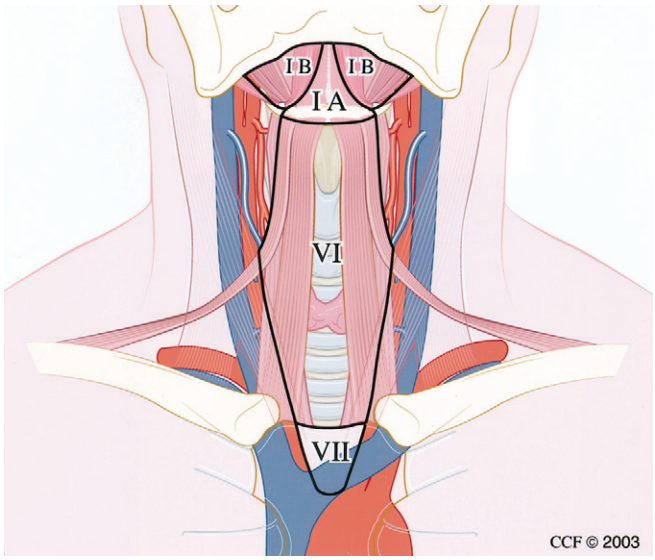


FIGURE 35-3 Diagram of anterior lymph node levels I, VI, and VII. Although large in area, most level VI lymph nodes are confined to the paratracheal region. (Courtesy Cleveland Clinic Foundation, 2003.)

the posterior border of the sternocleidomastoid muscle posteriorly, and by a horizontal plane extending posteriorly from the inferior border of the cricoid cartilage.

4. Level IV begins at the inferior border of level III and is bounded anteriorly by the strap muscles, posteriorly by the posterior edge of the sternocleidomastoid muscle, and inferiorly by the clavicle.
5. Level V is posterior to the posterior edge of the sternocleidomastoid muscle, anterior to the trapezius muscle, superior to the clavicle, and inferior to the base of skull.
6. Level VI is bounded by the hyoid bone superiorly, the common carotid arteries laterally, and the sternum inferiorly. Although level VI is large in area, the few lymph nodes that it contains are mostly in the paratracheal regions near the thyroid gland.
7. Level VII (superior mediastinum) lies between the common carotid arteries and is superior to the aortic arch and inferior to the upper border of the sternum.

Lymphatic drainage usually occurs in a superior to inferior direction and follows predictable patterns based on the primary site. Primary tumors of the lip and oral cavity generally metastasize to nodes in levels I, II, and III, although skip metastases may occur in lower levels. The upper lip primarily metastasizes ipsilaterally, whereas the lower lip has ipsilateral and contralateral drainage. Tumors in the oropharynx, hypopharynx, and larynx usually metastasize to levels II, III, and IV. Tumors of the nasopharynx spread to the retropharyngeal and parapharyngeal lymph nodes, as well as to levels II through V. Other sites that metastasize to the retropharyngeal lymph nodes are the soft palate, posterior and lateral oropharynx, and hypopharynx. Tumors of the subglottis, thyroid, hypopharynx, and cervical esophagus spread to levels VI and VII. In addition to the lower lip, the supraglottis, base of the tongue, and soft palate have a high incidence of bilateral metastases.

Therapeutic Options

Therapeutic options for patients with HNSCC include surgery, radiation therapy, chemotherapy, and combination regimens. In general, early-stage disease (stage I or II) is treated by surgery or radiation therapy. Late-stage disease (stage III or IV) is best treated by a combination of surgery and radiation therapy or chemotherapy and radiation therapy, or all three modalities, depending on the site of the primary. Because surgery was the first therapeutic option available to physicians, it has the longest track record of the three and established the head and neck surgeon as the leader of the treatment team for HNSCC. Photon irradiation is superior to surgery for eradicating microscopic disease and is an excellent alternative to surgery for early lesions. Tonsil, tongue base, and nasopharyngeal primary tumors are especially responsive to photon irradiation. Neutron and proton irradiation are used much less often in the head and neck, although experience has grown with their role in salivary gland malignancies and skull base cancers, respectively. Electrons are not commonly used in the head and neck for noncutaneous tumors. With the advent of intensity-modulated radiation therapy, which can reduce the photon dosage to surrounding normal tissue through computer three-dimensional planning, the dogma that patients may not receive more than 7200 cGy to tissue of the head and neck has been called into question. Hyperfractionation is the practice of administering radiation more than once daily, and results of the European Organization for Research and Treatment of Cancer have determined that hyperfractionation for HNSCC produces greater locoregional control than conventional once-daily regimens.[13] Radiation therapy is not as effective in treating large-volume, low-grade neoplasms or tumors in close proximity to the mandible because of the risk for osteoradionecrosis. The loss of salivary function with irradiation of the oral and oropharyngeal cavity can be disabling to patients, and its impact should not be minimized in the decision making process.

A landmark chemotherapy trial for HNSCC was the Veterans Affairs larynx trial, published in 1991.[14] Although chemotherapy alone is not curative in HNSCC, its role as a radiation sensitizer was established in this study. Two thirds of patients treated with radiation therapy and chemotherapy were able to keep their larynx, and survival was equal to that of patients treated with laryngectomy and radiation therapy. Recurrences after radiation therapy have been shown to be multifocal in the bed of the original tumor and the salvage surgeon should be familiar with the original tumor location and volume. Chemotherapy is commonly used in the treatment of incurable HNSCC, such as unresectable and metastatic disease, and can provide excellent symptom control in these patients.

Data from two large-scale, independent trials have examined the benefit of adding chemotherapy to postoperative irradiation for HNSCC.[15,16] Both the European Organization for Research and Treatment of Cancer Trial and the Radiation Therapy Oncology Group 9501/Intergroup treated advanced-stage, high-risk patients with cisplatin concurrently with postoperative radiation therapy and compared the outcomes with those of patients undergoing postoperative irradiation alone. In the Radiation Therapy Oncology Group, the 2-year locoregional control rate was 82% for the group receiving chemoradiation therapy versus 72% for the radiation therapy–alone group. Disease-free survival was significantly longer in the chemoradiation therapy patients, although overall survival was not

significantly different between the groups. Not unexpectedly, significantly more toxicity and treatment morbidity were seen in the combined-treatment group, and further prognostic indicators about which patients are at high risk for failure are needed to predict which groups warrant this more intensive adjuvant therapy.

The neck should be treated when there are clinically positive nodes or the risk for occult disease is more than 20%, based on the location and stage of the primary lesion. The decision to perform neck dissection or irradiate the neck is related to treatment of the primary lesion. If the index tumor is being treated with radiation and the neck is N0 (no clinically detectable disease) or N1, the nodes are usually treated with irradiation. For surgically treated primary lesions, N0 or N1 neck disease may also be treated surgically. Negative prognostic factors such as extracapsular spread of tumor, perineural invasion, vascular invasion, fixation to surrounding structures, and multiple positive nodes are indicators for postoperative adjuvant radiation therapy. For N2 or N3 neck disease, neck dissection with planned postoperative radiation therapy is performed. When chemoradiation therapy protocols are used in treating the primary lesion and there is a complete response in the primary tumor and an N2 or N3 neck, planned neck dissection 8 weeks after chemoradiation therapy will contain cancer in up to one third of specimens.[17] If the neck mass persists, the percentage of residual disease increases to two thirds. When patients have advanced neck disease that involves the carotid artery or deep neck musculature, radiation or chemoradiation therapy is given preoperatively in the hope that the tumor will reduce in size and become resectable. CT scans notoriously carry a high false-positive rate for determining carotid encasement. When carotid resection is necessary, the associated morbidity is high (major neurologic injury in 17%), with a 22% 2-year survival rate, and the decision to resect should be weighed carefully.

Radical neck dissection (RND) was attributed to Crile in 1906 and was considered the gold standard for the removal of nodal metastases (Fig. 35-4). Through a subsequent close reading of Crile's surgical notes, it was found that he had begun to modify his surgical technique to remove only selected regions of the neck, depending on the site of the primary tumor. Today, this has become common surgical practice for HNSCC. All modifications of neck dissection are described in relation to the standard RND, which removes nodal levels I through V and the sternocleidomastoid muscle, internal jugular vein, cranial nerve XI, cervical plexus, and submandibular gland. Preservation of the sternocleidomastoid muscle, internal jugular vein, or cranial nerve XI in any combination is referred to as a modified RND (MRND), and the structures preserved are specified for nomenclature. A modified neck dissection may also be referred to as a Bocca neck dissection, named after the surgeon who demonstrated that not only is MRND equally as effective in controlling neck disease as RND when structures are preserved that are not directly involved in tumor, but the functional outcomes of patients after MRND are also superior to those after RND.[18] Although resection of the sternocleidomastoid muscle or one internal jugular vein is relatively nonmorbid, loss of cranial nerve XI leaves a denervated trapezius muscle, which can cause a painful chronic frozen shoulder.

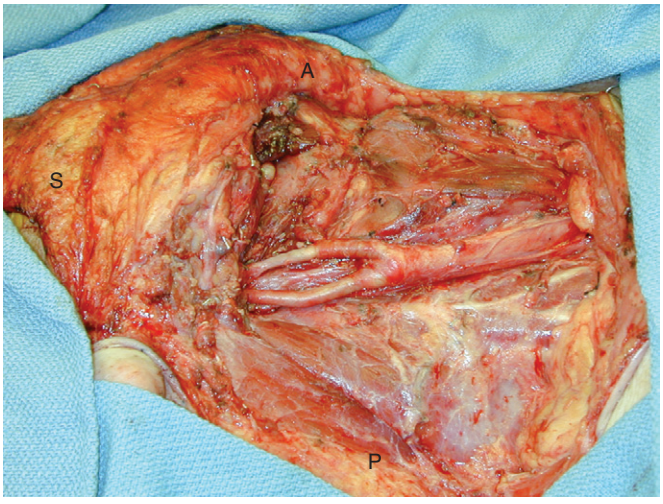


FIGURE 35-4 Proper appearance of the right neck after a radical neck dissection. In addition to all lymphatic tissue, the three structures of the internal jugular vein, sternocleidomastoid muscle, and spinal accessory nerve have been resected. *A,* Anterior; *P,* posterior; *S,* superior.

RND or MRND can be performed for removal of detectable nodal disease. Preservation of any of levels I through V during neck dissection is referred to as selective neck dissection and is based on knowledge of the patterns of spread to neck regions. Selective neck dissection is performed on a clinically negative (N0) neck, with preservation of nodal groups carrying less than a 20% chance of being involved with metastatic disease. Regional control has been shown to be as effective after selective neck dissection as after MRND in patients with a clinically negative neck. Recent studies evaluating treatment of an N0 neck have investigated the use of sentinel lymph node biopsy, which attempts to predict the disease status of the neck based on the first echelon of nodes that drain the tumor.[19] Although sentinel lymph node biopsy has been used extensively with melanoma, its use in HNSCC has come about more gradually. Early results using isosulfan blue dye alone have suggested that this technique cannot consistently identify the sentinel node in HNSCC. More recent results using a gamma probe have been more encouraging, although the isolated node should be serial step–sectioned at a thickness of 150 nm and be examined through permanent processing. The current recommendations are that the technique should be restricted to early-stage (T1 or T2) oral and oropharyngeal cancers, with clinically N0 necks; this continues to be an investigational tool pending validation by large randomized clinical trials.

ANATOMIC SITES

Lip

Anatomically, the lip is considered a subsite of the oral cavity. The lip begins at the junction of the vermilion border and skin and is composed of the vermilion surface, which refers to the mucosa that contacts the opposing lip. It is divided into the upper lip, lower lip, and oral commissures. Most lip cancers occur on the lower lip (90% to 95%) and less often on the upper lip (2% to 7%) and commissures (1%). White men 50 to 80 years of age are the most common group in which lip cancer develops. Sun exposure and pipe smoking are associated with lip cancer. Although SCC is the most common lip cancer (90%), the most common cancer of the upper lip is basal cell carcinoma.

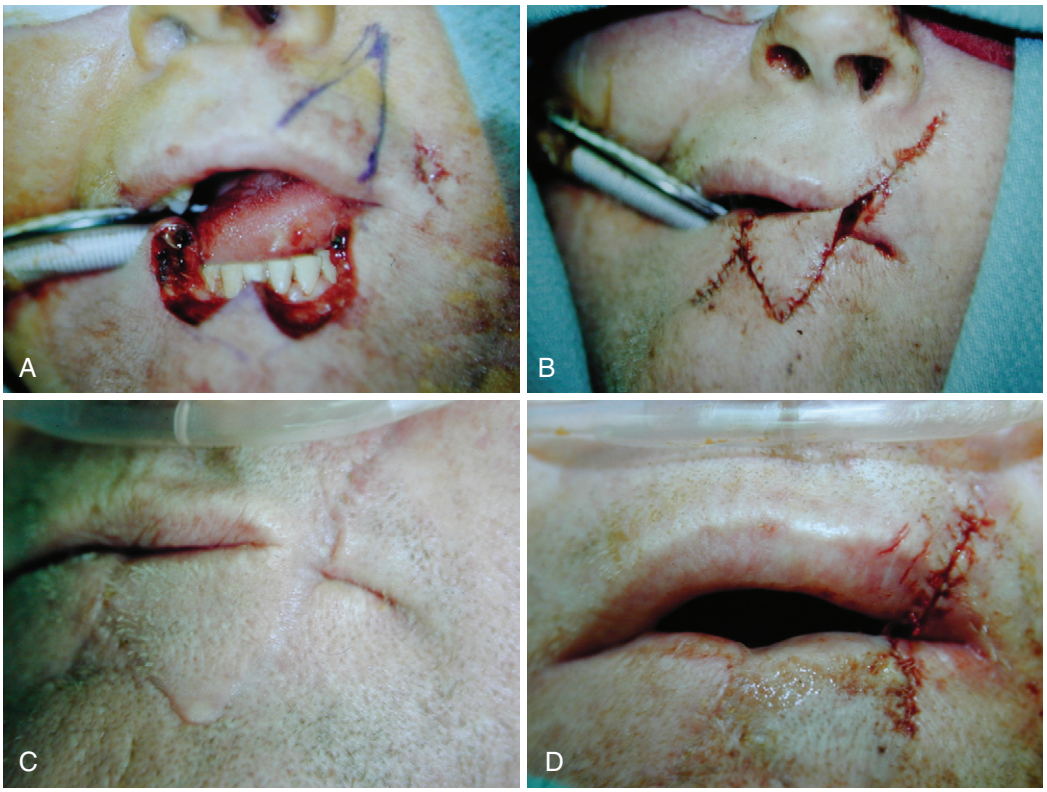


FIGURE 35-5 **A,** Squamous cell carcinoma resected from the lower lip, leaving approximately 25% of normal tissue. **B,** Abbé flap uses upper lip tissue pedicled on the labial artery. **C,** Prior to division of the flap after 6 weeks of healing. **D,** Appearance after pedicle division.

Other lip cancers include variants of SCC (e.g., spindle cell and adenoid squamous carcinoma), as well as mucosal melanoma and minor salivary gland cancers.

The most common clinical manifestation of lip cancer is an ulcerative lesion on the vermilion or skin surface. Palpation is necessary to determine the submucosal extent of the lesion and possible fixation to underlying bone. Sensation of the chin should be tested to determine involvement of the mental nerve. Poor prognostic indicators include nerve involvement, fixation to the maxilla or mandible, cancer arising on the upper lip or commissure, positive nodal disease, and age younger than 40 years at diagnosis. The most frequently involved nodal basins are the submental and submandibular levels. A depth of tumor invasion of 4 mm has been shown to be a cutoff above which the incidence of cervical nodal disease is significantly increased.[20]

Similar to the rest of the oral cavity, lip cancer staging is based on size at initial evaluation. Early-stage disease may be treated by surgery or radiation therapy with equal success. Local surgery (wide local excision) with negative margin control of at least 3 mm is the preferred treatment, with supraomohyoid neck dissection performed for tumors with clinically negative necks but deeper primary invasion or size larger than 3 cm. Neck dissection with postoperative radiation therapy for patients with clinically evident neck disease has an acceptable 91% regional control rate in the neck.[21] The overall 5-year cure rate of 90% drops to 50% in the presence of neck metastases. Postoperative irradiation is also indicated for advanced-stage primary disease, tumors with perineural involvement, or close or positive margins at the time of resection.

The goals of lip reconstruction include reinstitution of oral competence, cosmesis, and maintenance of dynamic function while allowing adequate access for oral hygiene. Fortunately, the surgeon can remove up to half of the lip and still close the defect primarily, particularly defects in the lower lip, which contains more excess tissue than the upper lip. A lower lip wedge excision should not be carried below the mental crease unless the tumor dictates its excision. Care is taken to achieve close approximation of the white line on either side of the defect at the vermilion border because the eye is drawn to any mismatch that exists at this critical aesthetic location.

Defects encompassing between half and two thirds of the lip require augmentation. The Estlander and Abbé flaps are lip switch flaps based on the sublabial or superior labial artery. The Estlander flap is used when the defect involves the commissure, whereas the Abbé flap is used for more midline defects and requires second-stage division of the pedicle (Fig. 35-5). The Karapandzic flap consists of circumoral incisions with circular rotation of the skin flaps while maintaining innervation of the orbicularis oris musculature. This one-stage procedure is used for defects involving more than two thirds of the lip. Microstomia is a potential complication from these types of flap reconstructions, and denture use may not be possible. For defects larger than two thirds, the Webster, Gillies, or Bernard types of repairs may also be used.

Oral Cavity

Because the oral cavity begins at the skin-vermilion junction, the lips are considered part of the oral cavity for staging

purposes. Other subsites in the oral cavity include the buccal mucosa, upper and lower alveolar ridges, retromolar trigone, floor of mouth, hard palate, and oral tongue. The tongue is divided into the oral tongue (two thirds of the tongue volume), anterior to the circumvallate papillae, and the base of tongue, which is not considered part of the oral cavity but rather the oropharynx. Staging of the oral cavity is based on size: T1, 0 to 2 cm; T2, 2 to 4 cm; T3, 4 to 6 cm; and T4, tumors larger than 6 cm or invading adjacent structures, including bone (cortical bone of the mandible or maxilla, not superficial erosion or tooth sockets), deep tongue musculature, or facial skin. SCC accounts for 90% of tumors located in these subsites, with a male preponderance in the fifth and sixth decades of life. There is a close association with alcohol and tobacco abuse.

Oral Tongue

The oral tongue begins at the junction between the tongue and floor of mouth and extends posteriorly to the circumvallate papillae. Tumors appear as exophytic, ulcerative, or submucosal masses that may be associated with tenderness or irritation with mastication. Benign tumors tend to be submucosal and include leiomyomas, neurofibromas, and granular cell tumors. Although granular cell tumors can arise in the larynx, they occur more frequently in the tongue and can be confused with SCC because of overlying pseudoepitheliomatous hyperplasia. Complete excision is curative, but histologic borders are notorious for extending beyond gross disease, and negative intraoperative margins are mandatory.

SCC is the most common type of malignancy, but leiomyosarcomas and rhabdomyosarcomas are also encountered (rarely). Neurotropic malignancies may involve the lingual or hypoglossal nerves, so tongue deviation or loss of sensation should be examined closely. Treatment of oral tongue cancer is primarily surgical, with wide local excision and negative margin control. The development of cervical metastases is related to the depth of invasion, perineural spread, advanced T stage, and tumor differentiation. Infiltration of more than 4 to 5 mm into the tongue musculature increases the incidence of occult cervical metastases. Metastases from the anterior of the tongue most frequently spread to the submental and submandibular regions. Tumors located more posteriorly often metastasize to levels II and III. Indications for postoperative radiation therapy include evidence of perineural or angiolymphatic spread and/or positive nodal disease.

Small tumors may be removed by wide local excision and primary closure or closure by secondary intention. Excision of larger tumors requires partial glossectomy or hemiglossectomy. Extirpation may result in significant dysfunction in terms of disarticulation and dysphagia from an inability to contact the palate, sense oral contents, or manipulate the tongue against the alveolus or lips. Reconstructive efforts should focus on maintaining tongue mobility without excess bulk. Split-thickness skin grafts, primary closure, or healing by secondary intention of larger tongue defects often results in tongue tethering. Thin, pliable fasciocutaneous flaps (e.g., the radial forearm free flap) are the preferred reconstructive technique for such defects. A palatal augmentation prosthesis may assist in maintaining palatal contact, important for speech and posterior propulsion of food boluses.

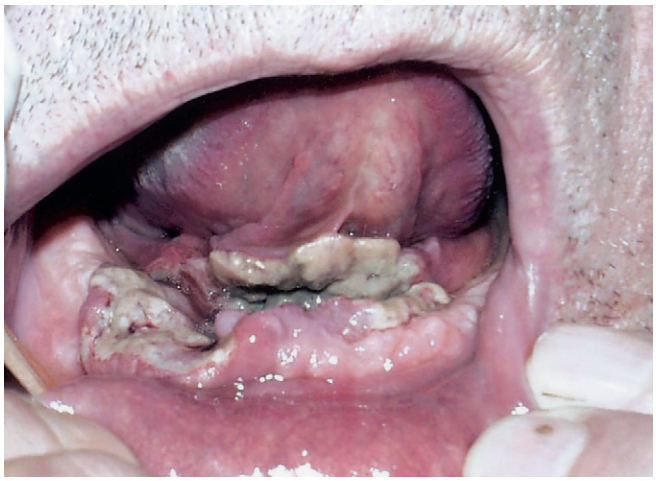


FIGURE 35-6 62-year-old man with squamous cell carcinoma of the anterior floor of mouth invading the mandible.

Floor of the Mouth

The floor of the mouth extends from the inner surface of the mandible medially to the ventral surface of the tongue and from the anteriormost frenulum posteriorly to the anterior tonsillar pillars. The mucosa of the floor of the mouth contains the openings of the sublingual gland and submandibular gland (via Wharton's ducts). The muscular floor is composed of the genioglossus, mylohyoid, and hyoglossus muscles, with the lingual nerve located immediately submucosally.

Bimanual palpation can often determine fixation of tumors of the floor of the mouth to the mandible. CT demonstrates the depth of mandibular bony invasion, and widening of the cranial neural foramen, such as the foramen ovale, suggests neurotropic intracranial spread in advanced tumors. Determining mandibular invasion is of utmost importance for preoperative planning (Fig. 35-6). Invasion into the tongue musculature necessitates partial glossectomy concurrently with removal of the lesion on the floor of the mouth.

Treatment of lesions on the floor of the mouth is primarily surgical, with excision of the involved tongue or mandible as necessary to obtain negative margins. Removal of bone with soft tissue in continuity is commonly referred to as a commando or composite resection. Involvement of the neck may occur by direct extension of tumor through the floor of the mouth musculature or by lymphatic spread. The primary lesion and neck specimen should be taken in continuity so that accompanying lymphatic channels are resected. Adjuvant radiation therapy has similar indications as in oral tongue cancers. The primary goal of reconstruction is separation of the oral cavity from the neck by creating a watertight oral closure. This prevents orocutaneous salivary fistula formation. Secondary goals are maintaining tongue mobility, creating a lingual-alveolar sulcus, and preserving mandibular continuity. Local flaps for soft tissue reconstruction include the platysmal and submental myocutaneous pedicled flaps. Larger defects, including mandibular resection, require complex reconstruction, which is most often performed with free flaps.

Alveolus

The alveolus and its accompanying gingiva constitute the dental surfaces of the maxilla and mandible and extend from the

gingivobuccal sulcus laterally to the floor of the mouth and hard palate medially. Posteriorly, the alveolus extends to the pterygopalatine arch and ascending ramus of the mandible, also referred to as the retromolar trigone. Because of the tight attachment between the mucosa and underlying bone, treatment of alveolar SCC often involves treatment of the maxilla or mandible. Of gingival carcinomas, 70% occur on the lower gum. The periosteum of the mandible is a strong tumor barrier, and tumors that abut the bone may often be resected along with the adjacent periosteum only. Tumors adherent to the periosteum should undergo excision with marginal mandibulectomy, which involves resection of the superior or inner cortical portions of the mandible, with preservation of a continuous rim. Even superficial tumors that invade the outermost part of the mandible may be resected with a marginal mandibulectomy, although this is not oncologically sound if the tumor is a recurrence after radiation therapy. Segmental mandibulectomy entails excision of the full thickness of the mandible, thus interrupting mandibular continuity, and is indicated for patients with gross bone invasion by tumor. Primary radiation therapy for mandibular tumors is not a viable treatment option because of the high likelihood of osteoradionecrosis and poor response of involved bone to radiation therapy.

Buccal Mucosa

The buccal mucosa extends from the inner surface of the opposing surfaces of the lips to the alveolar ridges and pterygomandibular raphe. Buccal cancer is uncommon and represents 5% of all oral cavity carcinomas. Smoking, alcohol abuse, lichen planus, dental trauma, snuff dipping, and tobacco chewing are causative factors associated with buccal cancer. Approximately 65% of patients with buccal cancer are initially found to have extension beyond the cheek mucosa. Lymphatic drainage is to the submandibular lymph nodes; however, tumors in the posterior aspect of the cheek may spread to level II initially. Stage I cancers have historically been treated by surgery and did not involve elective neck dissection because of the low rate of occult metastases. More recent studies, however, have suggested high rates of local recurrence for lesions treated by surgery alone, and adjuvant radiation therapy has been suggested, even for early-stage lesions.[22] Deep invasion may require through and through excision of cheek skin, thus necessitating internal and external linings, usually with a fasciocutaneous free flap.

Palate

The hard palate is defined as the area medial to the maxillary alveolar ridges and extending posterior to the edge of the palatine bone. Chronic inflammatory lesions such as viral lesions, zoster, and pemphigoid can mimic neoplasms, and biopsy is indicated for persistent lesions. Necrotizing sialometaplasia is a benign, self-limited process of the minor salivary glands that has a predilection for the palate and can clinically mimic malignancy. The most common intraoral site for Kaposi's sarcoma is the palate in immunosuppressed patients. Torus palatinus is a benign exostosis of the midline hard palate and may require surgery if it interferes with denture wearing.

Minor salivary gland tumors, along with SCC, make up most hard palate tumors. Adenoid cystic carcinoma, mucoepidermoid carcinoma, adenocarcinoma, and polymorphous low-grade adenocarcinoma are common malignancies of salivary gland origin that tend to arise at the junction of the hard and soft palate. Malignancies of the hard palate are treated by local excision, if found early, but most commonly require resection of bone because of close adherence of the mucosa to the palate. Inferior maxillectomy, subtotal maxillectomy, or total maxillectomy is indicated for progressively destructive tumors extending into the maxillary antrum. Adjuvant radiation therapy is given for advanced lesions. Reconstruction may be accomplished with soft tissue flaps for small defects, obturation with a dental prosthesis for defects with some remaining hard palate, or bony free tissue transfer for extensive palatal resections.

Oropharynx

The borders of the oropharynx include the circumvallate papillae anteriorly, plane of the superior surface of the soft palate superiorly, plane of the hyoid bone inferiorly, pharyngeal constrictors laterally and posteriorly, and medial aspect of the mandible laterally. The oropharynx includes the base of the tongue, inferior surface of the soft palate and uvula, anterior and posterior tonsillar pillars, glossotonsillar sulci, pharyngeal tonsils, and lateral and posterior pharyngeal walls. Similar to the oral cavity, T staging in the oropharynx is dependent on size. T4 tumors may extend out of the oropharynx posteriorly into the parapharyngeal space, inferiorly into the larynx, or laterally into the mandible.

Of tumors of the oropharynx, 90% are SCCs. Other tumors include lymphoma of the tonsils or tongue base or salivary gland neoplasms arising from minor salivary glands in the soft palate or tongue base. Initial symptoms include sore throat, bleeding, dysphagia and odynophagia, referred otalgia, and voice changes, including a muffled quality or hot potato voice. Trismus suggests involvement of the pterygoid musculature. Imaging studies should focus on invasion through the pharyngeal constrictors, bony involvement of the pterygoid plates or mandible, invasion of the parapharyngeal space or carotid artery, involvement of the prevertebral fascia, and extension into the larynx. Lymph node metastases generally occur in the upper jugular chain (levels II to IV), although lesions may skip to lower levels and spread to level V; such lesions are more common with oropharyngeal tumors than with tumors of the oral cavity. Bilateral metastases are more common with tongue base and soft palate lesions, especially those with midline lesions.

Treatment of oropharyngeal SCC has focused increasingly on conservation therapy with chemotherapy and radiation therapy. Many tumors of the oropharynx are poorly differentiated and respond well to radiation. Chemotherapy has been used as a radiation sensitizer in a number of studies and the local control rate achieved has been 90%, even in stage IV disease, although overall survival has not improved over more traditional surgery and radiation therapy.[23] A recent study of the cause of tonsil and tongue base cancers has suggested that when the disease is associated with HPV infection, the prognosis is significantly improved over non-HPV tumors. In a phase II trial of investigational therapy in patients with oropharyngeal and laryngeal cancers (ECOG 2399), patients with HPV positive tumors had a 73% reduction in risk of progression and a 64% reduction in risk of death when compared with HPV-negative patients.[24] This landmark study was the first to demonstrate that tumor HPV status is a strong and favorable prognostic marker in uniform patient populations with similar treatment protocols. Many physicians are advising that tumor HPV status should be incorporated as a stratification factor in patients with

oropharyngeal cancer, although basing treatment protocols on HPV status has yet to be definitively investigated.

Surgery is necessary for primary disease that involves the mandible, for resectable recurrent disease, and it has a role in very early superficial tumors that do not justify a full course of radiation therapy. Extensive surgery of the tongue base significantly alters a patient's ability to swallow. Reconstruction of the tongue with preservation of the larynx requires surgical techniques that maintain tongue mobility and suspend the larynx and neotongue to prevent aspiration.

Resection or contracture after irradiation of the soft palate may result in velopharyngeal insufficiency, which is manifested clinically as nasal regurgitation of liquids and solids and hypernasal speech. Augmentation of the soft palate may be performed surgically or via palatal obturation. Although a palatal obturator requires cleaning and is not permanent, patients can remove it for sleep. With surgical augmentation of the palate, a balance between reducing velopharyngeal insufficiency and causing obstructive sleep apnea is difficult to achieve. After tongue base resection, an inferiorly directed palatal obturator assists in achieving the contact at the tongue base that is necessary for the projection of food posteriorly during the oral and pharyngeal phases of swallowing.

Hypopharynx

The hypopharynx is the portion of the pharynx that extends inferiorly from the horizontal plane of the top of the hyoid bone to a horizontal plane extending posteriorly from the inferior border of the cricoid cartilage. The hypopharynx includes both piriform sinuses, lateral and posterior hypopharyngeal walls, and postcricoid region. The postcricoid area extends inferiorly from the two arytenoid cartilages to the inferior border of the cricoid cartilage, thereby connecting the piriform sinuses and forming the anterior hypopharyngeal wall. The piriform sinuses are inverted, pyramid-shaped potential spaces medial to the thyroid lamina; they begin at the pharyngoepiglottic folds and extend to the cervical esophagus at the inferior border of the cricoid cartilage.

Hypopharyngeal cancer is more common in men 55 to 70 years of age with a history of alcohol abuse and smoking. The exception is in the postcricoid area, in which cancers are more common worldwide in women. This is directly related to Plummer-Vinson syndrome, a combination of dysphagia, hypopharyngeal and esophageal webs, weight loss, and iron deficiency anemia, usually occurring in middle-aged women. In patients who fail to undergo treatment consisting of dilation, iron replacement, and vitamin therapy, postcricoid carcinoma may develop just proximal to the web.

Hypopharyngeal tumors are manifested as a chronic sore throat, dysphagia, referred otalgia, and a foreign body sensation in the throat. A high index of suspicion should be maintained because similar symptoms may be seen with the more common gastroesophageal reflux disease. In advanced disease, hoarseness may develop from direct involvement of the arytenoid, recurrent laryngeal nerve, or paraglottic space. The rich lymphatics that drain the hypopharyngeal region contribute to the fact that 70% of patients with hypopharyngeal cancer are initially seen with palpable lymphadenopathy. Patients with hypopharyngeal cancer have the highest rate of synchronous malignancies and the highest rate of development of second HNSCC primaries of any of the head and neck sites. Staging for hypopharyngeal cancer is based on the number of involved subsites or size of the tumor.

Physical examination for hypopharyngeal lesions includes fiberoptic endoscopy. Having the patient blow against closed lips and pinching the nose closed will inflate the potential spaces of the piriformis and assist in visualization of the tumor. Palpation of the larynx may demonstrate a loss of laryngeal crepitus. A fixed larynx suggests posterior extension into the prevertebral fascia and unresectability. Barium swallow may demonstrate mucosal abnormalities associated with an exophytic tumor and is useful for determining the extent of involvement of the cervical esophagus. It also assists in determining the presence and amount of aspiration present. CT can be used to determine the presence of thyroid cartilage invasion, direct extension into the neck, and pathologic lymphadenopathy. Biopsy of the hypopharynx usually requires direct laryngoscopy under general anesthesia.

The most common area for lymphatic spread is the upper jugular nodes, even with inferior tumors. Other regions include the paratracheal and retropharyngeal nodes. The presence of contralateral cervical metastases or level V involvement is a grave prognostic indicator. Treatment of hypopharyngeal cancer yields poor results in comparison to other sites in the head and neck, presumably because of the late stage of the disease at diagnosis. For early lesions confined to the medial wall of the piriform or posterior pharyngeal wall, radiation or chemoradiation therapy is effective as a primary treatment modality. Seldom is laryngeal-sparing partial pharyngectomy possible. Small tumors of the medial piriform wall or pharyngoepiglottic fold may be amenable to conservation surgery, but they must not involve the piriform apex and the patient must have mobile vocal cords and adequate pulmonary reserve.

The most common treatment of hypopharyngeal cancer is laryngopharyngectomy and bilateral neck dissection, including the paratracheal compartments, along with adjuvant radiation therapy. Trials of neoadjuvant chemotherapy followed by concomitant chemotherapy and radiation therapy have shown promise in organ preservation in hypopharyngeal cancer.[25] The estimated 5-year laryngeal preservation rate is 35%, and induction chemotherapy appears to decrease the rate of death from distant metastases.

After total laryngectomy and partial pharyngectomy, primary closure may be possible if at least 4 cm of viable pharyngeal mucosa remains. Primary closure using less than 4 cm of mucosa generally leads to stricture and an inability to swallow effectively. A pedicled cutaneous flap such as a pectoralis myocutaneous flap can be used to augment any remaining mucosa in these cases. When total laryngopharyngectomy with esophagectomy has been performed, a gastric pull-up may be used for reconstruction. More recently, free flap reconstruction with enteric flaps or tubed cutaneous flaps, such as radial forearm or anterolateral thigh flaps, has been used to reconstruct the total pharyngectomy defect.

Larynx

The three-dimensional boundaries of the larynx are complex, and exacting definitions are necessary before understanding the pathologic conditions affecting this organ system. The anterior border of the larynx is composed of the lingual surface of the epiglottis, thyrohyoid membrane, anterior commissure, and anterior wall of the subglottis, which consists of the thyroid

cartilage, cricothyroid membrane, and anterior arch of the cricoid cartilage. The posterior and lateral limits of the larynx are the arytenoids and interarytenoid region, aryepiglottic folds, and posterior wall of the subglottis, which is composed of the mucosa covering the cricoid cartilage. The superior limits are the tip and lateral borders of the epiglottis. The inferior limit is made up of the plane passing through the inferior edge of the cricoid cartilage.

For staging purposes, the larynx is divided into three regions—supraglottis, glottis, and subglottis. The supraglottis is composed of the epiglottis, laryngeal surfaces of the aryepiglottic folds, arytenoids, and false vocal folds. In addition to these supraglottic subsites, the epiglottis is divided into the suprahyoid and infrahyoid epiglottis, for a total of five supraglottic subsites. The inferior limit of the supraglottis is a horizontal plane through the ventricles, which is the lateral recess between the true and false vocal folds. This plane is also the superior border of the glottis; this is composed of the superior and inferior surfaces of the true vocal folds, extends inferiorly from the true vocal folds, and is 1 cm thick. Also included in the glottis are the anterior and posterior commissures. The subglottis extends from the lower border of the glottis to the lower margin of the cricoid cartilage.

Innervation of the larynx includes the superior laryngeal nerve, which supplies the cricothyroid and inferior constrictor muscles and contains afferent sensory fibers from the mucosa of the false vocal folds and piriform sinuses. The recurrent laryngeal nerve supplies motor innervation to all the intrinsic muscles of the larynx and sensation to the mucosa of the true vocal folds, subglottic region, and adjacent esophageal mucosa. The normal functions of the larynx are to provide airway patency, protect the tracheobronchial tree from aspiration, provide resistance for Valsalva maneuvers and coughing, and facilitate phonation. Tumors that involve the larynx impair these functions to a variable degree, depending on location, size, and depth of invasion.

Glottic tumors are often manifested early as hoarseness because the vibratory edge of the true vocal fold is normally responsible for the quality of the voice and is sensitive to even small lesions. Signs of airway compromise occur later in disease progression, when tumor bulk obstructs the glottic opening. Impaired movement of the vocal fold may cause hoarseness, aspiration, impaired cough, or obstructive symptoms. Impaired movement is caused by tumor bulk, direct invasion of the thyroarytenoid muscle, invasion of the cricoarytenoid joint, or invasion of the recurrent nerve. Hemoptysis occurs with hemorrhagic lesions.

When compared with glottic tumors, supraglottic lesions are relatively indolent and are initially seen at a later stage of disease (Fig. 35-7). Patients often complain of a sore throat or odynophagia. Referred otalgia is caused by Arnold's nerve, the vagal branch that supplies part of the ear sensation. Bulky tumors of the epiglottis are often associated with a hot potato or muffled voice quality because of airway compromise. Dysphagia may cause weight loss and malnutrition. Subglottic tumors are rare and most often manifest as airway obstruction, vocal fold immobility, or pain.

The respiratory and squamous epithelia of the larynx are most often the cause of laryngeal neoplasms, benign and malignant. Laryngeal papillomatosis is a benign exophytic growth of squamous epithelium with a tendency to recur, despite surgical excision. It has a bimodal distribution, referred to as the juvenile type and adult type. Granular cell tumors are also benign but may be confused with SCC because of a characteristic pseudoepitheliomatous hyperplasia that overlies this subepithelial lesion. Less frequent benign lesions include chondromas and rhabdomyomas. Non-neoplastic lesions of the larynx include vocal fold nodules and polyps, contact ulcers, subglottic stenosis, amyloidosis, and sarcoidosis. Finally, with exposure to carcinogens (e.g., tobacco), the epithelium of the larynx may undergo a series of precancerous changes, clinically referred to as leukoplakia (any white lesion of the mucosa) or erythroplakia (a red lesion), that consist of hyperplasia, metaplasia, or variable degrees of dysplasia.

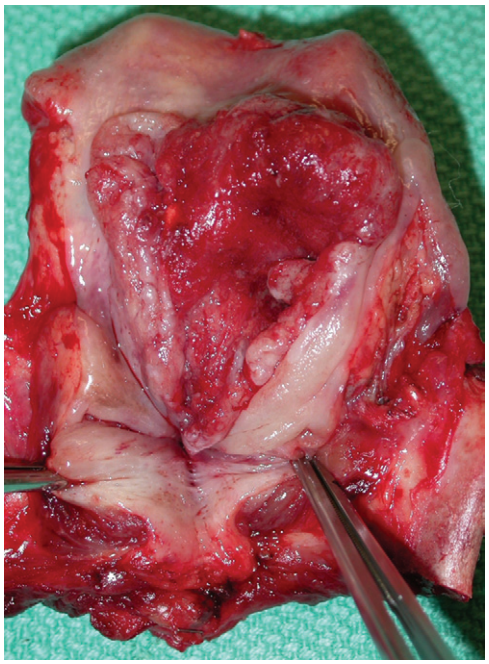


FIGURE 35-7 Pathologic specimen from a supracricoid laryngectomy for squamous cell carcinoma. The tumor involves almost the entire laryngeal surface of the epiglottis, as well as the anterior commissure of the true vocal folds. Both vocal folds have been resected back to the vocal processes of the arytenoids, which are preserved to continue phonation and protect the airway from aspiration.

The most common malignant lesion of the larynx is SCC, which is often classified as SCC in situ, microinvasive SCC, or invasive SCC. Spindle cell carcinoma and basaloid SCC are rare and represent more aggressive variants of SCC. Verrucous carcinoma is a highly differentiated variant of SCC that is locally destructive but does not metastasize and should respond to complete surgical excision. The nonepithelial components of the larynx may also undergo malignant transformation, leading to tumors of salivary origin such as adenocarcinoma, adenoid cystic carcinoma, and mucoepidermoid carcinoma. Other tumors include neuroendocrine carcinoma, adenosquamous carcinoma, chondrosarcoma, synovial sarcoma, and distant metastases from other organ systems.

The staging system for laryngeal cancers is based on subsite involvement and vocal fold mobility. Office examination includes flexible laryngoscopy to assess the location and

functional impairment. Stroboscopic laryngoscopy can detect subtle impairment of true fold mucosal waves that suggest significant tumor penetration. Direct laryngoscopy under anesthesia allows examination of all laryngeal subsites, along with the ability to perform biopsy. Specific sites that are important to examine in supraglottic tumors include the ventricle, anterior commissure, vallecula, base of the tongue, piriform sinus, and preepiglottic space. Key areas of glottic involvement include the false vocal fold, ventricle, anterior commissure, arytenoids, subglottis, and posterior commissure or postcricoid mucosa. Under general anesthesia, paralysis of the vocal fold is differentiated from arytenoid fixation by palpation of the vocal process portion of the arytenoid.

CT is routinely performed for laryngeal lesions and images the preepiglottic and paraglottic regions and extent of cartilage involvement, as well as determining direct extension into the deep neck structures. For the natural barriers and pathways of direct tumor spread, see the landmark histopathologic work of Kirchner.[26] CT examination should be performed with contrast agents and thin (1.5-mm) cuts through the larynx. Lymph node metastases are also identified by CT. The lymphatic drainage of the larynx differs in the supraglottic and glottic regions. Supraglottic epidermoid cancers metastasize early, with up to 50% of lesions having positive nodes. Contralateral and bilateral nodal metastases are common with supraglottic lesions because of the embryologic development of the supraglottis as a midline structure. Lymphatic drainage exits along the course of the superior laryngeal neurovascular pedicle and pierces the thyrohyoid membrane to drain to the subdigastric and superior jugular groups of nodes (levels II and III). Lymphatic drainage of tumors in the glottic and subglottic areas exits via the cricothyroid ligament and drains to the prelaryngeal (delphian) node, paratracheal nodes, and deep cervical nodes in the region of the inferior thyroid artery. Tumors confined to the glottis are only rarely associated with regional disease (4%), and positive nodes, when present, are most often ipsilateral.

Decision making in the treatment of laryngeal cancer is governed by tumor location and characteristics of tumor aggressiveness, as well as the patient's overall constitution and lifestyle. Poor prognostic factors include size, nodal metastasis, perineural invasion, and extracapsular spread. Low-grade epidermoid lesions of the larynx, such as dysplasia and carcinoma in situ, can be managed with local excision, such as microscopic excision of the mucosa. Concurrent denuding of the mucosa of both vocal folds near the anterior commissure can lead to the formation of an anterior web, which reduces voice quality and is a difficult complication to correct. Successful treatment of low-grade lesions includes close follow-up, with repeat office or operative laryngoscopy, as well as strict smoking cessation. For invasive disease, multiple treatment options are available, including conservation surgery and aggressive surgery, radiation therapy, and chemoradiation therapy. In general, conservation of the larynx in early-stage disease is key and can be accomplished with laryngeal preservation surgery or radiation therapy. Later stage disease that is still confined to the larynx is generally treated by chemoradiation therapy, with total laryngectomy used for salvage.

Laryngeal preservation surgery includes endoscopic surgery with cold steel, endoscopic laser resection, and open surgery, with preservation of some portion of the larynx to maintain the ability to talk. Transoral laser microsurgery, promoted by Ambrosch and colleagues[27] in Germany, has been used to treat not only all stages of laryngeal cancer but also oropharyngeal and hypopharyngeal tumors. Challenging the dogma that non–en bloc resection of tumors promotes locoregional recurrence, they have demonstrated comparable cancer survival while decreasing perioperative morbidity. In supraglottic cancers, this group reported 100% 5-year control rates for T1 and 89% for T2, with excellent functional outcomes, including minimal aspiration and short recovery periods.[27]

In recurrent glottic tumors after failure of radiation therapy, transoral laser microsurgery has demonstrated an overall 3-year survival rate of 74%, comparable to that of total laryngectomy.[28] Although laser microsurgery requires significant technical expertise, acceptance of this oncologic technique has been increasing, changing the approach to upper aerodigestive tract malignancies.

Open conservation laryngeal surgery entails maintaining a conduit for air flow through the remnant of the larynx to permit the ability to talk without aspiration. When deciding whether a patient is a candidate for laryngeal preservation surgery, factors such as pulmonary function and cardiovascular status must be examined, because these patients will often have to tolerate some amount of aspiration or airway compromise.

Pulmonary function testing, such as spirometry and arterial blood gas analysis, is performed preoperatively. An excellent functional test is to have the patient climb two flights of stairs successively without becoming short of breath. The least invasive of the open procedures is open cordectomy, which is indicated for small midfold lesions and for which 100% and 97% 5-year control rates for T1 and T2 lesions, respectively, have been reported.[29] Reconstruction is performed with a false vocal fold flap. For lesions involving the anterior commissure with less than 10 mm of inferior extension, an anterior frontal partial laryngectomy may be performed.

Conservation surgery options for more extensive tumors include vertical partial laryngectomy, supracricoid laryngectomy, and supraglottic laryngectomy. For T1 or T2 glottic lesions, vertical partial laryngectomy plus reconstruction with a false vocal cord pull-down or local muscle flap is indicated, as long as the cartilage is not involved. For T3 lesions not involving the preepiglottic space or arytenoid cartilage, supracricoid laryngectomy with cricohyoidopexy or cricohyoidoepiglottopexy is possible (Fig. 35-8). Excellent disease control has been achieved with this technique, largely because of removal of the paraglottic space and thyroid cartilage. Naudo and coworkers have shown that removal of feeding tubes and respiration without a tracheotomy can be achieved in 98% of patients.[30] The standard supraglottic laryngectomy preserves both true vocal folds, both arytenoids, the tongue base, and the hyoid bone (Fig. 35-9). Because there are numerous extensions of this operation, in which more than the standard structures are resected, cure rates are difficult to compare but, in general, T1 and T2 local control rates range from 85% to 100%, with decreased control for higher stage lesions.

If a decision has been made to undergo nonsurgical therapy, the patient must be able to complete the full course of radiation therapy, which usually includes 5 to 7 weeks of continuous daily therapy visits. Previous irradiation is a contraindication to further radiation therapy. Finally, the patient must be reliable in adhering to follow-up for years after treatment because recurrences may be indolent and difficult to detect.

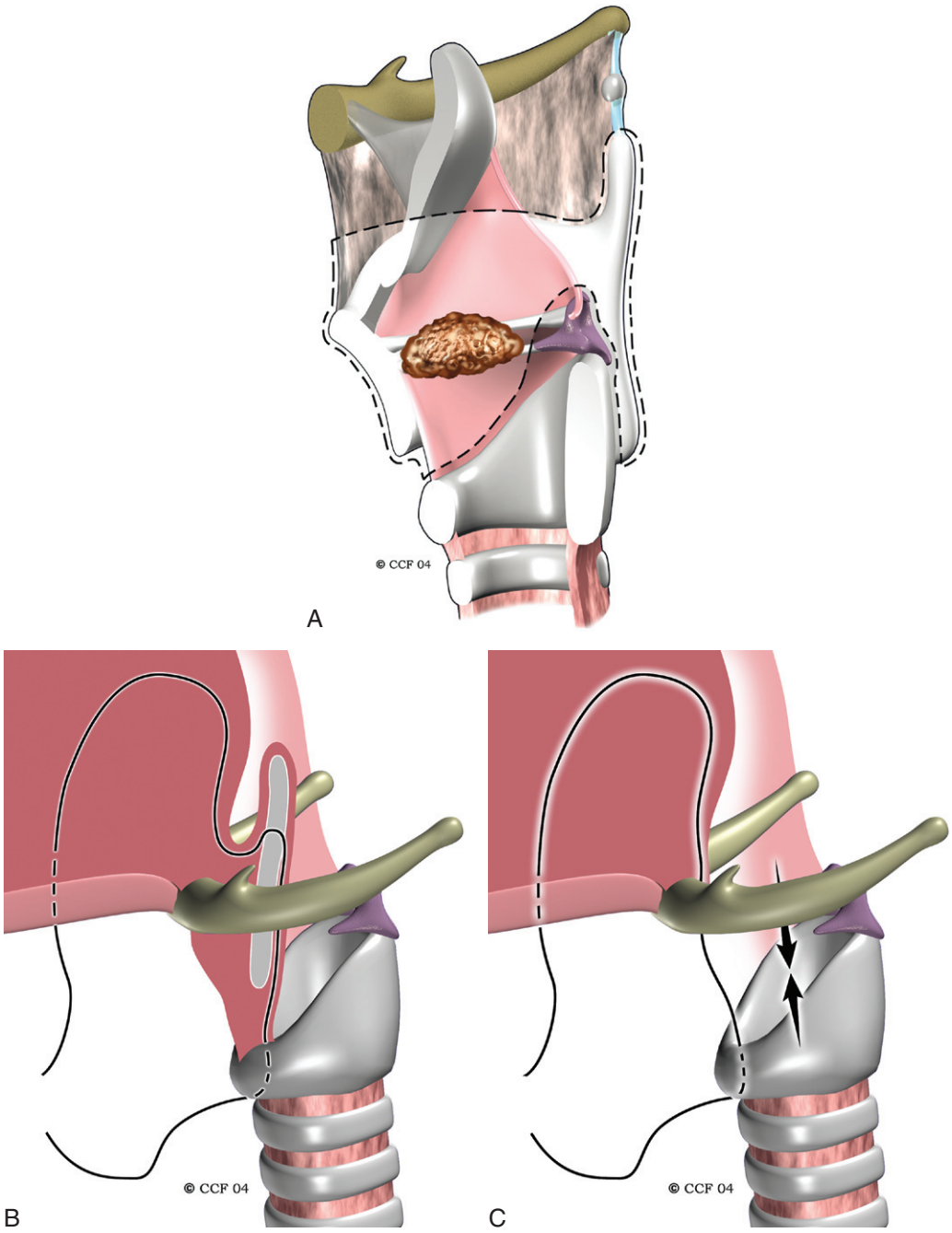


FIGURE 35-8 **A,** Lesion of the glottis deemed removable by supracricoid laryngectomy. The *dotted line* demonstrates resection of the true vocal fold to the arytenoid cartilages, including the entire laryngeal cartilage and paraglottic spaces laterally. **B,** Reconstruction by cricohyoidoepiglottopexy, with the cricoid cartilage sutured directly to the epiglottic remnant and hyoid bone, or cricohyoidopexy **(C),** with the cricoid sutured to the hyoid bone and tongue base directly. (Courtesy Cleveland Clinic Foundation, 2004.)

For neoadjuvant or concurrent chemotherapy, the patient must have sufficient constitutional health to withstand the chemotherapeutic agents. For early laryngeal cancer (T1 or T2), irradiation provides excellent disease control, with good to excellent post-therapy voice quality. For professional voice users with early lesions, irradiation is usually the choice of therapy.

The combination of chemotherapy and radiation therapy for advanced-stage disease (stages III and IV) was first brought into the mainstream with the Veterans Affairs larynx trial in 1991.[14] Induction chemotherapy followed by radiation therapy was found to provide 2-year survival equal to that after total laryngectomy with postoperative radiation therapy, in addition to being able to preserve the larynx in 64% of patients. More recently, trials with concurrent chemotherapy and radiation therapy have demonstrated even better local control of advanced laryngeal cancers. Pretreatment vocal cord fixation does not preclude conservative nonsurgical therapy, but persistent

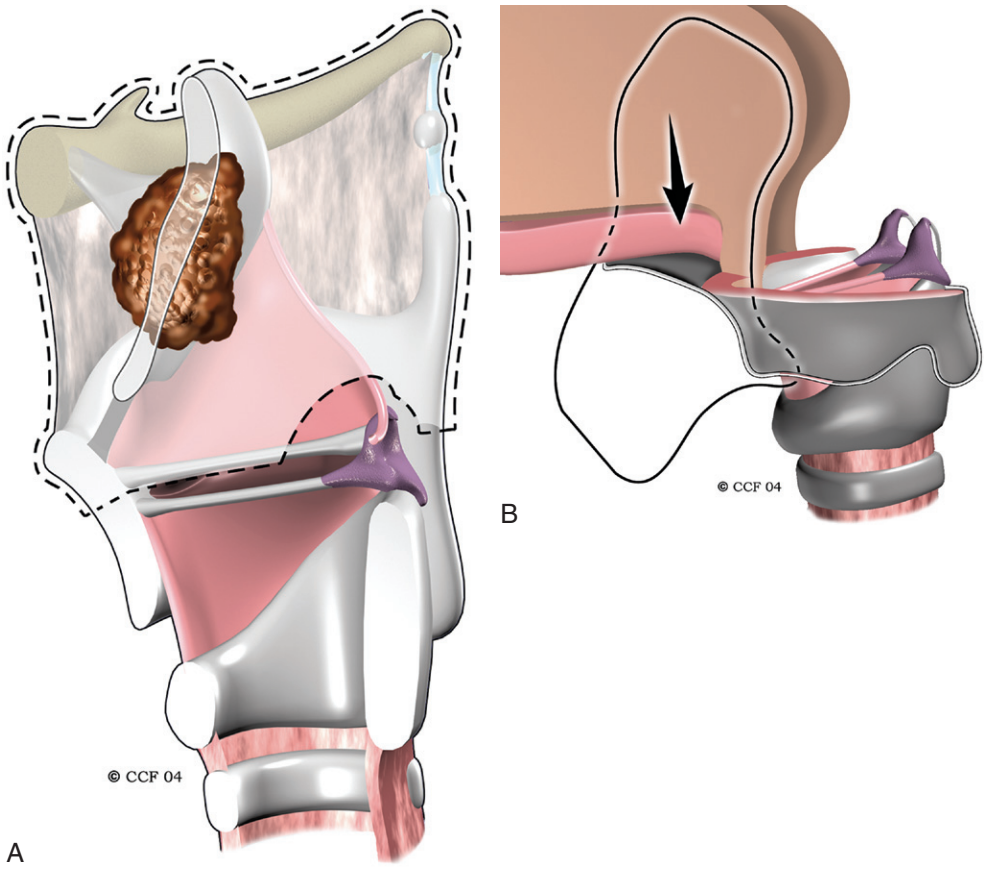


FIGURE 35-9 **A,** Supraglottic lesion, resectable by supraglottic laryngectomy. Shown are the borders of resection *(dotted line),* including the false vocal folds, hyoid bone, and preepiglottic space. **B,** Reconstruction of the remaining inferior segment of the thyroid cartilage sutured to the tongue base. (Courtesy Cleveland Clinic Foundation, 2004.)

immobility posttreatment is a poor prognostic sign and early surgical intervention should be considered.[31]

In patients who have disease extending outside the larynx, who fail conservative therapy (although some failures may still be amenable to conservation surgery), or who are not otherwise candidates for organ-preserving strategies, total laryngectomy is still commonly performed. It involves a permanent tracheostoma and loss of the voice, with permanent separation of the upper respiratory and digestive tracts.

Patients may experience a period of depression or social withdrawal after becoming aphonic. Speech and swallowing rehabilitation have become an integral part of laryngeal cancer treatment and should begin preoperatively. Speech rehabilitation options include speech with an electrolarynx, esophageal speech, and tracheoesophageal puncture. The electrolarynx is considered the easiest of the three methods to use and consists of a vibratory sound wave generator that is usually placed directly on the submandibular area or cheek. The patient mouths words to produce a monotone, electronic-sounding speech. Becoming understandable can take considerable time and patience.

Esophageal speech is produced by swallowing air into the esophagus and expulsing the air back through the pharynx, which vibrates as the air passes. The ability to master esophageal speech takes a motivated patient to be able to control the release of air through the upper esophageal sphincter, which occurs in only 20% of laryngectomized patients.

Finally, tracheoesophageal puncture is a surgically created conduit between the tracheal stoma and pharynx that is made at the time of laryngectomy or secondarily. This conduit is fitted with a one-way valve that allows passage of air posteriorly from the trachea to the pharynx but prevents food and liquid from entering anteriorly into the airway. By occluding the stomal opening with the thumb during exhalation, the patient can pass air into the pharynx, which vibrates and allows remarkable clarity of speech. Patients who are good candidates for tracheoesophageal puncture have an 80% success rate of achieving fluent speech.

Swallowing rehabilitation is a second role of the speech therapist when rehabilitating a laryngeal cancer patient, whether treated surgically or nonsurgically. Partial laryngectomy patients may have impaired pharyngeal movement and sensation, impaired vocal fold movement, decreased laryngeal elevation, and decreased subglottic pressure with poor cough, all contributing to possible aspiration.

Specially designed swallowing maneuvers and training in regard to food consistency are offered by the speech therapist to maintain an oral diet, although some patients may require gastric feeding or conversion to total laryngectomy if aspiration persists. Even laryngectomized patients have difficulty relearning the act of swallowing. Radiation therapy and chemotherapy, although organ-preserving, cause fibrosis, decreased sensation and movement, and decreased lubrication, which have a

negative impact on swallowing. Furthermore, because of the exposed circumferential ulcerated mucosa of the pharynx that occurs with chemoradiation therapy, pharyngeal stenosis may develop during the recovery phase and necessitate dilation and even pharyngeal augmentation surgery with healthy nonirradiated tissue. Thus, the speech therapist and surgeon must work as a team to rehabilitate a larynx cancer patient.

Nasal Cavity and Paranasal Sinuses

The nasal cavity consists of the nares, vestibule, septum, lateral nasal wall, and roof. The paranasal sinuses include the frontal, maxillary, ethmoid, and sphenoid sinuses. The lateral nasal wall includes the highly vascular inferior, middle, superior and, occasionally, supreme turbinates, as well as the ostiomeatal complex and nasolacrimal duct and orifice. The frontal sinuses are two asymmetrical air cavities within the frontal bone that drain into the nasal cavity via the frontal recesses. The ethmoid sinuses are a complex bony labyrinth directly beneath the anterior cranial fossa. The lamina papyracea is the paper-thin lateral wall of the ethmoid sinus that constitutes the medial wall of the orbit. The anterior ethmoids drain into the middle meatus (inferior to the middle turbinate), whereas the posterior ethmoids drain via the sphenoethmoidal recess. The sphenoid sinus lies in the middle of the sphenoid bone and also drains via the sphenoethmoidal recess. The vital structures of the optic nerves, carotid arteries, and cavernous sinuses are contained within the lateral walls of the sphenoid sinus, whereas the sella turcica and optic chiasm lie superiorly within the roof. The maxillary sinuses drain into the middle meatus and are bound posteriorly by the pterygopalatine and infratemporal fossae.

Tumors of the nasal cavity and paranasal sinuses tend to be seen initially at a late stage because their symptoms are often attributed to more mundane causes. Symptoms include epistaxis, nasal congestion, headache, and facial pain. Orbital involvement produces proptosis, orbital pain, diplopia, epiphora, and even vision loss. Nerve involvement is heralded by numbness in the distribution of the infraorbital nerve. A variety of benign tumors occur in the nasal region. Sinonasal papilloma (or schneiderian papilloma) is classified into three groups:

1. Septal papillomas (50%) arise on the septum. They are exophytic and not associated with malignant degeneration.
2. Inverted papilloma (47%).
3. Cylindrical cell papillomas (3%) arise on the lateral nasal wall or from the paranasal sinuses and are associated with malignant degeneration (10% to 15%), usually into SCC.

Previously believed to require radical extirpation, sinonasal papillomas require only local surgical excision with negative margins.

Other benign nasal lesions include hemangioma, benign fibrous histiocytoma, fibromatosis, leiomyoma, ameloblastoma, myxoma, hemangiopericytoma (a benign, aggressive lesion with a tendency to metastasize), fibromyxoma, and fibro-osseous and osseous lesions, such as fibrous dysplasia, ossifying fibroma, and osteoma. Intracranial tissues may extend into the nasal area and give rise to encephaloceles, meningoceles, and pituitary tumors. CT and MRI demonstrate the intracranial connection, and biopsy without previous imaging is unwarranted because of the risk for cerebrospinal fluid (CSF) leakage or uncontrollable bleeding from vascular tumors.

Malignancies of the sinonasal tract represent only 1% of all cancers or 3% of upper respiratory tract malignancies and have a 2:1 male-to-female ratio. Because respiratory epithelium can differentiate into squamous or glandular histology, SCC and adenocarcinoma represent two of the most common sinonasal cancers.[4] Sinonasal carcinoma is related to exposure to nickel, Thorotrast (used as a radiographic contrast agent in the United States from about 1930 to the mid-1950s), and softwood dust. Chronic exposure to hardwood dust or leatherworking has been associated with adenocarcinoma of the sinonasal tract. Other malignancies include olfactory neuroblastoma, malignant fibrous histiocytoma, midline malignant reticulosis (also known as lethal midline granuloma or polymorphic reticulosis), osteosarcoma, chondrosarcoma, mucosal melanoma, lymphoma, fibrosarcoma, leiomyosarcoma, angiosarcoma, teratocarcinoma, and metastases from other organ systems, especially renal cell carcinoma.

Since the publication of the 2002 AJCC staging manual, the nasal cavity and ethmoid sinuses have been considered as separate primary sites, in addition to the maxillary sinus.[1] The staging system is only for carcinomatous malignancies and does not include the frontal or sphenoid sinuses as separate sites because of the rarity of tumors arising in these sites. Staging is partly dependent on local spread of the tumor. Ohngren's line extends from the medial canthus to the mandibular angle. Maxillary tumors superior to Ohngren's line have a poorer prognosis than those inferior to the line because of the proximity to the orbit and cranial cavity. Local spread of tumors may occur along nerves or vessels or directly through bone. Advanced tumors of the maxillary sinuses commonly involve the pterygopalatine and infratemporal fossae. Widening of the foramen rotundum (V2) or foramen ovale (V3) on imaging suggests neural spread with intracranial involvement (Fig. 35-10). Because olfactory neuroblastomas are believed to arise from the olfactory neuroepithelium, these tumors commonly involve the cribriform plate and spread intracranially toward the frontal lobes. Sphenoidal tumors may include extension to the cavernous sinuses, carotid arteries, optic nerves, or the ophthalmic or maxillary branches of the trigeminal nerves. Lymph node metastases are in general uncommon (15%), and elective neck dissection or irradiation of a

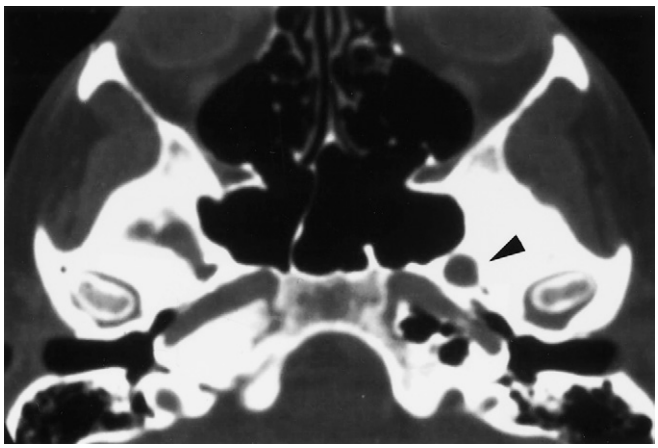


FIGURE 35-10 CT scan of 38-year-old woman with adenoid cystic carcinoma demonstrating perineural spread along V3 and widening of the foramen ovale *(arrowhead).* (Courtesy Dr. J. Netterville.)

clinically negative neck is most often unwarranted. Involved nodal groups include the retropharyngeal, parapharyngeal, submental, and upper jugulodigastric nodes.

The standard treatment of sinonasal malignancies is surgical resection, with postoperative radiation or chemoradiation therapy used for high-grade histology or advanced local disease. Because these cancers can involve the dentition, orbits, or brain, treatment requires a multidisciplinary team, including a head and neck surgeon, neurosurgeon, ophthalmologist, prosthodontist, oral surgeon, and reconstructive surgeon. After a preoperative workup consisting of imaging, endoscopy, and biopsy, a tumor map and operative plan are formulated. Vascular tumors are embolized by an interventional radiologist, preferably within 24 hours of surgery. Patients with tumors requiring skull base exploration may need a lumbar drain to decompress the dura from the cranium and reduce the risk for postoperative CSF leakage. Routine prophylactic use of a tracheotomy for craniofacial surgery to reduce the risk for postoperative pneumocephalus is controversial.

Low-grade tumors limited to the lateral nasal wall, ethmoid sinuses, or septum have increasingly been removed with endoscopic techniques. A lateral rhinotomy incision is the classic open approach for a medial maxillectomy and entails removal of the lateral nasal wall. If the tumor involves the inferior maxilla, an inferior maxillectomy, including removal of the hard palate and the medial, lateral, and posterior maxillary sinus walls, is performed. For tumors more superior in the maxillary sinus, a total maxillectomy, including excision of the roof, is performed. If the bone of the floor of the orbit is involved, removal with postoperative reconstruction is indicated. If the orbital periosteum is involved with tumor, it may be resected with preservation of the orbit, although more extensive involvement of fat or muscle necessitates orbital exenteration (Fig. 35-11).[32]

If the anterior cranial floor is involved with tumor, as it often is in olfactory neuroblastomas, craniofacial resection is indicated. This procedure combines a craniotomy approach with a transfacial approach. Surgical disruption of the cribriform region causes postoperative anosmia. Reconstruction of the anterior cranial fossa requires separation of the cranial vault from the nasal cavity with a pericranial flap, temporoparietal fascial flap, fascia lata free graft or, when extensive resection has been performed, a microvascular free flap. Unresectable lesions include those with brain involvement, carotid artery encasement, or bilateral optic nerve involvement.

Radiation therapy and chemotherapy for sinonasal malignancies are being used with increasing frequency. Sinonasal undifferentiated carcinoma, rhabdomyosarcoma, and midline reticulocytosis are examples of aggressive cancers in which neoadjuvant chemotherapy and radiation therapy play an integral role. Combining chemotherapy with radiation therapy and surgery for treatment of advanced sinonasal SCC has met with variable success.

Nasopharynx

The nasopharynx begins at the posterior nasal choana and ends at the horizontal plane between the posterior edge of the hard palate and posterior pharyngeal wall. The nasopharynx includes the vault, lateral walls, which contain the eustachian tube orifices and the fossae of Rosenmüller, roof, which is made up of the sphenoid rostrum, and posterior wall, which consists of the basiocciput or clivus. Both malignant and benign tumors of the nasopharynx are usually related to the normal histology, which includes squamous and respiratory epithelium, the lymphoid tissues of the adenoids, and deeper tissues, including fascia, cartilage, bone, and muscle. Benign tumors of the nasopharynx are rare and include fibromyxomatous polyps, papillomas, teratomas, and pedunculated fibromas. Angiofibroma, a benign tumor that affects young males, is the most common benign tumor of the nasopharynx. Rathke's pouch cysts arise high in the nasopharynx at the sphenovomerian junction. The cyst develops from a remnant of ectoderm that normally invaginates to form the anterior pituitary and may become infected later in life. Thornwaldt's bursa is located more inferiorly and arises from a remnant of the caudal notochord; it can contain a jelly-like material. It may also become infected in later life, and marsupialization is most often all that is required to treat it and

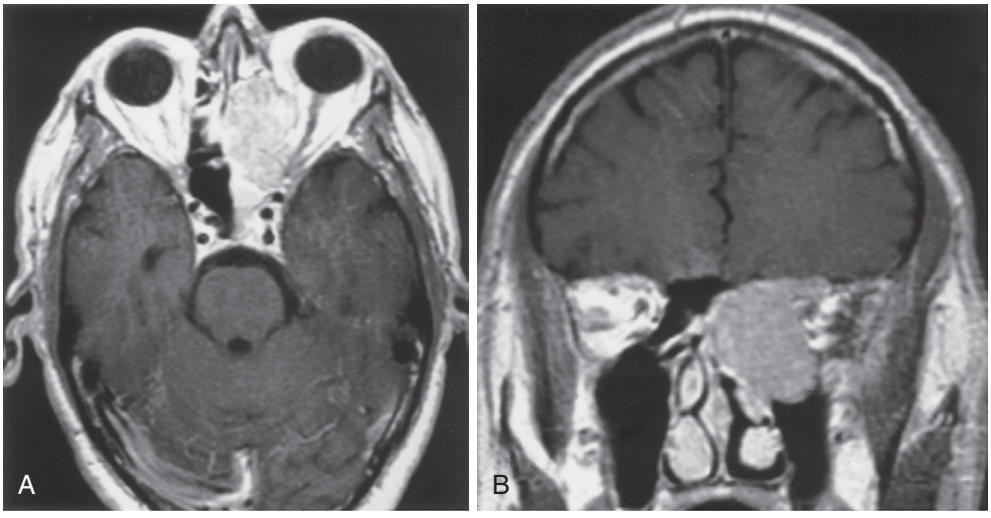


FIGURE 35-11 **A,** Axial MRI scan of patient with adenosquamous carcinoma of the ethmoids involving the orbital fat. Orbital exenteration was necessary. **B,** Coronal MRI scan of the same patient demonstrating tumor extension to the floor of the anterior cranial fossa. (Courtesy Dr. J. Netterville.)

Rathke's pouch cysts. Craniopharyngiomas, extracranial meningiomas, encephaloceles, hemangiomas, paragangliomas, chordomas (which can cause extensive destruction), and antral-choanal polyps can also be seen in the nasopharynx.

The clinical findings in patients with nasopharyngeal tumors include symptoms of nasal obstruction, serous otitis with effusion and associated conductive hearing loss, epistaxis, and nasal drainage. Findings such as a cervical mass, headache, otalgia, trismus, and cranial nerve involvement suggest malignancy. Examination of the nasopharynx was historically performed with a mirror and has greatly been improved with the use of a rigid or flexible nasopharyngoscope in the office. CT is excellent for determining bony destruction and widening of foramina. MRI is used to assess soft tissue involvement and intracranial extension, as well as nerve, cavernous sinus, and carotid involvement.

Angiofibromas are vascular lesions found exclusively in males, usually develop during puberty, and are commonly referred to as juvenile nasopharyngeal angiofibromas. Although they are benign tumors, angiofibromas often erode bone and cause significant structural and functional dysfunction, as well as bleeding. CT findings of a nasopharyngeal mass, anterior bowing of the posterior wall of the antrum, erosion of the sphenoid bone, erosion of the hard palate, erosion of the medial wall of the maxillary sinus, and displacement of the nasal septum in an adolescent male are highly suggestive of angiofibroma (Fig. 35-12). Surgery after embolization is the primary treatment modality and understanding the location of origin is critical for complete tumor extirpation. Tumors originate at the posterolateral wall of the roof of the nasal cavity, at the sphenopalatine foramen. Whether performed endoscopically or via an open approach, such as lateral rhinotomy or the Caldwell-Luc operation, complete removal of all tumor and bone in the sphenopalatine region is crucial to decrease the possibility of recurrence. Radiation has been successfully used as treatment for these tumors but, given the young age at diagnosis and the lifelong risks associated with radiation exposure, is usually reserved for unresectable angiofibromas and recurrences.

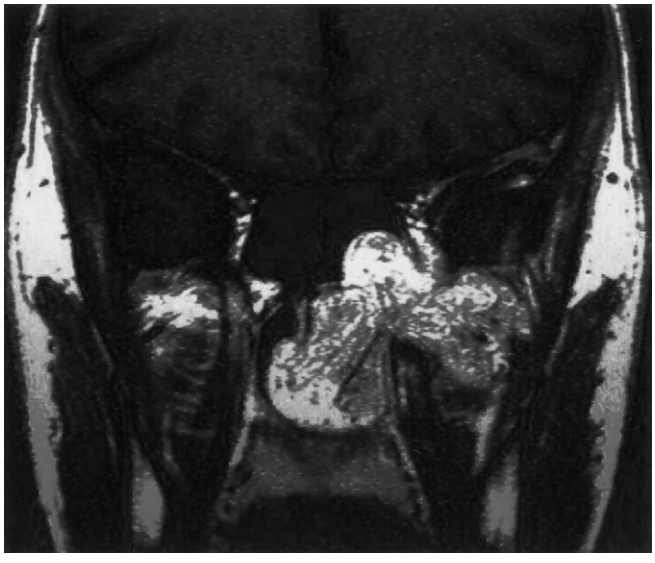


FIGURE 35-12 MRI scan of a 16-year-old boy with a left-sided juvenile angiofibroma. The tumor arose in the pterygomaxillary region and has extended into the nasopharynx and infratemporal fossa. (Courtesy Dr. J. Netterville.)

Possible malignancies include nasopharyngeal carcinoma, low-grade nasopharyngeal papillary adenocarcinoma, lymphoma, rhabdomyosarcoma, malignant schwannoma, liposarcoma, and aggressive chordoma. The staging system of malignant tumors of the nasopharynx is for epithelial tumors only and is based on confinement to the nasopharynx or spread to surrounding structures. Although nasopharyngeal carcinoma accounts for only 0.25% of all cancers in North America, it represents approximately 18% of all malignancies in China.[33] There is a strong correlation with Epstein-Barr virus, which has been demonstrated in all histologic subtypes of nasopharyngeal carcinoma. The World Health Organization has divided nasopharyngeal carcinoma into three histologic variants—keratinizing (25%), nonkeratinizing (15%), and undifferentiated (60%)—although more recent classifications combine nonkeratinizing and undifferentiated tumors.[33] The most common initial sign is neck node metastases, especially to the posterior cervical triangle, and inferiorly positioned positive nodes predict poor outcomes. Treatment is based on radiation therapy to the primary site and bilaterally in the neck. With the addition of cisplatin and 5-fluorouracil, the rate of distant metastases decreases and disease-free and overall survival increase.[34] Intracavitary irradiation is used to provide a boost at the primary site for advanced tumors and is used in cases of reirradiation. Surgery is reserved for persistent neck disease or for selected cases of local recurrence. It is unique that the risk for recurrence with nonkeratinizing and undifferentiated carcinoma appears to be chronic and does not level off at 5 years, as it does with most other cancers. Rhabdomyosarcoma is the most frequent soft tissue sarcoma in the pediatric population and is the most common sarcoma occurring in the head and neck. Excluding the orbit, the most common site in the head and neck is the nasopharynx. Treatment is based on multimodality therapy consisting of nonradical surgery and radiotherapy, plus multiagent chemotherapy.

Although surgery of the nasopharynx is used primarily for benign pathologies, a number of approaches have been described, both endoscopic and open, for the surrounding skull base region. The recent development of endoscopic skull base tumor resection has gained significantly in popularity, although the limits of the technique have yet to be clearly defined.[35] Endoscopic techniques not only avoid facial incisions but also allow shorter hospital stays. The most commonly described tumor removed via transnasal techniques is an inverting papilloma, which is excised in piecemeal fashion. Success has also been reported with the endoscopic removal of mucoceles. Numerous open surgical approaches have been described to obtain access to the central skull base. For tumors of the nasopharynx, the transpalatal approach offers excellent visualization. The transfacial approach of lateral rhinotomy with unilateral or bilateral medial maxillectomy creates a facial incision but offers greater lateral exposure. The midfacial degloving procedure allows excellent bilateral exposure of the maxillae, paranasal sinuses, and nasopharynx without facial incisions. The posterior wall of the maxillary sinus may be removed to allow access to the pterygomaxillary fossa and deeper infratemporal fossa. For disease located more laterally, the transmastoid, transcochlear, and translabyrinthine approaches described by Fisch are used alone or in combination with more anterior approaches.

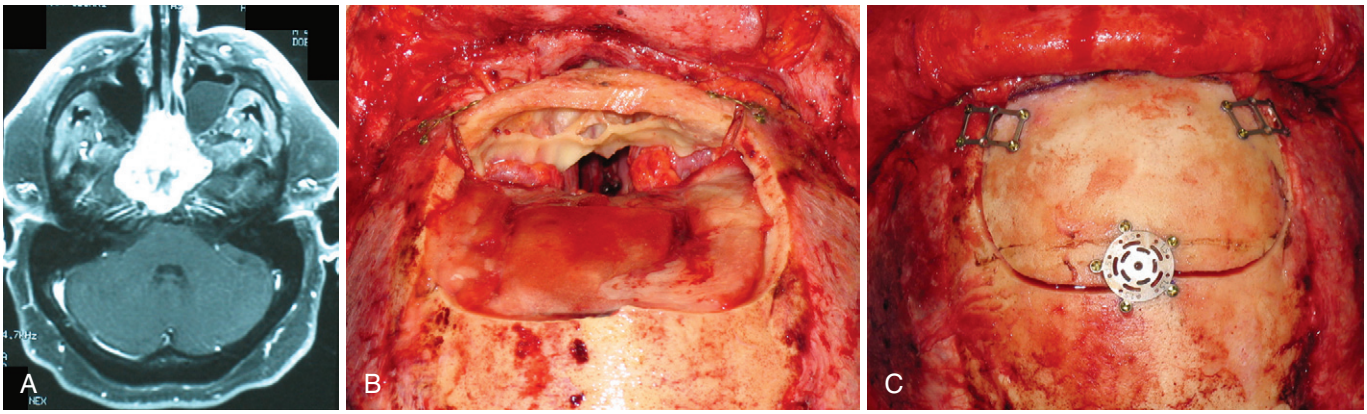


FIGURE 35-13 **A,** MRI scan of a 42-year-old man with a midline fibromyxoid sarcoma. **B,** Bicoronal incision with a combined subfrontal bar and craniotomy, allowing full access to the central anterior skull base. **C,** Replacement of the cranial bone along with a pericranial flap harvested from deep surface of bicoronal flap for reconstructing of skull base.

More extensive approaches include the lateral facial split and mandibular swing, frontal-orbital or frontal-orbital-zygomatic approach, and maxillary swing and, for disease of the high nasopharynx, the subfrontal approach affords excellent medial exposure (Fig. 35-13).

Pituitary Surgery

Although neurosurgery maintains the discipline responsible for the comprehensive management of hypophyseal disease, a collaboration between otolaryngologists with endoscopic sinus surgery skills and neurosurgeons has resulted in the development of minimally invasive pituitary surgery.[35] The endoscopic transnasal transsphenoidal approach provides excellent visualization of the operative field and avoids intraoral or anterior nasal incisions, nasal packing, and postoperative complications, such as septal deviation and lip anesthesia. Length of hospital stay, use of lumbar drains, and the need for nasal packing have been demonstrated to be significantly reduced with minimally invasive pituitary surgery as compared with open traditional approaches. Reconstruction of the sella by minimally invasive endoscopic repair has demonstrated that normal sphenoidal function can be maintained while obtaining excellent results in terms of a low incidence of CSF leakage and harvest site morbidity (Fig. 35-14).[36]

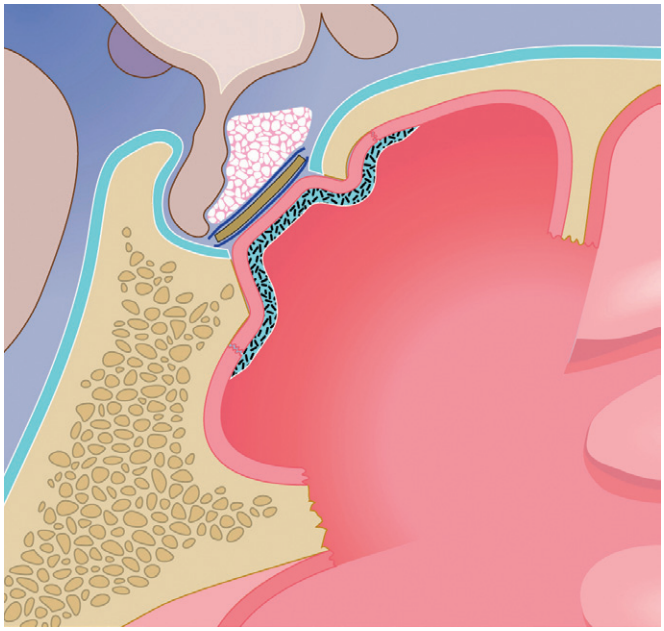


FIGURE 35-14 After endoscopically opening the sphenoid sinus in the minimally invasive hypophysectomy technique and resecting the pituitary tumor, sellar reconstruction is performed in a layered fashion. The sellar defect is partially filled with Gelfoam or fat, followed by layers of acellular human dermis, cartilage, acellular human dermis, mucosa, and fibrin glue. (From Lorenz RR, Dean RL, Chuang J, Citardi MJ: Endoscopic reconstruction of anterior and middle cranial fossa defects using acellular dermal allograft. Laryngoscope 113:496–501, 2003.)

Ear and Temporal Bone

When referring to tumors of the ear, the structures commonly involved include the external ear, middle ear, and inner ear. The external ear consists of the auricle or pinna and the external auditory canal to the tympanic membrane. The middle ear contains the tympanic cavity proper, ossicles, eustachian tube, epitympanic recess, and mastoid cavity. The borders of the middle ear include the tympanic membrane and squamous portion of the temporal bone laterally, petrous temporal bone medially, tegmen tympani or roof superiorly, carotid canal anteriorly, mastoid posteriorly, and floor of the tympanic bone inferiorly. The inner ear is contained within the petrous portion of the temporal bone and consists of the membranous and osseous labyrinth and internal auditory canal.

Evaluation of ear and temporal bone neoplasms requires appropriate physical examination and audiologic and vestibular testing, as well as radiologic assessment. Findings of hearing loss, vertigo, eustachian tube dysfunction with serous otitis media, cranial nerve deficits, pulsatile tinnitus, drainage, and deep boring pain are often associated with tumors and must be thoroughly evaluated. CT plays a crucial role in evaluating the temporal bone because of the complex anatomy contained within bony confines. MRI with gadolinium contrast is complementary and is used to define soft tissue anatomy (Fig. 35-15).

Neoplasms of the pinna are most often related to sun exposure and include basal cell carcinoma and SCC.

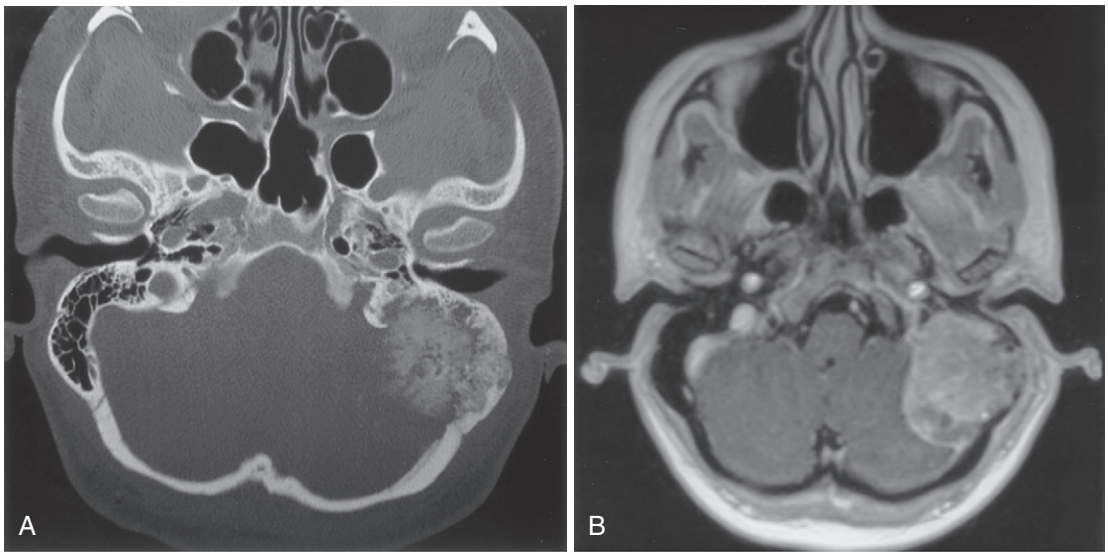


FIGURE 35-15 **A,** CT scan of a 19-year-old woman with osteosarcoma of the left temporal bone and bony destruction of the mastoid. **B,** MRI is useful for determining the extent of the tumor and the lack of brain invasion. (Courtesy Dr. J. Netterville.)

Keratoacanthoma is a benign tumor characterized by rapid growth and spontaneous involution and may be confused with SCC. In the external auditory canal, ceruminal gland adenocarcinomas, adenoid cystic carcinoma, and atypical fibroxanthomas may arise. Within the temporal bone, benign neoplasms include adenoma, paraganglioma (at the tympanic membrane and at the jugular bulb), acoustic neuroma, and meningioma. SCC is the most common cancer of the temporal bone; others include adenocarcinoma of middle ear or endolymphatic sac origin. In the pediatric population, soft tissue sarcomas such as rhabdomyosarcoma predominate. Metastases are an underrecognized cause of petrous bone tumors.

Malignancies of the pinna are treated similarly to skin cancers elsewhere on the face. Mohs microsurgery with frozen section control of margins minimizes the amount of normal tissue resected with the cutaneous malignancy. Involvement of underlying cartilage leads to more disseminated growth, necessitating partial or total auriculectomy. If the extent of disease is great, lateral temporal bone resection may be indicated, with attempted preservation of the facial nerve and inner ear. When the facial nerve or parotid gland is involved, lateral temporal bone resection with parotidectomy is performed. Radiation therapy may be used uncommonly for primary treatment or, more commonly, for adjuvant treatment in the case of perineural spread or poorly differentiated tumors.

Treatment of tumors involving the middle ear and bony canal consists of en bloc resection of structures at risk for involvement. Rarely, when the tumor involves only the external canal without bony destruction, sleeve resection of the canal can be performed. Lateral temporal bone resection removes the bony and cartilaginous canal, tympanic membrane, and ossicles. Subtotal temporal bone resection involves removal of the ear canal, middle ear, petrous bone, temporomandibular joint, and facial nerve. Involvement of the petrous apex necessitates total temporal bone resection, with removal of the carotid artery. SCC within the petrous apex is considered incurable, although adenoid cystic carcinoma and select low-grade sarcomas may be excised with total temporal bone resection. The goals of reconstruction of temporal bone defects are protection from CSF leaks and coverage of vital structures and remaining bone to prepare for postoperative radiation therapy. Techniques for facial nerve rehabilitation are covered below in the section on salivary gland malignancies. A prosthetic ear provides acceptable rehabilitation when a total auriculectomy has been performed.

Salivary Gland Neoplasms

The major salivary glands include the parotid glands, submandibular glands, and sublingual glands. There are also approximately 750 minor salivary glands scattered throughout the submucosa of the oral cavity, oropharynx, hypopharynx, larynx, parapharyngeal space, and nasopharynx. Salivary gland neoplasms are rare and constitute 3% to 4% of head and neck neoplasms. Most neoplasms arise in the parotid gland (70%), whereas tumors of the submandibular gland (22%) and sublingual and minor salivary glands (8%) are less common. The ratio of malignant to benign tumors varies by site as well—parotid gland, 80% benign and 20% malignant; submandibular gland and sublingual gland, 50% benign and 50% malignant; and minor salivary glands, 25% benign and 75% malignant.

The parotid gland is the largest salivary gland and is divided into the superficial lobe and deep lobe by the facial nerve. On imaging, the lobes can be differentiated by the retromandibular vein, which is commonly found at the division of the lobes. Deep lobe tumors lie within the parapharyngeal space. Stensen's duct is approximately 5 cm long; it pierces the buccal fat pad and opens in the oral cavity, opposite the second maxillary molar. The submandibular glands are closely associated with the lingual nerve in the submandibular triangle and empty via Wharton's duct into the papilla, just lateral to the frenulum. The sublingual gland lies on the inner table of the mandible and secretes via tiny openings (ducts of Rivinus) directly into the floor of the mouth or via several ducts that unite to form the common sublingual duct (Bartholin), which then merges with Wharton's duct.

Numerous non-neoplastic diseases commonly affect the salivary glands. Sialadenitis is an acute, subacute, or chronic

inflammation of a salivary gland. Acute sialadenitis commonly affects the parotid and submandibular glands and can be caused by bacterial (usually *Staphylococcus aureus*) or viral (mumps) infection. Chronic sialadenitis results from granulomatous inflammation of the glands and is commonly associated with sarcoidosis, actinomycosis, tuberculosis, and cat scratch disease. Sialolithiasis is the accumulation of obstructive calcifications within the glandular ductal system, more common in the submandibular gland (90%) than in the parotid (10%). When the calculi become obstructive, stasis of saliva may cause infection and create a painful, acutely swollen gland. Benign lymphoepithelial lesions of the salivary glands are non-neoplastic glandular enlargements associated with autoimmune diseases, such as Sjögren's syndrome.

Salivary gland neoplasms are most often manifested as slow-growing, well-circumscribed masses. Symptoms such as pain, rapid growth, nerve weakness, and paresthesias and signs of cervical lymphadenopathy and fixation to skin or underlying muscles suggest malignancy. When the initial symptom is complete unilateral facial paralysis, Bell's palsy may be misdiagnosed as the cause, and it is important to remember that all patients with Bell's palsy will show some improvement in facial movement within 6 months of the onset of weakness. Trismus is associated with involvement of the pterygoid musculature by deep parotid lobe malignancies. Bimanual palpation of submandibular masses assists in determining fixation to surrounding structures. CT and MRI tend to show irregular tumor borders and obliteration of fat planes in the parapharyngeal space with deep parotid lobe cancers. The accuracy of fine-needle aspiration cytology of the salivary glands has been well established. The sensitivity, specificity, and accuracy of parotid gland aspirates in one series were 92%, 100%, and 98%, respectively.[37] Excision of the gland is used to confirm the final diagnosis.

Benign tumors of the salivary glands include pleomorphic adenomas, various monomorphic adenomas (e.g., Warthin's tumor, oncocytomas, basal cell adenomas, canalicular adenomas, and myoepitheliomas), various ductal papillomas, and capillary hemangiomas. Pleomorphic adenomas account for 40% to 70% of all tumors of the salivary glands and usually occur in the tail of the parotid. Like all benign parotid tumors, the treatment of choice is surgical excision with a margin of normal tissue (e.g., superficial parotidectomy). In the parotid gland, if excision is possible without complete removal of the affected lobe, the postoperative cosmetic appearance will be superior to that in patients in whom a complete lobe is removed. Shelling out of pleomorphic adenomas is to be avoided because it has been shown to correlate with increased rates of recurrence.[38] The facial nerve should not be sacrificed when removing a benign lesion (Fig. 35-16). Warthin's tumor, or papillary cystadenoma lymphomatosum, is the second most common benign parotid tumor and occurs most often in older white men. Because of the high mitochondrial content within oncocytes, the oncocyte-rich Warthin tumor and oncocytomas will incorporate technetium-99m and appear as hot spots on radionuclide scans. If fine-needle aspiration suggests a slow-growing Warthin tumor with confirmatory technetium scanning in a patient with contraindications to surgery, the tumor may be closely monitored because it has no malignant potential.

Malignant salivary tumors are staged according to size; T1 is smaller than 2 cm, T2 is 2 to 4 cm, T3 is larger than 4 cm (or any tumor with macroscopic extraparenchymal extension), and T4 involves invasion of surrounding tissues. Malignant salivary tumors are listed in Box 35-1. Mucoepidermoid carcinoma is the most common malignant tumor of the parotid gland and can be divided into low-grade and high-grade tumors. High-grade lesions have a propensity for both regional and distant metastases and corresponding shorter survival rates than low-grade mucoepidermoid carcinomas. Adenoid cystic carcinoma constitutes 10% of all salivary neoplasms, with two thirds occurring in the minor salivary glands. The histologic types of adenoid cystic carcinoma are tubular, cribriform, and solid, listed in order from best to worst prognosis. An indolent growth pattern and a relentless propensity for perineural invasion characterize adenoid cystic carcinoma. Regional lymphatic spread is uncommon, although distant metastases occur within the first 5 years after diagnosis and may remain asymptomatic for decades. Malignant mixed tumors include cancers originating from pleomorphic adenomas, termed *carcinoma ex pleomorphic adenoma,* and de novo malignant mixed tumors. The risk for malignant transformation of benign pleomorphic adenomas is 1.5% within

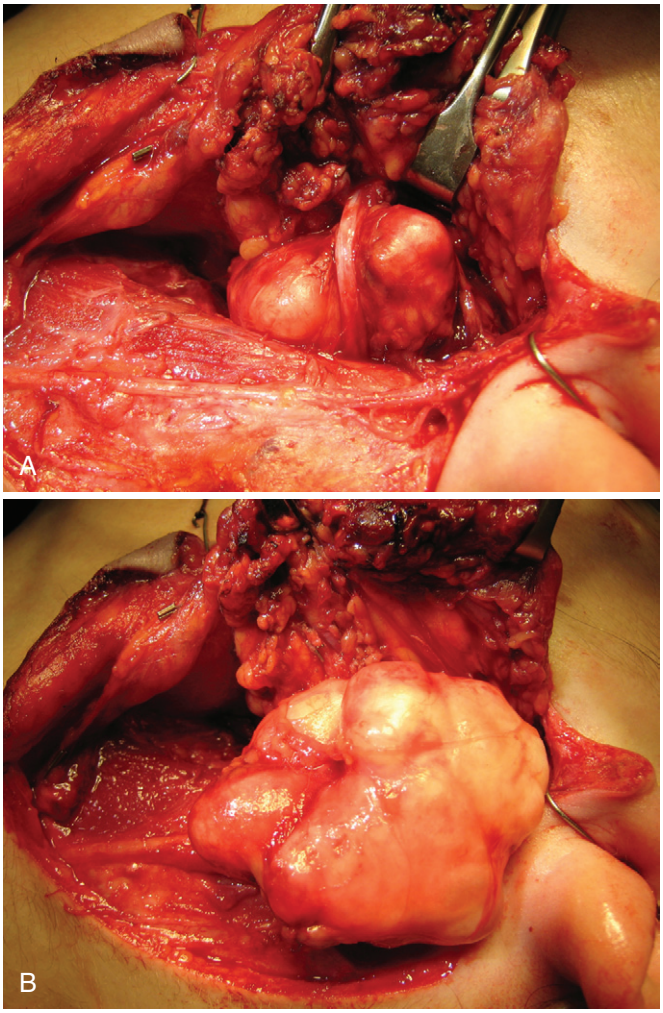


FIGURE 35-16 **A,** 32-year-old woman with a deep parotid lobe pleomorphic adenoma. The facial nerve is displaced laterally. **B,** Once the mass is separated from the prestyloid space, it is delivered around the facial nerve, emptying the compressed parapharyngeal space and avoiding facial nerve injury.

BOX 35-1 Tumors of the Major and Minor Salivary Glands

Benign
Pleomorphic adenoma
Warthin's tumor
Capillary hemangioma
Oncocytoma
Basal cell adenoma
Canalicular adenoma
Myoepithelioma
Sialadenoma papilliferum
Intraductal papilloma
Inverted ductal papilloma

Malignant
Acinic cell carcinoma
Mucoepidermoid carcinoma
Adenoid cystic carcinoma
Polymorphous low-grade adenocarcinoma
Epithelial-myoepithelial carcinoma
Basal cell adenocarcinoma
Sebaceous carcinoma
Papillary cystadenocarcinoma
Mucinous adenocarcinoma
Oncocytic carcinoma
Salivary duct carcinoma
Adenocarcinoma
Myoepithelial carcinoma
Malignant mixed tumor
Squamous cell carcinoma
Small cell carcinoma
Lymphoma
Metastatic carcinoma
Carcinoma ex pleomorphic adenoma

the first 5 years but increases to 9.5% once the benign tumor has been present for more than 15 years.[39] Most salivary gland lymphomas are of the non-Hodgkin's variety (85%). The risk for malignant lymphoma in patients with Sjögren's syndrome is 44-fold higher than in the normal population. Metastatic tumors are most often derived from cutaneous carcinomas and melanomas from the scalp, temporal area, and ear. Distant metastatic tumors are rare but may arise from the lung, kidneys, and breasts.

Treatment of salivary gland malignancies is en bloc surgical excision. Radiation therapy is administered postoperatively for high-grade malignancies demonstrating extraglandular disease, perineural invasion, direct invasion of surrounding tissue, or regional metastases. For tumors confined to the superficial lobe of the parotid gland, lateral lobectomy with preservation of the facial nerve may be performed. Gross tumor should not be left in situ but, if the facial nerve can be preserved by peeling tumor off the nerve, the nerve should be preserved and radiation therapy used for microscopic residual disease. For cancers of the deep lobe, total parotidectomy is performed. Elective neck dissections are performed for high-grade malignancies, such as high-grade mucoepidermoid carcinoma. In patients with gross facial nerve involvement, temporal bone resection is performed and the nerve is sacrificed proximally to obtain a negative margin. When the facial nerve is removed, rehabilitation with a simultaneous nerve graft may be performed in the hope of producing facial muscular tone. Although the primary goal of facial nerve rehabilitation is protection of the cornea from chronic exposure, other concerns include oral competency, nasal valve maintenance, and cosmesis. Upper lid gold weights, lateral tarsorrhaphies, static fascial slings, dynamic muscular slings, and delayed reinnervation procedures are also used for facial rehabilitation. Submandibular gland and minor salivary gland malignancies are treated similarly to parotid gland cancers, by en bloc resection. Submandibular gland malignancies are removed with level I contents and accompanying MRND. Gross involvement of the hypoglossal or lingual nerves requires sacrificing them and obtaining a negative margin by following the nerves toward the skull base. Adenoid cystic cancers are highly neurotropic; treatment consists of removal of gross tumor with radiation therapy for the microscopic disease that is assumed to exist at the periphery of the tumor.

Neck and Unknown Primary

The workup of a neck mass is different in children than in adults because of differing causes. Cervical masses are common in children and most often represent inflammatory processes or congenital abnormalities. Of pediatric neck masses that are persistent, 2% to 15% that are removed will be malignant. Pediatric evaluation requires thorough head and neck examination, including endoscopy of the nasopharynx and larynx. The most common cause of cervical adenopathy is viral upper respiratory tract infections. The associated lymphadenopathy generally subsides within 2 weeks, although mononucleosis-related lymphadenopathy may persist for 4 to 6 weeks. The location of the mass, as well as its character, most often leads to the diagnosis. Lymphadenopathy not attributable to viral infections may represent a less common infectious process. Bacterial cervical adenitis is most often caused by group A beta-hemolytic streptococci or *S. aureus*. Scrofula is cervical adenitis secondary to tuberculosis and is relatively uncommon in industrialized countries, although atypical mycobacteria may also cause cervical adenitis. Cat scratch disease should be suspected if there is a history of cat contact, and indirect fluorescence antibody testing for *Bartonella henselae* should be performed. Midline masses include thyroglossal duct cysts, enlarged lymph nodes, dermoid cysts, hemangiomas, and pyramidal lobes of the thyroid. Nonlymphoid masses anterior to the sternocleidomastoid muscle are usually branchial cleft cysts. A soft compressible mass of the posterior triangle may represent a lymphangioma (or cystic hygroma), which usually develops before the age of 2 years. Cervical teratomas are present at birth and may involve compression of the airway or esophagus. Malignancies most commonly encountered in pediatric neck masses include sarcomas, lymphomas, and metastatic thyroid carcinoma.

In adults, neck masses represent malignancies more often than in children. It should be emphasized that persistent masses larger than 2 cm represent cancer in 80% of cases. In addition to head and neck examination, CT assists in evaluating not only the masses but also potential primary sites. Fine-needle aspiration (<22-gauge needle) is performed as one of the initial steps in the workup of neck masses; it has an overall accuracy of 95% for benign neck masses and 87% for malignant masses (Fig. 35-17).[40] As in children, the location of the mass has a bearing on the likelihood of diagnosis: midline masses may represent thyroglossal duct cysts, dermoid tumors, delphian nodes, thyroid

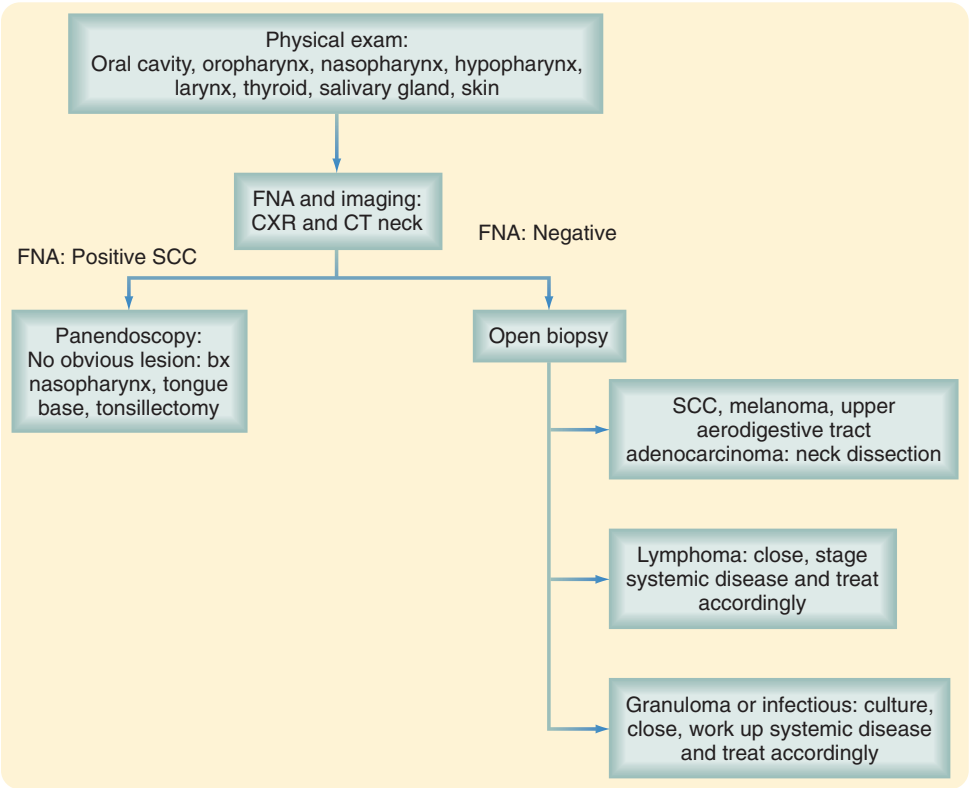


FIGURE 35-17 Workup of an asymptomatic unilateral neck mass in adults. *CXR,* Chest x-ray; *FNA,* fine-needle aspiration.

masses, lipomas, or sebaceous cysts. Thyroglossal duct cysts represent the vestigial tract of descent that the thyroid followed from the foramen cecum to its normal location below the cricoid. The cyst may become enlarged later in life concurrent with an upper respiratory tract infection. Surgical excision should include the central portion of the hyoid bone (Sistrunk procedure), or recurrence is more likely.

Persistent lateral neck masses in adults may represent enlarged benign or malignant lymph nodes, neuromas or neurofibromas, carotid body tumors, branchial cleft cysts, lipomas, sebaceous cysts, parathyroid cysts, or a primary soft tissue tumor. Enlarged lymph nodes may be have an infectious cause, similar to those in the pediatric population, lymphoma, regional metastases from SCC, melanoma, thyroid carcinoma, or salivary gland tumors, or distant metastases. Usually, lymphadenopathy in an adult is indicative of metastatic HNSCC, with lymphoma being less likely. Metastatic SCC is most frequently from the nasopharynx, oropharynx, or hypopharynx and its presence is a negative prognostic indicator. In all cases of metastases to the neck, lymphadenectomy as treatment is valuable only in cases of SCC, salivary gland tumors, melanoma, and thyroid carcinoma. Otherwise, removal of metastatic lymph nodes is indicated for diagnosis only, and systemic treatment must be initiated. In cases of multiple lymph node enlargement, a diagnosis of HIV infection, toxoplasmosis, or fungal infection should be investigated.

Less frequently, benign neck masses can develop in adults. The branchial cleft apparatus that persists after birth may give rise to a number of neck masses. First branchial cleft cysts develop in the preauricular or submandibular area, are intimately associated with the external auditory canal and parotid gland, and may require dissection of the facial nerve during excision. Second and third branchial cleft cysts and tracts develop anterior to the sternocleidomastoid muscle and often become symptomatic after upper respiratory tract infections. Although the second branchial cleft communicates with the ipsilateral tonsillar fossa, the third communicates with the piriform sinus. Removal of the cyst and tract necessitates dissection along the course of embryologic descent. Second branchial cleft tracts course between the internal and external carotid arteries. Third branchial cleft tracts course posterior to both branches of the carotid artery. Occasionally, a carcinoma may be found within the cyst. Debate continues about whether the carcinoma represents a cystic metastasis from the tongue base or tonsil or whether cancer may occur de novo within a branchial cleft cyst.[41]

Carotid body tumors or chemodectomas are more properly referred to as paragangliomas and arise from the branchiomeric paraganglia at the carotid body. These tumors are usually benign, unifocal, and nonhereditary; they are manifested as a nonpainful mass at the carotid bifurcation and have a characteristic lyre sign on carotid arteriography (Fig. 35-18). Because of their highly vascular nature, biopsy is contraindicated. Preoperative embolization is performed for tumors larger than 3 cm. The most frequent sequela from resection is cranial nerve injury, most commonly of the superior laryngeal nerve, but also the vagal nerve or hypoglossal nerve with large tumors.[42] Tumors larger than 5 cm are associated with a need for concurrent carotid artery replacement. The term *first-bite syndrome* was coined to describe the phenomenon of pain with the initiation of mastication; it is believed to be caused by removal of the sympathetic nerves surrounding the carotid bifurcation and reinnervation of the parotid secretory glands by parasympathetic fibers. Excision

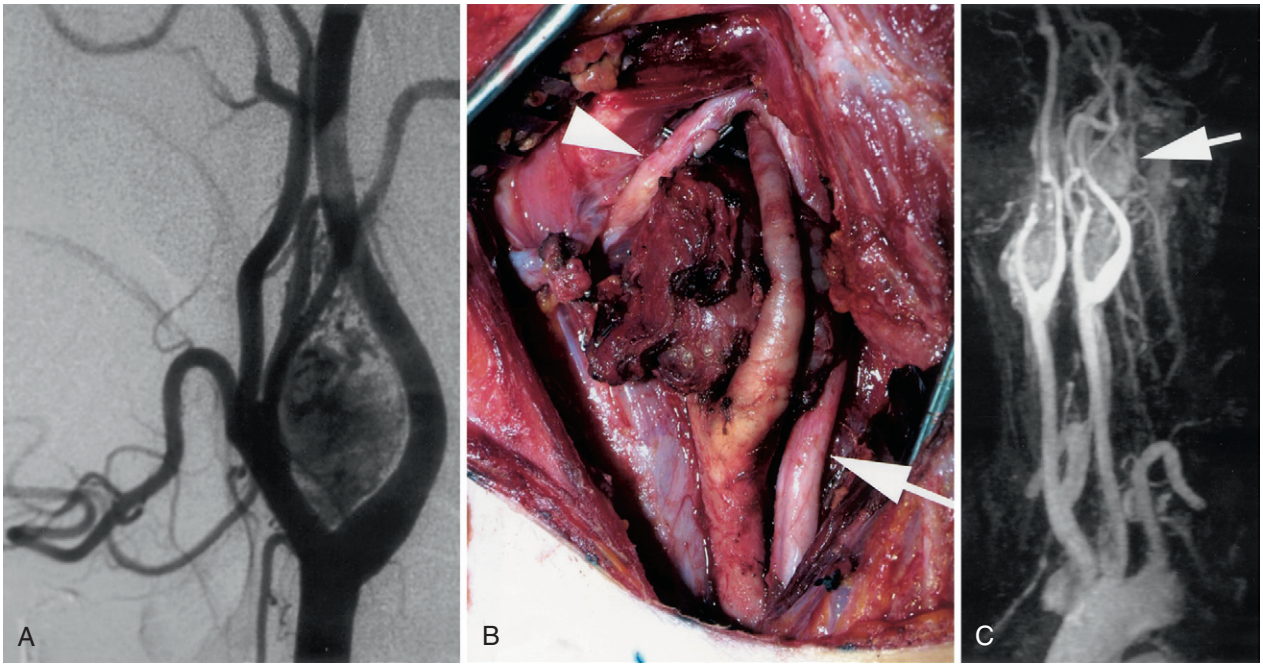


FIGURE 35-18 **A,** Characteristic lyre sign on an arteriogram of a carotid body paraganglioma demonstrating splaying of the internal and external carotid arteries. **B,** The tumor lies between the arteries, superficial to the vagus nerve *(arrow)* and deep to the hypoglossal nerve *(arrowhead).* **C,** MR angiography scan of a different patient demonstrating bilateral carotid body tumors in addition to a separate, more superior, left vagal paraganglioma *(arrow).* (Courtesy Dr. J. Netterville.)

of bilateral carotid body tumors may lead to baroreceptor failure, with wide fluctuations in blood pressure.

Tumors of the parapharyngeal space are distinguished by their location; they are prestyloid, usually of salivary gland origin, or poststyloid, usually vascular or neurogenic in origin. Initial symptoms may consist of a superior neck mass, fullness of the parotid gland or tonsillar fossa, trismus, dysphagia, Horner's syndrome, or cranial nerve impairment. Tumors include paraganglioma, salivary gland neoplasms, schwannoma or neurilemoma, lipoma, sarcoma, and lymphadenopathy. Access to these tumors is usually performed transcervically and care must be taken to preserve uninvolved structures, such as the carotid artery and major cranial nerves (Fig. 35-19). A mandibulotomy approach is rarely required.

TRACHEOTOMY

Tracheotomy is generally used for patients requiring prolonged mechanical ventilation to reduce the risk of damage to the larynx, assist ventilation and pulmonary hygiene, and improve patient comfort and oral care. There is no hard rule about how long a translaryngeal endotracheal tube can be left in place. Some laryngologists recommend conversion to a tracheotomy after 3 days of intubation, although most use 2 to 3 weeks as a limit. Other common reasons for tracheotomy include chronic aspiration, acute airway obstruction secondary to facial or laryngeal trauma or oral or deep neck space infections, or perioperatively during radical cancer ablation.

The term *tracheotomy* implies formation of an opening that will close spontaneously once the tracheotomy tube has been decannulated. Closure via secondary intention generally occurs over a period of 5 to 7 days and the healing process should not be hastened by suturing the overlying skin closed, or an abscess

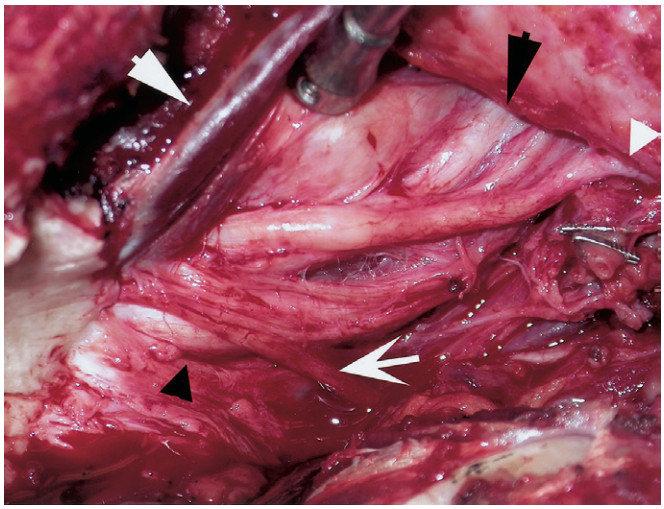


FIGURE 35-19 Left poststyloid space after removal of a parapharyngeal space tumor and lateral temporal bone resection. The carotid is seen anteriorly *(black arrowhead)* where it enters the skull base, whereas the internal jugular vein *(large white arrowhead)* is retracted posteriorly. The vagus nerve *(large black arrowhead)* is intimately associated with the hypoglossal nerve *(small white arrowhead),* and separation of the two nerves at this level often leads to vocal cord paralysis. The glossopharyngeal nerve is seen anteriorly *(large white arrow).*

may form in this highly contaminated wound. The term *tracheostomy* implies the formation of a permanent opening that remains open after removal of the tube. The surgeon can form a tracheostomy by suturing an inferiorly based tracheal ring flap to the skin at the time of surgery. Although this flap allows safer

replacement of the tracheal tube should it become accidentally decannulated, once the mucocutaneous junction forms, a surgical procedure with rotational skin flaps is required to close the tracheostomy. A permanent tracheostomy should be considered for patients with extended mechanical ventilation, chronic aspiration, obstructive sleep apnea, and/or uncorrectable upper airway obstruction.

Preoperative assessment should include a history of previous tracheotomy or neck surgery, laryngeal pathology, bleeding difficulties, or cervical spine injuries. Perioperative complications of tracheotomy include bleeding, aspiration, pneumothorax and pneumomediastinum, recurrent laryngeal nerve injury, and hypoxia. Long-term problems include the formation of granulation tissue at the skin and within the trachea, collapse of tracheal cartilage and airway obstruction, and tracheoinnominate artery and tracheoesophageal fistulas.

Although the traditional open tracheotomy technique is still primarily used and preferred, percutaneous tracheotomy is being done more often. There have been reports of increased and decreased complication rates with the percutaneous technique versus the open technique.[43,44] Although one might suspect that the trauma from dilating the tracheal rings in the percutaneous technique might be associated with a substantial increase in long-term tracheal stenosis, this does not always seem to be the case; percutaneous tracheotomies have become common in many intensive care units in patients with favorable anatomy and supportive clinical settings.

VOCAL CORD PARALYSIS

More appropriately termed *vocal fold immobility,* loss of vocal cord function remains a common occurrence. The recurrent laryngeal nerve supplies all the laryngeal musculature except for the cricothyroid muscle, which is supplied by the superior laryngeal nerve. Paralysis of the laryngeal muscles may occur from a lesion in the central nervous system or, usually, with peripheral nerve involvement (90%). Once the vagus nerve exits the jugular foramen, the superior laryngeal nerve divides superiorly in the parapharyngeal space and passes deep to the carotid artery. On the left side, the recurrent laryngeal nerve separates from the vagus nerve in the thorax, passes around the aortic arch at the ductus arteriosus, and travels superiorly in the tracheoesophageal groove to the cricothyroid joint. Probably as a result of the left recurrent nerve's longer course, left vocal cord paralysis is more common than on the right. The right recurrent nerve separates from the vagus and passes around the right subclavian artery and back to the larynx (Fig. 35-20). A nonrecurrent recurrent laryngeal nerve is a rare finding (0.5% to 1.0%) on the right side; when present, the nerve separates from the vagus before descending into the chest, passes directly to the larynx, and is associated with a retroesophageal right subclavian artery. Approaches to the

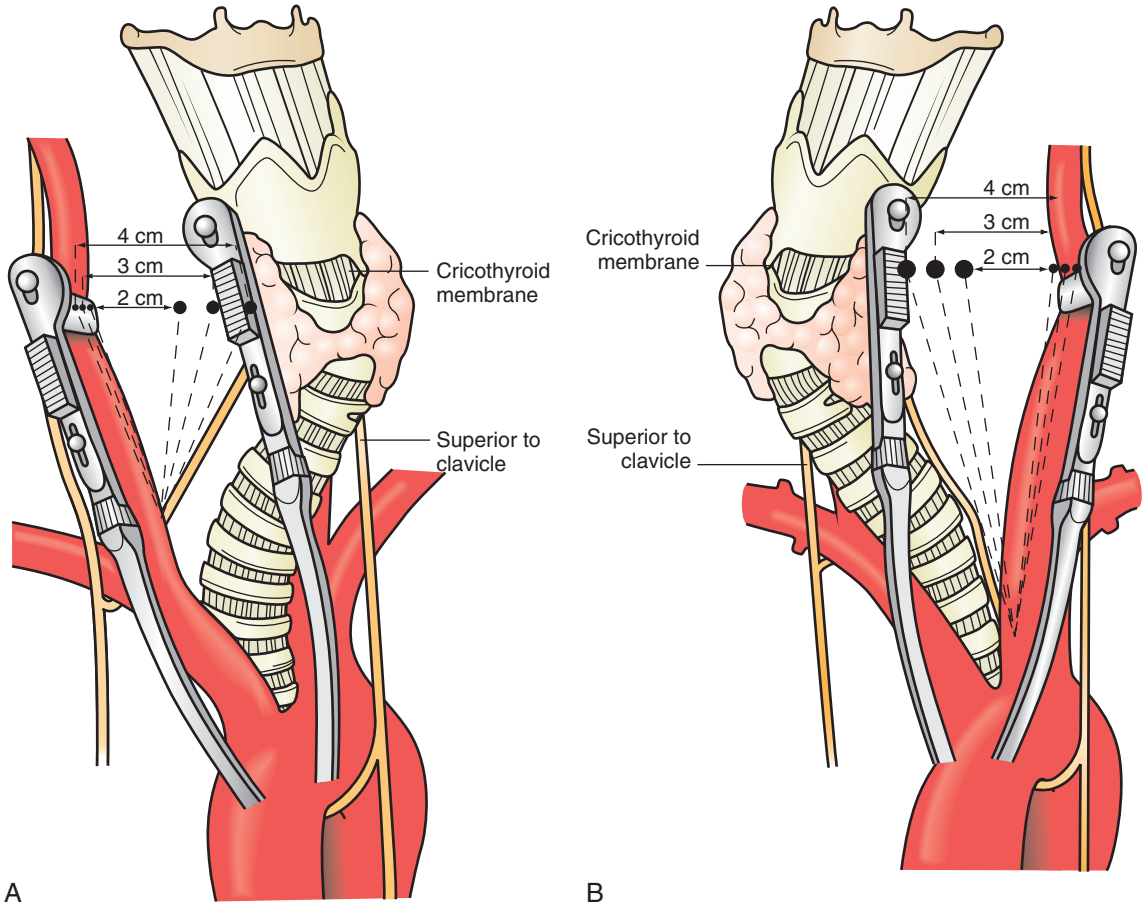


FIGURE 35-20 Anatomy of the right **(A)** and left **(B)** recurrent laryngeal nerves. The more diagonal course on the right side predisposes patients to traction injury during anterior cervical neck surgery. (From Netterville JL, Koriwchak MJ, Winkle M, et al: Vocal fold paralysis following the anterior approach to the cervical spine. Ann Otol Rhinol Laryngol 105:85–91, 1996.)

cervical spine should generally be performed from the left to reduce traction injury on the recurrent nerve because right-sided approaches have been associated with a higher rate of laryngeal nerve injury.[45]

Dysfunction of the superior laryngeal nerve usually occurs after thyroidectomy because the nerve is in close proximity to the superior thyroid vascular pedicle and affected patients may have difficulty achieving precision in pitch, noticeable usually in professional voice users. Injury to the recurrent laryngeal nerve results in vocal fold paresis or paralysis. Patients with unilateral vocal cord immobility may have hoarseness, ineffective cough, dysphagia, aspiration, or airway compromise or may be completely asymptomatic because of their ability to compensate. Definitive diagnosis is made via laryngoscopy and subtle weakness may require stroboscopic examination. Causes of paralysis include surgical trauma (usually thyroidectomy), malignancies of the thyroid, mediastinum, esophagus, or larynx, mediastinal compression, viral neuropathy, collagen vascular disease, sarcoidosis, diabetic neuropathy, and other reported factors. The cause remains unknown in 20% of patients. Because re-creating volitional abduction and adduction of the vocal cord is not currently feasible, the goal of treatment entails creating sufficient medialization of the involved vocal cord to allow efficient voicing and cough, as well as reduce hoarseness and aspiration. Medialization may be accomplished with intracordal injection of various substances, including fat, Gelfoam, and human cadaveric collagen preparations. Because of the risk for granuloma formation, Teflon injection is rarely used today. Medialization thyroplasty, with or without concurrent arytenoid adduction, consists of a surgically created window in the thyroid cartilage with the insertion of Silastic, hydroxyapatite, or Gore-Tex and has shown excellent results. Laryngeal reinnervation via an ansa cervicalis–recurrent laryngeal nerve anastomosis provides medialization with tone to the paralyzed cord but takes several months to become effective.[46] Bilateral vocal fold paralysis is an uncommon scenario manifested by both vocal folds remaining near the midline position. Patients maintain a strong voice because the vocal folds continue to vibrate, but they might suffer life-threatening airway obstruction and stridor and require immediate reintubation or tracheotomy.

RECONSTRUCTION

Perhaps the area of head and neck surgery that has undergone the most advancement in the past 25 years is reconstruction, fueled largely by the advent of microvascular free flaps. Today, there is almost no defect that cannot be repaired, which this has afforded the ablative surgeon more leeway in obtaining tumor-free margins. The head and neck region is unique in the intricacy of its form and function, and careful reconstruction is needed to return patients back to their premorbid condition. Focus is usually on speech, swallowing, and cosmesis when considering rehabilitative goals. Swallowing may be impaired by resection of local tissues of the oral cavity, oropharynx, hypopharynx, larynx, and cervical esophagus. Loss of innervation, sensory or motor, locally or at the skull base, can severely impair swallowing. Irradiation leads to fibrosis of local tissues, as well as loss of saliva and taste, and may cause stenosis years after treatment is finished. Speech rehabilitation of speech has been discussed earlier (see "Larynx"). Because of the proximity and complexity of the airway and digestive tracts at the oral cavity, oropharynx, larynx, and hypopharynx, the ability to maintain the two functions is closely related. Frequently, aspiration occurs when the swallowing process is impeded. Although a tracheotomy tube helps protect the airway somewhat from aspiration and allows increased pulmonary suctioning, it also tethers the larynx to the skin and often exacerbates dysphagia. Once dysfunction has occurred, the physician is hampered by trying to maintain balance among airway, speech, and swallowing, and one function may have to be further impaired to improve another. In a severely dysfunctional upper airway, total sacrifice of one function may have to be accepted, and laryngectomy or a permanent gastric tube may be required.

Cosmetic deformities are most obvious in the head and neck area. Functional deficits not only occur in speech and swallowing but also affect eyelid function, oral competence, and maintenance of a nasal and oral airway. General principles of facial restoration include reconstructing the underlying bony framework, replacing skin with skin of matching quality, minimizing scar visibility and contracture, and reconstructing in zones of facial units. Skin should be matched by color, thickness, and hair-bearing units, when possible. The aesthetic facial units include the forehead, eyes and periorbital area, midface, nose (which itself contains several subunits), and lips and mentum. A spectrum of reconstructive options exists, with healing by secondary intention and primary closure at one end and extensive reconstruction such as microvascular free flaps at the other. The option that is selected depends on the location and severity of the defect, overall health of the patient, available donor sites for flaps, status of the tissue adjacent to the defect (irradiated, infected, previously operated), and functionality of the area to be reconstructed. Not only must the reconstructive surgeon choose which option is best for a given defect, but secondary and tertiary options should be also planned in case of flap failure or recurrent disease.

Healing by secondary intention is an excellent option in several clinical scenarios. Mucosal defects with an underlying layer of vascularized muscle or bone that will not contract to the point of impeding function may be left to close by secondary intention. Examples include small tonsillectomy defects, tongue resections, and some laryngeal mucosal defects. Primary closure is likely to be the most commonly used option for closure of cutaneous defects. Attempts should be made to keep incisions within the lines of relaxed skin tension. These lines are caused by muscular insertion into the skin and form when there is mimetic motion. Incisions that parallel the lines of relaxed skin tension not only respect the aesthetic units of the face but also have the least amount of tension along them, which decreases scarring. A Z-plasty may be used to reorient an unfavorable line of closure into a relaxed skin tension line.

Skin grafts are generally used for oral cavity, ear, or maxillectomy defects, and for coverage of donor sites, such as the radial forearm and fibular free flaps and deltopectoral flap. Skin grafts are completely dependent for nutrition on the tissue over which they are placed and can heal well over muscle, perichondrium, and periosteum. They do not take well over bone or cartilage, nor on tissue that has been irradiated or infected or is hypovascular. Split-thickness skin grafts contain the epidermis and a portion of the dermis and are harvested with a dermatome at approximately 0.012- to 0.018-inch thickness. Thinner grafts require less nutrients to remain viable but will also contract more when healing. Grafts may be meshed to allow greater surface coverage, but these types of grafts are generally restricted to the

scalp or over muscle because of a less cosmetic result. A nonadherent antibiotic-impregnated bolster is commonly used to maintain stability between the split-thickness skin graft and recipient bed for 5 days to allow transmission of nutrients and capillary ingrowth while healing. Harvest sites include the anterior and lateral aspects of the thighs and buttocks.

Full-thickness skin grafts are characterized by a better color match, texture, and contour and less contracture but success rates lower than with split-thickness skin grafts. Commonly used donor sites include the postauricular, upper eyelid, and supraclavicular fossa skin. Composite grafts are occasionally needed for cartilage and skin reconstruction of the nasal ala and may be harvested from the conchal bowl without significantly affecting the appearance of the pinna. Acellular cadaveric human dermis that has been prepared by removing immunogenic cells while leaving the collagen matrix intact has grown in popularity as a skin graft substitute and avoids the need for a donor site.

Local skin flaps have an excellent tissue match because of their proximity to the defect. Commonly used designs include advancement, rotation, transposition, rhomboid, and bilobed flaps. Similar to primary closure, local flaps should be designed to be incorporated into the lines of relaxed skin tension. Although local flaps depend on the subdermal plexus of capillaries, regional flaps have an axial blood supply. This latter vascular pedicle is necessary for flap viability because greater distances are spanned by the flap and it is contained within the subcutaneous fascia, as in a fasciocutaneous flap, or within an underlying muscle, as in a myocutaneous flap. The deltopectoral, or Bakamjian, flap was one of the early regional flaps and was used extensively in head and neck reconstruction. Based on the intercostal perforating branches from the internal mammary artery, the flap is based medially and is designed over the upper pectoralis and deltoid regions. Because of the pliability of the transferred skin, it can be swung upward for skin defects or pharyngeal reconstruction.

Perhaps the development with the most significant impact on head and neck reconstruction was introduction of the pectoralis myocutaneous flap in 1978. Based on the pectoral branch of the thoracoacromial artery, the artery pierces the pectoralis muscle from the deep surface. A skin paddle designed over the muscle, or simply the muscle itself, may be transferred to reconstruct defects up to the nasopharynx. Historically, the pectoralis muscle was tunneled under the intervening skin to preserve the ipsilateral deltopectoral flap in case it was needed for future coverage. Division of the pectoral nerve branches ensures atrophy of the muscle and reduces the bulge over the clavicle. In addition to reconstruction of mucosal defects with the vascularized skin, coverage of an exposed carotid artery is an excellent use of the myogenous flap. The trapezius muscle offers multiple soft tissue flaps that may be rotated into head and neck defects. The lower trapezius myocutaneous flap, based on the dorsal scapular artery, has already been referred to as an excellent choice for lateral temporal bone defects. Finally, the submental and platysmal flaps are based on the facial artery and provide excellent local flap coverage for oral and oropharyngeal defects.

A free flap entails removal of composite tissue from a distant site, along with its blood supply, and reimplantation of the vasculature in the reconstructive field. Although the first successful human microvasculature transfer was a jejunal interposition flap in 1959, the modern era of microvasculature reconstruction did not arise until the 1970s, with improvements in instrumentation and technique. The current selection of donor sites allows the benefit of choosing among sites with large-caliber, long vascular pedicles that are anatomically consistent. In addition to favorable vascularity, optimal donor sites allow a simultaneous two-team approach of ablation and harvesting, possibility of a sensate flap, composite transfer of bone stock capable of accepting osseointegrated implants, transfer of secretory mucosa, or any combinations of these options. Patient selection for free flap reconstruction is of critical importance. Advanced age is not a contraindication to microvascular reconstruction, although previous recipient bed irradiation, contraction of tissues after secondary reconstruction, or previous free flap failure should raise concern in the reconstructive surgeon. Complete loss of a free tissue transfer should occur in less than 5% of cases.

The radial aspect of the forearm has emerged as the workhorse of soft tissue free flaps in head and neck reconstruction. A fasciocutaneous flap with sensate capabilities, the radial forearm flap is based on the radial artery and its venae comitantes, cephalic vein, or both for drainage. Variations of the flap include harvest of partial radius bone or palmaris longus tendon for bony or suspensory reconstruction, respectively. The main advantage of the radial forearm flap is the thinness and pliability of the harvested skin, which makes it ideal not only for external cutaneous defects but also for reconstruction of the floor of the mouth or tongue (Fig. 35-21), soft palate and oropharyngeal wall, and pharynx, and for skull base reconstruction. Although the donor site is more cosmetically obvious than other donor sites, long-term morbidity of the harvest is minimal. Other soft tissue flaps include the lateral arm flap, anterolateral thigh and lateral thigh flaps, latissimus dorsi flap, and rectus abdominis flap. The lateral arm flap is an excellent alternative to the radial forearm flap when the patient exhibits a dominant radial artery supply to the hand, which is a contraindication to use of the forearm site. The lateral arm flap is based on the posterior branches of the radial collateral vessels. It offers slightly more bulk than the radial forearm flap does but is compromised to some extent by vessels that are smaller in caliber. Experience with thigh flaps has shown excellent results in tubed reconstruction of the pharynx. Both the latissimus dorsi and rectus abdominis flaps can be transferred as myogenous or myocutaneous flaps. Although skin match is not ideal, these flaps are best suited to large defects, including skull base repair or maxillectomy defects with orbital exenteration (Fig. 35-22). Harvest of the rectus abdominis may lead to the complication of postoperative hernia formation.

Enteric flaps include the gastro-omental flap and the jejunal flap. Disadvantages of these donor sites include the need for a laparotomy, which may preclude a two-team approach. In addition, the acceptable ischemia time is shortest with the enteric flaps because of their high tissue oxygen and nutrient demand. Unlike other donor sites, the pedicle of these flaps cannot be divided even years postoperatively because the flap tissues do not incorporate blood supply from the surrounding tissue bed. The main advantages of enteric flaps are their pliability and ability to continue secreting mucus. In an irradiated patient who suffers from xerostomia, enteric reconstruction of recurrent oral or oropharyngeal tumors affords the opportunity to improve his or her quality of life significantly. The omentum of the gastro-omental flap may be draped into the neck to provide contour and bulk to a neck that has previously been dissected.

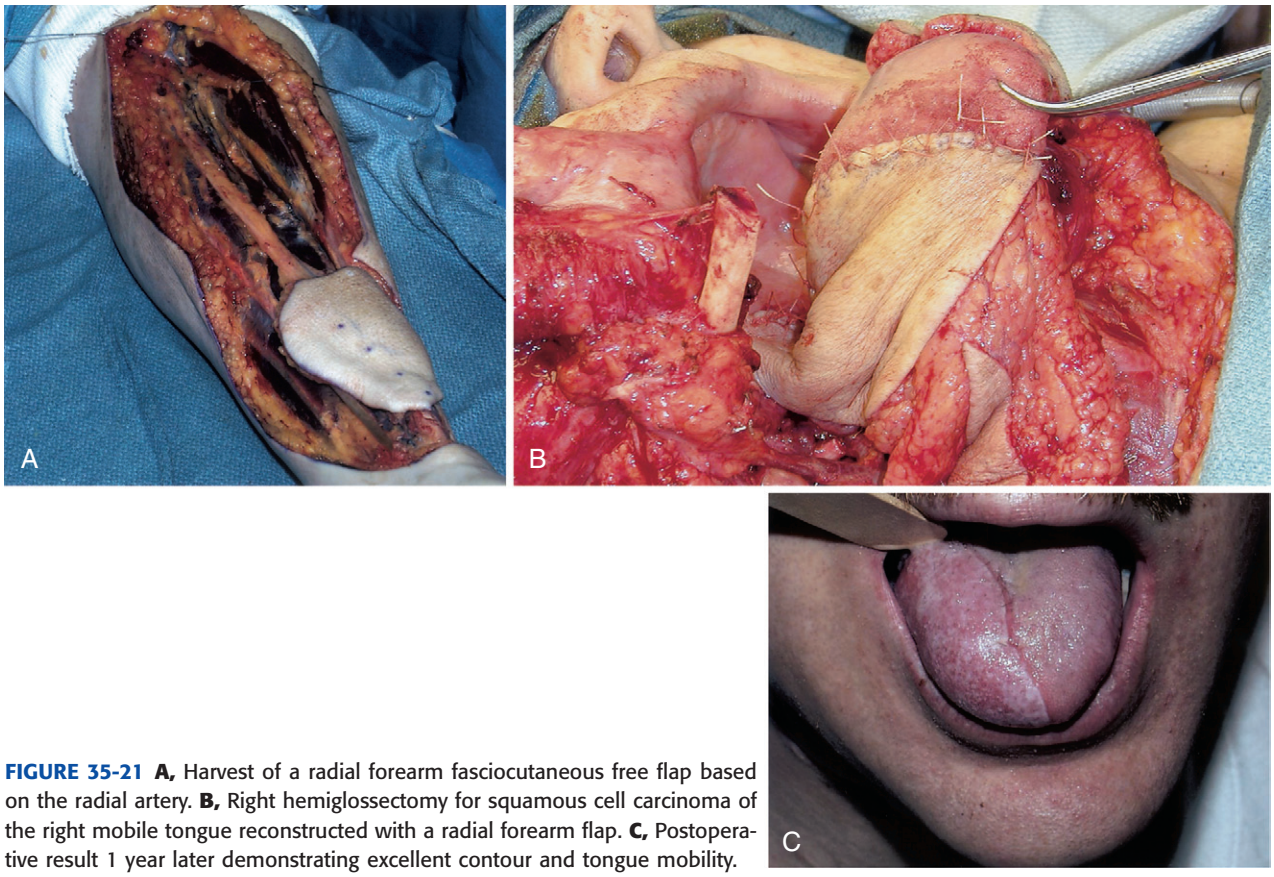


FIGURE 35-21 **A,** Harvest of a radial forearm fasciocutaneous free flap based on the radial artery. **B,** Right hemiglossectomy for squamous cell carcinoma of the right mobile tongue reconstructed with a radial forearm flap. **C,** Postoperative result 1 year later demonstrating excellent contour and tongue mobility.

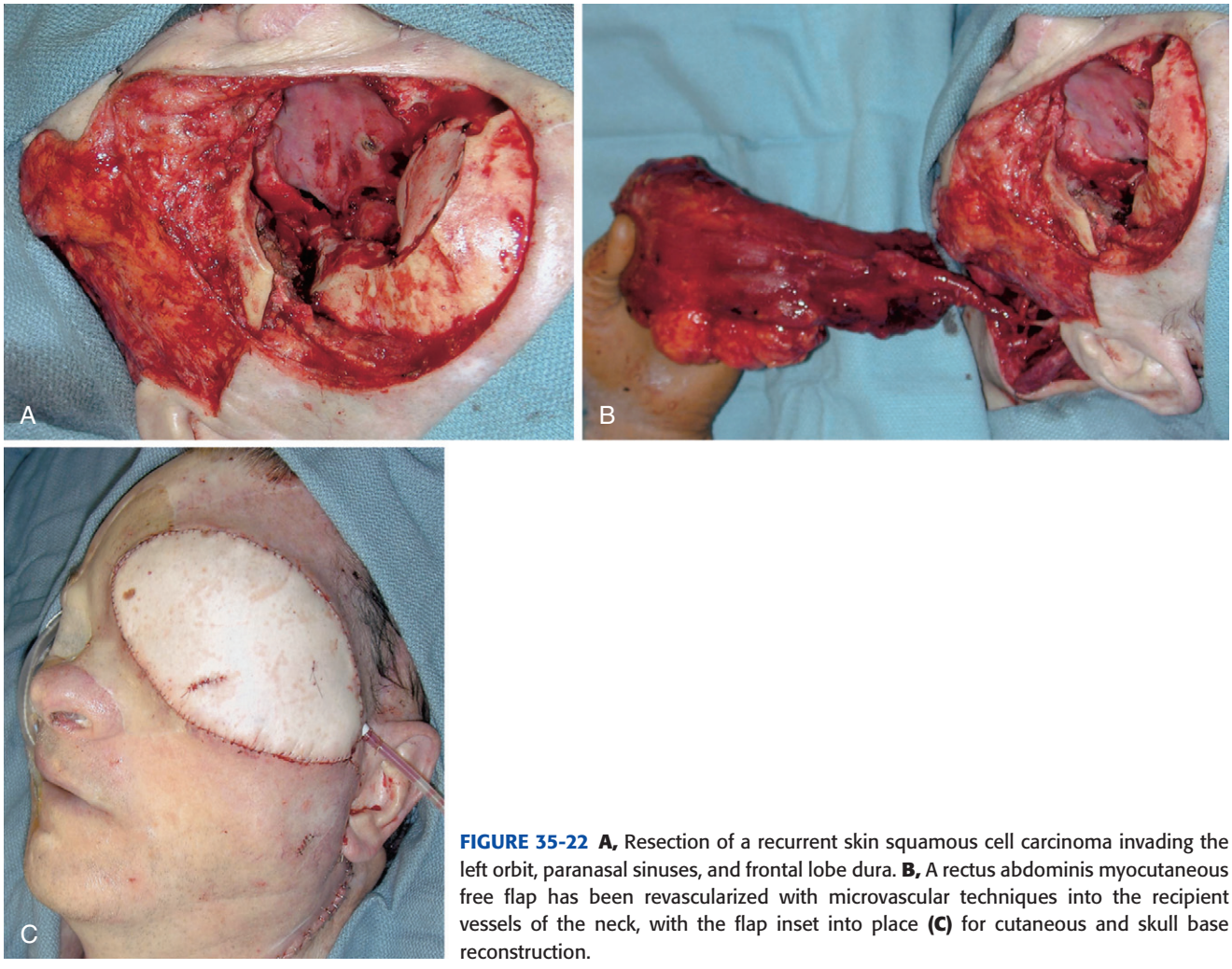


FIGURE 35-22 **A,** Resection of a recurrent skin squamous cell carcinoma invading the left orbit, paranasal sinuses, and frontal lobe dura. **B,** A rectus abdominis myocutaneous free flap has been revascularized with microvascular techniques into the recipient vessels of the neck, with the flap inset into place **(C)** for cutaneous and skull base reconstruction.

The most commonly used osseous free flaps include the fibula, scapula, and iliac crest. The fibular free flap is based on the peroneal artery and vein, and the blood supply to the foot should be investigated before harvesting this flap.[47] Up to 25 cm of fibula may be harvested for mandibular or maxillary reconstruction with an osseous or osteocutaneous graft, and donor site morbidity is minimal (Fig. 35-23). The bone stock of the fibula is sufficient to allow osseointegrated implantation for dentition or prosthetic anchors. The iliac crest osteocutaneous free flap allows even greater bone stock and is already naturally shaped in the form of a mandibular angle. Like the rectus abdominis flap, the iliac crest is hampered by the potential for postoperative hernias and has a relatively short vascular pedicle. Although the scapular free flap has the least bone stock of the three osseous flaps, it offers the advantage of simultaneous muscular, cutaneous, and bony reconstruction based on separate pedicles, thus allowing tremendous versatility in flap orientation. The megaflap includes the lateral border of the scapula based on the angular artery or the periosteal branch of the circumflex scapular artery, scapular or parascapular skin paddle based on cutaneous branches of the circumflex scapular artery, and latissimus dorsi and serratus anterior muscles supplied by the thoracodorsal artery. All arterial branches lead to the subscapular artery where it branches from the axillary artery, and revascularization of all segments may be accomplished with a single arterial anastomosis.

Perhaps the ultimate in head and neck reconstruction lies in the possibility of replacing ablated tissue with identical cadaveric donor tissue. In 1998, the first successful human laryngeal transplantation was performed with microvascular reconstruction (Fig. 35-24).[48] Not only the larynx but also the pharynx, thyroid, parathyroids, and trachea were transplanted. Since the initial laryngeal transplant, further transplants of both the larynx and trachea have been performed successfully, but until nontoxic

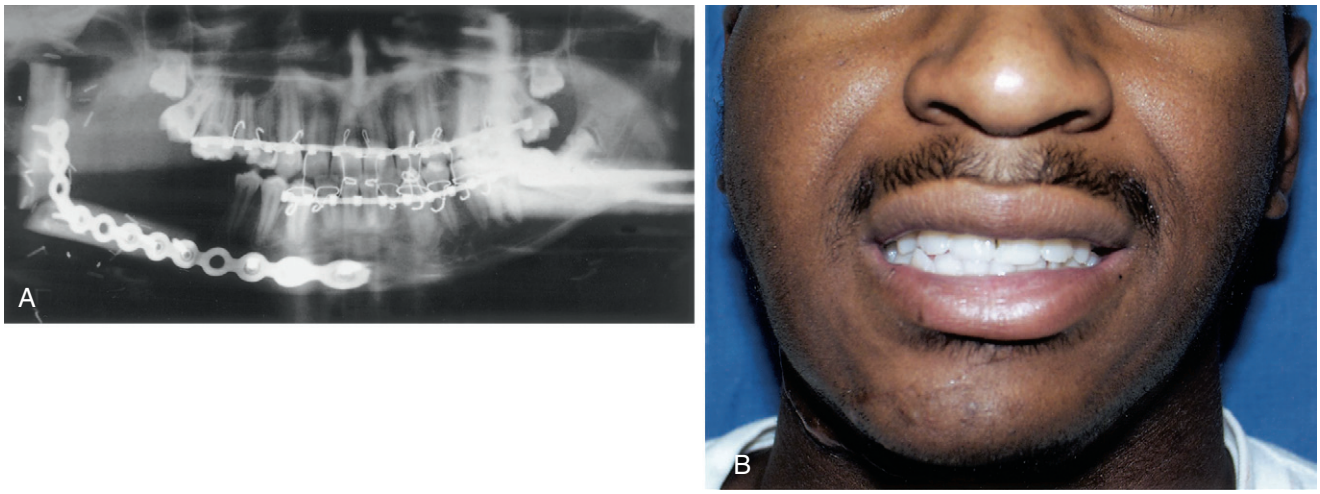


FIGURE 35-23 **A,** Immediate postoperative radiograph of a 35-year-old man after resection of an osteosarcoma of the mandibular ramus and reconstruction with a fibular osseocutaneous free flap. **B,** At 6 months postoperatively, the patient's dental occlusion has been preserved, along with excellent facial contour.

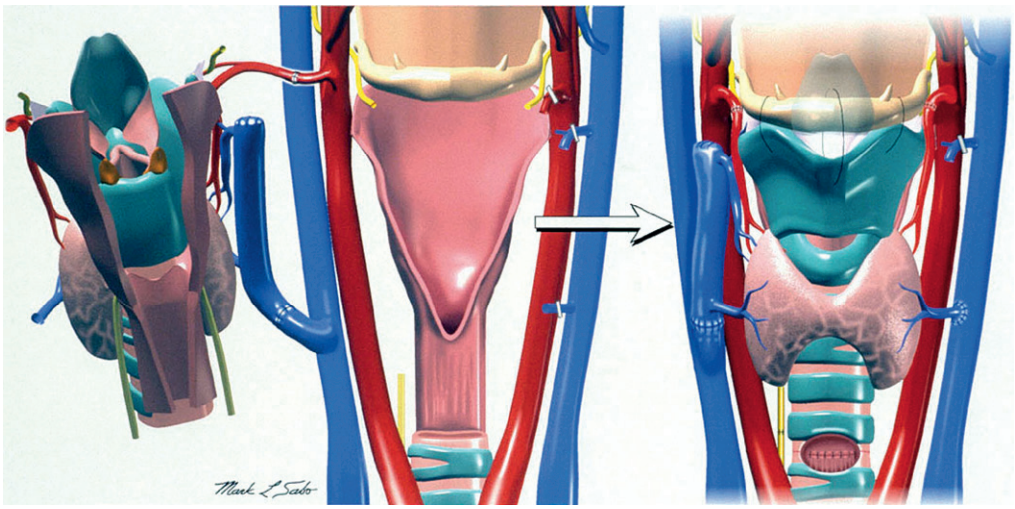


FIGURE 35-24 Schematic of the first successful laryngeal transplantation, performed in 1998. Not only was the larynx transplanted, but the thyroid, parathyroids, pharynx, and five rings of trachea accompanied the vascularized and innervated organ. (From Strome M, Stein J, Esclamado R, et al: Laryngeal transplantation and 48-month follow-up. N Engl J Med 344:1676–1679, 2001.)

immunosuppressive drugs and protection against fostering tumor recurrence have been developed, nonvital organ transplantation are unlikely to become commonplace.

SELECTED REFERENCES

Bocca E, Pignataro: A conservation technique in radical neck dissection. Ann Otol Rhinol Laryngol 76:975–987, 1967.

A landmark paper demonstrating equal control of metastatic neck disease with radical neck dissection and modified radical neck dissection while avoiding the morbidity of unnecessary removal of neck structures.

Fakhry C, Westra WH, Li S, et al: Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. J Natl Cancer Inst 100:261–269, 2008.

A recent phase II trial that suggests that when HNSCC is associated with HPV infection, the prognosis is significantly improved over non-HPV tumors. This landmark study was the first to demonstrate that tumor HPV status is a favorable prognostic marker in uniform patient populations with similar treatment protocols. Many physicians advise that tumor HPV status should be incorporated as a stratification factor in patients with oropharyngeal cancer, although basing treatment protocols on HPV status has yet to be definitively investigated.

Naudo P, Laccourreye O, Weinstein G, et al: Complications and functional outcome after supracricoid partial laryngectomy with cricohyoidoepiglottopexy. Otolaryngol Head Neck Surg 118:124–129, 1998.

This paper describes the outstanding functional results of supracricoid laryngectomy in terms of speech and swallowing while obtaining excellent local control of disease.

The Department of Veterans Affairs Laryngeal Cancer Study Group: Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. N Engl J Med 324:1685–1690, 1991.

This multi-institutional randomized trial demonstrated equal success between chemoradiation therapy and surgery with irradiation for laryngeal carcinoma while allowing patients who responded to the conservation treatment to keep their larynx.

REFERENCES

1. Edge SB, Byrd DR, Compton CC, et al, editors: AJCC cancer staging manual, ed 7, New York, 2010, Springer-Verlag.
2. Chaturvedi AK, Engels EA, Anderson WF, et al: Incidence trends for human papillomavirus–related and unrelated oral squamous cell carcinomas in the United States. J Clin Oncol 26:612–619, 2008.
3. Johnson N: Tobacco use and oral cancer: a global perspective. J Dent Educ 65:328–339, 2001.
4. Cooper JS, Porter K, Mallin K, et al: The National Cancer Database report on cancer of the head and neck: 10-year update. Head Neck 31:748–758, 2009.
5. Gillison ML: Current topics in the epidemiology of oral cavity and oropharyngeal cancers. Head Neck 29:779–792, 2007.
6. Stadler M, Patel M, Couch M, et al: Molecular biology of head and neck cancer. Hemat Oncol Clin N Am 22:1099–1124, 2008.
7. Li C, Hu Z, Lu J, et al: Genetic polymorphisms in DNA base-excision repair genes ADPRT, XRCC1, and APE1 and the risk of squamous cell carcinoma of the head and neck. Cancer 110:867–875, 2007.
8. Califano J, van der Riet P, Westra W, et al: Genetic progression model for head and neck cancer: Implications for field cancerization. Cancer Res 56:2488–2492, 1996.
9. Hugo H, Ackland ML, Blick T, et al: Epithelial-mesenchymal and mesenchymal-epithelial transitions in carcinoma progression. J Cell Physiol 213:374–383, 2007.
10. Kalyankrishna S, Grandis JR: Epidermal growth factor receptor biology in head and neck cancer. J Clin Oncol 24:2666–2672, 2006.
11. Pollak MN, Schernhammer ES, Hankinson SE: Insulin-like growth factors and neoplasia. Nat Rev Cancer 4:505–518, 2004.
12. Kutler DI, Wong RJ, Kraus DH: Functional imaging in head and neck cancer. Curr Oncol Rep 7:137–144, 2005.
13. Bourhis J, Wibault P, Lusinchi A, et al: Status of accelerated fractionation radiotherapy in head and neck squamous cell carcinomas. Curr Opin Oncol 9:262–266, 1997.
14. The Department of Veterans Affairs Laryngeal Cancer Study Group: Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. N Engl J Med 324:1685–1690, 1991.
15. Bernier J, Domenge C, Ozashin M, et al: Postoperative irradiation with or without concurrent chemotherapy for locally advanced head and neck cancer. N Engl J Med 350:1945–1952, 2004.
16. Cooper JS, Pajak TF, Forastiere AA, et al: Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous cell carcinoma of the head and neck. N Engl J Med 350:1937–1944, 2004.
17. Roy S, Tibesar RJ, Daly K, et al: Role of planned neck dissection for advanced metastatic disease in tongue base or tonsil squamous cell carcinoma treated with radiotherapy. Head Neck 24:474–481, 2002.
18. Bocca E, Pignataro O: A conservation technique in radical neck dissection. Ann Otol Rhinol Laryngol 76:975–987, 1967.
19. Kuriakose MA, Trivedi NP: Sentinel node biopsy in head and neck squamous cell carcinoma. Curr Opin Otolaryngol Head Neck Surg 17:100–110, 2009.
20. O'Brien CJ, Lauer CS, Fredricks S, et al: Tumor thickness influences prognosis of T1 and T2 oral cavity cancer—but what thickness? Head Neck 25:937–945, 2003.
21. Gooris PJ, Vermey A, de Visscher JG, et al: Supraomohyoid neck dissection in the management of cervical lymph node metastases of squamous cell carcinoma of the lower lip. Head Neck 24:678–683, 2002.
22. Strome SE, To W, Strawderman M, et al: Squamous cell carcinoma of the buccal mucosa. Otolaryngol Head Neck Surg 120:375–379, 1999.
23. Adelstein DJ, Saxton JP, Rybicki LA, et al: Multiagent concurrent chemoradiotherapy for locoregionally advanced squamous cell head and neck cancer: Mature results from a single institution. J Clin Oncol 24:1064–1071, 2006.
24. Fakhry C, Westra WH, Li S, et al: Improved survival of patients with human papillomavirus–positive head and neck squamous cell carcinoma in a prospective clinical trial. J Natl Cancer Inst 100:261–269, 2008.

25. Lefebvre JL, Chevalier D, Luboinski B, et al: Larynx preservation in piriform sinus cancer: Preliminary results of a European Organization for Research and Treatment of Cancer phase III trial. EORTC Head and Neck Cancer Cooperative Group. J Natl Cancer Inst 88:890–899, 1996.

26. Kirchner JA: Vocal fold histopathology: A symposium, San Diego, Calif, 1986, College-Hill Press.

27. Ambrosch P, Kron M, Steiner W: Carbon dioxide laser microsurgery for early supraglottic carcinoma. Ann Otol Rhinol Laryngol 107:680–688, 1998.

28. Steiner W, Vogt P, Ambrosch P, Kron M: Transoral carbon dioxide laser microsurgery for recurrent glottic carcinoma after radiotherapy. Head Neck 26:477–484, 2004.

29. Muscatello L, Laccourreye O, Biacabe B, et al: Laryngofissure and cordectomy for glottic carcinoma limited to the mid third of the mobile true vocal cord. Laryngoscope 107:1507–1510, 1997.

30. Naudo P, Laccourreye O, Weinstein G, et al: Complications and functional outcome after supracricoid partial laryngectomy with cricohyoidoepiglottopexy. Otolaryngol Head Neck Surg 118:124–129, 1998.

31. Solares CA, Wood B, Rodriguez CP, et al: Does vocal cord fixation preclude nonsurgical management of laryngeal cancer? Laryngoscope 119:1130–1134, 2009.

32. Imola MJ, Schramm VL: Orbital preservation in surgical management of sinonasal malignancy. Laryngoscope 112:1357–1365, 2002.

33. Vasef MA, Ferlito A, Weiss LM: Clinicopathological consultation: Nasopharyngeal carcinoma, with emphasis on its relationship to Epstein-Barr virus. Ann Otol Rhinol Laryngol 106:348–356, 1997.

34. Al-Sarraf M, LeBlanc M, Giri PB, et al: Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized Intergroup Study 0099. J Clin Oncol 16:1310–1317, 1998.

35. Jia WH, Huang QH, Liao J, et al: Trends in incidence and mortality of nasopharyngeal carcinoma over a 20–25 year period (1978/1983–2002) in Sihui and Cangwu counties in southern China. BMC Cancer 6:178, 2006.

36. Lorenz RR, Dean RL, Chuang J, Citardi MJ: Endoscopic reconstruction of anterior and middle cranial fossa defects using acellular dermal allograft. Laryngoscope 113:496–501, 2003.

37. Stewart CJ, MacKenzie K, McGarry GW, et al: Fine-needle aspiration cytology of salivary gland: A review of 341 cases. Diagn Cytopathol 22:139–146, 2000.

38. Witt RL: The significance of the margin in parotid surgery for pleomorphic adenoma. Laryngoscope 112:2141–2154, 2002.

39. Seifert G: Histopathology of malignant salivary gland tumours. Eur J Cancer B Oral Oncol 28B:49–52, 1992.

40. Amedee RG, Dhurandhar NR: Fine-needle aspiration biopsy. Laryngoscope 111:1551–1557, 2001.

41. Zimmermann CE, von Domarus H, Moubayed P: Carcinoma in situ in a lateral cervical cyst. Head Neck 24:965–969, 2002.

42. Cohen SM, Burkey BB, Netterville JL: Surgical management of parapharyngeal space masses. Head Neck 27:669–675, 2005.

43. van Heurn LW, Goei R, de Ploeg I, et al: Late complications of percutaneous dilatational tracheotomy. Chest 110:1572–1576, 1996.

44. Kost KM: Endoscopic percutaneous dilatational tracheotomy: A prospective evaluation of 500 consecutive cases. Laryngoscope 115:1–30, 2005.

45. Netterville JL, Koriwchak MJ, Winkle M, et al: Vocal fold paralysis following the anterior approach to the cervical spine. Ann Otol Rhinol Laryngol 105:85–91, 1996.

46 Lorenz RR, Teker AM, Strome M, et al: Ansa cervicalis-to-recurrent laryngeal nerve anastomosis for unilateral vocal fold paralysis: A single institutional experience. Ann Otol Rhinol Laryngol 117:40–45, 2008.

47. Lorenz RR, Esclamado R: Preoperative magnetic resonance angiography in fibular free flap reconstruction of head and neck defects. Head Neck 23:844–850, 2001.

48. Strome M, Stein J, Esclamado R, et al: Laryngeal transplantation and 40-month follow-up. N Engl J Med 344:1676–1679, 2001.