Chapter 62: Malignant Neoplasms

Michael J. Kaplan, Michael E. Johns

Numerous factors conspire to challenge the otolaryngologist-head and neck surgeon approaching salivary gland tumors. The salivary glands are the site of a large variety of histopathologic types of benign and malignant tumors that have variable biologic courses. Some of the malignant tumors are often difficult to distinguish from one another on routine hematoxylin-eosin staining. Some recurrent histologically benign tumors appear multicentric and are then so difficult to cure that irradiation is often considered. Some malignant tumors on the other hand are so slow in their growth that a 20-year survival with active disease is possible. The relative rarity of salivary gland tumors makes epidemiologic studies difficult. The American Cancer Society (1983) estimates their incidence to be between 1 and 2 per 100.000 of population. This represents about 1% of all head and neck tumours. Approximately 750 related deaths occur annually. The experience of any single surgeon or any single institution is necessarily limited, making a random study impractical and the analysis of data difficult. The limited amount of pretreatment information available and the intricate and complex anatomy of the branches of the facial nerve and the parotid and submandibular glands complicate operative management of salivary gland cancer. These factors - limited availability, intricate anatomy, complex and varied pathology, unpredictable biologic course, and prolonged risk - account for the difficulty in planning a rational therapeutic approach to salivary gland tumors.

Nevertheless, the embryology, anatomy, and collected experiences of many institutions allow the formation of a working model. The salivary glands can be divided into two groups: the major salivary glands, consisting of the parotid, submandibular, and sublingual glands; and the minor salivary glands, consisting of the 600 to 1000 small glands distributed in the upper aerodigestive tract. The parotid gland is by far the most common site of salivary gland tumors. Approximately 85% occur there, and of these, 80% are benign. From 10% to 15% of tumors occur in the submandibular gland, and of these 50% to 60% are benign. The remaining 5% of tumors occur in the sublingual and minor salivary glands; of these estimated 25% to 50% are benign (Tables 62-1 and 62-2).

The fundamental aim in treating parotid tumors is the same as with any cancer: the elimination of disease with a minimum of deformity and the reconstruction of any residual functional and cosmetic defect.

Embryology and Anatomy

Embryology

The physician wishing to treat diseases of the salivary glands finds that an understanding of their anatomy and embryology is essential to success. These topics are covered in detail in earlier chapters, but a brief review as it pertains to tumors is warranted here.

The major and minor salivary glands both arise by the proliferation and ingrowth of a solid anlage of cells from the oral epithelium into the underlying mesenchymal tissues. As these ingrowths develop, they hollow out and arborize to form tubules composed of a double layer of epithelial cells. These cells then differentiate into the ductal system, the acini, and other component cells of the salivary gland unit. This process begins at about the fourth to sixth week of development (Fig. 62-1). The parotid gland develops first but is encapsulated last, allowing lymph nodes to become entrapped within its substance.

Two basic theories of histogenesis of salivary gland malignancies exist: a stem cell model and a multicellular adult model. Both theories strive to account for the vast phenotypic heterogeneity exhibited by these neoplasms. Both theories account for the observation that salivary gland tumors can be categorized into two major types: those originating from the excretory duct, resulting in the epithelial type of malignancy, and those originating more proximally in the salivary gland, resulting in the more glandular type of malignancy. The bicellular stem cell theory suggests that neoplasms arise from either of two undifferentiated basal reserve cells: the excretory duct reserve cell and the intercalated duct reserve cell. The excretory duct reserve cell gives rise to squamous cell carcinomas and mucoepidermoid carcinomas, and the intercalated duct reserve cell gives rise to mixed tumors, adenocarcinomas, adenoid cystic carcinomas, and acinic cell carcinomas. The multicellular theory of histogenesis suggests that neoplasms arise from the adult mature differentiated counterpart of the salivary gland unit that the neoplastic cell mimics. In this theory, oncocytic tumors arise from the striated duct cells with their numerous mitochondria at the basal surface, acinic cell carcinomas originate from the acini, squamous cell carcinomas and mucoepidermoid carcinomas arise from the excretory duct cells, and mixed tumors arise from the intercalated duct cells. Batsakis et al (1988) recently reviewed some of the implications of the stem cell model and myoepithelial differentiation and regulation. Dardick et al (1990) counter with a review of recent evidence in support of the multicellular theory.

Anatomy

The parotid gland

The parotid compartment is the space anterior to the ear containing the parotid gland, the facial nerve, and other nerves in its superficial portion, and blood and lymphatic vessels in its deeper portions (Fig. 62-2). It is important to recognize that this somewhat triangular-shaped compartment is three dimensional, with an anterior diagonal border, a posterior diagnoal border, a superior border, and a deep border. The following is a list of the contents of the parotid compartment.

1. Nerve compartment (superficial portion)

a. Great auricular nerve

b. Auriculotemporal nerve

c. Facial nerve

2. Venous compartment (middle portion)

a. Superficial temporal vein, uniting with

b. Internal maxillary vein, to form

c. Posterior facial vein, which divides into

d. Anterior branch of posterior facial vein and

e. Posterior branch of posterior facial vein, which joins

f. Posterior auricular vein, to form

g. External jugular vein

3. Arterial compartment (deep portion)

a. External carotid artery

b. Internal maxillary artery

c. Superficial temporal artery.

The ramus of the mandible with the masseter muscle superficial to it and the internal pterygoid muscle deep to it form the anterior border of the parotid compartment. Posteriorly, the external auditory bony and cartilaginous canal, the mastoid process, and the base of the styloid process, and more inferiorly, the sternocleidomastoid and posterior belly of the digastric muscle form the posterior border of the compartment. The zygomatic arch represents the superior border. The deep portion of the parotid compartment is in juxtaposition to the lateral pharyngeal space and rests on the styloid muscles, the stylomandibular ligament and membrane, and the carotid sheath. Because of this close relationship to the lateral pharyngeal space, parotid tumors may appear intraorally, pushing the soft palate and tonsillar fossa anteromedially. They have often been described as dumbbell or round tumors. A round tumor passes posterior to the stylomandibular ligament into the lateral pharyngeal space (Fig. 62-3). A dumbbell tumor passes through the narrow space between the mandible and the stylomandibular ligament to enter the lateral pharyngeal space. In passing through this small area, it has a waistlike constriction that creates the dumbbell shape (Fig. 62-4).

The parotid gland is a unilobular gland with numerous processes but with not true superficial and deep lobes. Between the ramus of the mandible and the posterior belly of the digastric muscle is a small constriction of the gland, the isthmus. Near this area, the facial nerve, in dividing into its major branches, separates the gland into two portions: a lateral portion superficial to the facial nerve and a deep portion medial to the facial nerve. Surgically, these are often referred to as the *superficial* and *deep lobes;* however, they are simply the product of surgical dissection and are not true separate anatomic units.

Although not found in every gland, three to five processes of the parotid gland exist, making it extremely difficult to perform a true total parotidectomy. Three superficial processes are the condylar process (near the temporomandibular joint), the meatal process (in the medial area of the incisura of the external auditory canal), and the posterior process (projecting between the mastoid and the sternocleidomastoid muscle). Two deep processes are the glenoid process, which rests on the vaginal process of the tympanic portion of the temporal bone, and the stylomandibular process, which projects anteromedially above the stylomandibular ligament (Fig. 62-5).

The parotid (or Stensen's) duct drains the parotid gland. It is found along the anterior border of the parotid below the zygoma, crosses the masseter and buccal fat pad, and then penetrates the buccinator muscle before opening intraorally opposite the second maxillary molar. Topographically the duct can be found along a line from the external auditory meatus to the base of the columella. The duct is 4 to 7 cm long.

Facial nerve

Following its emergence from the temporal bone through the stylomastoid foramen, the facial nerve is intimately associated with the parotid gland as the nerve divides into its main branches. The stylomastoid foramen is immediately posterior to the base of the styloid process and anterior to the attachment of the digastric muscle to the mastoid tip at the digastric ridge (see Fig. 62-2). In difficult cases, the facial nerve can be found here by removing the mastoid tip (see Fig. 62-1). The facial nerve then travels anteriorly and laterally toward the parotid gland. Before entering the gland, it sends off branches to the posterior auricular muscle, the posterior belly of the digastric muscle, and the stylohyoid muscle. The facial nerve then enters the parotid gland superficial to the external carotid artery and posterior to the facial vein. As it enters the gland, it branches at the pes anserinus into two divisions, the upper temporal facial division and the lower cervical facial division. Its subsequent branching is variable, but at least five major branches, which may interconnect, exit from the gland to innervate the muscles of facial expression. Fig. 62-6 shows common variations (Davis et al, 1956). As is apparent, the course of the facial nerve brances is unpredictable. During surgery it is necessary to locate each branch individually when facial nerve dissection is required. Surgical approaches are discussed later.

Branches of the external carotid artery supply the parotid gland, and the retromandibular vein drains it. Lymphatic draiange is via intraglandular and extraglandular lymph nodes and then to the deep jugular chain (Fig. 62-7).

Submandibular glands

The submandibular glands, containing both serous- and mucus-secreting glandular elements and weighing 10 to 15 g each, lie anteroinferior to the mandible (Figs. 62-8 and 62-9). Each gland contains a superficial portion above the mylohyoid muscle and a deep portion between the mylohyoid and the hyoglossus muscle (Fig. 62-9). Posteriorly, the stylomandibular ligament separates the submandibular gland from the parotid gland. The submandibular gland is crossed by the anterior facial veni and by branches of the facial nerve, usually the margin of the mandibular and cervical branches. The facial artery, which must be ligated twice in excising the gland, makes a groove in the deep portion. The submandibular

duct or Wharton's duct runs between the mylohyoid and hyoglossus muscles and along the genioglossus muscle to enter the oral cavity by the lingual frenulum. It is about 5 cm in length. The hypoglossal nerve lies below the duct, and the lingual nerve lies above it. The lingual and facial arteries supply the gland, and the anterior facial vein drains it. The lymphatic drainage is into the submandibular nodes and from here to the jugular nodes.

Table 62-9. Malignancy and prognosis among patients with parotid carcinoma and facial nerve paralysis

	Neck metastases (%)	**10-year survival rate (%)**
Eneroth (1972)	77	0
Conley (1975)	84	14.&

Sublingual gland and minor salivary glands

The sublingual gland, which weighs only 2 g, is the smallest of the major salivary glands. It is located above the mylohyoid line of the mandible, resting in the sublingual depression on the inner surface of the mandible near the symphysis (Fig. 62-9). Eight to twenty ducts exit from the superior surface of the gland in the sublingual fold of the floor of the mouth. The sublingual branch of the lingual artery and submental branch of the facial artery supply the gland, and the lymphatic drainage goes to the submental and submandibular nodes.

Between 600 and 1000 small, independent, predominantly mucous salivary glands are distributed throughout the upper aerodigestive tract. They are particularly abundant in the palate and the buccal, labial, and lingual areas. The palate is the most common site of minor salivary gland tumors, followed by the upper lip and the cheek.

Factors Influencing Survival

To develop a rational therapeutic plan for tumors of the salivary glands, the surgeon must be fully cognizant of the factors that may affect survival. Each of the following factors should be considered:

Histopathologic diagnosis

Incidence of lymph node metastasis

Pain

Facial nerve paralysis

Skin involvement

Stage

Location

Recurrence

Distant metastasis

Radiation sensitivity

Chemotherapeutic sensitivity.

In recent years, papers have appeared suggesting or refuting an association of DNA aneuploidy with poor prognosis. Similar reports have correlated DNA content with prognosis, to some extent, in well-differentiated thyroid cancer and perhaps squamous cell carcinoma. At this time, such data should be considered preliminary. In addition, retrospective reviews have from time to time cited other epidemiologic factors, such as the patient's sex or a history of radiation or sun exposure.

Because knowledge about the clinical behavior and biologic course of salivary gland tumors of submandibular, sublingual, and minor salivary gland tumors is limited, the following review of data is directed primarily toward parotid malignancies. When appropriate, comments regarding tumors in these other sites are mentioned. In general, submandibular gland malignancies appear to behave in a somewhat more aggressive way than do parotid malignancies. Minor salivary gland tumors, of which adenoid cystic carcinoma is the most common, appear to behave even more aggressively.

Although uncommon, salivary gland tumors in children require particular vigilance in view of the higher frequency of malignancies in children compared to adults. Of epithelial and nonepithelial salivary gland tumors in children, 35% (149 of 428) were found to be malignant (Schuller and McCabe, 1977) (Table 62-3). Hemangiomas were the most common tumors seen. The most common epithelial tumor was the benign mixed tumor, which occurred more often than the most common malignant tumor, mucoepidermoid carcinoma. A more recent review by Shikhani and Johns (1988) of 21 children at Johns Hopkins and 472 cases in the English literature demonstrated that 50% of children's salivary gland tumors were malignant. The most common tumors were the same as in the earlier report cited, with 85% parotid in origin and 12% submandibular.

In past discussions of salivary gland tumors, one of the major obstacles has been the lack of a universally accepted pathologic classification system. It currently appears necessary to place parotid tumors into different categories based on their histologic appearance for two reasons. First, the biologic course does differ for different histologic types. Second, some histopathologic varieties are so rare that the biologic course is uncertain. These should be kept separate until it can be determined from their behavior that they should be placed within a more general histopathologic category. Oversimplification of the complexities of salivary pathology, as found in data that lump together tumors with possibly disparate behavior, make that data incomprehensible or useless.

In a series of articles on salivary gland tumors, Batsakis and co-workers have described a classification system (Batsakis and Regezi, 1978, 1979; Batsakis et al, 1978, 1979b). They classify salivary gland tumors as follows:

I. Benign lesions

A. Mixed tumor (pleomorphic adenoma)

B. Adenolymphoma (Warthin's tumor)

C. Oncocytosis, oncocytoma

D. Monomorphic adenoma

1. Basal cell adenoma

2. Glycogen-rich adenoma and clear cell adenoma

3. Others

E. Sebaceous adenoma

F. Sebaceous lymphadenoma

G. Papillary ductal adenoma

H. Benign lymphoepithelial lesion

II. Malignant lesions

A. Carcinoma ex pleomorphic adenoma (carcinoma arising in or from a mixed tumor)

B. Mucoepidermoid carcinoma

1. Low-grade

2. High-grade

C. Hybrid basal cell adenoma/adenoid cystic carcinoma

D. Adenoid cystic carcinoma

E. Acinic cell carcinoma

F. Adenocarcinoma

1. Mucus-producing adenopapillary and nonpapillary carcinoma

2. Salivary duct carcinoma (ductal carcinoma)

G. Oncocytic carcinoma (malignant oncocytoma)

H. Clear cell carcinoma

I. Epithelial or myoepithelial carcinoma of intercalated ducts

J. Squamous cell carcinoma

K. Undifferentiated carcinoma

L. Miscellaneous (including sebaceous carcinoma, Stensen's duct carcinoma, melanomas, and carcinoma ex lymphoepithelial lesion)

M. Metastatic carcinomas.

More recently Batsakis and others, as will be discussed, have demonstrated that there are high- and low-grade adenocarcinomas. Adenocarcinomas that arise from the intercalated ducts tend to have a low-grade potential. These include terminal duct carcinoma and epimyoepithelial carcinoma (Batsakis and Luna, 1989; Luna et al, 1987). Tumors arising from the larger excretory ducts, such as salivary duct carcinoma, are high grade (Brandwein et al, 1990; Luna et al, 1987).

In discussing the factors influencing survival, this chapter uses Batsakis' classification. To expand the data on parotid tumors beyond the limited experience of any one surgeon or any one institution, the current literature has been reviewed (Table 62-4). Only data from series in which the tumors were classified largely according to the system just outlined have been used. Today it appears that the adenocarcinomas can be discussed in terms of high-grade malignancies (adenocarcinoma NOS, salivary duct carcinoma (rare but very aggressive)), and the group of less common lower-grade adenocarcinomas (including mucus-producing adenopapillary and nonpapillary carcinoma, clear cell carcinoma, epithelial or myoepithelial carcinoma of intercalated ducts, and polymorphous low-grade adenocarcinoma). This breakdown is rarely apparent in retrospective series in the literature. No attempts have been made to draw conclusions regarding the miscellaneous group of rare cancers because of insufficient data. The following outline, which is a slight modification of Batsakis, may make it easier to discuss malignant salivary gland tumors.

II. Malignant lesions

A. Mucoepidermoid carcinoma

1. High-grade

2. Low-grade

B. Adenoid cystic carcinoma

C. Acinic cell carcinoma

D. Adenocarcinoma

1. High-grade

a. Adenocarcinoma

b. Salivary duct carcinoma (ductal carcinoma)

c. Oncocytic malignancy

2. Low-grade

a. Mucus-producing adenopapillary and non-papillary carcinoma

b. Clear cell carcinoma

c. Epithelial or myoepithelial carcinoma of intercalated ducts

d. Terminal duct carcinoma

E. Carcinoma ex pleomorphic adenoma or malignant mixed tumor

F. Squamous cell carcinoma

G. Undifferentiated carcinoma

H. Miscellaneous (including sebaceous carcinoma, melanomas, and carcinoma ex lymphoepithelial lesion)

I. Hybrid basal cell adenoma/adenoid cystic carcinoma

J. Metastatic carcinoma.

Histopathology

The correlation of histopathology with biologic behavior has allowed the more common malignant salivary gland cancers to be divided into two groups: low grade and high grade. The low-grade cancers include acinic cell carcinomas and low-grade mucoepidermoid carcinomas (and the rare low-grade carcinomas included in heading D above). The high-grade malignancies include adenocarcinoma (with the exception of the previously discussed terminal duct carcinoma and epimyoepithelial carcinoma), adenoid cystic carcinoma, carcinoma ex mixed tumor (as well as true malignant mixed tumors), squamous cell carcinoma, and high-grade mucoepidermoid carcinoma.

Table 62-4 shows 5-year survival statistics. Data such as this should be viewed with an appreciation of the obvious limitations of retrospective accrual, and despite accrual over an extended period of time, limited numbers. It should also be pointed out that treatment has clearly evolved, making possible suspect retrospective historical comparisons. Spiro et al

(1989) for instance, point out that comparing 319 patients seen before 1966 with 165 patients seen between 1966 and 1982 resulted in improved 5-year and 10-year survivals in the more recent group (80% versus 65% and 60% versus 50% respectively). This could be from a number of factors including smaller tumors at presentation and the use of postoperative irradiation.

It is important to realize that long after the first 5 years patients continue to die from their tumors. Table 62-5 shows survival rates at 10 years; only the low-grade mucoepidermoid and acinic cell carcinomas have 10-year survival rates comparable to 5-year rates. Although obtaining data of longer survivals is more difficult, a few authors have reported them (Conley, 1975; Eneroth and Hamberger, 1974; Fu et al, 1977; Spiro et al, 1975; Spitz and Batsakis, 1984). These data demonstrate that survival rates continue to decrease after 5 years. In fact, 20-year determinant survival rates in one series demonstrated that the only tumors for which the 5-year survival predicted long-term survival was the low-grade mucoepidermoid and squamous cell carcinomas (Eneroth and Hamberger, 1974). Even though it is a low-grade tumor, acinic cell carcinoma decreased from an 80% (at 5 years) to a 60% determinant survival rate (at 20 years).

Separation of mucoepidermoid carcinomas into low-grade and high-grade histologic patterns has been fruitful in determining biologic course. The relative ratio of epidermoid to mucous cells determines the grade of the tumor: the greater the epidermoid component, the higher the grade and the worse the prognosis.

Most adenocarcinomas are high grade. Some, such as salivary duct carcinoma appear to have particularly unrelenting course, with about a 50% rate each of nodal and distant metastases, and a corresponding poor survival, with a mean survival of about 2.5 years (Brandwein et al, 1990). Rare low-grade adenocarcinomas do exist. Hamper et al (1989) reported 21 cases over 15 years of epithelial-myoepithelial duct carcinoma in which no patients died of their tumor. Lymph node metastases were present however, and one quarter o the patients had local recurrences. Among the first 33 (Corio et al, 1982; Daley et al, 1984; Donath et al, 1972) and two recent additional reported cases, (Arora et al, 1990 and Carillo et al, 1990), 16 had at least one recurrence, and one patient died.

Attempts to correlate histologic features with survival in adenoid cystic carcinoma and acinic cell carcinoma have been less consistent. Eby et al (1972) stated that the solid pattern of adenoid cystic carcinomas was more aggressive than the cribriform pattern. This statement has not been confirmed (Spiro et al, 1974). Perzin et al (1978) divided adenoid cystic carcinoma into three histologic patterns: tubular, cribriform, and solid. They found a recurrence rate of 59% for patients with the tubular pattern, compared with 89% for the cribriform pattern and 100% for the solid pattern. Patients with the tubular pattern had a median survival of 9 years, whereas the median survival for the cribriform pattern was 8 years and for the solid tumor was 5 years. Controversy remains among pathologists regarding this histologic subclassification, and it should be remembered that the presence of all three patterns in a single tumor is not unusual. Currently subclassification of adenoid cystic carcinomas should not be used in establishing management principles. Batsakis et al (1979a) have retrospectively classified acinic cell carcinoma into high-grade and low-grade patterns. Of patients with low-grade tumors, 5% died of their disease; 58% of patients with high-grade tumors died of their disease. Others have attempted to classify acinic cell carcinomas in a

different way (Spiro et al, 1978b). In the group that included carcinomas that were completely encapsulated the 10-year survival rate was 71%. The second group included tumors that were incompletely encapsulated and in which blood vessel or capsule invasion existed. In this group the 10-year survival was 33%. A third group, in which no 10-year survivors existed, included tumors that showed a papillary-cystic pattern.

Retrospective classification of carcinomas as high grade and low grade based on histologic patterns remains controversial for adenoid cystic carcinomas and acinic cell carcinomas. Such classification may correlate with biologic outcome. These factors should be kept in mind, with the use of adjuvant radiation therapy or chemotherapy discussed for these tumors.

Lymph node metastasis

It is well accepted and amply documented that the presence of clinically positive nodes alters prognosis. Positive nodes indicate surgical management of the neck. Indications for a prophylactic neck dissection, however, are controversial. Many surgeons might agree that if a 25% or greater likelihood of occult metastases exists, a neck dissection should be done. Others might argue, however, that there is no evidence demonstrating that waiting for occult metastases to become clinically manifest adversely affects the ultimate outcome of the disease process.

Knowing which of the histologic classes of tumors have a propensity for lymphatic metastasis is important. To attempt to answer this question, the pooled data from many studies, including the University of Virginia, were reviewed (Conley, 1975; Hollander and Cunningham, 1973; Rosenfeld et al, 1966; Spiro et al, 1975). Table 62-6 summarizes the incidence of cervical metastases that developed at any time in the course of the disease. Only the high-grade mucoepidermoid and squamous cell carcinomas have a propensity for neck metastases greater than 25%.

At the time of initial presentation, Spiro et al (1975) found the incidence of cervical metastasis to be 13%. They found the incidence of occult metastases to be 16% or less for all the parotid cancers except squamous cell carcinoma, which has a 40% incidence of occult metastasis (Table 62-7 and Spiro et al, 1975). High-grade mucoepidermoid carcinomas had a 16% occult metastasis rate.

Occult metastasis in acinic cell carcinomas and adenoid cystic carcinomas are rare. In adenoid cystic carcinoma, regional spread occur by contiguous growth and rarely if ever occurs by lymphatic extension (Marsh and Allen, 1979). Because of the rare neck metastases in acinic cell carcinomas, earlier proponents of routine neck dissection in acinic cell carcinomas no longer recommend it (Bjorkland and Eneroth, 1980; Eneroth and Hamberger, 1974)

The size of the tumor is also a critical factor in the incidence of lymph node metastases. Using a staging system that, in a modified form, is currently the American Joint Committee's Staging System, Spiro found that stage I tumors of the parotid had a 1% incidence of neck metastases, stage II tumors a 14% incidence, and stage III tumors a 67% incidence (Spiro et al, 1975). Fu et al (1977) similarly demonstrated that smaller tumors have

a lower incidence of neck metastases. In his system, stage I and II tumors had a 13% incidence, whereas stage III tumors had a 33% incidence. A subsequent system discusses the size or stage of tumor.

In addition to this epidemiologic information, treatment planning can be modified during parotidectomy when the first-echelon lymph nodes are exposed. Metastases would probably occur first in these parotid and subdigastric nodes. The physician should recall that postoperative irradiation, when used as an adjunct to surgery, may in itself control occult metastasis.

Another factor that has a high association with regional node metastasis is facial nerve paralysis. Eneroth (1972) recorded a 77% incidence and Conley and Hamaker (1975) recorded a 66% incidence of lymph node metastasis in patients who had facial nerve paralysis.

In summary, the evidence suggests that in untreated parotid cancers the incidence of cervical metastasis is quite low. More important, occult metastasis is rare in all but squamous cell carcinomas. Large tumors and tumors associated with facial nerve paralysis, however, do have a high association with regional node metastasis, but there is no information to suggest that the clinically negative neck is best treated by a prophylactic neck dissection. The use of postoperative irradiation as an adjunct to surgery may control occult metastasis.

With all this in mind, the following philosophy for treatment of the clinically negative neck has evolved. At the time of parotidectomy, the periparotid, upper jugular, and posterior submandibular triangle nodes are inspected. Suspicious nodes are either biopsied or included in the parotid dissection. Whether further surgery is carried out or postoperative irradiation therapy used is based on the pathology report on the tumor itself and the nodes sampled. With advanced tumors for which postoperative irradiation is used, we include the neck in the radiation port. The presence of histologically positive nodes in the neck is an indication for a neck dissection.

Pain

What is the significance of pain in a patient with a parotid mass? Pain may be due to inflammation in benign settings or either inflammation and neural invasion in malignancies. In reviewing 802 parotid tumors Eneroth (1964) found pain to be an initial symptom in 34 of 665 patients with benign tumors (5.1%) and 9 of 137 patients with malignant tumors (6.5%). Pain is thus not a criterion of malignancy, however, the presence of pain correlates with a poor prognosis. Spiro et al (1975) found a 5-year survival rate in 35% of patients with painful malignant tumors, whereas asymptomatic patients with malignant tumors had an overall 5-year survival rate of 68%. Mustard and Anderson (1964) reported a similarly low 5-year survival rate (33%) in patients with painful malignancies.

Facial nerve paralysis

Although there are a few case reports of facial nerve paralysis secondary to a benign parotid tumor (we have seen three cases ourselves), facial nerve paralysis associated with a parotid mass indicates malignancy. Moreover, it indicates a malignant tumor with a dismal prognosis. Eneroth (1964) found no cases of facial nerve paralysis among 1780 benign parotid

tumors; among 378 parotid tumors he found 46 cases of facial nerve paralysis. In the latter grou the average survival interval from the time of paralysis was 2.7 years, and all patients died within 5 years. In a subsequent multiinstitutional study Eneroth reviewed 1029 malignant parotid tumors, of which 14% had facial nerve paralysis, and the 5-year survival rate was 9% (Eneroth et al, 1977). Other reviews have confirmed this poor prognostic sign. Conley and Hamaker (1975), in reviewing 279 parotid malignancies, found that 9 of 34 patients were free of disease at 5 years, and 4 of 26 patients available for follow-up at 10 years were free of disease. Spiro et al (1975) found a 5-year survival rate of 14% in 43 patients with malignancy and facial nerve paralysis.

The incidence of facial nerve involvement, estimated to be between 12% and 14%, varies with the histology of the tumor (Table 62-8). Adenoid cystic carcinoma and undifferentiated carcinomas have the highest rate of facial nerve paralysis. It can be concluded that facial nerve paralysis occurring in the presence of a parotid mass indicates malignancy, a high likelihood of cervical metastasis, and a poor prognosis (Table 62-9).

Skin involvement

Skin involvement by parotid tumors is fortunately rare today as it indicates advanced malignancy and poor survival. In addition to numerous anecdotal reports, North et al (1990) in reviewing 87 patients demonstrated in a multi-variate analysis that skin involvement was one of five important prognostic factors. Even with wide resection including skin, prognosis is poor because other factors such as large size or facial nerve paralysis are also present. For such tumors especially, the use of adjuvant chemotherapy and high linear energy transfer (LET) radiation such as fast neutrons needs further investigation.

Stage

The size of a parotid mass may be the most important factor in staging parotid malignancy (Table 62-10). The T class is determined by the size of the tumor; T1 is 0 to 2 cm, T2 is 2 to 4 cm, T3 is 4 to 6 cm, and T4 is greater than 6 cm (American Joint Committee, 1988).

Table 62-10. Proposed staging system for major salivary gland cancer

Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor < 2 cm in greatest dimension
T2	Tumor 2-4 cm in greatest dimension
T3	Tumor 4-6 cm in greatest dimension
T4	Tumor > 6 cm in greatest dimension

All categories are subdivided: (a) no local extension
(b) local extension

(Local extension is clinical/macroscopic invasion of skin, soft tissue, bone, or nerve. Microscopic evidence alone is not considered local extension for classification purposes.)

Nx	Regional nodes cannot be assessed
N0	No regional lymph node metastases
N1	Single ipsilateral node < 3 cm in diameter
N2a	Single ipsilateral node 3-6 cm in diameter
N2b	Multiple ipsilateral node, none > 6 cm
N2c	Bilateral or contralateral nodes, none > 6 cm
N3	Metastasis in a lymph node > 6 cm
Mx	Presence of distant metastases cannot be assessed
M0	No distant metastases
M1	Distant metastases

Stage I	T1a	N0	M0
	T2a	N0	M0
Stage II	T1b	N0	M0
	T2b	N0	M0
	T3a	N0	M0
Stage III	T3b	N0	M0
	T4a	N0	M0
	Any T (exc T4b)	N1	M0
Stage IV	T4b	Any N	M0
	Any T	N2, N3	M0
	Any T	Any N	M1.

Spiro et al (1975, 1978a, 1978b) have done much work correlating the stage of disease with prognosis and the incidence of lymph node and distant metastasis. In Spiro's system, T1 lesions are 0 to 3 cm, T2 lesions are 3 to 6 cm, and T3 lesions are greater than 6 cm. Five-year survival rates were 85%, 67%, and 14%, respectively (Spiro et al, 1975). Using the same staging system as Spiro, Fu et al (1977) reported 5-year and 10-year determinant survival rates for stages 1, 2, and 3 parotid cancers: 88% and 83% for stage I, 76% and 76% for stage II, and 49% and 32% for stage III. Clearly size is a major prognostic indicator of survival.

Size or stage also correlates well with the incidence of distant metastasis in the studies of Spiro et al (1974, 1975, 1978a, 1978b). Only 2% o patients with stage I lesions had distant metastases, whereas 39% of patients with stage III lesions had distant metastases.

In the same studies, size also correlated with recurrence rate. In patients with T1 lesions, the recurrence rate was 7%, whereas in those with T3 lesions it was 58%. In their study of mucoepidermoid carcinomas, the authors found that distant metastases as well as lymph node metastasis, recurrence, and overall survival, correlated well with the stage of disease. In 1981, a retrospective multiinstitutional study of 861 patients with salivary gland tumors was published and formed the basis for the 1980 American Joint Committee on Cancer staging for major salivary gland cancers (Levitt et al, 1981). Four clinically recognized parameters were incorporated into the TNM system: size of tumor, local extension, presence of lymph nodes, and presence of metastases. In 1988 the AJCC staging system was slightly modified (see Table 62-10) to clarify, for staging purposes, the meaning of local extension and to simplify and standardize the staging of neck nodes.

As prognosis of salivary gland malignancies appears to depend to a great extent on size (or stage) of the primary tumor - frequently more so than histology - staging should be used. It plays a key role in treatment planning.

Location

Because the deep portion of the parotid gland is less accessible surgically, it is reasonable to ask whether a malignant tumor of the deep portion has a less favorable prognosis than one in the superficial portion. Nigro and Spiro (1977) studied 36 patients with malignancies of the deep portion and found no difference between the survival of those patients and that of all patients with carcinomas of the paroti. The 5-, 10-, and 15-year survival rates for deep lobe tumors were 61%, 52%, and 48% respectively. These figures are similar to earlier stated survival rates in all sites of the parotid. The authors did not, however, that if the mass appears in the oral cavity (via the parapharyngeal space), then a decreased survival rate is seen.

Some tumors occasionally occur bilaterally and multicentrically. After the Warthin's tumor, the acinic cell carcinoma is the most frequent tumor to do so. Chong et al (1974) suggested the need for total parotidectomy with acinic cell carcinomas because of this potential for multicentricity and reported an improved rate of local control with total parotidectomy.

It should be kept in mind that the parotid gland is not anatomically divided into two lobes. Surgery divides the gland into a superficial portion and a deep portion related to the course of the facial nerve. Because of surgical access, it is more difficult to obtain a cuff of normal tissue around a deep lobe tumor. Studies suggest, however, that for parotid malignancies not appearing in the parapharyngeal space, the survival differential is not statistically significant. Obtaining a positive histologic margin may influence the treatment planned for such an individual.

Recurrence

Parotid carcinomas too often recur. Considering all tumors collectively, reports show their recurrence rate to be between 27% and 38% (Hodgkinson and Woods, 1976; Spiro et al, 1975; Woods et al, 1975). Not surprisingly, the incidence of recurrence is higher in high-grade tumors (Table 62-11; Woods et al, 1975). It is particularly significant that in two thirds of the patients in the series by Hodgkinson and Woods (1976) who had a 38% local recurrence rate within 5 years, the facial nerve had been sacrificed. This emphasizes that even with aggressive surgery, recurrences are frequent. Historically, such data lead to the increased use of postoperative irradiation as part of the initial treatment for the more aggressive tumors. That irradiation is effective in reducing recurrences is now well established. However, the results of treatment of recurrences themselves remains poor, spurring interest in chemotherapy and high-linear transfer (high LET) radiation, such as fast neutron irradiation.

Table 62-11. Incidence of local recurrence in patients with malignant parotid carcinomas

Histologic type	No. of recurrence/total
Mucoepidermoid	3/62
Acinic cell	5/34
Adenoid cystic	17/28
Adenocarcinoma	25/54
Arising from mixed tumor	9/15
Squamous cell	14/22
Undifferentiated	7/11.

Once a parotid carcinoma recurs, the duration of average survival is decreased. In reviewing 109 recurrences in 56 patients (an average of 2 recurrences per patient), Kagan et al (1976) reported a 3.7-year median survival from the time of first recurrence. Hanna et al (1976) found a 5-year disease-free rate of only 37% for recurrent malignant parotid tumors. Others have reported a 5-year disease-free rate between 17% and 49% (Hollander and Cunningham, 1973; Rafla-Demetrious, 1970). Rodriguez-Bigas et al (1989) reported on 99 patients with recurrent or metastatic tumors, of whom only 33 could be treated with curative intent. In only 5 of these 33 (15%) was 5-year survival achieved; the histology of these five included three adenoid cystic carcinomas, which often achieve longer survival. When compared to the 5-year survival rate of 67% for nonrecurrent malignant cancers, it is evident that recurrence is an extremely poor prognostic sign. Even if both surgery and irradiation are used initially, aggressive management salvages few patients. Protocols investigating the use of chemotherapy and/or high-LET radiation are needed.

Distant metastases

The presence of distant metastases obviously indicates a poor prognosis. Overall, approximately 21% of parotid tumors demonstrate distant metastases, with almost a third of high-grade tumors eventually failing at distant sites (Table 62-12). Even for low-grade tumors the incidence is 9% to 13%. For adenoid cystic carcinoma the rate is nearly 50% (Fu et al, 1977; Rafla, 1977; Spiro et al, 1975). The two most frequent sites of metastases are lung and bone. The average time of survival from the onset of distant metastases varies with the type of tumor. For malignant mixed tumor Jackson et al (1983) have reported a median survival of 1.76 years. For adenoid cystic carcinomas, survivals in excess of 10 years have been reported (Jackson et al, 1983; Tannock and Sutherland, 1980). Especially for malignant mixed tumors, squamous cell carcinomas, adenocarcinomas, and undifferentiated carcinomas, the aggressive behavior of parotid tumors as manifested by the high incidence of distant metastasis (higher than that seen in squamous cell carcinomas of the upper aerodigestive tract sites) suggests that adjuvant chemotherapy needs to be considered.

Table 62-12. Incidence of distant metastasis among patients with parotid carcinomas

Histologic type		No. of metastasis/total	(%)
Mucoepidermoid		22/232	(9%)
Acinic cell		3/24	(13%)
Adenoid cystic		34/82	(41%)
Arising from mixed tumor		5/25	(20%)
Squamous cell carcinoma		3/21	(14%)
Adenocarcinoma		32/110	(29%)
Undifferentiated		13/35	(37%)
Total	All:	112/529	(21%)
	High-grade:	87/273	(32%).

Epidemiologic and other factors

In addition to the nine major factors already discussed, a number of epidemiologic factors may be related to salivary gland tumors. Prior irradiation appears to be fairly a well-documented risk factor. This was shown by Spitz and Batsakis (1984) in a retrospective review of 498 tumors. Spitz et al (1990) also demonstrated this in a case control investigation of risk factors, as have other researchers in radiation following treatment of benign skin disorders (Maxon et al, 1981; Modan et al, 19074). There is one report linking exposure to diagnostic dental and medical radiation with subsequent salivary gland tumors (Preston-Marin, 1988). The latency of possible radiation-induced tumors appears to be in the range of 10 to 25 years. Other possible epidemiologic factors for which some evidence exists include alcohol exposure (Spitz et al, 1990), hairspray use (Spitz et al, 1990), and coexisting nonmelanotic skin cancer (Spitz and Batsakis, 1984).

It has been noted that women with malignant salivary gland tumors seem to fare better than men (Friedman et al, 1986; Spitz and Batsakis, 1984). Like the observation that those under the age of 35 fare better than those over the age of 60, this observation may reflect the incidence of less aggressive tumors among younger people and possibly among women. Spitz and Batsakis (1984) have suggested that blacks do better than whites; others have not found this to be so (Lawrence and Lawrence, 1981; Spiro et al, 1982).

Radiation sensitivity

Because of the high incidence of local recurrence, soft-tissue invasion, and distant metastasis, there is a need for a treatment adjunct to surgery. For many years it had been reported that parotid tumors were resistant to radiation (Evans, 1966). Evidence, albeit retrospective, has now accumulated that convincingly demonstrates that in many clinical situations radiation therapy reduces recurrences and improves survival.

Historically, several papers appeared in the 1970s suggesting a role for radiation therapy in the treatment of salivary gland cancer. King and Fletcher (1971) reported an 81% local control rate for recurrent or inoperable tumors. However, their follow-up was as short as 2 years (2-20 years). This contrasts with Elkon et al (1978) who found that only 2 of 19

patients with cervical nodes or skull base involvement achieved local control with irradiation. Rossman (1975) demonstrated a dose-response relationship using radiation as a sole modality. Although he reported few patients with limited (2-6 year) followup, all 5 patients receiving high-dose radiation (> 1800 ret) had local control, whereas only 1 of 6 receiving lower doses of radiation achieved local control. Elkon et al (1978) appeared to show that using radiation in microscopically positive margins was helpful; only 1 of 17 such patients had recurrences. Similarly, Fu et al (1977) reported a local failure rate of 14% among 35 patients with microscopic residual disease treated with radiation, compared to 54% of patients treated with surgery alone. When used in a planned combined manner, several early papers suggested a role for radiation. Rossman (1975) reported a 17% recurrence rate for combined treatment compared to 65% for surgery alone. Woods et al (1975) reported Mayo Clinic data showing an 11.5% recurrence rate for combined treatment versus 36% for surgery alone. Similarly, Tapley (1977) showed a 9% recurrence rate among 33 patients treated with combined treatment, compared with a 30% recurrence rate among 54 patients receiving surgery alone. Shidnia et al (1980) demonstrated a 20% improvement in the disease-free rate when combined treatment was used as against surgery alone.

More recent compilations of retrospective data using multivariate analysis continue to support the use of planned postoperative irradiation in many situations. Theriault and Fitpatrick (1986) reported the 10-year relapse-free rate to be 62% among 169 patients treated with postoperative radiation between 1958 and 1980, whereas the 10-year relapse-free rate among the 67 patients who underwent surgery alone was 22%. There was no difference in stage or nodal metastases (the two most critical prognostic factors in their multivariate analysis) between these two groups. North et al (1990) reported that among 50 patients treated with postoperative radiation between 1975 and 1987 there was a 96% local control rate, compared with 74% among the 19 patients receiving surgery alone. Among recurrences, 3 of 14 (21%) were salvaged with surgery and postoperative irradiation; none of the four recurrences receiving surgery alone were salvaged. Armstrong et al (1990), using a matched-pair retrospective analysis, reported the advantages of using postoperative radiation over surgery alone in stage III to IV of disease to be 5-year survival (51% versus 9.5%) and local control (51% versus 17%). For those with nodal disease the 5-year survival was 49% versus 19% and local control was 69% versus 40%.

Recognizing that the data is retrospective and that follow-up periods rarely exceeds 5 years, we nevertheless find the data compelling. It appears abundantly clear that the addition of radiation in many instances is highly likely to reduce the incidence of recurrence and lengthen the disease-free interval. Whether this improves survival is difficult to prove in the absence of prospective trials, but also appears likely (Armstrong et al (1990); North et al (1990)). Surgery and postoperative high-dose radiation (approximately 60 Gy using photons or 4 meV using electrons) is now well established as a frequent principal treatment modality.

Precisely when should radiation be used? Tu et al (1982) reported that radiation was helpful in four situations: high-grade tumors, locally advanced disease, facial nerve involvement, and recurrent tumors. Guillamondegui et al (1975) listed seven indications: high-grade tumors, recurrent tumors, deep-lobe tumors, gross or microscopic residual disease, tumors adjacent to the facial nerve, regional nodal metastases, or invasion of adjacent tissue (muscle, bone, skin, nerves, or extraparotid extension). Our recommendations are in full agreement, but can be simplified by using the current AJCC staging system. All stage II, III,

and IV tumors should be irradiated because these include local extension, increased size, and/or cervical lymph node metastases; obviously M1 disease is a special case. In addition stage I (T1a/T2a, N0, ie, < 4 cm without apparent local extension) should be irradiated if the histology is high grade or if there are microscopically positive margins. Data that separates deep-lobe involvement per se is difficult to obtain, but it is logical to assume that microscopically positive margins would be more likely in deep-lobe tumors. In recurrent disease if full-course irradiation is still possible, we fully agree that it or high-LET radiation should be part of the management.

In the past decade there has been an accumulating data base concerning the role of high-LET radiation in recurrent or inoperable salivary gland malignancy. In an excellent review Koh et al (1989) summarized the rationale behind its use and the data to date. The radiobiologic advantages of high-LET radiation include a lower oxygen enhancement ratio, decreased variation of radiosensitivity across the cell cycle, and decreased ability of tumor cells to repair sublethal damage and potentially lethal damage. Since 1987, 277 patients with inoperable or recurrent salivary gland malignancies in six reports have been treated with fast neutron irradiation (Battermann and Mijnheer, 1986; Catterall and Errington, 1987; Duncan et al, 1987; Griffin et al, 1988a, 1988b; Saroja, 1987). Added to 27 earlier patients, 302 such patients have been treated, with local control reported to be 67%. Although follow-up is necessarily short, this is in marked contrast to the roughly 25% of local control from photon and electron irradiation data among similar patients. Eighteen additional patients have been treated with neon ion radiotherapy, which produces biologic behavior similar to neutrons, with 5-year actuarial survival of 59% and local control of 61% (Linstadt et al, 1991). A prospective randomized trial instituted jointly by the Radiation Therapy Oncology Group (RTOG) and the Medical Research Council (MRC) of Great Britain compared neutrons to photons: the loco-regional control rate at 2 years was 67% versus 17% ($p < .005$), and 2-year survival was 62% versus 25% ($p = 0.10$) (Griffin et al, 1988a). The study was discontinued or ethical reasons because the results were so overwhelming. It should be noted that reirradiation was often possible, with an incidence of severe late complications of about 20%. Given the lack of alternatives in previously irradiated patients who have had prior surgery, high-LET reirradiation, when available, may be the most reasonable option.

Chemotherapy sensitivity

The treatment of parotid malignancies is an evolving process. Only 40 years ago Foote and Frazell (1954) introduced a classification system that enabled comparative study of these malignancies. Collected histopathologic reviews and electron microscopy have enhanced their system of classification. In the last 20 years, the limitations of surgery have been learned, and the increased use of postoperative radiation therapy appears to have improved local control. In the last 10 years, increased familiarity with chemotherapy protocols and recognition of the high frequency of distant metastases among parotid cancers have prompted the initial investigation of the potential value of adjunctive chemotherapy. In 1981 a multiinstitutional study collected 39 cases of histopathologically confirmed salivary gland carcinoma treated with known dosages of chemotherapy and documented responses. A literature survey added 46 additional cases, allowing Suen and Johns (1982) to review 85 cases of chemotherapy-treated salivary gland cancer (Table 62-13). All patients had advanced disease and were treated for palliation. Between 1981 and 1984, Kaplan et al (1986) reviewed 21 additional evaluable cases, and 10 cases from the University of Virginia. There is still too little

information available to draw definite conclusions; nevertheless, certain trends were observed.

In the determination of chemotherapy sensitivity, the different histopathologic types seem to fall into two groups. One group is the adenocarcinoma-like cancers (adenoid cystic carcinoma, adenocarcinoma, carcinoma ex mixed tumor, and acinic cell carcinoma). The other group is the epidermoid-like cancers (squamous cell carcinoma and mucoepidermoid carcinoma). For the adenocarcinoma-like tumors, adriamycin, cisplatinum, and 5-fluorouracil appear to have some effect. The addition of cyclophosphamide to adriamycin is worthy of investigation. For the epidermoid-like carcinomas, methotrexate and cisplatinum appear to have some effect.

Because of insufficient data, it is not known whether combination regimens have an advantage over single drugs. To further understand the chemotherapeutic sensitivity of these infrequent tumors, multiinstitutional cooperative studies are needed to accumulate adequate numbers of cases for study. Appropriate animal models of cell culture models may also prove helpful to assessing drug sensitivity in the future. One sensible suggestion for future studies is to begin with single drugs to assess drug effectiveness before combining the effective drugs in protocols to improve initial response rates.

Management Principles

The most critical prognostic factors in salivary gland malignancies are (1) size of the tumor (0-2 and 2-4 cm versus larger tumors), (2) histology (low-grade versus high-grade tumors), (3) local extension (VII paresis, skin involvement, muscle/bone invasion), (4) lymph node metastases, and (5) distant metastases. These factors, incorporated into the 1988 AJC staging system, allow the formation of a rational treatment plan, one that is well supported by the literature (Table 62-14).

Table 62-14. Principles of treatment for salivary gland carcinoma

Stage/Histology
I, Low-grade (0-4 cm, no local extension)
I, High-grade
II-IV wuith N0M0 (Local extension and/or > 4 cm)
Any T, N1-3 (Positive nodes)

Surgical procedure (Extent of parotidectomy)
Superficial (partial) or total as needed
Superficial (partial) or total as needed
To fit disease: may include mastoid tip, mandible, muscles
To fit disease

Surgical procedure (If submandibular tumor)
Submandibular triangle resection
Wide excision submandibular triangle
Will require at least conservation neck dissection
To resect primary and the nodes will require neck dissection

VII nerve; submandibular: V, XII

Preserve

Preserve

Preserve functioning branches if possible

Preserve functioning branches if possible

Neck dissection

No

No

No

Yes

Postoperative RT (4 meV)

No, unless positvie margins or recurrent

Yes

Yes

Yes

Resected VII branches requiring reconstruction should be reconstructed immediately, usually with a cable graft.

If positive nodes are found at surgery, neck dissection is indicated. In SCC, some would include a neck dissection, others would not because postoperative RT is included.

If available, high-LET radiation should be considered postoperatively in recurrent previously irradiated or in unresectable tumors.&

Column 1 of Table 62-14 shows tumors with the best prognosis, including the smaller low-grade mucoepidermoid carcinomas and smaller acinic cell carcinomas. The rare low-grade adenocarcinomas might also fall in this group if the pathologist was confident of the diagnosis. The stages of these low-grade tumors, which are less than 4 cm in size, without local extension (T1a, T2a) and without nodes or metastases (N0M0) are I or II. Treatment is identical to that for benign tumors - an appropriate parotidectomy sufficient to remove the tumor with a generous cuff of normal parotid around it, preserving the facial nerve. The lymph nodes around the digastric triangle should be evaluated at the time of surgery, and in the unlikely event that they are involved, a neck dissection should be done (see column 3). The tumors in this group (surgically staged I and II of low-grade histology, and with negative surgical margins) are the only ones for which postoperative irradiation is not recommended.

High-grade tumors with otherwise identical features are in column 2. Surgery is identical, but postoperative irradiation will be administered in all cases.

Larger malignant tumors (> 4 cm) or those with local extension (including facial nerve paresis), regardless of specific histology, are addressed in columns 3 and 4. Surgery is likely to consist of a total parotidectomy, and may require partial resection of muscle, mastoid, mandible, or skin. Facial nerve branches involved preoperatively will be included in the resection and grafted primarily. On rare occasions it may be necessary to sacrifice some uninvolved branches. The treatment of the uninvolved neck is controversial, but as

postoperative irradiation (from the skull base to the clavicle) will be included, it appears reasonable to include a neck dissection only if positive nodes are discovered. Preoperative MRI, in addition to assisting in the planning of the extent of resection and planning radiation ports, may find nonpalpable suspicious nodes. If the main branch of the facial nerve is sacrificed, a negative proximal frozen section should be sought before immediate cable grafting is performed. This may require a mastoidectomy.

For primary tumors of the submandibular gland, a similar management plan is included in Table 62-14. Low-grade stage I to II tumors may be resected by a submandibular triangle dissection. This may need to be extended superiorly to include the tongue musculature, the lingual nerve, and the inferior edge of the mandible, or inferiorly to include the hypoglossal nerve and adjacent muscles in larger tumors and high-grade tumors. A complete neck dissection is performed when there are positive nodes or if it facilitates complete excision of the primary tumor. The indications for postoperative irradiation are the same as for parotid primaries.

For recurrent disease, surgical resection should be considered if feasible. Frequently this is not the case. Postoperatively conventional irradiation should be used in previously unirradiated patients. High-LET irradiation should be considered for unresectable disease, grossly positive margins, or where conventional RT is not possible.

In metastatic disease, a decision must first be made about whether it is appropriate to try to achieve local control in the parotid and the neck. One must take into account the amount of morbidity local treatment would lead to as well as the extent of the metastases. Because prolonged survival is possible in some high-grade tumors, it is often appropriate to treat the primary tumor. Isolated pulmonary metastases from adenoid cystic carcinoma have been approached surgically with possible overall survival advantage. As discussed earlier, the results of chemotherapy have been disappointing.

As in all malignancies, treatment must be individualized and tailored to meet the specific needs of the patient. Tumor factors alone do not dictate treatment. Age, medical and nutritional status, and underlying sociologic and emotional factors may require a surgeon to modify the treatment routine to meet the specific requirements of an individual patient.

Surgery

As emphasized in the discussion of management principles, surgery remains the mainstay of treatment for resectable salivary gland malignancies. In the discussion of surgical techniques that follows, our primary emphasis is directed toward the submandibular and parotid glands, and in particular toward the various approaches to the parotid and parapharyngeal spaces. The technical aspects of treating minor salivary gland tumors are not addressed because those tumors must be treated in relation to the anatomic region in which they are found. References to chapters on the oral cavity, oral pharynx, larynx, nose, and paranasal sinuses should be noted; the surgical techniques described in those chapters should be used.

Preoperative diagnostic aids

MRI and CT. It is frequently unnecessary to obtain preoperative radiologic information because it is highly unlikely to affect the decision to proceed with surgery. This is especially so in the otherwise healthy patient whose only sign or symptom is the mass itself palpable in the parotid gland. However, in larger masses or parapharyngeal masses, preoperative delineation of the facial nerve, the accurate extent of extraparotid involvement and distinguishing an intraparotid deep lobe tumor from a parapharyngeal space primary, and the suggestion of nodal involvement may all assist in treatment planning. If a metastasis or a nonsalivary gland malignancy is suspected from the clinical setting, a CT scan may assist in accurately placing the needle for FNA, especially in deep-lobe or parapharyngeal space tumors. In the submandibular space, MRI or CT may accomplish the same goals as well as distinguishing whether a mass is adjacent to the submandibular gland or within it.

MRI appears to offer several advantages compared to CT in examining parotid masses. Contrast resolution is superior in general (Byrne et al, 1989; Mandelblatt et al, 1987; Som et al, 1988; Tabor and Curtin, 1989). It often demonstrates the relationship of the tumor to the facial nerve (Teresi et al, 1987a) as well as determining accurately an intraparotid versus and extraparotid origin (Teresi et al, 1987b). This is especially helpful in the parapharyngeal space (Cross et al, 1989; Som et al, 1988), where some histologic correlation may also be definitive. For instance, glomus tumors displace the internal carotid artery anteriorly, whereas salivary gland tumors displace it posteriorly (Som et al, 1988). The multiplanar imaging capacity of MRI often provides the surgeon with a more accurate appreciation of the anatomic extent of the tumor in this area.

Although histologic diagnosis is not the aim of MRI, some correlative information is available (Byrne et al, 1989; Som and Biller, 1989; Swartz et al, 1989). For instance, pleomorphic adenomas are generally homogeneous and smoothly marginated whereas adenolymphoma (Warthin's tumor) is heterogeneous and well marginated. Signals of benign and low-grade malignancies are usually low T1-weighted and high T2-weighted, reflecting seromucinous secretions. High-grade tumors frequently have poorly defined margins and bioth T1 and T2 images may be low in signal intensity. The signal intensity of high-grade tumors is similar to fibrosis and sialolithiasis although inflammatory lesions exhibit thickening of the deep cervical fascia and infiltration of subcutaneous fat. Such information must of course be correlated with the clinical setting. If obtaining true pathologic information before surgery is indicated, then clearly fine-needle aspiration is necessary.

There are other indications for CT or MRI. CT or MRI may assist the radiation oncologist in planning postoperative radiation fields. In a patient with multiple cystic lesions of the parotid, especially with cervical adenopathy, HIV infection should be suspected (Holliday et al, 1988; Shugar et al, 1988). If a FNA were to be done, a lymphoepithelial lesion would be found. Surgery is unnecessary in this setting, but one should keep in mind that there is an increased incidence of lymphoma in patients with AIDS.

Other diagnostic imaging. In addition to CT and MRI, a number of other imaging techniques have been advocated as helpful for diagnosing salivary gland tumors. These include sialograms (sometimes with CT), ultrasonograms, and radionuclide imaging. If the clinical setting suggests an inflammatory or infectious process, an ultrasound, which is less

expensive than a CT, may show an abscess that is in need of drainage. Sialograms may show stones or sialectasis. In the setting of a mass lesion, however, these tests offer little. Their results do not differentiate benign from malignant tumors and rarely alter the therapeutic approach. For the majority of smaller parotid neoplasms that occur in the superficial lobe (particularly in the tail of the parotid) without evidence of facial nerve or lymph node involvement, no pretreatment information is usually required. If information is needed regarding the anatomic extent of disease, CT and especially MRI are far more helpful. Before MRI was available, CT sialography was proposed as a tool, but more recently few seem to feel it offers any advantage to MRI (Byrne et al, 1989).

Because benign Warthin's tumors (and oncocytomas) scan positively with technetium-99 radionuclide imaging, this technique has been advocated for patients who are high surgical risks. If a tumor "lights up", surgery is deemed unnecessary. A more reliable and less expensive method in such high-surgical risk patients, however, is fine-needle aspiration. This technique is highly accurate, and Warthin's tumors and oncocytomas with a consistent clinical picture usually pose no diagnostic dilemma. We therefore see no indication for radionuclide scanning in the diagnosis of salivary gland tumors when FNA is available.

Fine-needle aspiration. Fine-needle aspiration (FNA) with a 22-gauge or smaller needle has become a valuable pretreatment diagnostic test in many centers (Abele et al, 1987; Frable, 1983; Sismanis et al, 1981). When properaly practiced and interpreted, the procedure is well tolerated, safe, and inexpensive; its results are at least as correlative with final histology as frozen sections are, and are rarely misleading. Complications of fine-needle aspiration are exceedingly rare. A small hematoma may occur at the FNA site. Seeding in the needle tracks or facial nerve injury has not been reported in the head and neck, and in fact only two such cases have been reported in any site (Ferrucci et al, 1979; Sinner and Zajicek, 1976). Proper use of FNA in salivary gland lesions requires particularly close cooperation between the surgeon and the cytopathologist and a recognition that not infrequently the cytopathologist is unable to make a complete and accurate diagnosis. However, a misleading diagnosis is rare. Difficulties might result from an unsatisfactory specimen (in which case no clinical information is derived). More commonly it may be the result of difficulty with the underlying histology. The more common problem areas are cellular benign mixed tumors with either some nuclear atypia or with no stroma, cystic lesions and mucoepidermoid carcinomas, and lymphoid lesions or rare tumors. In such cases the cytopathologist can best assist the clinician by describing the FNA and discussing the differential diagnosis with the clinician. In experienced hands misleading diagnoses (false positives and false negatives) are rare. For squamous cell carcinoma of the head and neck the sensitivity of fine-needle aspiration is well over 90% and its specificity is nearly 100% (Feldman et al, 1983), in salivary gland cytopathology results are not as good. As experience continues to accumulate, however, interpretation has become increasingly accurate and helpful. This sensitivity and specificity are responsible for the expanded use of FNA in salivary gland neoplasms.

When FNA of salivary glands was first introduced 25 years ago, Eneroth and his group reported false-positive rates of about 1% for benign lesions (3 of 274 and 4 of 413 respectively), with "suspicious" cases of benign mixed tumors almost always turning out on histology to be non-malignant (Eneroth et al, 1967a and b; Mavec et al, 1964). However, their results with malignant tumors were much worse. Mavec et al (1964) had the wrong diagnosis in 42 of 91 malignancies, and of 55 adenoid cystic carcinomas, mucoepidermoid carcinomas,

acinic cell carcinomas, and adenocarcinomas, only 16 were diagnosed. Eneroth (1967a and b) similarly had a high (46%) false-negative rate among malignant tumors. Early investigators learned from this. A decade later Persson and Zettergent (1973) reported on 216 FNAs with histologic confirmation. In 96% of benign tumors the diagnosis was complete and accurate; only 1 diagnosis of 161 was misleading (a suspected squamous cell carcinoma). Persson and Zettergen's false-negative rate among the 34 malignant tumors was 9%, with two malignant mixed tumors called benign and a mucoepidermoid carcinoma called a cyst. Lindberg and Akerman (1976) discussed their learning process with 461 aspirates (including 214 bening and 38 malignant) in which 63% had complete and accurate correlation with histology, 18% had nonmisleading agreement, 11% had unsatisfactory aspirates, and 8% had false reports. Upon revision of the diagnoses based on accumulation of further experience, 45 (up from 38) would have been called malignant, only 7 (not 20) would have remained false negatives, and 25 (not 19) would have been diagnosed as malignant but not requiring description rather than a complete histologic diagnosis. Qizilbash et al (1985) reported 146 satisfactory FNAs among 160 attempts. Among 77 benign or nontumor cases, 69 diagnoses were complete and accurate and the other 8 were correctly reported as being nonmalignant. Among the malignant cases, 11 of 14 diagnoses were complete and accurate with two (both lymphomas) of the three false negatives attributed to initial personal inexperience. Nettle and Orrell (1989) reported one false-positive and five false-negative diagnoses among 25 malignant and 74 benign tumors, or an 80% specificity and 99% sensitivity for a malignant diagnosis on FNA. Among these, 68% were complete and accurate, with only the 6 (of 99) being misleading. The most difficult to diagnose were mucoepidermoid carcinoma and unusual pleomorphic adenomas. Jayaram et al (1989) confirmed these were the two areas that were the most troublesome for the cytopathologist.

When confronted with a diagnostic dilemma, the cytopathologist and the clinician discuss the rendered descriptive cytopathologic diagnosis, both to decide whether a repeat FNA should be done and to discuss the implications of the uncertainty. In most cases where nuclear atypicality is seen in the setting of a visible biphasic mixture of mesenchymal (usually fernlike stroma) and epithelial elements typical of pleomorphic adenoma, the diagnosis will be the relatively common pleomorphic adenoma and not malignancy. The diagnosis o pleomorphic adenoma may also be difficult when the usual biphasic pattern is missing and only stroma or only epithelial cells are present. The presence of intracellular mucin or squamous cells, or of cystic changes may also pose diagnostic problems. For mucoepidermoid carcinoma, Cohen et al (1990) reviewed the experience of research at the University of California, San Francisco, with 34 such malignancies among a total of 47 malignancies seen in 96 salivary gland FNA specimens. The presence of intermediate cells (79%) or the presence of both overlapping epithelial cells (91%) and squamous cells (77%) correlated best with the diagnosis of mucoepidermoid carcinoma, with a sensitivity of 97%, a specificity of 100%, and a positive and negative predictive value of 99% and 98% respectively, using stepwise logistic regression analysis. Distinguishing high-grade from low-grade mucoepidermoid carcinoma was based on the presence of nuclear atypia (19% versus 89%), necrosis (6% versus 28%) and stringy extracellular mucin (81% versus 44%). Cystic changes in mucoepidermoid carcinomas may be difficult to distinguish from atypical benign cysts containing mucin and necrotic debris.

As in all tests, clinical judgment is necessary to interpret fine-needle aspirates. We stress that the technique itself and interpretation of results requires considerable experience; success varies from center to center as individual experience is gained. If the cytologic diagnosis is at odds with clinical judgment, clinical judgment dictates further investigation and appropriate treatment. A recent short review of salivary gland FNA cytopathologic appearance may be found in research by Bottles (1990).

Frozen section. The use of frozen sections in the evaluation of parotid tumors is controversial (Hillel and Fee, 1983; Wheelis and Yarington, 1984), and has similar difficulties as fine-needle aspiration when the underlying histology is difficult to interpret. Cohen et al (1990) specifically compared FNA with frozen section diagnoses, noting that problem cases were often problems for either technique. They reported an overall accuracy rate for frozen section diagnosis of 71% compared to an 88% accuracy rate for FNA. Layfield et al (1987) similarly reported an 11% false-negative rate for frozen section diagnosis compared to a 4.7% false-negative rate for FNA.

In patients who clinically appear to have a malignant tumor and in whom needle-aspiration biopsy has not provided a malignant diagnosis, a frozen section may be attempted to confirm clinical suspicion. If a nearby lymph node appears to be involved, an excisional biopsy of it may clarify the situation. Only if a pathologist familiar with the particular clinical setting and experienced in salivary gland pathology renders a firm diagnosis of malignancy in this setting should one consider proceeding with the complete surgical procedure appropriate for the malignancy. A conservative alternative is to perform only the parotidectomy and await permanent section diagnosis. Even in the most capable hands, the necessarily rapid interpretation of salivary gland frozen section material may be difficult, with error rates in distinguishing benign from malignant diseases reported to be as high as 25%.

Open biopsy. Open biopsy is rarely indicated. It provides useful histopathologic guidance for the use of palliative irradiation or chemotherapy only in those patients who are poor surgical candidates and have an obvious malignancy and on whom needle aspiration has not provided a diagnosis.

Intraoral open biopsy of a parapharyngeal tumor should be avoided. Such a biopsy in essence connects the parapharyngeal space with the oral cavity, contaminating the subsequent operative field with flora from the oral mucosa, necessitating a wider excision that includes the oral mucosa, and increasing the subsequent chance of postoperative infection. If one waits until the mucosa heals, the considerable inflammation, edema, and possible infection may delay the surgical procedure.

The preoperative workup routinely should include an MRI scan with gadolinium to delineate the anatomic relationships of the tumor, rule out a vascular tumor, and determine the location of the carotid artery. An MRI may also strongly suggest that a mass may have a nerve origin. An FNA via an extraoral or intraoral route (with CT guidance if necessary), may lead to a tissue diagnosis. Even if it does not, however, the surgical approach is not altered. Because of the location of the tumor, an en bloc resection is rarely feasible, and the external surgical approach (discussed later) both establishes tissue for histopathology and removes the tumor as well as possible.

Surgical techniques

Parotidectomy and CN VII identification. When a parotidectomy is performed, the patient's face is turned away from the surgeon, and a pad is placed beneath the ipsilateral shoulder. Epinephrine (1:100.000) is injected subcutaneously along the planned incision line to induce vasoconstriction so as to minimize bothersome arteriolar bleeding at the time of the incision. No lidocaine is used because it may produce temporary facial nerve paralysis.

Some surgeons have recommended the instillation of methylene blue into the ductal system suggesting it makes the facial nerve stand out white against the blue ducts and acinar system. However, either overinjection or subsequent transection of salivary gland tissue leads to leakage of the methylene blue into the operative field. Moreover, a surgeon skilled in parotid surgery does not require color coding to identify and preserve the facial nerve.

When the operative field is draped, it is important to be able to see facial muscle function while the facial nerve is being dissected. Consequently, a sterile, clear plastic drape, not a towel, should be used anterior to the incision to cover the rest of the face, including the eye, corner of the mouth, and nose.

Any properly designed incision that allows closure and produces a good cosmetic result is appropriate. An incision that begins anterior to the attachment of the anterior helix just superior to the zygomatic arch and descends to the tragus is preferred. The incision is hidden behind the inner free margin of the tragus, over the incisura; it is then directed behind the lobule of the pinna in a soft curve that continues onto the neck along the anterior border of the sternomastoid toward the greater cornu of the hyoid.

The incision is carried down to parotomasseteric fascia, which has an easily identifiable silvery sheen. The anterior skin flap is raised 1 cm anterior to the parotid gland. If greater exposure is needed superiorly, the incision can be carried into the temporal hairline with a horizontal anterior excision. If greater exposure is needed inferiorly, the incision can be extended to the greater cornu of the hyoid bone. With both these extensions the anterior facial skin flap can be elevated almost to the midline. To minimize the trauma of retractors, the skin flap is sutured anteriorly.

The fascia that extends from the sternocleidomastoid muscle onto the parotid is then incised, allowing the tail of the parotid to be separated from the sternocleidomastoid muscle. Generally the greater auricular nerve is sectioned, but on occasion it may be mobilized and reflected posteriorly (Fig. 62-10). The posterior facial vein can generally be preserved when a superficial parotidectomy is being performed because the dissection is superficial to it.

With the tail of the parotid mobilized and the anterior border of the sternocleidomastoid retracted, the digastric muscle is identified (Fig. 62-11). To help identify the facial nerve, the digastric muscle can be followed superiorly toward the mastoid tip and digastric groove where the muscle inserts.

Blunt dissection then separates the parotid gland from its attachment to the cartilage of the external auditory canal. As this dissection progresses, the tragal pointer comes into view (Fig. 62-12). The facial nerve lies approximately 1 cm deep and slightly anteroinferior

to the tragal pointer. The tympanomastoid suture line is another landmark for identification of the facial nerve. It can be palpated at this point in the dissection, and the facial nerve exits from the skull base through the stylomastoid foramen approximately 6 to 8 mm deep to the inferior end of the tympanomastoid suture line. This relationship is nearly always constant. The facial nerve exits between the styloid process, which also can be palpated, and the attachment of the digastric muscle to the digastric ridge (Fig. 62-13). Careful dissection of this small area with a narrow fine hemostat in the direction parallel to the course of the facial nerve separates the soft tissue until the facial nerve is identified. For the majority of parotid tumors, this posterior approach leads to the easy identification of the facial nerve.

Alternative approaches to the facial nerve are necessary when a tumor mass sits over the main trunk of the facial nerve or when previous surgery or a recurrent tumor has obscured the anatomy.

The most common alternative approach uses the identification of the marginal mandibular nerve. The posterior facial vein is identified and followed superiorly ot its entry into the parotid gland. The marginal mandibular nerve crosses superficial to the posterior facial vein (Fig. 62-14) and is then followed posteriorly to the main trunk.

Especially useful on patients who have heavy scarring from previous surgery or with recurrent tumor in the area of the main trunk is identification of the facial nerve proximal to the prior operative field. With either a mallet and gouge or an otologic drill, the mastoid tip is removed for identification of the nerve as it exits from the stylomastoid canal (Fig. 62-15). To identify the facial nerve in a nonoperated area, a mastoidectomy may be occasionally necessary to locate and trace the descending portion of the facial nerve in its intratemporal approach.

Other methods for identifying the facial nerve involve identifying other distal branches. For example, the buccal branch can be identified as it courses parallel to the parotid duct. The parotid duct is identified as it crosses the masseter muscle (Fig. 62-14).

Once the main trunk of the facial nerve is identified, a curved mosquito hemostat is used to create a tunnel just superficial to the nerve, and the overlying parotid tissue is incised (Fig. 62-16, A). The pes anserinus is reached where the facial nerve begins to branch. The farthest branch from the tumor is followed out to the periphery of the gland. As each tunnel over a nerve branch is made, a No. 12 blade is used to cut the overlying parotid tissue (Fig. 62-16, B). Having followed the first branch out to the periphery, the surgeon returns to find the next branch and creates a second tunnel. This tunnel is sharply connected to the previously dissected tunnel over the previously dissected facial nerve branch (Fig. 62-16, C). This pattern is successively followed as the gland is reflected downward in the plane of the facial nerve by serial identification of each nerve branch until the entire superficial portion of the gland that includes the tumor is thus gained (Fig. 62-17). For an inferiorly located tail of parotid tumor, the superficial parotidectomy progresses from superior to inferior as the underlying facial nerve brances are successively identified, tunnels made and connected, and the superficial parotid with the tumor removed.

Although the majority of parotid gland tumors arise in the more abundant superficial portion of the gland, about 10% to 12% of tumors lie medial to the facial nerve, that is, in the deep portion of the gland. Although anatomically no deep lobe exists, the deep portion of the gland medial to the nerve is often referred to as the deep lobe of the parotid. With the standard approach just described, tumors involving the deep lobe generally can be removed, preserving the facial nerve branches. However, maintaining a margin of normal salivary gland tissue around the tumor is more difficult. In approaching the deep lobe tumor, the superficial gland is first removed by a standard superficial parotidectomy. The exposed branches of the facial nerve are then dissected from the deep lobe. Rubber spaghetti-like bands placed around the branches of the nerve can aid retraction of facial nerve branches. The deep lobe tumor and as much surrounding normal tissue as possible is then dissected from the mandible and stylomandibular membrane by diligent mobilization from all four sides, including its deep attachments.

Parapharyngeal space tumors. Tumors that involve the parapharyngeal space or retromandibular area can be approached in two ways. Usually a submandibular approach is sufficient. Occasionally, an osteotomy of the mandibular ramus to reflect the mandible superiorly is necessary to provide more exposure of the parapharyngeal space.

Submandibular approach. In the submandibular approach to the parapharyngeal space, the first step in obtaining exposure is excision of the submandibular gland. In a natural skin crease 3 to 4 cm inferior to the mandible, a skin incision is made that extends from the greater cornu of the hyoid laterally for about 5 cm. This incision is an extension of the inferior parotidectomy incision (Fig. 62-18) and is continued to a subplatysmal plane in order to identify the superficial layer of the deep cervical fascia. The anterior border of the sternocleidomastoid muscle is identified posteriorly and the anterior belly of the digastric muscle is identified anteriorly. Just deep to the deep cervical fascia the anterior facial vein is ligated and divided. Retraction of the superior ligature, which is usually taut, protects the marginal mandibular nerve that runs just superficial to the anterior facial vein. We nevertheless recommend that identifying it positively is the best method to ensure its preservation.

With the fascia elevated, the gland is exposed and dissection begins superiorly where the external maxillary artery is ligated and divided (Fig. 62019). The mylohyoid muscle is retracted anteriorly, and the submandibular gland is retracted posteroinferiorly. This step exposes the lingual nerve and Wharton's duct (Fig. 62-20). The submandibular duct and the submandibular gland, with its associated venous plexus, are ligated and divided. Division of the ganglion allows the lingual nerve to retract superiorly.

Inferior dissection of the gland should proceed with care to preserve the hypoglossal nerve that lies between the mylohyoid and hypoglossus muscle. Inferior retraction of the anterior belly and tendon of the digastric muscle exposes this nerve, The external maxillary artery is ligated and divided a second time (Fig. 62-21), and the submandibular gland is removed.

Following the parotidectomy and submandibular gland excision, access to the parapharyngeal space is obtained by a sharp incising of the sylomandibular ligament at its attachment to the mandible (Fig. 62-22). This incision allows for anterior dislocation of the

mandible (Fig. 62-34). This approach provides sufficient exposure so that most tumors of the parapharyngeal space or those that extend into the parapharyngeal space from the tail of the parotid or from the deep lobe can be bluntly dissected with the index finger.

Osteotomy. Larger tumors or those close to the neurovascular bundle of the carotid sheath require an osteotomy, which is the second approach to the parapharyngeal space and provides greater exposure. After a superficial parotidectomy an incision is made along the inferior body and angle of the mandibular ramus, taking care to protect the marginal mandibular nerve. The masseter and internal pterygoid muscles are then elevated from the agnle of the mandible. Before making the mandibular osteotomy, holes for the subsequent rewiring of the mandible are drilled, and a step or V type of osteotomy is performed (Fig. 62-24). The ramus of the mandible can then be swung superiorly, providing wide exposure of the parapharyngeal and pterygoid areas (Fig. 62-25). Following excision of the tumor, the mandible is reapproximated, with figure-of-eight wire placed in the previously created drill holes. With careful reapproximation, significant alveolar nerve regeneration can occur within a year.

After irrigation and placement of suction drains, the wound is closed in layers and the drains are left in place for 24 to 48 hours, depending on the amount of drainage. We prefer Jackson-Pratt drains when a radical neck dissection is not used; larger Hemovac drains are used in conjunction with a neck dissection.

For benign tumors and for smaller malignant tumors confined to the anatomic areas just described, these approaches work well. For larger lesions that cross the various planes, however, a combination of methods must be used, keeping in mind that removal of the tumor with a margin of normal tissue is paramount. The resection of malignant tumors may require resection of the facial nerve, masseter and internal pterygoid muscles, and mandible, or even a mastoidectomy. The extent of tumor determines the extent of surgery; no standard approach exists.

When the facial nerve has to be resected because of involvement by malignancy, frozen sections of the proximal and distal stumps are obtained to rule out perineural spread. The nerve is resected back to clear margins, and facial nerve reconstruction is carried out at the time of primary resection. Postoperative radiation does not adversely affect facial nerve regeneration.

Complications. The complications of parotid surgery include facial nerve injury, gustatory sweating, salivary fistula, infection, hematoma, and recurrence of tumor. Facial nerve injury and repair is discussed in Chapter 63. Postoperative hematomas are unusual when adequate hemostasis has been obtained at the time of the procedure. In patients with bleeding diathesis, functioning suction drainage and careful attention to hemostasis should prevent the problem. When a hematoma does appear, treatment is simply the evacuation of the hematoma and the regaining of adequate hemostasis. Because infection is so unusual after uncomplicated parotid surgery, prophylactic antibiotics do not seem warranted. In a chronically infected gland or in a more extensive procedure, especially one in which the oral cavity is to be extended, perioperative antibiotics are indicated.

Frey's syndrome. Frey's syndroem (gustatory sweating, or auricular temporal syndrome) is a symptom complex that includes localized facial sweating and flushing during the mastication of food. Its incidence is unknown but is estimated to affect between 35% and 60% of postparotidectomy patients (Gordon and Fiddian, 1976; Hays et al, 1982). Some suggest that, if specifically investigated, all patients would show this. Gustatory sweating is seen in the anterior skin flap and may also be seen in the distribution of the greater auricular nerve and branches of the cervical plexus. First seen several months after surgery, it may be socially noticeable. The probable pathophysiology involves aberrant regeneration of nerve fibers from the postganglionic secretomotor parasympathetic innervation to the parotid gland occurring through the severed axon sheath of the postganglionic sympathetic fibers that supply the sweat glands of the skin (Fig. 62-26 and 62-27).

Minor's starch/iodine test can objectively measure the area of gustatory sweating. The suspected area of skin is painted with iodine solution and the solution is allowed to dry on the face. Starch powder is then dusted on the area. The patient then chews on a lemon wedge or similar sialogogue for 2 minutes. Gustatory sweating is demonstrated by appearance of dark blue-black spots, the result of sweat dissolving the starch powder, which then reacts with the iodine. Because the majority of patients are not bothered enough by these symptoms to seek medical therapy, treatment is generally supportive. Numerous surgical treatments have been proposed, including tympanic neurectomy, subdermal insertion of fascia lata grafts, and the rotation of sternocleidomastoid muscle flaps into the parotid bed. Glycopyrrolate is a simple possibly effective medical treatment (Hays et al, 1982). Hays and co-workers reported success in 14 of 16 patients using a 1% glycopyrrolate roll-on lotion. They also noted a very low rate of anticholinergic side effects, such as blurred vision and dry mouth.

Salivary fistula. Postoperative salivary fistulas are uncommon. They may appear either as an opening, draining clear fluid, in the suture line just below the lobule of the pinna, or occasionally as saliva accumulating under a healed flap. The latter is more likely to occur if Stensen's duct has been ligated. In most instances a salivary fistula is a self-limited condition that responds to a pressure dressing.

Recurrent benign mixed tumors. This chapter has already extensively discussed recurrence of malignant tumors. The recurrence of benign mixed tumors, however, deserves special discussion. Even though superficial parotidectomy that includes a cuff of normal tissue is the minimal acceptable procedure for dealing with pleomorphic adenomas, local recurrences of benign mixed tumors occur. The incidence of mixed tumor recurrence has been estimated to be between 2% and 30% (Fee et al, 1978; Grage et al, 1961; Hanna et al, 1976). Time to recurrence is measured in years, with a significant percentage occurring more than 10 years from the time of initial surgery. When evaluating a patient with a possible recurrent benign mixed tumor it should be remembered that malignant mixed tumors, although rare, usually occur in a patient who has had a prevsious benign tumor.

The surgical approach to recurrent benign mixed tumors should incorporate the surgical techniques discussed in this text, noting that by definition a recurrence happens in a previously operated field. Generally the facial nerve can be dissected away from the tumor, even from recurrent benign mixed tumors, but the incidence of postoperative paresis is greater than at the initial operation. Fee et al (1978) noted a 52% incidence of transitory facial paresis or paralysis and an 8% incidence of a permanent facial paralysis involving more than one

fifth of the facial nerve distribution. On rare occasions the facial nerve must be sacrificed to cure the patient of the tumor (Conley, 1975; Hanna et al, 1976; Work et al, 1976). In general, a total parotidectomy is planned for recurrent tumors and the relationship of tumor to facial nerve dictates whether any facial nerve branches need resection and grafting.

The role of irradiation in treating recurrent benign mixed tumors is controversial. Following superficial parotidectomy for mixed tumor, should one radiate a patient with apositive margin or one in whom the capsule was violated? Is irradiation a useful adjunct to total parotidectomy in treating recurrent benign mixed tumors?

Summary

Treatment of parotid cancers continues to evolve. About 40 years ago Foote and Frazell (1953) introduced an acceptable classification system that first allowed study of these malignancies. Continual revision, collected histopathologic reviews, and electron microscopy have added sophistication to this initial study. In 1988 the AJCC simplified and clarified its recommended staging system making it a useful communicative and treatment planning tool. The limitations of surgery have been learned in the past 30 years, and the widespread use of postoperative radiation therapy has appeared to improve local control. High-LET irradiation, though of limited availability, is promising in recurrent and advanced disease. The increased investigation of chemotherapy in the last 10 years is the result of an increased awareness of the frequency of distant metastases. However, the results of chemotherapy remain disappointing. The role of biologic modifiers is unknown. Investigation at a molecular biology and genetic level is just beginning. To make further progress in the understanding of these infrequent malignancies, cooperative studies will be needed to accumulate adequate numbers of cases for study and to plan prospective trials of new therapy.