

Chapter 90: Malignant Cervical Adenopathy

Roy B. Sessions, Catherine P. Hudkins

The proper evaluation and management of a neck mass in an adult can require an impressive amount of anatomic, pathologic, immunologic, and oncologic information. Except for thyroid cancer, most adult neck masses represent metastatic squamous carcinoma that is located in lymph nodes (Slaughter et al, 1960) and that has metastasized from a primary tumor in the regional aerodigestive tract. In the pediatric population, on the other hand, most cervical masses are nonmalignant (Moussatus and Battes, 1963; Skandalakis et al, 1960; Slaughter et al, 1956).

A differential diagnosis must be considered, of course, in all patients who present with a neck mass. It is difficult to improve on the outline developed by Suen and Wetmore (1981), which is presented as follows:

1. Neoplasm

- A. Benign

1. Vascular - hemangioma, lymphangioma, arteriovenous malformation, aneurysm

2. Chemodectoma

3. Neural - neurofibroma, schwannoma

4. Lipoma

5. Fibroma

6. Miscellaneous - fibromatosis

- B. Malignant

1. Neck primary

- a. Lymphoma

- b. Sarcoma

- c. Thyroid carcinoma

- d. Salivary gland carcinoma

- e. Branchial cleft cyst carcinomas

- f. Thyroglossal duct cyst carcinomas

2. Metastatic

- a. Head and neck primary - mucosal surfaces, skin, salivary glands, thyroid
- b. Infraclavicular primary - lung, kidney, prostate, gonads, stomach, breast
- c. Leukemia

II. Infection

A. Abscess

B. Cervical lymphadenitis

1. Bacterial

2. Granulomatosis - tuberculosis, actinomycosis, sarcoidosis

3. Viral - infectious mononucleosis

III. Congenital

A. Thyroglossal duct cyst

B. Branchial cleft cyst

C. Dermoid cyst

D. Teratoma

IV. Miscellaneous

A. Zenker's (hypopharyngeal) diverticulum

B. External laryngocele

C. Amyloidosis

D. Neuroma (traumatic)

V. Normal structures

A. Hyoid

B. Carotid bulb

C. Transverse process of vertebrae

D. Normal neck nodules (hyperplasia).

In this chapter, our purpose is to discuss the management of cervical nodal metastases from aerodigestive squamous carcinoma (ADSC). This section reviews extensive literature in order to develop a practical therapy plan that is based on a thoughtful appraisal of the information available on cervical metastatic disease. These recommendations will need to be updated continually as new knowledge becomes available.

Anatomy

The scope of this discussion does not allow a detailed description of the complex anatomy of the neck; however, a review of the lymphatics of the area enhances the overall understanding of cervical adenopathy. The anatomy of the neck is distinguished by a certain consistency that is useful in the management of neoplastic conditions.

Anatomic triangles

The neck can be divided into two major triangles, the anterior and the posterior. The anterior cervical triangle (ACT) has a caudal apex and a cephalic base and is bounded posteriorly by the anterior edge of the sternocleidomastoid muscle (SCM), anteriorly by the midline of the neck and cephalically by the inferior rim of the horizontal ramus of the mandible. The apex of the ACT lies at the level of the clavicular head, in the sternal notch. The posterior cervical triangle (PCT) is bounded by the SCM anteriorly, the clavicle caudally, and the trapezius muscle posteriorly. Its apex lies at the mastoid tip. Both the anterior and posterior cervical triangles are subdivided into smaller triangles, a fact noteworthy for anatomic as well as practical reasons (Fig. 90-1).

The ACT contains the submandibular, suprahyoid (submental), and the superior and inferior carotid triangles. The submandibular triangle is outlined by the two converging bellies of the digastric muscle and the inferior margin of the mandible. The mylohyoid and hyoglossus muscles form the floor of this compartment, and within its borders lie the submandibular gland, part of the parotid gland, a group of lymph nodes, and the hypoglossal nerve. The suprahyoid triangle is bordered by the hyoid bone below and the anterior belly of the digastric muscle above, and abuts its counterpart from the opposite side at the midline. The floor of the suprahyoid triangle is the mylohyoid muscle, superficial to which usually are two lymph nodes.

The superior belly of the omohyoid muscle divides the remainder of the ACT into the superior and inferior carotid triangles. The inferior triangle is bounded by the midline of the neck, the superior belly of the omohyoid muscle above, and the anterior margin of the lower part of the SCM below. In this triangle are located the sternohyoid and sternothyroid muscles, part of the thyroid gland, the larynx, and the trachea. The superior carotid triangle is bounded behind by the SCM, below by the superior belly of the omohyoid muscle, and above by the stylohyoid muscle and the posterior belly of the digastric muscle. The floor of this triangle is formed by the thyrohyoid and hypoglossus muscles and the middle and inferior pharyngeal constrictor muscles. Within this triangle are the great vessels and associated lymph nodes as well as the hypoglossal nerve.

The PCT is unequally divided into subdivision by the inferior belly of the omohyoid muscle. The larger occipital triangle is bounded in front by the SCM, behind by the trapezius muscle, and below by the omohyoid muscle. Its floor is formed by the splenius capitis, levator scapulae, and the medial and posterior scalene muscles. The triangle is crossed by the spinal accessory nerve and its associated lymph nodes. The smaller subclavian triangle is bounded above by the inferior belly of the omohyoid muscle, below by the clavicle, and in front by the SCM. Its floor is formed by the first rib and the first digitation of the anterior scalene muscle. Within this triangle lie the brachial plexus, subclavian artery and vein, and some of the branches of the thyrocervical trunk.

To simplify and consolidate discussion of the neck nodes, we use a level designation that refers to the neck topographically. Cervical nodes are reported in terms of five anatomic levels (Fig. 90-2). Level I refers to the area of the submandibular and suprahyoid (submental) triangles; levels II, III, and IV refer to the areas containing the chain of nodes along the upper, middle, and lower one third of the jugular vein, respectively; and level V describes nodes along the spinal accessory nerve and within the posterior cervical triangle. Thus levels I to IV correspond to the anterior cervical triangle, whereas level V represents the posterior cervical triangle.

Lymph nodes

There are approximately 300 lymph nodes in the head and neck that comprise about 30% of the total in the human body (Hellstrom and Hellstrom, 1971; Million et al, 1982). The following outline organizes this anatomic system in the head and neck:

- I. Lymph nodes of head
 - A. Occipital
 - B. Posterior auricular (postauricular)
 - C. Anterior auricular (preauricular)
 - D. Parotid
 - E. Facial
 - F. Deep facial
 - G. Lingual
- II. Lymph nodes of neck
 - A. Superficial cervical
 - B. Anterior cervical
 - C. Submental

- D. Submaxillary
- E. Deep cervical
 - 1. Retropharyngeal
 - 2. Jugular
 - a. Superior
 - b. Inferior
 - 3. Spinal accessory
 - 4. Transverse cervical.

Lymphatic vessels of the first order arise from lymphatic capillary plexuses that then enter lymph nodes as afferent vessels. From these nodes efferent vessels usually pass to one or a series of lymph nodes before joining the thoracic duct on the left side of the neck or the lymphatic duct on the right.

Because the lymphatic system originates embryologically from the venous system, the lymph nodes and lymphatic trunk are associated with veins. The nodes are situated along the lymphatic vessels so that the lymph and chyle pass through them on their way to the bloodstream. The lymphatic drainage of any particular area of the head and neck generally reflects the venous density of that same site from the standpoint of direction as well as volume. The nasopharynx and piriform sinuses have the most profuse networks of capillary lymphatics, whereas the paranasal sinuses, middle ear, and true vocal cords have few or no lymphatics.

Head lymph nodes

A description of the lymph nodes of the neck must include those lymphatics that originate in the head and facial areas because their efferent drainage is into the cervical nodes (Fig. 90-3, A).

One to three occipital nodes are on the back of the head, close to the margin of the trapezius muscle. The two posterior auricular (postauricular) nodes are on the insertion site of the SCM; their counterparts, the anterior auricular (preauricular) nodes lie anterior to the tragus and are separate from the substance of the parotid gland. The parotid nodes themselves are divided into superficial and deep nodes, of which the former lie within the substance of the gland (Fig. 90-3, B), and the latter lie on the lateral wall of the pharynx, deep to the gland.

Neck lymph nodes

The infraorbital (maxillary), buccinator, supramandibular, and submental nodes all drain into the superior deep cervical chain by way of the submandibular nodes. The primary deep lymphatic chains in the neck are the internal jugular, spinal accessory, and transverse cervical (Fig. 90-3, B).

Internal jugular

The internal jugular group is the chief collecting system for most regions in the head and neck; it contains 10 to 20 nodes on each side that lie adjacent to various parts of the internal jugular vein from the skull base to the termination of the lymphatic trunks at the base of the neck. The highest nodes are actually in the lateral pharyngeal space and are known as the parapharyngeal or retropharyngeal nodes. These nodes are deep to the SCM and posterior to the digastric muscle and the tail of the parotid gland. *Gray's Anatomy* lists these with the head nodes rather than with the neck nodes, but they are related intimately to the neck (Fig. 90-4).

The remaining cervical nodes in the jugular chain are divided into superior and inferior. The superior group lie anterior or lateral to the internal jugular vein. These nodes can appear clinically in front of, deep to, or behind the SCM near the angle of the jaw. Proceeding inferiorly, the relationship of the nodes to the vein and muscle changes. The middle to upper nodes lie deep to the internal jugular vein, whereas the inferior groups lie more anterior and medial to this vascular structure, close to the trachea. The nodes of the upper jugular group also are known as the subdigastric nodes and, either directly or indirectly, are the nodes most frequently involved in ADSC.

Spinal accessory

The spinal accessory chain contains approximately 20 lymph nodes that generally lie along the nerve. These nodes blend above with the upper jugular chain nodes and below with the supraclavicular or transverse cervical group. There is no distinction between the upper spinal accessory nodes and the jugulodigastric nodes, and some consider these part of level II.

Transverse cervical

The transverse cervical chain has from 4 to 12 nodes and connects the spinal accessory chain with the internal jugular nodes (Schuller, 1984). These nodes are located just superior to and along the clavicle and are a continuation of the axillary chain and blend with the deepest jugular nodes. These deep conduit then empty into the lymphatic trunk that drains into the thoracic duct on the left and the lymphatic duct on the right. These large lymphatic channels also drain the thorax and abdomen (Million and Cassisi, 1984) and thus the supraclavicular (Virchow's) nodes receive lymph from below the clavicles as well as from the head and neck and upper extremities.

Other nodal groups

Other primary nodal stations should be mentioned. Three to six submandibular nodes are situated beneath the body of the mandible in the submandibular triangle (level I) and rest on the superficial surface of the submandibular gland (see Fig. 90-3, A). One constant node, the so-called node of Stahr (Gray, 1954), lies along the facial artery located just where that vessel crosses the horizontal ramus of the mandible. This node is important surgically because of its proximity to the marginal mandibular nerve. The submental or suprahyoid nodes are situated between the anterior bellies of the digastric muscle and are superficial to the mylohyoid muscle, draining into the adjacent submandibular nodes as well as directly into the deep midjugular nodes. The submandibular nodes drain into the adjacent superior group of deep cervical lymphatics.

Superficial facial and cervical lymphatics

The superficial cervical nodes lie close to the external jugular vein and therefore are superficial to the SCM (see Fig. 90-3, A). These nodes drain into the superior deep jugular chain. Their importance is critical at times but is seldom mentioned (Ballantyne, 1976).

The anterior nodes that form an irregular and inconstant group on the front of the larynx and trachea can be important. The most important of these are the prelaryngeal (Delphian) nodes, which are located in the midline on the cricothyroid ligament, and the pretracheal nodes. These drain the lower part of the larynx, the thyroid isthmus, and the upper trachea into the deep cervical nodes.

Drainage patterns

Although some evidence suggests an alteration of lymphatic flow in the neoplastic as well as the postsurgical state (Welsh and Welsh, 1966), the physician can use the anatomic knowledge of the norm to understand better the pathogenesis of malignant disease of the aerodigestive tract. Such knowledge forms the basis of a logical management plan for cancers affecting the area. Nodal groups are way stations for given areas. Clinical investigators have compiled statistics on many patients with cervical nodal metastasis in a way that allows the oncologist to compare the actual metastatic pattern to the theoretic norm (Feind, 1972).

The nodal groups of the head as well as the superficial nodes of the neck are first-echelon stations that drain ultimately into the deep lymphatic system. The occipital nodes drain the scalp over the occipital portion of the skull; the postauricular (mastoid) nodes drain this area as well as the posterior aspects of the pinna and the external auditory canal; and the preauricular nodes (superficial parotid nodes) drain the anterior or lateral portion of the auricle as well as the skin of the adjacent temporal region. These three groups of nodes send efferent lymph channels into the superior deep nodes. The parotid nodes are drainage stations for the root of the nose, the eyelids, the frontotemporal skin, the external auditory meatus, and the tympanic cavity (Schuller et al, 1980; Spiro et al, 1974).

The efferent drainage flows ultimately into the superior deep cervical nodes. The deep parotid nodes lie on the lateral wall of the pharynx and drain the nasal part of the pharynx and the posterior nasal cavity. The eyelids, the conjunctiva, the skin and mucous membranes

of the nose, and the mucosa of the cheek drain into the facial nodes; the efferents of these nodes drain into the submandibular nodes and then into the superior deep cervical nodes. The parotid lymph nodes are far more important than the facial ones for drainage of the eyelids and conjunctiva although the facial nodes do provide some exit for lesions affecting these structures (Gray, 1954).

The clinical importance of the retropharyngeal nodes is often overlooked. These nodes lie behind the upper part of the pharynx and in front of the first cervical vertebra, and drain the posterior nasal cavity and auditory tubes as well as the hypopharyngeal and oropharyngeal walls. These nodes often are critical to planning therapy for lesions in these areas because efferents from these structures drain into the superior deep cervical nodes (see Fig. 90-4).

The submandibular nodes primarily drain structures from above. The sides and the vestibular aspects of the nose, the upper lip, the most lateral part of the lower lip, the gums, the anterior aspect of the tongue margin, and part of the lateral floor of the mouth all drain into the submandibular lymph nodes. In addition, some secondary afferent lymph vessels from the adjacent submental nodes exist; thus the submandibular nodes indirectly drain the lower lip and the tip of the tongue. There are no lymphatic vessels between the larynx and the submandibular lymph nodes; this fact forms the basis for a recent trend toward modifying the classic techniques of neck surgery for laryngeal cancer. Although most of the submental efferent vessels go to the adjacent submandibular nodes, one direct vessel connects with the middle deep cervical nodes bilaterally.

The deep cervical lymphatics are the most significant lymphatics in the head and neck area. The superior deep jugular nodes receive drainage from the soft palate, palatine tonsil and pillars, posterior oral tongue and tongue base, piriform sinuses, and supraglottic larynx. Also, these nodes form a secondary echelon of drainage for the retropharyngeal, spinal accessory, parotid, superficial cervical, and submandibular nodes. Essentially, these superior nodes receive deep efferent vessels from all the other head and neck nodes, with the exception of the inferior deep cervical nodes.

The middle deep cervical nodes receive primary drainage from the supraglottic larynx, lower piriform sinus, and the posterior cricoid area. This middle group of deep jugular nodes serves as a secondary-echelon station for the inferior retropharyngeal nodes and the superior jugular nodes. A few paratracheal nodes are situated along the recurrent laryngeal nerves on the lateral aspects of the trachea and esophagus. This inferior group of nodes is linked with the supraclavicular nodes and thus indirectly drains the back of the scalp and neck, the superficial pectoral region, part of the arm, and occasionally part of the superior surface of the liver (Gray, 1954).

The spinal accessory nodes receive drainage from the parietal and occipital regions of the scalp and from the upper retropharyngeal and parapharyngeal nodes draining the nasopharynx and paranasal sinuses. The more cephalic spinal accessory nodes drain into the superior deep cervical nodes, whereas the more inferior ones have efferent connections primarily with the supraclavicular nodes.

Those nodes in the supraclavicular area usually receive metastases from infraclavicular primary tumors, but at times their enlargement can reflect cervical esophageal or thyroid

metastasis. Infrequently nasopharyngeal carcinoma can present with adenopathy that is isolated to this area (Lindberg, 1972).

Metastatic patterns

Patterns of metastatic involvement of the cervical lymph nodes have been determined in studies of substantial numbers of patients with ADSC. Lindberg's classic study (1972) is the most frequently quoted, and others (Feind, 1972) have corroborated his findings. In lesions of the oral tongue, the lymph nodes most often involved are in the high deep cervical (subdiaphragmatic) and submandibular triangle groups. Midjugular nodes sometimes are involved. It is significant that submental, low jugular, and posterior cervical nodes are seldom involved. Patients with floor-of-the-mouth carcinomas show a consistent pattern of submandibular and upper deep cervical nodal involvement. Submental nodal involvement is infrequent and low jugular or posterior cervical nodal involvement is rare. Lesions of the oropharynx show a consistent pattern of metastasis directly to the high deep cervical nodes, whereas submandibular and submental nodal involvement is rare.

Within the oropharyngeal group of lesions some notable variations occur: the retromolar trigone/anterior tonsillar pillar area demonstrates a predilection for submandibular as well as high deep cervical metastasis, whereas posterior cervical metastasis is rare. With palatal lesions, bilateral spread to the high deep cervical nodes is relatively common. Primary tonsillar tumors are noteworthy because metastasis to the posterior cervical nodes is common, and the incidence of spread to the middle and lower jugular chain is substantial. The tongue base demonstrates a high probability of bilateral metastasis, and the most frequently involved area is the high deep cervical, followed by the middle deep cervical. Low deep cervical and posterior cervical nodes rarely harbor tongue base metastases. Finally, of the oropharyngeal lesions, the posterior pharyngeal wall, as expected, frequently is associated with bilateral metastasis in the upper and middle cervical areas. Importantly, the posterior cervical nodes also are frequently involved, whereas supraclavicular area involvement is rare.

Diagnosis and Staging

When a primary tumor in a patient presenting with a neck mass is obvious, evaluation is not complicated. More problematic is evaluation of the neck mass that presents without an obvious primary lesion. The critical distinction is between metastatic squamous carcinoma and other masses. Fine-needle aspiration for cytologic analysis has become an acceptable and helpful diagnostic tool, and earlier concerns over tumor seeding in the needle tract have been largely dispelled (Weymuller et al, 1983). The diagnostic accuracy of this method is directly related to the physician's skill in needle placement as well as the cytologist's experience and knowledge. Fine-needle techniques are especially helpful in analyzing a neck mass that does not have an obvious source. In such cases the general distinction between squamous cell carcinoma and lymphoma, when made, saves the patient unnecessary endoscopic and biopsy procedures in the aerodigestive tract. Fine-needle cytologic techniques are inadequate for definitive diagnosis and subcategorization of lymphomas, but they do demonstrate a lymphoid rather than a squamous cytologic pattern. In such a circumstance, the next diagnostic step can be an excisional nodal biopsy rather than endoscopic procedures that are designed to find a squamous cell primary neoplasm that does not exist. If the cytologic pattern suggests squamous cell carcinoma, a search for the primary tumor will be part of the initial workup.

When the primary neoplasm is located, the neck mass can then be incorporated into the overall treatment plan, but in an unmolested state. Some authors do not believe that a premature biopsy of a metastatic node has any effect on the ultimate results of treatment and thus question the need for this ritualistic approach to neck masses (Futrell et al, 1971).

Staging allows a rational clinical assessment and an orderly appraisal of the patient's disease as well as a means to study the disease process. The American Joint Committee on Cancer (1988) assigns N1 to N3 ratings to different degrees of neck adenopathy with further subgroupings of a, b, and c for certain stages. The following is standard staging of neck disease and reflects the designations used here:

- Nx Nodes cannot be assess
- N0 No nodes containing metastasis
- N1 A single ipsilateral node metastasis, 3 cm or less in diameter
- N2a A single ipsilateral positive node more than 3 cm but not more than 6 cm in diameter
- N2b Multiple positive ipsilateral nodes, none more than 6 cm in diameter
- N2c Bilateral or contralateral positive nodes, none more than 6 cm in diameter
- N3 Massive adenopathy, greater than 6 cm in diameter.

Although variations in staging systems are available, much effort has been made in standardization, and the oncologist is urged to adhere to the AJC recommendations. The AJC system is a clinical staging system and refers to the evaluation of disease before surgical intervention. Thus the accuracy of staging relates to the physician's diagnostic ability and thoroughness. Accuracy depends somewhat on how far disease has advanced; the more advanced the cancer, the more accurate the staging. For example, patients with T1N0 lesions are more likely to be staged incorrectly than those with T3N3 lesions. Unfortunately, errors at the low end of the scale may have a more harmful effect if understaging leads to insufficient treatment of the patient (Nahum, 1982).

Sako (1964) and Spiro et al (1974) address the question of accuracy in the assessment of cervical adenopathy by routine physical examination. Sako analyzed 235 head and neck tumor patients in whom a concomitant radical neck dissection was done. The accuracy of preoperative evaluation was 72% for palpable and 72% for nonpalpable nodes. Spiro et al (1974) did a more extensive analysis of 966 patients who had ipsilateral neck dissections in whom histologic examination was used to verify the clinical impression of the presence or absence of metastatic nodes. The authors reported a somewhat higher overall accuracy rate: 15% false-negative and 19% false positive. They also noted a higher accuracy rate in patients with bilateral disease.

Other factors also affect the physician's ability to palpate subtle disease. Posterior cervical and midneck disease is more easily palpable than disease in levels I and II. The obese

neck, the short neck, and previous radiation all contribute to physical diagnostic difficulties.

There is a substantial body of literature supporting the value of the CT scan in clinical staging of metastases to the cervical nodes (Lydiatt et al, 1989; Mancuso and Dillon, 1989; Mancuso et al, 1980, 1983). Optimally, CT scan is capable of detecting foci of metastases in normal-sized nodes, and multiple positive nodes not detected by physical examination. It can also demonstrate involvement of nodes that are not readily palpable, such as the retropharyngeal nodes, and can demonstrate capsular rupture. Many studies now confirm an accuracy in excess of 90% for CT scan of neck disease, and its usefulness in staging is clear. Less information and experience are available for MRI, but reports available so far suggest equal accuracy in detecting enlarged but nonpalpable nodes. MRI is of less value in detecting central necrosis, small foci of metastases, or extracapsular spread. Essentially, imaging is part of clinical diagnosis and staging should not be concluded without the use of these technologies. Detection of neck metastasis is important because once the neck becomes clinically positive, the tumor automatically assumes either a stage III or IV designation. As expected, a linear relationship exists between stage and mortality (Spiro and Strong, 1971), and accurate staging has major implications for prognosis and treatment.

Biology of Metastasis

Metastasis has been defined as the transfer of disease from one organ or part to another not directly connected to it. This is a complex process that involves escape of tumor cells from the primary site by invasion into vascular and/or lymphatic channels, followed by dissemination to distant sites where the tumor emboli are arrested in the microcirculation (DeVita et al, 1982). The cells must then invade parenchyma, survive, and grow in a hostile environment. This process as well as its outcome is influenced by both host factors and tumor cell properties (Sugarbaker and Ketchum, 1977). These concepts are still poorly understood but ongoing research continues to provide new information.

Perhaps most poorly understood are the characteristics of the tumor cells themselves that influence tissue invasion and modulate the body's immune responses. Such factors as cell motility and the elaboration of specific tissue-destructive enzymes are probably crucial to invasion into normal tissues by malignant cells. Additionally, a variety of inhibitory substances are produced or stimulated by tumors, affecting both lymphocyte function and proliferation (Fidler and Hart, 1982).

A very important characteristic of tumor cells is the degree to which they express antigens on their cell surfaces. The T-cell system responds to antigens on the tumor cell surface to initiate the lysis of those cells to which it is sensitized. This sequence involves recognition of foreign antigens as the requisite first step, and not all tumor cells express immunogenic antigens. Tumor antigenicity appears to be correlated with differentiation. For example, several studies have suggested that T cells recognize well-differentiated tumor cells that express major histocompatibility class 1 (MHC-1) antigens; however, they are unable to recognize poorly differentiated cells that do not present this antigen on their surfaces (Gidlund et al, 1981; Racz et al, 1989; Stern et al, 1980). Also, the cells in any given tumor are antigenically heterogeneous, implying varied vulnerability to cytotoxicity mediated by T cells. Interestingly, cloned cells from metastases themselves are antigenically much more uniform. This implies that cells with high metastatic potential (ie, cells without antigens recognizable

to the immune system) exist in the parent tumor and it is these that survive the complicated metastatic process. The human immune system, in effect, weeds out the most "effective" tumor cells.

For years it has been recognized that head and neck cancer patients exhibit derangements of cellular immunity as evidenced by decreased cell-mediated response to skin testing (Brooks and Clifford, 1981; Lee, 1975; Maisel and Ogura, 1976). Additionally, nonspecific suppression of immune response is evident in malnourished patients; malnourishment is common in patients with head and neck cancer (Law et al, 1974), and a similar pattern is recognized with chronic alcohol and tobacco abuse (Lundy, 1975; Schuller and Chretien, 1978; Treves et al, 1981).

Tumors associated with a marked local inflammatory response around the primary site have decreased rates of cervical metastases and thus better prognoses. Such tumors also tend to be better differentiated and less infiltrative at their periphery. Poorly differentiated tumors with a greater infiltrative capacity are associated with minimal inflammatory response and poorer prognoses (Lane et al, 1961).

Regional lymph nodes are frequently reactive in response to nearby tumor. Not uncommonly, a surgeon finds that a clinically enlarged node that is suspected to be malignant is actually hyperplastic, implying regional immune system activation. There are data that address the issue of the prognostic significance of activated regional lymph nodes, and these generally suggest that there is a correlation. Inactivated, lymphocyte-depleted lymph nodes seem to be associated with a less favorable prognosis than are those that demonstrate reactive patterns (Berg and Huvos, 1973; Berlinger et al, 1976; Black et al, 1971; Carter, 1974; Ferlito, 1976). Other authors, however, have cautioned against using lymph node morphology to predict prognosis (Futrell et al, 1971; McGavran and Bauer, 1975). Furthermore, Batsakis (1979) points out that any morphologic features of significance are erased by radiation therapy.

These morphologic and clinical changes are crude assessment of a complex and dynamic process that occurs at the cellular level and which is probably critical in determining outcome. It is clear that T-cell mediated cytotoxicity is a major mechanism in killing tumor cells, especially when they are well differentiated. However, this mechanism cannot be activated if tumor cells have no recognizable surface antigens; thus, tumor cells escape detection and subsequent lysis. Recent work has focused on the role of natural killer (NK) cell activity. NK activity is attributed to several cell types, including T cells and lymphocytes (Fidler and Hart, 1982). NK activity is presumably a primitive defense mechanism because it does not recognize altered antigens, only the presence of "alien" cells and therefore it represents a second cell-mediated defense against tumor. It is of the greatest importance that NK activity is activated by a different mechanism than the one that activates T-cell cytotoxicity. There is speculation that these NK cells are the ones primarily involved with regulating the cells that are capable of metastatic spread, that is, those not recognized and destroyed by other immunologic mechanisms. In support of this, *in vitro* studies have shown that poorly differentiated tumors lacking MHC-1 antigens are sensitive to NK cell lysis, and well-differentiated tumors are not (Racz et al, 1989).

Analysis of NK activity in head and neck cancer patients suggests a strong correlation between metastatic disease (both nodal and distant) and decreased NK activity (Schantz and Ordoniez, 1987). No such correlation has been noted with local recurrence (Schantz and Poissobn, 1986). NK activity is also correlated with degree of in vivo tumor differentiation. Such activity is predictive of metastatic disease in patients with moderate to poorly differentiated tumors, but not in well differentiated ones (Racz et al, 1989; Schantz and Poisson, 1986). Additional studies of NK cell activity in regional nodes of cancer patients reveal that nodes with metastatic deposits have decreased NK activity when compared to normal nodes from the same patient. Furthermore, there is no difference in NK activity between lymph nodes from normal controls and lymph nodes from cancer patients that do not contain metastasis (Kessler et al, 1988; Wustrow and Zenner, 1985). Interestingly, patients exhibiting extracapsular nodal spread or tumor infiltrating the neck have elevated levels of NK activity (Schantz and Poisson, 1986). Whether deficient NK cell activity is the primary defect that allows tumor cells to "escape" immunologic surveillance and so cause metastatic spread is not clear. It may be that the location of the presentation of tumor cells to the immune system makes a difference, and that the presence of malignancy in the stroma of the neck is a better stimulus to NK cells than tumor presence in a lymph node. Other factors, such as levels of prostaglandins, undoubtedly modulate the immune response (Mandell-Brown et al, 1986). So far we have only provocative clues to the factors that control tumor spread and much remains to be learned in this fascinating area of investigation.

Although it is intuitively obvious that the regional lymph nodes are crucial in head and neck cancer, what exactly happens at this level is not clear. Are the nodes simply "filters", or are they responsible for initiating the immune response to tumor, especially when antigenicity is low? Disturbing questions have been raised about the importance of the regional nodes to systemic immunity, and, inevitably, about the effects of treatment of the nodes on host immune response. Crile (1969) was the first to suggest that reactive regional nodes in breast cancer patients should not be removed because they granted a higher level of systemic immunity and resistance to metastasis. There is work in the transplant literature that suggests that regional lymphadenectomy alone alters systemic host resistance (Flannery et al, 1973). Whether this is applicable to human neoplasms is not known. Temporary postoperative depression of T- and B-cell function is well documented, and the intensity and duration of the depression are related to preoperative immunocompetence, length of surgery, and transfusion (Berenbaum et al, 1973; Jubert et al, 1973; Slade et al, 1975). It is also known that surgical treatment of neck nodes alters drainage and that this can result in subsequent regional metastases in unusual locations (Northrup et al, 1972). Finally, chemotherapy and radiation therapy each have a clear impact on systemic and regional lymphocytes. Thus, there are concerns that immune function is being altered by these treatment modalities.

On the other hand, contemporary data do not support this theoretic concern. The data of Vikram et al (1980) compare a group of patients with stage III and IV ADSC treated with combined surgery and full-course radiation therapy to a similar group treated with surgery alone. With regard to distant metastasis, the rate is essentially the same in both groups (20%), despite a substantial enhancement in disease control in the group that received combined therapy. Interestingly, however, the incidence of second primary occurrence increased significantly in the combined-therapy group. Whether or not this reflects a manifestation of alteration of the immune system is unknown.

Traditional teaching holds that carcinomas are spread by the lymphatics whereas mesenchymal tumors are spread by the bloodstream. Lymphatic and vascular systems, however, have numerous connections (del Regato, 1977), and studies have shown, at least experimentally, that disseminating tumor cells pass from one system to another (Fisher and Fisher, 1966; Zeiderman and Buss, 1954). The two systems are inseparable, and the division into lymphatic spread and hematogenous spread is somewhat arbitrary and used for the sake of simplicity. The mere presence of tumor cells in the circulation does not constitute a metastasis (Salsbury, 1975) because most cells entering the bloodstream are destroyed rapidly (Butler and Gulliano, 1975; Fidler, 1970). The probability of metastasis, however, does increase in direct proportion to the number of tumor cells entering the blood stream. In general, larger primary tumors are associated with increased numbers of blood-borne tumor cells (Sugarbaker, 1979). Perhaps this fact is related partly to the more extensive necrosis and hemorrhage usually associated with large lesions. Not surprisingly, then, in ADSC a higher rate of regional metastasis is associated with more advanced primary disease (Spiro and Strong, 1971), and there is a significant incidence of distant blood-borne metastasis.

Natural History of Neck Disease

Contemporary methods approach both the primary tumor and the neck in a single treatment plan. This requires an in-depth knowledge of patterns of spread as well as of those factors that influence local, regional, and systemic control. We have previously discussed details of lymphatic drainage of various sites in the head and neck, and these patterns are consistent. The probability of lymphatic spread, whether subclinical or obvious, is dictated by a number of factors, including the site, size, and degree of differentiation of the primary tumor, perineural and perivascular invasion, inflammatory response, and possibly cellular DNA content (ploidy).

Primary site

Spread is dictated by local anatomy, and each site has its own pattern. The probability of lymphatic spread is related to the abundance of capillary lymphatics in the given primary site. Areas with the most dense capillary network of lymphatics are the nasopharynx, the tongue, and the hypopharynx, and the rate at which neoplasms metastasize from them, as expected, is high (Pietrantonio and Fior, 1958). On the other hand, areas such as the laryngeal glottis and the paranasal sinuses have a sparse lymphatic network and demonstrate a proportionately lower rate of metastasis when invaded by neoplasm.

The probability of metastatic disease occurring at any given primary site has been determined both by studying the incidence of positive nodes found in elective neck dissection specimens and by calculating the percentage of N0 necks that, left untreated, become positive (assuming, of course, control of the primary). These studies have been laboriously compiled by Mendenhall et al (1980). These statistics have been outlined to show (1) the percentage of each type of head and neck primary tumor that appears with positive clinical neck disease; (2) the percentage of each type of such tumors that appear as N0 but after elective neck dissection turn out to be histologically positive; and (3) the percentage of each type of primary tumor that presents as N0 and, when left untreated, becomes clinically positive. These data, plus the bibliographic references used in this exhaustive study, are listed in Table 90-1.

Primary tumor size

Another important factor in the evolution of cervical metastasis is the size of the primary tumor. Lindberg (1972) compiled an analysis of each site relative to primary stage in a revealing study of 2044 patients (Table 90-2). In many primary sites such as the oral tongue, floor of mouth, retromolar trigone/anterior tonsillar pillar, soft palate, oropharyngeal walls, and larynx, small primary lesions were associated with a high incidence of N0 necks and, except in the supraglottic larynx, a low percentage of advanced neck disease. On the other hand, primary sites such as the tonsillar fossa, base of tongue, hypopharynx, and nasopharynx had relatively low incidences of N0 necks even with small primaries, and these same sites were distinguished by a rather large percentage of advanced neck disease, even in early primary stages. These more ominous areas often develop tumors in which the first clinical sign is the development of a neck node. According to Lindberg's data, the correlation of the T stage with the N stage is common to all sites; that is, the more advanced the primary tumor, the higher the percentage of patients with cervical metastasis.

Biller et al (1971) compiled other data about the supraglottic larynx regarding the probability of metastasis in relationship to T stage. These figures were similar to Lindberg's in the supraglottic larynx:

T Stage	Number	Metastases (%)
T1	51	31
T2	63	39
T3	21	52
T4	8	75

Total: 143

Using current staging methods for mobile tongue lesions, Teichgracher and Clairmont (1984) also analyzed T stage in predicting N stage. Their data essentially agreed with the earlier data of both Lindberg (1972) and Spiro et al (1974).

Current investigations suggest a strong correlation between tumor thickness and regional node involvement. This has been evaluated only for oral cavity tumors. Mohit-Tabatabai et al (1986) found that lesions < 1.5 mm thick developed cervical metastasis in < 2% of cases. This incidence increased to 33% for lesions 1.6 to 3.5 mm in thickness, and jumped to 60% for lesions > 3.5 mm ($p < 0.001$). Spiro et al (1986) found a high risk (40%) of nodal metastasis if tumor thickness exceeded 2 mm. These data are supported by Moore et al (1986). Frierson and Cooper (1986) found a similar pattern for the lower lip although the significant thickness was determined to be 6 mm. However, Close et al (1987) could not demonstrate that tumor thickness was correlated to neck disease.

The issue of tumor thickness and depth of invasion demonstrates a significant weakness of our current staging methods for primary tumors. The data cited suggest that a T2 primary that is only 2 mm thick is of less concern than a T1 that is 10 mm deep because the incidence of regional metastasis and its impact on survival should be much lower. Current staging may well underestimate the more deeply invasive T1 tumor and ascribe too much

importance to the surface dimensions of a very superficial T2 lesion. Essentially, failure to think of lesions in a three-dimensional way leads to inaccurate staging.

Degree of differentiation of tumor

Many studies have correlated the risk of cervical metastasis with the grade of tumor at the primary site. The more poorly differentiated the tumor is, the more aggressive it is believed to be, and the greater the risk of regional metastasis. McGavran et al (1961) found a statistically significant incidence of metastasis in high-grade carcinomas of the larynx. Mendelsohn et al (1976), Lund et al (1975), and Frierson and Cooper (1986) found the same correlation for tongue cancer. Close et al (1987) and Jakobsson et al (1973) demonstrated a higher incidence of node involvement in moderate to poorly differentiated cancers of the oral cavity.

Perineural invasion

The information regarding perineural invasion is conflicting. Several investigators found strong correlation between perineural invasion at the primary site and cervical node metastasis (Frierson and Cooper, 1986; Goepfert et al, 1984). Close et al (1987), however, found no such trend, and Soo et al (1986) could only correlate this characteristic with subsequent recurrence (Fig. 90-5).

Perivascular invasion

In a retrospective review of 43 patients with carcinoma of the oral cavity and oropharynx, Close et al (1987) concluded that intravascular invasion by tumor at the primary site is the single most important pathologic predictor of regional nodal disease ($p < 0.0009$). This finding was supported by studies by Crissman et al (1984), Poleksic and Kalwaic (1978), and Rasgon et al (1989). Close also noted that when vascular invasion was limited to a single vessel, nodal involvement was unlikely; however, extensive invasion of vessels was associated with a very high probability of nodal metastasis. Presumably, invasion into vascular structures is a result of more aggressive tumor behavior; also, it results in the tumor "emboli" necessary to create metastasis (Fig. 90-6).

Inflammatory response

Inflammatory infiltrate at the primary site is another factor and its significance is not universally accepted although most studies support the concept that a weak local inflammatory response is correlated with risk of neck metastasis (Frierson and Cooper, 1986; Mohit-Tabatabai et al, 1986; Rasgon et al, 1989; Van Nagell et al, 1978). Patients who are able to mount a significant reaction at the primary site tend to have a lower incidence of metastasis (Fig. 90-7).

Tumor DNA content

Flow cytometric analysis of tumor cellular DNA content has been used in evaluating various solid tumors for the last decade (Williams and Daly, 1990). Normal or diploid cells contain a constant amount of DNA. Malignant cells are known to contain greater amounts of

DNA than normal, and this is referred to as *aneuploidy*. Degrees of aneuploidy can be quantified and the cell cycle phase of the tumor cells can be determined. These measurements of cellular DNA have been shown to have significant prognostic significance in cancers of the breast (Winchester et al, 1990) and colon (Quirke et al, 1986; Sciallero et al, 1988; van der Ingh et al, 1985; Williams and Daly, 1990). Less is known about the significance of ploidy status in ADSC, and the available information is conflicting. Kokal et al (1987) evaluated 76 patients with squamous carcinoma of the oral cavity and found that local recurrence was significantly higher in the aneuploid group as compared with the diploid group. However, Farrar et al (1989) examined 60 patients with localized tongue carcinomas and found no correlation between aneuploid status and recurrence, metastasis, or survival. It appears that decreasing histologic differentiation and increasing tumor size are correlated with aneuploidy (Hemmer et al, 1990), and this may account for the variation in rates of aneuploidy found in unselected series of tumors as well as the confusion about the significance of these data. In addition, aneuploidy rate may vary by site (Holm, 1982). Information is preliminary at this time, and only future prospective studies will define the role of cytometry of DNA content as a prognostic indicator.

The grave consequences of nodal metastases cannot be overstated. Schuller et al (1980) and Spiro et al (1974) have effectively made the point that the single most important factor in determining survival in patients with ADSC is the presence or absence of lymph node metastasis. Spiro demonstrated that once nodal metastasis was documented histologically, whether the patient had clinically negative or palpable nodes, and whether the nodes were solitary, multiple, or even bilateral, the cure rates were uniformly decreased by 50%. Other data (Cady and Catlin, 1969; Harrold, 1971; O'Brien and Catlin, 1965) show decreased survival rates correlated to the presence of cervical metastasis. Recent information analyzing contemporary stage III and IV survival data compared to historic data from a similar population sample suggests that although cervical metastasis still affects survival, it does so to a lesser degree than before the routine use of combined surgical and radiation treatment (Vikram et al, 1980). This probably attests to the effectiveness of combined treatment modalities.

Extracapsular spread

Data compiled by Snow et al (1982), Johnson et al (1981, 1985) and Carter et al (1987) regarding both the frequency of and the poor prognosis associated with extracapsular spread (ECS) are striking. They have shown that ECS is commonly encountered. Even in small lymph nodes its incidence approaches 25%, and overall the incidence of histologically documented ECS is nearly 60% in patients with cervical metastasis. This is significant because the presence of ECS apparently decreased survival by 50% and also decreased the disease-free interval from 18 months to 6 months overall in this study.

The high scores of failure to control disease in the neck with surgery alone (Strong et al, 1966) probably reflect the high rate of ECS that has since been demonstrated. This is a strong argument for the use of postoperative radiation therapy when any disease is found in the cervical lymph nodes.

Sites of nodal involvement

Various studies show that survival rate decreases with positive nodes at multiple rather than single sites (Schuller et al, 1980; Sessions, 1976; Spiro et al, 1974). In addition, as nodal metastasis progressively involves lower levels of the neck that are more remote from the primary site, the prognosis steadily worsens (Spiro et al, 1974). Posterior triangle involvement is associated with the worst prognosis. Finally, noncontiguous metastasis is associated with an even worse prognosis. The most extreme example of noncontiguous cervical metastasis is at the contralateral site, at best an ominous occurrence.

Contralaterality of metastasis

Any discussion of the probability of metastasis must address the phenomenon of contralaterality of metastasis. In general lesions in well-lateralized primary sites (piriform sinus, lateral floor of mouth) tend to metastasize to the ipsilateral side of the neck, and lesions in a more midline position (supraglottic larynx, base of tongue, posterior pharyngeal wall) demonstrate a higher incidence of bilateral metastasis. In the more midline lesions, the initial spread tends to be toward the side with the predominance of tumor. These generalizations, however, are fraught with exceptions; any lesion with ipsilateral metastasis creates a risk for contralateral disease, especially if the ipsilateral nodes are multiple or large (Million and Cassissi, 1984). Biller et al (1971) analyzed contralateral metastasis in the larynx, base of tongue, vallecula, piriform sinus, and posterior pharyngeal wall. These data reveal that in the supraglottic larynx, the incidence of contralateral metastasis, whether at the time of initial treatment or delayed, is 13% to 50%, depending on the T stage. Base-of-tongue data is similar, whereas piriform sinus and transglottic larynx data demonstrate a much lower incidence of contralateral disease, despite a high ipsilateral rate of metastasis. Leipzig et al (1982) reported an overall incidence of contralateral metastasis of 30% in tongue carcinoma in all stages, suggesting that even in smaller lesions located in either the anterior or posterior tongue, management of the contralateral neck should be considered.

Despite the emphasis that is consistently placed on the bilaterality of lymphatic drainage from the tongue base, little attention has been given to this anatomic fact in the more anterior aspects of the tongue. Diagrams adapted from the original work of Jamison and Dobson (Gray, 1954) clearly point out that, except for the most lateral part of the mobile tongue, there are ample lymphatic channels that drain to either side of the neck (Fig. 90-8). Johnson et al (1980), Leipzig et al (1982), and others (Drroulias and Whitehurst, 1976) have provided data that clinically reflect this phenomenon. Spiro et al (1974) studied 1069 patients with squamous carcinoma of the oral cavity and oropharynx, of whom 83 patients (8.5%) had bilateral cervical metastasis.

In patients with laterally oriented primary lesions, the initial appearance of cervical adenopathy is rarely contralateral; when it is, the development of ipsilateral nodal disease usually follows, regardless of the state of the primary tumor. Thus contralaterality is almost always a manifestation of bilaterality of metastasis. Isolated contralateral metastasis can occur, but in our experience, does so rarely. When contralateral metastasis does occur from well-lateralized lesions, the subdiaphragmatic node is most often involved but it may be bypassed, with the midjugular or low jugular nodes affected next (Million and Cassissi, 1984).

Studies recognize that surgical treatment and/or radiation therapy can alter lymphatic flow (Fisch, 1968; Welsh and Welsh, 1966) and may affect contralateral metastasis by shunt lymph flow through the submental and submandibular lymphatics. Significantly, Biller et al (1971) found that a substantial number of patients who had ipsilateral histologically negative nodes at the time of neck dissection developed delayed contralateral neck disease. Skolnick et al (1980) revealed that the rate of failure following radical neck dissection in the contralateral neck was higher in patients who had histologically negative necks than in those who had positive necks. This suggests that neck dissection may have a shunting effect on the cells to the contralateral neck.

The possible effect that ipsilateral neck treatment has on inducing contralateral disease is disconcerting and should influence the physician's planning of the prophylactic or elective treatment of the N0 contralateral neck in patients with clinically positive (N+) ipsilateral necks. This circumstance would seem to indicate bilateral rather than only unilateral postoperative radiation therapy.

Advanced neck disease: the "fixed" neck mass

The adherency of nodes to adjacent cervical tissues remains a formidable problem. There is a distinction between decreased mobility of a neck mass due to bulk and actual fixation to neck structures. Previously only a subjective assessment, the issue of what structures a malignant mass involves can now be evaluated with CT scans, arteriography, or MRI. In general, true fixation is an ominous finding; Spiro et al (1974) indicate that the outlook for survival is greatly decreased once "fixation" is noted. These adherent neck masses are generally the larger ones and their poor prognosis is recognized in the revised staging of neck disease (AJC, 1988). The designation N3 now only applies to massive adenopathy, and smaller multiple contralateral or bilateral nodes are all considered subsets of N2 because of their more favorable prognosis with current treatment. Issues of resectability are difficult to quantify because they depend on the structures to which the mass is attached, the philosophy of the individual surgeon, and the patient's wishes. All decisions must be tempered with consideration of surgical morbidity and the overall poor prognosis. This point is well made by Santos et al (1975) who showed that in patients with fixation of nodes at the time of neck dissection, the incidence of recurrent neck disease and distant metastasis was very high and survival was very poor.

A primary or recurrent tumor that involves the carotid artery is a particularly difficult problem. Until the 1970s tumor adherent to the carotid artery was widely regarded as unresectable. A more aggressive approach to resecting the carotid with the tumor yielded disappointing results (Hiranandani, 1971; Kennedy et al, 1977; Santos et al, 1975) with neck recurrence rates of 45% to 50%, distant metastatic rates of 60% to 70% and only a 5% to 7% 5-year survival rate. In addition, surgical morbidity and mortality from stroke was very high (up to 45%) prior to the employment of techniques involving reconstruction of the carotid artery that substantially reduced mortality and morbidity. Fee et al (1983) have reported the use of I-125 implants intraoperatively in combination with aggressive treatment of carotid disease, and have increased local control to almost 70%. However, the distant metastatic rate is still 50%, and there has been a disappointingly poor survival rate that is unchanged from older reports. The prognosis for tumor attached to the carotid artery is very poor; improvement in survival rates will probably require the development of effective adjuvant

chemotherapy.

Management

The basic therapeutic approach to metastatic cervical disease is currently in a state of flux. Such traditional concepts as the need for en bloc and continuity resections are thought to be of uncertain value. A basic premise in modern head and neck oncology is complete acceptance of the role of radiation therapy combined with surgical extirpation of stage III and IV disease. The recent literature emphasizes substantial progress in our ability to control head and neck disease, but the percentage of patients who die of distant metastasis has not improved (Vikram et al, 1984a to 1984d); the opposite may even be true (Goepfert, 1984).

Distant metastasis apparently has changed in its patterns of occurrence. Using historic comparisons from the same institution, Vikram (1984) has pointed out that before postoperative radiation therapy was routinely used in stage III and IV head and neck carcinomas, a high percentage of patients who developed distant metastasis had failure at the primary site; by contrast, in the more contemporary analysis, more than 50% of the patients with distant metastases were free of disease in the head and neck when distant metastasis appeared. This change in the pattern of presentation reflects improvement of local and regional control. Although the use of combination therapy has enhanced overall survival, essentially the natural history of the disease process is being altered and the numbers in Vikram's analysis support this statement by showing an alarming increase in the incidence of second primary tumors in the contemporary population sample.

Until methods are found to attack systemic disease and also to protect the high-risk patient from second primary neoplasms, it appears that advanced head and neck disease will not be greatly affected. The major controversies regarding neck management, however, do not involve this type of disease, but instead focus on how the N0 neck should be approached.

Clinically negative neck

Widely divergent opinions exist on how to manage the N0 neck. There seems to be increasing awareness of the neck's importance to overall survival; however, many oncologists maintain that the N0 neck has been surgically overtreated for some time. Before contemporary radiation therapy methods and the more recently accepted modifications of classic neck dissection techniques, treatment was relatively straightforward; if clinical neck disease or a reasonable probability of neck metastasis existed, a standard radical neck dissection was done. Now, even with its acceptable level of morbidity, this procedure is almost never used prophylactically. Instead, various modified techniques and/or radiation therapy are used when the tumor burden is thought to be minimal (N0). The knowledge that radiation therapy, elective neck dissection, or combined treatment are equal in their ability to cure or suppress the development of occult metastases in regional lymphatics from any given primary tumor has led to a more deliberate and restrained approach to the clinically negative neck (Fletcher, 1972; Million and Cassisi, 1984). The understandable urge to leave all such necks untreated and to wait for the appearance of clinical disease, however, should be discouraged for several reasons:

1. The development of clinical neck disease puts these patients at higher risk for distant metastasis.

2. The failure rate in neck initially N0 that become N+ before treatment is undertaken may be increased (Spiro et al, 1974), and the survival rate may be decreased.

3. Providing the clinical follow-up necessary to detect the earliest conversion of a neck from N0 to N+ is impossible, and valuable time is lost in instituting treatment.

Physicians, then, are faced with the dilemma of which N0 necks to treat prophylactically and which to observe; they must rely on the data relating to the probability of metastasis from various primary tumor sites and also on information about histomorphologic features of the primary tumor. Even though the ready use of radiation therapy or modified neck dissection may lead to overtreatment in some N0 patients, we support a liberal approach. T stage and probability of cervical metastasis are directly related in most lesions (Spiro et al, 1974; Lindberg, 1972), and we arbitrarily believe that if a probability of metastasis greater than 15% exists in any given lesion, the neck should be treated prophylactically. For example, such primary sites as the tongue base, hypopharynx, and pharyngeal wall have a high overall incidence of metastasis at all T stages, and data analysis shows a substantial probability of histologic or subclinical metastasis for lesions in this group. The supraglottic larynx, oral tongue, faucial arch, and tonsil fossae are associated with a lesser percentage of overall metastasis, but in all except very small lesions of these structures the eventual metastatic rate is sufficient to warrant neck management. The small lesion affecting the lip or gingiva usually can be managed with observation of the neck, although some suggest a more aggressive approach to lip cancer (Marshall and Edgerton, 1977). Clinical judgment is also essential in determining whether or not a neck can be adequately evaluated. The short, heavy neck is sometimes impossible to evaluate accurately. CT scan or MRI evidence of possible involved nodes must be considered. Histomorphologic features of primary tumors are clearly important prognostic indicators, and those that are available are tumor grade and size and possibly the degree of peritumor inflammatory response. The thickness of the primary as a reflection of size is probably important and may impact on surgical decision making. Finally, the patient's ability to return for follow-up visits can affect the decision.

Once the decision is made to treat the neck therapeutically, even the choice of what to do is controversial. We accept the accuracy of the literature indicating the ability of radiation therapy to control or cure subclinical (histologic) cervical metastasis in most cases (Fletcher, 1972; Mendenhall et al, 1984). We also believe that certain modifications of the classic neck dissection that spare the internal jugular vein, sternocleidomastoid muscle, and spinal accessory nerve are acceptable methods for analyzing and staging the neck. Furthermore, selective procedures that remove only those nodes that are at highest risk for metastasis are being used more frequently, and there is growing support for their appropriateness in this setting. The most frequently used selective procedure is the supraomohyoid dissection advocated by Medina and Byers (1989). They have accumulated data that demonstrate the oncologic soundness of this procedure in carefully selected circumstances, with neck recurrence rates that compare with those obtained with the standard radical neck dissection. Byers (1985, 1988) has studied a large series of patients undergoing various selective procedures and confirmed their usefulness in certain patients.

How one manages the primary site has a major influence on management of the N0 neck. For example, if the primary site is to be radiated, we recommend including the neck as well. On the other hand, if surgery is used to treat the primary lesion, a selective neck dissection is often done on one or both sides. Because we continue to question the therapeutic effectiveness of the various neck dissections, we think that surgery should be followed by radiation therapy if histologic disease is found in the neck specimen. We view all selective neck dissections as staging procedures and believe they are especially helpful in evaluating the neck in treating lesions of the supraglottic larynx and oral cavity. On the other hand, we question the thoroughness of such procedures in harvesting the potential nodal sites that are associated with hypopharyngeal, transglottic laryngeal, and oropharyngeal lesions; a special effort must be made to incorporate the lower neck because it is at high risk in these lesions.

Because the probability of metastasis in transglottic, hypopharyngeal, and pharyngeal wall lesions is quite high, we routinely treat the neck, regardless of T stage. When the primary lesion is treated surgically, neck dissections are warranted, even if these lesions appear with N0 necks. If the primary site in this group of lesions is to be radiated, the neck(s) are included.

Clinically positive neck

The management plan for the neck with palpable adenopathy depends on several factors:

1. Location of the adenopathy
2. Stage of the cervical disease
3. Location of the primary site
4. The presence or absence of systemic metastasis.

The surgeon should realize that incurability is not necessarily a contraindication to treatment of head and neck disease. We believe that locoregional control is valuable, even though distant metastasis is present. In general, however, when treatment failure is inevitable because of recognized distant metastasis, a less radical approach to the head and neck area is undertaken. Radiation therapy (RT) often affords a degree of control that benefits the patient by allowing a less agonizing death. As the sole treatment modality RT is not likely to cure a large tumor burden (Wizenberg et al, 1972) because it does not effectively control lymph nodes greater than 3 cm in a substantial percentage of patients.

N1 neck

When the primary site is known, distant metastasis is not suspected, and the neck is staged N1, the usual approach is resection of the primary tumor in conjunction with a neck dissection. Postoperative RT usually is administered to the primary site and to both sides of the neck if the adenopathy is histologically positive. Some authors do not recommend postoperative RT if only solitary nodal metastasis exists (Suen and Wetmore, 1981). In our experience, however, methods that do not use combination therapy in this case are associated

with a significantly higher percentage of failure. Strong (1969) reported that after radical neck dissection, recurrences in the dissected neck occurred in 37% of the patients with metastasis at one cervical level and in 71% of those with spread to many levels. Other reports have shown similar associations (Henschke et al, 1964; Strong et al, 1966). On the other hand, DeSanto et al (1982) studied a group of ADSC patients with presumed or likely neck disease who had radical neck dissection alone; they showed a recurrence rate of 7.5%, 20%, and 37% respectively for stage N0, N1, and N2. When this group was compared to a similar one who had received RT in addition to neck dissection, the authors concluded that RT as an adjunct to surgery did not alter treatment results significantly. In effect, they questioned the premise that more treatment is better. These data, however, do not account for control or lack of control of primary disease. Most oncologists today believe that in patients with N1 necks who have histologic confirmation of the clinical staging, RT along with surgery is preferable over either modality alone (O'Brien et al, 1987). Because clinical staging has a consistent inaccuracy factor, histologic confirmation is especially important (DeSanto et al, 1982; Sako, 1964; Spiro et al, 1974).

With regard to RT to the opposite side of the neck, certain primary lesions have a higher probability of contralateral metastasis than others. Besides this natural risk factor, the effect ipsilateral neck surgery has on the shunting of tumor cells to the contralateral side is uncertain. We believe that if histologic confirmation of ipsilateral cervical metastasis is made, the postoperative RT employed should include the contralateral neck.

The scope of this chapter does not allow a comparison of the relative merits of the various types of neck dissection. A variety of techniques of lesser magnitude than the traditional radical neck dissection are in use, and the terminology has become confusing and imprecise. Such terms as *functional*, *modified*, *modified radical*, *supraomohyoid*, *upper neck dissection*, and others are widely used in an unstandardized and confusing manner, making it impossible to compare data from one institution to another. The Committee on Head and Neck Oncology of the American Academy of Otolaryngology-Head and Neck Surgery has recently adopted and recommended a standardized method for categorizing these operations (Robbins et al, 1991). While there will always be surgeons who will disagree with any such list, it is hoped that the following will serve as a method of naming and classifying the variety of neck dissection operations in use today, thus allowing standardization of terminology with improved reporting and data evaluation:

1. Radical neck dissection
2. Modified radical neck dissection
3. Selective neck dissection
 - a. Supraomohyoid neck dissection
 - b. Posterolateral neck dissection
 - c. Lateral neck dissection
 - d. Anterior neck dissection

4. Extended neck dissection.

Radical neck dissection refers to the removal of all ipsilateral cervical lymph nodal groups extending from the inferior border of the mandible superiorly to the clavicle inferiorly and from the lateral border of the sternohyoid muscle, hyoid bone, and contralateral anterior belly of the digastric muscle anteriorly to the anterior border of the trapezius muscle posteriorly. Included are all lymph nodes from level I through V. The spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle are also removed. It does not include removal of the suboccipital, periparotid, buccal, retropharyngeal, or paratracheal nodes.

Modified radical neck dissection refers to the excision of all lymph nodes routinely removed by the radical neck dissection while preserving one or more nonlymphatic structures: spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle. The structure(s) preserved should be specifically named, for example, "modified radical neck dissection with preservation of the spinal accessory nerve".

Selective neck dissection refers to any type of cervical lymphadenectomy where there is preservation of one or more lymph node groups removed by the radical neck dissection. Four subtypes are recognized:

1. **Supraomohyoid** neck dissection refers to the removal of lymph nodes contained in the submental and submandibular triangles (level I), the upper jugular nodes (level II), and the midjugular lymph nodes (level III). The posterior limit of the dissection is marked by the cutaneous branches of the cervical plexus and the posterior border of the sternocleidomastoid muscle. The inferior limit is the superior belly of the omohyoid muscle where it crosses the internal jugular vein.

2. **Posterolateral** neck dissection refers to the removal of the suboccipital lymph nodes, retroauricular lymph nodes, upper, middle, and lower jugular lymph nodes (levels II, III, and IV), and the nodes of the posterior triangle (level V). This procedure is most commonly used to remove nodal disease metastatic from cutaneous melanoma of the posterior scalp and neck.

3. **Lateral** neck dissection refers to the removal of the upper, middle, and lower jugular lymph nodes (levels II, III, and IV). Anatomically these groups are located in the lateral compartment of the neck.

4. **Anterior** neck dissection refers to the removal of lymph nodes surrounding the visceral structures of the anterior neck. These lymph nodes include the pretracheal and paratracheal as well as the precricoid (Delphian) nodes. The superior limit of dissection is the hyoid bone, the inferior limit is the suprasternal notch, and the lateral limits are the common carotid arteries.

Other variations of neck dissection in which there is preservation of lymph node groups should be designated as a selective neck dissection with the specific lymph node groups removed listed individually. In all selective dissections, the spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle are routinely preserved. If one or more of these are removed, this should be stated in the procedure title.

Extended radical neck dissection refers to the removal of one or more additional lymph node groups and/or non-lymphatic structures not encompassed by a radical neck dissection, such as the parapharyngeal, superior mediastinal, or paratracheal nodes; the carotid artery; the hypoglossal or vagus nerves; and the paraspinal muscles.

In general we limit selective neck dissections to N0 necks, and use the modified radical neck dissection for the N1 neck. However, when a solitary node occurs in the middle to upper neck and the primary site is not hypopharyngeal or transglottic laryngeal, we sometimes use a selective neck dissection.

The surgeon should not think that lymph nodes associated with the spinal accessory nerve exist only in the posterior cervical triangle (level V); the proximal nodes of this chain are virtually subdiaphragmatic and thus are anterior cervical or level II nodes. The upper part of level II poses special problems, and when a nodal mass lies adjacent to the spinal accessory nerve, we believe that modifications of classic methods are usually ill advised. Also, because most modified procedures do not deal adequately with the lower neck, we do not think these techniques should be used for oropharyngeal, hypopharyngeal, or transglottic laryngeal lesions unless they are adapted to include that area of the neck. Patients with a solitary mass in the upper neck in which the primary tumor is in the oral cavity occasionally are treated by primary resection in continuity with a neck dissection that includes levels I, II, and III. Because the submandibular triangle is rarely involved in primary laryngeal tumors (Feldman and Applebaum, 1977; Skolnick et al, 1976), we modify the classic methods to exclude this area from dissection.

N2 and more involved necks

N2a and N2b necks usually are treated in a straightforward fashion: composite resection of the primary tumor with a radical neck dissection. The surgery is followed by RT to both necks and the primary site. The various methods of altering the dose levels of radiation to different parts of the neck are discussed elsewhere and will not be detailed here. Suffice it to say that larger tumor burdens are treated with higher radiation levels. The N0 neck might be treated with 5000 to 5500 rad in 4 to 6 weeks (Million and Cassisi, 1984) for prophylactic control of presumed histologic neck disease; necks with N2-3 disease require substantially higher doses for control of disease. Shrinking field techniques and interstitial implantation are often useful in boosting those levels even higher. The principle of shrinking fields of radiation is used to minimize the effects of intense treatment on the outer perimeter of tissue where only histologic disease exists. In patients with node(s) adherent or even fixed to adjacent structures, RT can be administered preoperatively in an attempt to render the neck disease more resectable. The primary tumor site, of course, should be included in the RT in an attempt to make it less likely to reseed the neck. If the neck become operable following this method, the surgery is performed as usual, but with a guarded outlook for survival.

The N2c neck is managed with bilateral neck dissections, either both of a selective type, or with a radical neck dissection on the most involved side and a selective dissection on the contralateral side. If ligating both jugular veins is necessary to remove substantial contralateral adenopathy, we prefer staging the procedure to avoid the morbidity of postoperative edema or increased intracranial pressure (McGuire and McCabe, 1980; Mooney et al, 1969; Moore and Frazell, 1964; Rufino and MacComb, 1966; Sugarbaker and Wiley,

1951), even though it is known that alternate venous drainage occurs through the emissary, pterygoid, orbital, pharyngeal, and esophageal venous plexuses (Batson, 1944; Gius and Grier, 1950).

The management of the N3 neck must be tempered by the realization that, no matter that the treatment, the probability of cure is small. Every surgeon must develop a treatment philosophy that is in keeping with his or her personal feelings about the nature of life and death. Generally, an aggressive posture toward such neck disease is justified only when the primary site is controlled. We believe that distant metastasis is less of a contraindication to neck dissection that is uncontrolled primary cancer.

Summary

This discussion of the neck is an overview of a complex subject. The diversity of thinking and the burgeoning information available have made simple solutions impossible. Although we have attempted to avoid dogma when possible, scholarly analysis must culminate in a practical method the oncologist use to manage the problem at hand. We especially hope the gravity of cervical metastasis is more keenly appreciated. No matter how limited, cervical metastasis represents relatively advanced cancer, a fact that is reflected in the clinical staging system employed. Finally, present investigative endeavors will undoubtedly revolutionize our approach to these problems someday, but given the current state of knowledge and technology, our methods must continue to reflect traditional principles of diagnosis, surgery, and radiation therapy.