**Chapter 7 Head and Neck Cancers**

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**Specific Head and Neck Cancers**

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**Principles**

Head and neck cancers comprise a heterogeneous group of tumors exclusive of intracranial lesions. Tumors from various sites of origin have distinct behavior

patterns and prognoses and require different management. Each primary site is considered separately after a discussion of common features.

**I. Epidemiology and etiology**

A. **Incidence.** Primary head and neck malignant tumors constitute 5% of all newly diagnosed cancers in humans and result in about 16,000 deaths per year. One

to three cases occurs annually per 100,000 population in the United States. The incidence of squamous cell carcinoma is significantly higher in male patients

(male-to-female ratio, 3:1 to 4:1).

B. **Etiology.** Substantial alcohol intake and cigarette smoking are major risk factors for head and neck cancers. A variety of hereditary, environmental,

occupational, and hygienic factors are of lesser importance. Conditions associated with increased incidence of specific head and neck cancers are discussed in

their respective sections.

C. **Multiple cancers.** Second primary cancers in the upper respiratory passage are present in about 5% of patients with head and neck cancers at the time of

diagnosis. Eventually, secondary cancers occur in 20% of all of these patients. This development is most frequent in patients who continue to consume alcohol

and smoke cigarettes. The multiplicity of neoplasms suggests that the entire respiratory mucosa may be predisposed to develop malignant tumors, a so-called

field defect. These patients may also develop cancer of the lung.

**II. Pathology and natural history**

A. **Histology.** Squamous cell carcinomas constitute at least 95% of head and neck cancers, except those in the hard palate and salivary glands. Minor salivary

gland adenocarcinomas can occur throughout the upper aerodigestive tract. Tumors with other histologies are infrequently seen.

B. **Metastases.** Head and neck cancers spread predominantly by local invasion of adjacent tissues and dissemination through lymphatic channels. Hematogenous

dissemination, most commonly to the lungs, is a relatively late phenomenon.

**III. Diagnosis**

A. **Common symptoms or signs**

1. Mass, often painless

2. Mucosal ulcer, often with mass

3. Localized (often referred) pain in the mouth (teeth), throat, or ear

4. Odynophagia or dysphagia

5. Visual disturbances related to cranial nerve palsies, proptosis, blindness

6. Hearing loss, usually unilateral, and often associated with serous otitis

7. Persistent unilateral “sinusitis,” nasal obstruction, or bleeding

8. Unilateral tonsillar enlargement in adults

9. Five to 10% of white plaques (leukoplakia) may be cancer *in situ.* This condition must be differentiated from *Candida* species infection (can be wiped off) and

lichen planus (fine white lines often related to denture irritation).

B. **Laboratory investigation.** The pretreatment diagnostic evaluation of head and neck cancer must both document the extent of disease and exclude a coincident

second primary cancer in the upper aerodigestive tract. A chest radiograph and a computed tomography (CT) or magnetic resonance imaging (MRI) scan from

the base of the skull to the thoracic inlet are included in the evaluation of location and extent of the cancer.

C. **Endoscopy** includes direct visualization of the nasopharynx, larynx, hypopharynx, cervical esophagus, and proximal trachea. In patients without obvious

tumors, biopsies may be performed during endoscopy of high-risk areas: the nasopharynx, pharyngeal tongue, tonsillar fossa, and pyriform sinus. Endoscopy is

useful in the following circumstances:

1. To document the presence, site, and extent of tumors in the upper aerodigestive tract

2. To search for other primary cancers in patients with already recognized cancers in the upper aerodigestive tract

3. To evaluate patients with metastases of unknown origin (MUO) to neck lymph nodes

D. **Evaluating patients with probable MUO to neck lymph nodes.** A premature biopsy of a suspect node can compromise both treatment and likelihood of cure if

the origin is head and neck cancer. Management of patients with MUO is discussed in Chapter 20.

1. **Criteria for endoscopy in patients with cervical adenopathy**

a. The enlarged node is firm and nontender or growing, and there is no evidence to suggest inflammatory disease (e.g., no response to a 2-week course of

antibiotics).

b. The patient is at high risk for cancer (older than 40 years of age and a history of tobacco or alcohol abuse).

c. No primary tumor is found on visual, digital, and mirror examination.

2. **Biopsy of the suspect node** should be done only when:

a. Fine-needle aspiration cytology fails to reveal the diagnosis, and

b. Thorough physical examination fails to reveal a primary tumor, and

c. CT or MRI examination does not disclose a primary tumor, and

d. Endoscopy fails to reveal a primary site

**IV. Staging system and prognostic factors**

A. **Staging classification.** The TNM staging system for head and neck cancers is widely used. The definitions for the system, histopathologic grades, and stage

groupings are shown in Table 7.1.

**Table 7.1** TNM staging and stage grouping for head and neck cancers *a*

B. **Discordant clinical and pathologic evaluation of stage.** In some instances, biopsies of an apparently invasive cancer are interpreted as cancer *in situ,*

cellular atypia, or dysplasia. This histologic interpretation requires additional biopsies, particularly at the margin of the gross tumor, because the initial biopsies

may not have been representative of the lesion. If these biopsies are not conclusive, the entire gross tumor may be excised, if practical, for more complete

examination. After the primary cancer has been positively identified, treatment planning can proceed based on likely extension of the tumor into adjacent tissues.

C. **Prognostic factors**

1. **Primary site.** The site of origin of a cancer in the head and neck strongly influences the prognosis. For example, a cancer 1 cm in greatest dimension on a

true vocal fold is more curable than a primary lesion of similar size arising subglottically or in the pyriform sinus.

2. **Extent of tumor.** The local extent of the primary tumor and metastases is an important prognostic indicator and is reflected in the TNM staging system.

3. **Histologic grade.** Epidermoid carcinomas of the upper aerodigestive tract are usually subdivided by grade ( Table 7.1). Tumor grade correlates somewhat

with biologic behavior; less well-differentiated primary cancers tend to grow more rapidly and be more locally or regionally extensive at the time of initial

diagnosis.

**V. Prevention**

A. **Abstinence.** The limiting or elimination of alcohol and tobacco consumption (including chewing tobacco) and good oral hygiene remain the mainstay of

prevention for most head and neck cancers.

B. **Chemoprevention.** Isoretinoin (13-*cis*-retinoic acid) can reverse severe oral leukoplakia. Continued maintenance therapy with attendant toxicity (rashes,

conjunctivitis, hypertriglyceridemia) is required to sustain the effect. Isoretinoin also appears to reduce the occurrence of second neoplasms in patients treated

for primary head and neck squamous cell carcinomas; the drug does not prevent recurrence of the original neoplasm, however.

**VI. Management**

A. **Principles of treatment.** Before commitment for therapy of all patients, there should be input from members of a multidisciplinary group that includes a surgeon,

radiation oncologist, medical oncologist, and dentist. Patients must be frequently examined after treatment. Recurrent or persistent tumors can usually be

recognized within 2 years of initial treatment.

1. **Anatomic barriers,** such as bone and peripheral nerves, may be a greater deterrent to surgical removal than to irradiation. Thus, cancers arising in the

mucosa of the nasopharynx or posterior pharyngeal wall are usually irradiated by choice because of anatomic barriers. In other primary sites, such as the

vocal fold and retina, the extreme morbidity of loss of voice or sight associated with obtaining a tumor-free margin surgically usually makes radiation therapy

(RT) preferable.

2. **Surgery.** The primary cancer should be widely excised with tumor-free margins of normal tissues. Preservation of function (i.e., swallowing or speech) is a

prime consideration. Cosmesis is secondary to adequate resection. Ipsilateral neck dissection is often an extension of this operation.

Tumor extension into bone requires sophisticated partial resection, when appropriate, or complete resection followed by an insertion of a prosthesis or some

type of flap construction. When the primary tumor is closely adjacent to or involves the mandible, an *en bloc* resection of the primary tumor, cervical nodes, and

intervening mandible may be done (called *composite resection*).

3. **RT** can control cancers arising in the head and neck with preservation of an intact anatomic part and consequently with preservation of function and

cosmesis.

a. **The volume** at the primary tumor site must include a margin outside of all cancer cells and so is comparable to that which would be removed surgically.

The anatomic sites of actual or likely spread of cancer, such as the regional lymph nodes, are frequently included in continuity with the primary tumor site.

The primary and high-risk sites may be treated simultaneously or consecutively by the same or different methods.

b. **Large total doses** (i.e., 6500 to 7500 cGy) of radiation, approaching the tolerance of normal tissues, are usually required to eradicate squamous cell

carcinomas arising in the mucosa of the head and neck. Occasionally, the usual daily dose of 180 to 200 cGy may be delivered at less than 24-hour

intervals (accelerated fractionation), or several smaller increments may be used every 24 hours (hyperfractionation).

B. **Treatment of the primary cancer**

1. **T1 or T2 cancer at the primary site.** Either RT or surgery can usually treat small malignancies with equal success. The choice of modality depends on the

tumor’s location, accessibility, and histologic grade and the patient’s vocation, health, and treatment preference. Tumors of high grade are often best treated

with RT. Deeply invasive tumors and tumors adjacent to or invading bone are often best managed surgically.

2. **T3 or T4 cancer at the primary site.** The management of T3 lesions should usually combine surgery with preoperative or postoperative RT. Neither

sequence has been demonstrated to be clearly superior. If surgery is not considered feasible, patients may be treated with either high-dose RT alone or RT

preceded by or followed by chemotherapy. The addition of chemotherapy to RT is still being investigated.

3. **Postoperative RT.** After the removal of all grossly detectable cancer, doses of 4500 to 6000 cGy result in a very high frequency (90% to 95%) of tumor

control with few detectable sequelae. Advantages of this sequence include an appraisal of tumor extent that is unaltered by irradiation and performance of

surgery in unirradiated tissue with possibly fewer technical problems and more rapid healing. Such planned use of RT should begin as soon as wound

healing permits. **Postoperative RT is indicated** when:

a. The cancer is poorly differentiated, or

b. The cancer is histologically identified at or near the surgical margins, or

c. There is extensive involvement of the lymphatics by tumor, or

d. Multiple cervical lymph nodes contain cancer, or

e. The tumor extends through the capsule of the node into surrounding tissues

C. **Treatment of cervical lymph nodes** is determined by the site and extent of the primary tumor, the proposed treatment modality for the primary lesion, and the N

staging of the cervical nodes. A primary resection for proven or suspected metastases to cervical lymph nodes should involve *en bloc* removal of all lymph

nodes and adjacent normal tissues.

1. **Neck dissection** (ND) may be a “radical neck dissection” or one of a variety of partial neck dissections. Less extensive dissections include removal of

tumor-involved lymph nodes that do not respond adequately to primary irradiation. Definitions and indications vary among surgeons.

a. **A classic radical ND** removes *en bloc* all tissue from the mandible to the clavicle, from the anterior border of the trapezius to the midline strap muscles,

and between the superficial layer of the deep cervical fascia (platysma) and the deep layer of the deep cervical fascia. Among the resected structures are

the sternocleidomastoid muscle, internal jugular vein, and 11th cranial (accessory) nerve.

b. **A modified radical ND** spares certain structures, usually the accessory nerve or the sternocleidomastoid muscle. It is usually reserved for the treatment

of patients with clinically negative cervical lymph nodes, planned postoperative neck irradiation, or minimal tumor in neck nodes. The most common

variant is the supraomohyoid dissection, which removes nodes from levels 1, 2, and 3.

c. **A partial ND** results in only partial removal of the lymph nodes. In its extreme, a partial ND involves removal of only a solitary nodal mass.

2. **Patients without enlarged cervical lymph nodes** have an incidence of tumor-containing nodes as high as 60%. Exceptions to this high incidence include

cancers of the vocal fold or paranasal sinuses, small lip cancers, and low-grade salivary gland malignancies. For most other head and neck cancer sites, the

homolateral cervical nodes should be treated with either RT or ND, even if not grossly involved with metastases.

3. **Patients with enlarged cervical lymph nodes**

a. **ND** is usually is performed whenever the primary site is treated surgically. **RT should follow ND** when:

1. Any node is larger than 3 cm in greatest dimension, or

2. Any of the conditions listed in section B.3 are present

b. **RT** is usually the treatment of choice for primary carcinomas of the nasopharynx, pharyngeal tongue, soft palate, or tonsillar region or when the

tumor-involved nodes cannot be resected. **ND should follow RT** when the tumor-involved nodes do not completely grossly respond to RT or when the

tumor-involved nodes were initially unresectable but become resectable.

D. **Role of chemotherapy in head and neck cancers.** Many nonrandomized studies and early reports have shown impressive response rates for head and neck

carcinomas treated with various chemotherapeutic regimens, but no clear improvement in overall survival. Responses to chemotherapy are best with high-grade

tumors. The patient’s nutritional status, performance status, and comorbid conditions greatly affect the significance of the response.

1. **Single agents.** Methotrexate, bleomycin, carboplatin, cisplatin, vinorelbine, epirubicin, and 5-fluorouracil (5-FU) are active single agents, each achieving

significant tumor reduction in 15% to 30% of patients.

2. **Combination chemotherapy regimens.** The most useful regimens combine cisplatin and 5-FU (PF regimen) without leucovorin or with it (PFL regimen).

Adding other drugs to this combination has not improved results. Representative regimens, which are given every 21 to 28 days, include the following:

a. **PF**

Cisplatin, 100 mg/m2 IV on day 1

5-FU, 1000 mg/m2/day by continuous IV infusion (CIV) for 5 days (total, 5 g/m 2)

b. **PFL**

Cisplatin, 25 mg/m2 IV on days 1 through 5 by CIV (total, 125 mg/m2)

5-FU, 800 mg/m2/day on days 2 through 6 by CIV (total, 4 g/m2)

Leucovorin, 500 mg/m2 on days 1 through 6 by CIV (total, 3 g/m2)

3. **Beneficial effects of chemotherapy** have been best demonstrated in laryngeal and nasopharyngeal carcinomas.

a. **Laryngeal carcinoma.** Chemotherapy followed by definitive RT achieves laryngeal preservation in a high percentage of patients with advanced cancer

but does not improve overall survival. The precise contribution of chemotherapy to this benefit, however, is uncertain.

b. **Nasopharyngeal carcinoma.** Studies in the Western world of patients with N2 and N3 disease have shown improved 3-year relapse-free survival and

overall survival when compared with those treated with RT alone. Studies in Asia, however, have failed to demonstrate a benefit from the addition of

chemotherapy to intensive RT programs.

4. **Induction chemotherapy** (before surgery or RT) for locally advanced disease

a. Induction chemotherapy results in tumor regression in 60% to 90% and in complete responses (CRs) in 25% to 70% of patients with locally advanced

head and neck cancers, many of which can be pathologically documented. Patients with CRs have better survival than those with partial responses, but

this is not a valid statistical comparison.

b. Patients who achieve a CR with chemotherapy may require only additional RT (i.e., surgery may not be necessary). The appropriate sequence of

chemotherapy, RT, and surgery has not been well defined.

c. Induction chemotherapy results in a decreased frequency of subsequent distant metastases, but survival data are conflicting. Although individual reports

have supported using 5-FU and cisplatin induction chemotherapy for stage III and IV head and neck carcinomas without distant metastasis (i.e., with

substage M0), meta-analyses of phase III trials show no advantage in either locoregional control or survival.

5. **Simultaneous chemoradiotherapy** is popular and shows promise for locally advanced head and neck cancers but is difficult to evaluate. Such treatment is

considered for patients in good general condition and with good performance status because it can be associated with substantial toxicity.

a. Locoregional control is achieved in 35% to 70% of patients treated with chemoradiotherapy versus 15% to 45% of patients treated with conventional or

hyperfractionated RT. Three-year survival with chemoradiotherapy may be better than with RT alone. Extension and confirmation of these observations is

necessary before this approach becomes widely adopted.

b. A regimen used at Duke University with “acceptable” toxicity is given during the first and sixth weeks of RT, and for two cycles after the completion of RT.

Cisplatin, 12 mg/m2/day by CIV for 5 days (total, 60 mg/m2), and

5-FU, 600 mg/m2 by CIV for 5 days (total, 3 g/m2)

6. **Postoperative adjuvant chemotherapy** decreases the occurrence of distant metastases and may increase survival in high-risk groups (including those who

achieved a response to preoperative chemotherapy) but has no effect on disease-free survival or overall survival.

7. **Local recurrence and metastatic disease.** Combination chemotherapy with PF achieves response rates of about 45% (reported range, 10% to 75%), but

the duration of response is short (usually less than 2 months). No combination improves survival rates. Patients with disseminated head and neck cancers

usually die within 6 months.

E. **Persistent tumor.** When a cancer reappears at the previously treated primary site, it results from incomplete destruction of all tumor cells. Although this is often

called *recurrence,* it is actually regrowth of a persistent tumor. If a discrete new tumor arises separately from a previously treated primary site, it represents a

new or second cancer. Irradiation or additional surgery can often salvage surgical failures. Surgery is usually the treatment of choice to salvage RT failures;

such attempted surgical rescue is associated with increased morbidity related to late radiation-induced tissue changes.

F. **Adverse effects of treatment**

1. **Complications of radical surgery**

a. Cosmetic and functional deformity

b. Speech impediment or loss

c. Aspiration pneumonia

d. Shoulder or arm weakness, paresthesias, and pain with ND

2. **Toxicity of chemotherapy administered with RT** may be significant

a. Severe stomatitis, diarrhea

b. Nephropathy, fluid and electrolyte imbalance, divalent cation deficiency

c. Neuropathy

d. Malnutrition

e. Pancytopenia

f. Hospitalizations to treat complications

3. **Adverse effects of RT.** The frequency and severity of sequelae of RT are related to the specific sites irradiated, the condition of the normal tissues before

irradiation, the total and incremental doses, the pattern of application, the quality of the radiation, concurrent disease, and the use of medications.

a. **Acute, self-limiting sequelae**

1. **Skin and conjunctival “reactions”** include erythema, discoloration, and rarely superficial ulceration. These sequelae disappear after a few weeks.

2. **Epilation** of the scalp may be permanent or temporary depending on the total dose. The regrown hair may be of a different character than the original

in color and density. Permanent epilation of the face (beard) or eyebrows requires relatively high doses. Eyelashes may be permanently lost with

lower doses.

3. **Mucositis** in the oral cavity, hypopharynx, or cervical esophagus may result in dysphagia.

4. **Edema** involving the endolarynx may cause hoarseness.

5. **Lhermitte’s syndrome** is transitory and consists of electric shock–like sensations in the upper or lower limbs, precipitated by flexion of the neck. This

is related to inclusion of the cervical spinal cord in a tissue volume taken to relatively high doses.

6. **Serous otitis media,** which may follow irradiation of the middle ear, resolves spontaneously.

b. **Chronic sequelae**

1. **Xerostomia** is secondary to irradiation of the salivary glands, primarily the parotids, to high doses. Partial suppression and change of consistency of

the saliva may be permanent.

2. **Myelopathy** of the cervical spinal cord is the most dreaded long-term sequela. This condition follows exposure to very high doses (less than 1%

incidence at 6000 cGy in 200-cGy daily increments).

3. **Cataracts** may follow irradiation of the lens. This sequela, which is more common in elderly patients and those with diabetes, usually can be avoided

by careful technical application. Cataracts due to irradiation can be successfully treated surgically.

4. **Ulceration** of soft tissue is a rare long-term consequence and is usually related to irradiation to a high total dose, often in conjunction with surgery.

5. **Necrosis of the mandible** is infrequent and can be nearly eliminated by careful irradiation techniques and good dental care.

G. **Supportive care**

1. **Adequate nutrition** can be maintained by diet supplements between meals, nasoesophageal or gastrostomy tube feedings, or hyperalimentation.

2. **Opportunistic infections** frequently occur in debilitated patients during therapy and must be treated. Oral candidiasis is the most common infection in head

and neck cancer patients (see Chapter 35, section VI.B).

3. **Dental care**

a. All patients who are likely to receive high doses of radiation to the oral cavity, including a portion of the mandible or the salivary glands, should have a

dental consultation before therapy.

b. Fluoride gel treatment during and after the period of RT reduces dental problems.

c. Dentures should not be worn during RT and for a period of 6 to 9 months after its completion. These dentures should have a soft lining and not result in

local sites of pressure.

4. **Psychological support**

a. Reiterate the appropriateness and necessity of particular treatments.

b. Explain postsurgical reconstruction and rehabilitation.

c. Reinforce patient avoidance of alcoholic beverages and tobacco.

d. Emphasize the maintenance of good oral hygiene.

e. Emphasize the importance of long-term follow-up.

**VII. Special clinical problems**

A. **Increasing induration of neck or facial tissues in a previously irradiated area** may indicate persistent cancer. If involved by carcinoma, the skin is usually

tense, brawny, and purplish in color, often fixed to the underlying tissues or bone, and usually associated with an enlarging mass. Occasionally, no discrete

masses are palpable, but the involved tissues are firm to stony hard. In contrast, postirradiation induration is usually flat, smooth, and confined to areas of high

dose. A biopsy is often hazardous. Treatment can usually be undertaken using clinical criteria without tissue diagnosis.

B. **Unsightly cosmetic facial defects** pose major problems for both patients and those who must interact with them. Health professionals should combine a

professional, detached view of physical defects with compassion.

C. **Massive facial edema** is an occasional end-stage problem in advanced head and neck cancer and is usually caused by venous or lymphatic obstruction in the

neck or mediastinum. These patients usually die from cerebral edema, hemorrhage, or inanition.

D. **Arterial rupture with exsanguination** may result from tumor erosion through the carotid or other major arteries and is usually rapidly fatal. RT should be

attempted in patients with tumor adjacent to a major vessel. It may control the tumor, stimulate fibrosis, and avert or delay this disaster.

E. **Airway obstruction** can be a cause of death for patients with untreated or uncontrolled cancer of the upper respiratory passages.

1. **Emergency tracheostomy** may be required in patients with a severely compromised upper air passage (e.g., stridor) before treatment.

2. **Prednisone,** 40 to 60 mg/day PO, may provide temporary relief for some patients when other modalities have been ineffective. Patients who cannot swallow

can receive methylprednisolone, 40 mg SC.

3. **Antibiotics** for the treatment of superimposed infection may relieve airway or swallowing difficulties and reduce accompanying foul odors.

4. **Chemotherapy** may be used in patients who have already received maximum tolerable doses of radiation in an attempt to achieve tumor reduction.

F. **Inability to swallow** may be a complication of uncontrolled head and neck tumors. Alimentation support is probably not warranted in patients whose cancer is

refractory to RT and chemotherapy because prolonged survival may be accompanied by airway obstruction, facial edema, or intractable pain.

G. **Infection** of bulky, necrotic tumors may be associated with fever, pain, or swelling and may be caused by normal mouth flora. Symptomatic relief can sometimes

be obtained using a broad-spectrum antibiotic (e.g., metronidazole).

**Specific Head and Neck Cancers**

The relative occurrence, sex predominance, most common site, and histology of the constituents of head and neck cancers are compared in Table 7.2.

**Table 7.2** Features of head and neck cancers by site of origin

**I. Lip** (sites: vermilion border and mucosal surfaces)

A. **Natural history**

1. **Risk factors** include smoking, long-standing hyperkeratosis, sun and wind exposure, chronic irritation, and xeroderma pigmentosum.

2. **Presentation.** Ninety-five percent occur on the lower lip. The presenting sign or symptom is usually a recurrent scab, sore, blister, or ulcer with or without a

mass.

3. **Lymphatic drainage.** First to submental and submaxillary nodes, and then to upper anterior cervical (jugular) and intraparotid nodes. Lymphadenopathy is

seen in 5% to 10% of patients at presentation and is related to the size of the primary cancer.

B. **Differential diagnosis**

1. Keratoacanthoma is a self-limiting, exophytic lesion of sun-exposed skin that may mimic squamous cell carcinoma. It arises rapidly and resolves

spontaneously within months.

2. Infected hyperkeratosis

3. Leukoplakia

4. Syphilitic chancre

C. **Staging of lip carcinomas.** See Table 7.1 for TX, T0, Tis, N, and M stages, for histopathologic grades, and for stage groupings.

T1 Tumor £2 cm

T2 Tumor >2 cm but £4 cm

T3 Tumor >4 cm

T4 Tumor invades adjacent structures (e.g., through cortical bone, inferior alveolar nerve, floor of mouth, skin of face)

D. **Treatment of primary lesions.** Because lip carcinoma is often detected early, it is equally curable by surgery, various irradiation techniques, or chemosurgery.

Therefore, the choice of therapy is determined by the condition of tissues, expected cosmetic results, patient’s age, comfort, convenience, and treatment costs.

Treatment modalities are as follows:

1. **Leukoplakia, severe dysplasia, and small carcinoma *in situ*:** vermilionectomy (lip shave)

2. **T1 and Tis (lesions £ 1 cm):** RT or surgical excision

3. **T1 to T4 (lesions >1 cm):** RT is cosmetically preferred, but excision and reconstruction give similar curative results.

4. **Commissure involvement:** RT is cosmetically and functionally preferable if the commissure is involved.

E. **Treatment of regional nodes**

1. **Clinically negative neck.** Observe or irradiate the first echelon of nodes in large or poorly differentiated primary tumors.

2. **Clinically positive neck.** ND with or without contralateral suprahyoid dissection. Postoperative RT is given based on the findings of ND.

F. **Recurrences.** Most treatment failures occur locally.

1. **Surgical failures** are best treated with RT or additional surgery and RT failures with surgery.

2. **Delayed neck dissections** for subsequently appearing cervical metastases do not appear to affect survival.

G. **Local tumor control rate** exceeds 90% for cancers up to 3 cm and is 75% to 80% for larger cancers.

**II. Oral cavity** (sites: floor of mouth, oral tongue, buccal mucosa, gingiva, alveolar ridges, retromolar trigone, hard palate)

A. **Natural history**

1. **Risk factors** include smoking, excessive consumption of alcohol, poor oral hygiene, prolonged focal denture irritation, betel nut chewing, and syphilis

2. **Presentation.** Most oral cavity cancers first appear as a painless ulcer or mass. If symptomatic, patients complain of local pain; difficulty chewing,

swallowing, eating, or speaking; or that dentures do not fit well.

3. **Lymphatic drainage** involves the upper jugular and submandibular nodes. The likelihood of bilateral adenopathy increases as the lesion approaches the

midline. Lymphadenopathy occurs in about 40% of patients at presentation.

B. **Diagnosis.** Obtain x-ray films of the chest and mandible to detect distant metastases and bone erosion or mental nerve foramen enlargement (an indication of

perineural infiltration); panoramic views of the mandible are preferred.

C. **Staging of oral cavity carcinomas.** See Table 7.1 for TX, T0, Tis, N, and M stages, for histopathologic grades, and for stage groupings.

T1 Tumor £2 cm

T2 Tumor >2 cm but £4 cm

T3 Tumor >4 cm

T4 Tumor invades adjacent structures (e.g., through cortical bone, into deep muscle of tongue, maxillary sinus, skin). Superficial

erosion alone of bone or tooth socket by a gingival primary is not sufficient to classify the lesion as T4.

D. **Treatment of primary lesions**

1. **Oral tongue and floor of mouth carcinoma**

a. **Very small lesions (¾1 cm).** Surgical excision, interstitial RT, or external RT through the peroral cone; the neck is not treated electively.

b. **T1 or T2 lesions.** Surgery, if location allows a wide excision without functional deformity; or, combination external and interstitial RT. The choice between

surgery and RT is made according to the patient’s health and psychological, social, and occupational factors.

c. **Extensive lesions.** RT alone or combination RT and surgical resection. Surgery (alone or with RT) is preferred for mandibular invasion or attachment,

verrucous carcinoma, or unreliable patients.

d. **Local tumor control rate** exceeds 90% for T1 and T2 tumors.

2. **Gingiva and hard palate carcinoma.** Most tumors of the upper gingiva and hard palate are salivary gland adenocarcinomas. Gingival and palatal lesions

involve bone early on. Surgery is usually preferred.

a. **Early lesions.** Surgery

b. **Advanced lesions.** Surgery and RT

c. **Local tumor control.** Small tumors are usually locally controlled. The control rate of T4 lesions is about 40%.

3. **Buccal mucosa carcinoma**

a. **T1 lesions.** Surgery or RT

b. **T2 or T3 lesions.** RT

c. **T4 lesions.** Surgery and RT, if feasible

d. **Local tumor control rate** exceeds 90% for T1 lesions but drops to 50% to 60% for extensive tumors.

4. **Retromolar trigone carcinoma**

a. **Early lesion.** Surgery

b. **Advanced lesion** (usually involves bone). Surgery, often with RT

c. **Local tumor control.** Most T1 and T2 tumors are controlled.

E. **Treatment of regional nodes**

1. **Clinically negative neck**

a. **T1 primary.** Observe if the patient is reliable and the lesion is low grade.

b. **T2 to T4 primary, or a high-grade lesion**

1. If primary lesion is treated surgically, perform elective ND.

2. If primary lesion is treated with RT, treat nodes with RT.

3. If primary lesion is treated with both modalities, the cervical nodes can be treated with either modality.

2. **Clinically positive neck nodes**

a. If the primary lesion is treated surgically, do ND.

b. If the primary lesion is treated with RT, irradiate the neck and do ND for residual enlarged nodes or nodes originally larger than 3 cm.

c. If the cervical lymphadenopathy is fixed, begin treatment with RT. If the nodes become mobile during RT, do a neck dissection after 5000 cGy. If the

nodes remain immobile, complete the full course of RT.

3. **Indications for neck irradiation after ND**

a. Multiple tumor-containing nodes, or

b. Node greater than 3 cm or tumor extends outside capsule, or

c. High-grade malignancy

**III. Oropharynx** (sites: base of tongue, anterior and posterior tonsillar pillars, glossotonsillar sulci, lateral and posterior pharyngeal walls; extends from the plane of

the inferior surface of the soft palate to the plane of the superior surface of the hyoid [or floor of the vallecula])

A. **Natural history**

1. **Presentation**

a. Cancers arising in the pharyngeal tongue may be clinically silent until extensive. The lesion may be entirely submucosal and recognizable only by

induration.

b. Tonsillar and pharyngeal tongue tumors frequently are initially recognized by nodal metastases.

c. Symptoms include odynophagia (referred), local pain, otalgia, dysphagia, and trismus (an indication of deep infiltration of muscle by tumor).

2. **Lymphatic drainage.** Lesions of the pharyngeal tongue and tonsillar fossa metastasize to the upper jugular nodes. The incidence of nodal metastases at the

time cancer is detected varies with the primary site.

B. **Diagnosis.** These lesions can be visualized and are palpable. A CT scan or MRI of the neck is helpful to detect masses in the tongue and vallecula and to

visualize a pharyngeal wall mass, abnormal thickening, or enlarged lymph nodes.

C. **Staging of oropharyngeal carcinomas.** See Table 7.1 for TX, T0, Tis, N, and M stages, for histopathologic grades, and for stage groupings.

T1 Tumor £2 cm

T2 Tumor >2 cm but £4 cm

T3 Tumor >4 cm

T4 Tumor invades adjacent structures (e.g., pterygoid muscles, mandible, hard palate, deep muscle of tongue, larynx)

D. **Treatment of primary lesions**

1. **Soft palate carcinoma.** Forty to 50% of patients have cervical nodal metastases at the time of diagnosis.

a. **Small lesions.** Usually RT

b. **Large lesions.** RT alone is preferred because extensive surgical resection can result in compromise of ability to speak and swallow.

c. **Local tumor control rate** is 80% to 90% for T1 to T2 tumors and 75% to 80% for T3 to T4 tumors.

2. **Tonsillar region carcinoma.** Nodal metastases are detected in 70% of patients at the time of diagnosis.

a. **Early lesions.** Surgery (composite resection with ND) or RT

b. **Advanced lesions.** Surgery and RT

c. **Local tumor control rate** exceeds 85% for T1 and T2 cancers, 50% to 75% for T3 cancers, and 25% for T4 cancers.

d. **Approximate 5-year survival.** Invasion of the pharyngeal tongue or trismus markedly decreases likelihood of cure.

Stage Five-year survival (%) NodesFive-year survival (%)

T1,T2 70 All N0 80

T3,T4 20 All N1 45

All N3 10

3. **Anterior tonsillar pillar carcinoma** (may be included in oral cavity carcinoma) is better differentiated histologically and has less of a propensity for early

metastasis than other oropharyngeal sites.

a. **Early lesions.** Surgery or RT

b. **Advanced lesions,** particularly if deeply infiltrative or involving the base of tongue or bone, are treated with surgery or combined surgery and RT

c. **Local tumor control rate** exceeds 85% for T1 to T2 cancers

4. **Pharyngeal tongue carcinoma.** Lymphadenopathy is detected in 80% of patients at presentation and is bilateral in nearly 50%.

a. **Early lesions** (uncommon). Surgery or RT

b. **Advanced lesions** (across the midline). RT alone because the alternative of total glossectomy in unacceptable to most patients

c. **Local tumor control rate** is about 75% for T1 cancers, 60% for T3 cancers, and 15% for T4 cancers.

5. **Pharyngeal wall carcinoma.** Most lesions that extend well onto the posterior wall are not curable by surgery.

a. **Early lesions.** RT

b. **Advanced lesions.** Combined RT and surgery

c. **Local tumor control rate** ranges from 30% to 50% for T2 to T3 cancers; T1 cancers are rare.

E. **Treatment of regional nodes.** Because most of the cancers of this region require RT as primary or adjuvant therapy, RT rather than surgery is commonly used

in the treatment of cervical node metastases.

1. **N0 and N1.** If surgery is used to treat the primary site, then ND is done; if RT is used to treat the primary, then RT is used for the neck.

2. **N2A.** Similar to N0 and N1, but ND is often required for residual disease.

3. **N2B.** RT, followed by modified ND

4. **N3A.** RT and ND, if possible

5. **N3B.** Treat each side individually

6. **Indications for RT after ND**

a. Multiple tumor-containing nodes, or

b. Node greater than 3 cm or tumor perforating the capsule, or

c. High-grade pathology

F. **Follow-up of oropharyngeal carcinoma.** Careful and frequent follow-up visits are essential for the following reasons:

1. Surgical salvage of RT failures can be successful.

2. Incidence of subsequent second malignancies is 5% to 10%.

**IV. Nasopharynx** (sites: from the posterior choana to the level of the free border of the soft palate)

A. **Natural history.** Nasopharyngeal carcinoma is the second most common malignancy in southern China and is high in incidence among some native American

populations. Nonkeratinizing nasopharyngeal carcinomas are uniformly associated with Epstein-Barr virus; patients usually have increased levels of

immunoglobulin A antibody to the viral capsid antigen and early antigen.

1. **Pathology.** About 85% are squamous cell carcinomas or its lymphoepithelial variants (Schmincke’s or Regaud’s tumor), 10% lymphomas, and 5% other

histologic types (undifferentiated carcinoma, melanoma, plasmacytoma, angiofibroma of childhood).

2. **Presentation.** Nasopharyngeal tumors spread directly through the pharyngeal space to the structures in or near the cavernous sinus and the foramina of the

middle cranial fossa (including the gasserian ganglion and its branches). Destruction in the parasphenoid bones and nerve compression can result in severe

pain and nerve palsy. Cranial nerve VI, which passes around the brain stem and along the cavernous sinus, is usually the first nerve to be affected, resulting

in a lateral rectus muscle paresis.

a. **Common symptoms and signs.** Enlarged neck nodes, headache, epistaxis, nasal obstruction (often unilateral), unilateral decreased hearing secondary

to eustachian tube obstruction, sore throat (inferior extension), and pain on neck extension.

b. **Retrosphenoidal syndrome** usually starts with the sixth cranial nerve and subsequently involves cranial nerves II through VI. Symptoms include

unilateral ophthalmoplegia, pain, ptosis, trigeminal neuralgia, and unilateral weakness of muscles of mastication.

c. **Syndrome of the retroparotid space** results from nodal compression of cranial nerves IX through XII and of sympathetic nerves at the base of the skull.

Symptoms include difficulties with swallowing, taste, salivation, and respiration; weakness of the trapezius, sternocleidomastoid muscles, homolateral

tongue, and soft palate; and Horner’s syndrome.

3. **Lymphatic drainage.** Because the tumor is relatively anaplastic and the nasopharynx has a rich lymphatic network, these carcinomas may spread to lymph

nodes when the primary tumor is small.

a. First involved are the retropharyngeal and lateral pharyngeal nodes, followed by the upper cervical nodes. Involvement of the high, posterior cervical

nodes is characteristic.

b. Lymphadenopathy is present in 80% of patients at presentation; 50% is bilateral.

B. **Diagnosis.** Carefully examine regional lymph nodes. Rhinoscopy, indirect nasopharyngoscopy, and triple endoscopy are performed. A CT scan or MRI of the

base of the skull, pharynx, and neck is essential.

C. **Staging of nasopharyngeal carcinomas.** See Table 7.1 for TX, T0, Tis, N, and M stages and for histopathologic grades.

1. **Primary tumor stage**

T1 Tumor confined to nasopharynx

T2 Tumor extends to soft tissues of oropharynx or nasal fossa

T2a Without parapharyngeal extension

T2b With parapharyngeal extension

T3 Tumor invades bony structures or paranasal sinuses

T4 Tumor with intracranial extension or involvement of cranial nerves, infratemporal fossa, hypopharynx, or orbit

2. **Stage groupings**

I T1 N0 M0

IIA T2a N0 M0

IIB T1,2a N1 M0; T2b N0, N1 M0

III T1,2 N2 M0; T3 N0,1,2 M0

IVAT4 N0,1,2 M0

IVBAny T N3 M0

IVCAny T Any N M1

D. **Treatment of primary tumors**

1. **RT** alone (bilateral) is used for both the primary tumor and the regional nodal metastases.

2. **Surgery** is not feasible because of the inadequacy of the surgical margins at the base of the skull and the frequent involvement of the retropharyngeal and

cervical nodes bilaterally.

E. **Treatment of regional nodes.** RT is the treatment of choice. Neck dissection is reserved for adenopathy that persists or regrows after irradiation in patients with

apparently controlled primary tumors.

F. **Gross reappearance of the cancer** at the primary site can be retreated with additional external-beam RT or the placement of a removable radioactive source in

the nasopharynx. Such retreatment is only moderately successful and may often produce long-term side effects.

G. **Local tumor control rate** exceeds 90% for T1 to T3 primary cancers. Control of cervical adenopathy by RT is equally successful.

H. **Chemotherapy for nasopharyngeal carcinoma.** See Principles, section VI.D.3.

**V. Hypopharynx** (sites: pyriform fossa, lateral and posterior hypopharyngeal walls, postcricoid region; the hypopharynx extends from the plane of the superior

border of the hyoid bone, or floor of the vallecula, to the plane of the lower border of the cricoid cartilage)

A. **Natural history**

1. **Presentation.** Odynophagia, dysphagia, and referred otalgia are common presenting symptoms. Late clinical findings include cough, aspiration pneumonia,

hoarseness, and neck masses.

2. **Direct extension.** These tumors behave aggressively with early direct extension; they are usually detected in an advanced stage.

3. **Lymphatic drainage** involves the retropharyngeal and midjugular nodes. Lymphadenopathy is present in 80% of patients at presentation.

B. **Diagnosis.** Indirect laryngoscopy, direct laryngoscopy, and CT scan or MRI of the neck are performed.

C. **Staging of hypopharyngeal carcinomas.** See Table 7.1 for TX, T0, Tis, N, and M stages, for histopathologic grades, and for stage groupings.

T1Tumor limited to one subsite of hypopharynx and £2 cm

T2Tumor involves more than one subsite of hypopharynx or an adjacent site, or measures >2 cm but £4 cm without

fixation of hemilarynx

T3Tumor is >4 cm or with fixation of hemilarynx

T4Tumor invades adjacent structures (e.g., thyroid or cricoid cartilage, carotid artery, soft tissues of neck, prevertebral

fascia or muscles, thyroid or esophagus)

D. **Treatment of primary lesions**

1. **Pyriform sinus tumors**

a. **Small, exophytic lesions** (particularly in upper pyriform sinus). RT

b. **Other early T1 or T2 lesions.** Total or partial laryngectomy, and partial or total pharyngectomy and RT combined

c. **T3 to T4 lesions.** Laryngopharyngectomy and RT. If inoperable because of involvement of the posterior pharyngeal wall or massive neck disease, treat

with RT alone.

2. **Posterior pharyngeal wall tumors.** RT alone

3. **Persistent or recurrent disease.** Salvage is poor.

E. **Treatment of regional nodes**

1. **Clinically negative neck.** Prophylactic RT or ND

2. **Clinically positive neck.** Combined ND and RT

F. **Tumor control.** Many T1 and T2 tumors can be locally controlled. The likelihood of control of cervical node metastases varies with the size and number of

nodes.

**VI. Larynx**

A. **Natural history.** Although cancer of the larynx represents only 2% of the total risk for cancer in humans, it is the most frequent head and neck cancer except for

skin cancer. There is a direct etiologic relationship to cigarette smoking. Alcohol ingestion probably is less important as an etiologic agent than for other head

and neck cancers. The clinical presentation depends on the primary site and extent of the cancer. Tumors arising from the true vocal folds, which are usually

diagnosed when smaller, are less likely to infiltrate surrounding tissues or to metastasize to regional lymph nodes than are tumors arising subglottically or

supraglottically.

1. **Presentation.** Persistent hoarseness is the usual presenting symptom for patients with cancers arising on the true vocal folds (glottis). At other primary sites,

sore throat with dysphagia or nonpainful, regional adenopathy may develop.

2. **Lymphatic drainage**

a. **Glottic (true vocal fold) carcinomas.** The true vocal folds are devoid of lymphatics. Therefore, cervical node metastases develop only when the tumor

has extended to adjacent structures.

b. **Supraglottic carcinomas.** This group of tumors are drained by a rich lymphatic network. About 40% to 50% of these patients develop regional

adenopathy involving the upper (subdigastric) or middle internal jugular nodes (levels 2 and 3).

c. **Subglottic carcinomas.** Lymphatics, which are sparse, extend through the cricothyroid membrane to the pretracheal (Delphian) nodes or the lower

internal jugular nodes.

3. **Curability** is related to the site of origin, ranging from most curable to least curable as follows: true vocal fold cancers; tumors arising from the false folds,

epiglottis, ventricles, aryepiglottic folds; tumors arising in the subglottis (infrequently controlled).

B. **Diagnosis**

1. **Studies.** Indirect laryngoscopy, performed during deep breathing and phonation, can determine the mobility of the vocal folds and arytenoids. Direct

laryngoscopy facilitates biopsy and may provide better visualization of the ventricles and subglottic larynx. CT and MRI are useful to determine tumor extent,

particularly when the thyroid cartilage and pre-epiglottic space are involved.

2. **Differential diagnosis**

a. Hyperkeratosis

b. Laryngocele

c. Polyps (which appear as glistening, pedunculated masses)

d. Papillomas (which are white, grapelike growths)

C. **Staging of laryngeal carcinomas.** See Table 7.1 for TX, T0, Tis, N, and M stages, for histopathologic grades, and for stage groupings.

1. **T1 and T2 for glottic carcinomas**

T1 Tumor limited to the vocal folds with normal mobility (may involve anterior or posterior commissures)

T1a Tumor limited to one vocal fold

T1b Tumor involves both vocal folds

T2 Tumor extends to supraglottis or subglottis, or with impaired vocal fold mobility

2. **T1 and T2 for supraglottic carcinomas**

T1Tumor limited to one subsite of supraglottis with normal fold mobility

T2Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis

without fixation of the larynx (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus)

3. **T1 and T2 for subglottic carcinomas**

T1Tumor limited to the subglottis

T2Tumor extends to vocal folds with normal or impaired mobility

4. **T3 and T4 for glottic, supraglottic, and subglottic carcinomas**

T3Tumor limited to the larynx with vocal fold fixation (for supraglottic tumors: and/or invades postcricoid area or

preepiglottic tissues)

T4Tumor invades through the thyroid cartilage or to other tissues beyond the larynx (e.g., soft tissues of neck, thyroid,

trachea, pharynx, esophagus)

D. **Treatment principles for laryngeal carcinomas**

1. **Treatment of primary site**

a. **The overriding requirement** for treatment is preservation of the patient’s life, voice, and swallowing reflex. These considerations have led to the

increasing use of RT alone or more limited surgical procedures combined with RT.

b. **Salvage (total) laryngectomy** is usually required for patients in whom more conservative treatments fail.

c. **Deeply infiltrative tumors** are more difficult to evaluate because of accompanying distortion and edema. Laryngectomy is therefore favored in many of

these patients.

d. **Sequential chemotherapy and definitive RT** is effective for achieving laryngeal preservation in a high percentage of patients with advanced cancer in

both glottic and supraglottic lesions without compromising overall survival. It is not known, however, whether administering higher doses of RT alone

would achieve the same result.

e. **Sequelae of therapy**

1. Total laryngectomy necessitates tracheostomy and loss of normal voice. About 50% to 70% of patients develop satisfactory esophageal speech.

2. RT of the larynx is rarely associated with painful chondritis and edema of the laryngeal structures.

2. **Treatment of regional nodes.** Glottic carcinomas are treated without ND, unless cervical nodes are palpable (less than 10%). Supraglottic and subglottic

carcinomas usually require some form of cervical node therapy. Clinically positive nodes are generally managed with ND.

E. **Glottic carcinoma** (sites: true vocal folds, including the anterior and posterior commissures)

1. **Treatment of primary tumor**

a. **Tis.** RT or “cord-stripping” for focal areas of disease

b. **T1 to T2.** RT is preferable to surgery (either cordectomy or vertical laryngectomy). Involvement of the arytenoid or more than one third of the opposing

fold is a contraindication to hemilaryngectomy. Postoperative RT is given after hemilaryngectomy if the tumor is close to the surgical margins.

c. **T3.** Lesions that fix the true vocal folds can be divided into two groups: relatively smaller lesions, which respond to irradiation (local control is 50% to 60%

with possible surgical salvage) and extensive tumors (bilateral, compromised airway) that require surgery and usually postoperative RT.

d. **T4.** Total laryngectomy and RT

2. **Treatment of persistent or recurrent disease**

a. Surgery for RT failure. The surgical salvage rate for early glottic cancer is about 85%.

b. RT or total laryngectomy for failure of partial laryngectomy or cordectomy

c. RT for failure of total laryngectomy. Salvage rates are poor. (RT usually should be used as a postoperative adjuvant.)

3. **Tumor control**

a. **T1.** Greater than 80% with RT and approaches 100% with surgical salvage

b. **T2.** From 60% to 70% with RT and approaches 90% to 100% with surgical salvage

c. **T3.** From 60% to 65% with RT and 75% with surgery plus RT. Ultimate control of 80% to 85% with surgical salvage. From 60% to 65% voice preservation

with primary RT

d. **T4.** From 40% to 45% with laryngectomy. Up to 50% with RT and surgical salvage.

F. **Supraglottic carcinoma** (sites: epiglottis, aryepiglottic folds, vallecula, arytenoid, false folds)

1. **Treatment of primary tumor**

a. **T1.** RT or supraglottic resection

b. **T2 to T3.** RT frequently controls exophytic cancers. Surgery, which is reserved for RT failures, is favored for infiltrative disease or lesions involving the

base of the epiglottis or false folds. Surgical procedures include supraglottic or total laryngectomy.

c. **T4.** Surgery and RT

2. **Indications for postoperative RT**

a. Bulky or infiltrating lesions, or

b. Close or positive operative margins, or

c. Multiple positive lymph nodes, or

d. Deep connective tissue, thyroid cartilage, or perineural involvement, or

e. Poorly differentiated histology

3. **RT treatment failures** usually require total laryngectomy. The surgical salvage rate is 80% for RT failures.

4. **Local tumor control rates** are 90% to 95% for T1 and T2 lesions, about 80% for T3 lesions, and 40% to 50% for T4 lesions.

G. **Subglottic carcinoma** (sites: extends from 10 mm below the free margin of the vocal fold [inferior limit of the vocalis muscle] to the lower margin of the cricoid

cartilage)

1. **Treatment of primary tumor**

a. **Early lesions.** RT or total laryngectomy

b. **Advanced lesions.** Total laryngectomy and RT

c. **Approximate 5-year survival rate** without evidence of disease is less than 25%.

**VII. Nasal cavity and paranasal sinuses**

A. **Natural history.** Although cancers often involve both the nasal cavity and paranasal sinuses at the time of diagnosis, it is important to separate those cancers

limited to the nasal fossa from those arising in the sinuses. Most tumors of the nasal cavity and paranasal sinuses are squamous cell carcinomas. Some

adenocarcinomas, sarcomas, plasmacytomas, lymphomas, minor salivary gland tumors, and olfactory neuroblastomas also occur.

1. **Presentation.** Symptoms and signs often mimic inflammatory sinusitis and include local pain, tenderness, toothache, bloody nasal discharge, loosening of

teeth, and interference with fit of dentures. Other symptoms are visual disturbances, proptosis, nasal obstruction, trismus, and a bulging cheek mass that can

ulcerate through the skin and palate.

2. **Lymphatic drainage** involves the retropharyngeal, submaxillary, and upper anterior and posterior cervical nodes. At the time of presentation,

lymphadenopathy is present in 15% of patients who have early disease and in more patients with advanced disease.

B. **Diagnosis**

1. **Studies.** Rhinoscopy, endoscopy, sinoscopy, and CT scan or MRI of the involved structures are performed. Bone destruction on radiographs is the hallmark

of malignancy, although it can also occur in certain benign conditions (e.g., papilloma, osteomyelitis).

2. **Differential diagnosis**

a. Inverting papilloma of the nasal cavity

b. Destructive mucocele of the sinus

c. Allergic fungal sinusitis

3. **Staging.** The reader is referred to a current staging manual for staging of these tumors.

C. **Treatment of primary lesions**

1. **Paranasal sinuses**

a. **Surgery** is usually indicated because of the frequency of osseous involvement. The desire to obtain a wide margin beyond the tumor is tempered by a

reluctance to produce serious sequelae. If disease extends through the periorbita, orbital exenteration is performed. Reconstructive and cosmetic surgery

using prosthetic devices is often necessary.

b. **RT** is nearly always necessary because the resection margins are often minimal or positive and the neoplasm is frequently of high grade.

2. **Nasal cavity tumors**

a. **Early lesions.** RT is preferable if surgery will produce a deformity. Surgery is favored if bone is destroyed or if the lesion is a sarcoma.

b. **Advanced lesions.** A combination of surgical resection and RT is most commonly used. RT alone is used for lymphomas, plasmacytomas,

rhabdomyosarcomas, lethal midline granuloma, malignant histiocytosis, and olfactory neuroblastoma (see Chapter 19, section VIII). Adjuvant

chemotherapy is used for rhabdomyosarcoma, Ewing’s sarcoma, osteogenic sarcoma, and neuroblastoma.

c. **Local tumor control rate** approaches 100% for stage I tumors.

3. **Nasal vestibule carcinomas**

a. **Early lesions.** RT is preferable if surgery will produce a deformity.

b. **Advanced lesions.** RT alone

c. **Recurrent or persistent disease after RT.** Surgery, cryosurgery, chemosurgery, and laser surgery have all been advocated.

d. **Local tumor control rate** exceeds 90% for small tumors.

4. **Ethmoid sinus carcinoma.** Surgery and RT. Approximate 5-year survival rate is 30%.

5. **Frontal and sphenoid sinus carcinomas.** RT alone. Results are dismal.

6. **Maxillary antrum carcinoma.** Fenestration before surgical extirpation provides tissue biopsy, decreases tumor bulk through curettage, and allows for

drainage of necrotic debris during treatment. Treatment is as follows:

a. **Early lesions.** Surgery alone

b. **Advanced lesions.** Surgery with either preoperative or postoperative RT.

c. **Very advanced lesions.** Chemotherapy initially, then surgery and RT

d. **Unresectable disease.** Chemotherapy and high-dose RT

e. **Recurrences.** Surgery, RT, or chemotherapy, alone or in combination, is used. Salvage is very poor.

f. **Approximate 5-year survival** is 60% for patients with T1 or T2 lesions and 30% to 40% overall.

D. **Treatment of regional nodes**

1. **T1,2 N0.** No treatment

2. **T3,4 N0.** Prophylactic upper neck RT

3. **Any T N1,2,3.** If surgery is part of the management of the primary lesion, then ND is done. If RT is being used primarily, partial ND may still be necessary for

initial large or residual tumors.

E. **Sequelae.** Most failures are local. Subsequent cosmetic surgery or prosthetic reconstruction should await healing and a reasonable likelihood of local control.

Delayed homolateral cataract may follow RT.

**VIII. Salivary glands**

A. **Natural history.** The parotid gland accounts for 80% of the salivary gland neoplasms in adults. About 75% of parotid tumors are benign. In contrast, nearly half

of tumors arising in the submaxillary or minor salivary glands are malignant.

1. **Histology of malignant tumors**

a. Mucoepidermoid tumors (high and low grade)

b. Adenoid cystic carcinoma (high and low grade)

c. Undifferentiated carcinoma

d. Malignant mixed tumors (epithelial and mesenchymal components)

e. Adenocarcinoma

f. Squamous cell carcinoma (considered to be high grade)

g. Acinic cell tumors

h. Malignant lymphoma

2. **Presentation.** Most malignant salivary gland tumors appear as a painless swelling. Local pain (particularly along the distribution of an adjacent nerve) and

development of nerve palsy are highly indicative of malignancy.

3. **Tumor spread.** The malignant neoplasms tend to spread by direct extension and infiltration, but high-grade tumors also metastasize distantly or to regional

nodes. Adenoid cystic carcinomas tend to infiltrate along nerve trunks; they may recur months or years after initial therapy (see Chapter 19, section VI).

4. **Lymphatic drainage**

a. **Parotid gland tumors** metastasize to intraparotid, submaxillary, and upper cervical nodes.

b. **Submaxillary gland tumors** metastasize to subdigastric, submaxillary, and upper jugular nodes.

B. **Diagnosis**

1. **Studies.** A CT scan or an MRI should be obtained.

2. **Differential diagnosis.** Most salivary gland swellings are caused by inflammation or ductal obstruction. The intraparotid lymph nodes receive afferent

lymphatic drainage from the skin of the face, scalp, ear, and buccal mucosa. Symptoms and signs to differentiate benign from malignant parotid masses are

shown in Table 7.3.

**Table 7.3** Differential diagnosis of parotid gland masses

C. **Staging of major salivary gland carcinomas.** Regional lymph node (N) and distant metastases (M) classifications are shown in Table 7.1.

1. **Primary tumor stage**

TXPrimary tumor cannot be assessed

T0No evidence of primary tumor

T1Tumor £2 cm without extraparenchymal extension

T2Tumor >2 cm but £4 cm extraparenchymal extension

T3Tumor >4 cm but £6 cm or having extraparenchymal extension without seventh cranial nerve involvement

T4Tumor invades base of skull or seventh nerve or is >6 cm

2. **Stage groupings for major salivary gland carcinomas**

I T1,2,3 N0 M0

II T3 N0 M0

IIIT1,2 N1 M0

IVT4 N0 M0; T3,4 N1 M0; any T N2,3 M0; any T any N M1

D. **Treatment of parotid gland carcinoma.** Wide surgical excision (total parotidectomy) is the standard treatment. However, there is a tendency to use less radical

surgery in combination with postoperative RT to spare the facial nerve (when not involved by the cancer) while decreasing the possibility of local recurrence. For

example, superficial lobectomy may be considered if it is the only lobe involved.

1. **Prophylactic ND** is performed for high-grade parotid tumors, but not for low-grade tumors.

2. **Postparotidectomy sequelae**

a. Facial nerve palsy

b. Auriculotemporal syndrome of gustatory sweating

3. **Use of radiotherapy**

a. **Postoperative RT** is generally given to the tumor site when:

1. The tumor is high grade, or

2. Resection margins are positive or close, or

3. Tumor is peeled off the facial nerve or there is histologic evidence of perineural involvement, or

4. Tumor invades deeply, or

5. Tumor excision is for recurrence

b. **Curative RT** is attempted only if the patient is unresectable or medically inoperable.

c. **Recurrent benign tumors.** RT is advocated after reexcision (or after the initial treatment if the resection margins are positive).

4. **Chemotherapy** (see section E)

E. **Treatment of submaxillary gland carcinoma**

1. **Surgery.** Wide resection of contents of submaxillary space (including nerves, surrounding muscle, and periosteum) with ND

2. **Postoperative RT** indications are similar to those for the parotid gland.

3. **Chemotherapy** for salivary gland cancers has not been extensively investigated. Doxorubicin, fluorouracil, and methotrexate used alone or in combination

occasionally result in substantial tumor response.

F. **Results of treatment**

1. **Malignant salivary gland tumors**

a. **Local control rate.** Overall, 75%; high-grade and squamous cell carcinoma, 30%; low-grade carcinoma, 80%

b. **Survival rate.** Recurrences can occur 10 or 15 years after treatment. Therefore, 5-year survival statistics are not reliable.

2. **Benign mixed tumors** have a recurrence rate of 25% after lumpectomy and 2% after lobectomy. One fourth of recurrences are malignant.

**Suggested Reading**

American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* 5th ed. Philadelphia: Lippincott-Raven; 1997.

Brizel DM, et al. Hyperfractionated irradiation with or without concurrent chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 1998;338:1798.

Chua DTT, et al. Preliminary report of the Asian-Oceanian Clinical Oncology Association randomized trial comparing cisplatin and epirubicin followed by radiotherapy versus radiotherapy alone in the

treatment of patients with locoregionally advanced nasopharyngeal carcinoma. *Cancer* 1998;83:2270.

Clark JR, et al. Induction chemotherapy with cisplatin, fluorouracil, and high-dose leucovorin for squamous cell carcinoma of the head and neck: long term results. *J Clin Oncol* 1997;15:3100.

Harari PM. Why has induction chemotherapy for advanced head and neck cancer become a United States community standard of practice? *J Clin Oncol* 1997;15:2050.

Harrison LB, Sessions RB, Wong WK, eds. *Head and Neck Cancer: A Multidisciplinary Approach.* Philadelphia: Lippincott-Raven; 1999.

Laccourreye O, et al. Cisplatin-fluorouracil exclusive chemotherapy for T1-T3 N0 glottic squamous cell carcinoma complete clinical responders: five-year results. *J Clin Oncol* 1996;14:2331.

Vokes EE, ed. Head and neck cancer. *Semin Oncol* 1994;21:279 (entire issue).

Wendt TG, et al. Simultaneous radiochemotherapy versus radiotherapy alone in advanced head and neck cancer: a randomized multicenter study. *J Clin Oncol* 1998; 16:1318.

Chapter 8 Lung Cancer

Manual of Clinical Oncology