

FIFTH EDITION

Jatin Shah's  
**HEAD AND NECK**  
SURGERY AND ONCOLOGY

JATIN **SHAH** | SNEHAL **PATEL** | BHUVANESH **SINGH** | RICHARD **WONG**



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# HEAD AND NECK SURGERY AND ONCOLOGY

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JATIN SHAH'S HEAD AND NECK SURGERY AND ONCOLOGY, FIFTH EDITION

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# Preface

The stimulus for the senior author to write a book on head and neck surgery came from Prof. Arnold Maran, of Scotland, at an advanced course in head and neck surgery in Singapore in 1982. This led to the publication of the first edition of the book on operative surgery in two volumes in 1987 and 1990. The surgical techniques described in the first edition were the culmination of the influence of my surgical mentors in general surgery, Drs. Manubhai Patel and A.B. Kothari from Baroda, India, and in head and neck surgery, Drs. H. Randall Tollefsen, Hollon Farr, and Elliott Strong, from Memorial Hospital in New York. Subsequent editions of the book included diagnostic workup, perioperative care, radiology, pathology, adjuvant therapies such as radiation and chemotherapy, systemic therapy algorithms on selection of therapy, and finally outcomes of treatment. The book had a global influence in head and neck surgery as exemplified by its demand for multiple language translations. Over the years, the book has been translated and published in Portuguese, Spanish, Chinese, Greek, Russian, and Polish. We anticipate that this edition will also be available for translation into other languages. From a single author book for the first two editions, the book has been enriched with the addition of Drs. Snehal Patel, Bhuvanesh Singh, and Richard Wong as authors and editors in subsequent editions. The book has maintained its leadership position in the head and neck literature for over 30 years with three major book awards.

The fifth edition of this book continues to build its strength on the previous four editions and reflects the shifting paradigms in the understanding of the etiology and biological behavior of head and neck cancers and its contemporary management. Advancing knowledge as a result of new discoveries in basic sciences and advances in technology has led to better understanding of the natural history of these tumors. Thus a new edition becomes necessary to incorporate new information and changes to the practice patterns of the past. This edition has numerous new illustrations, data, therapeutic algorithms, and shifting paradigms in the management of several tumors. As with the previous editions, the mainstay of the book is based on description of diagnostic approaches, therapeutic decisions, surgical techniques, and results of treatment. However, there is a significant expansion on the discussion of selection of therapy and the rationale behind that. In addition, principles of radiation oncology, systemic therapy, maxillofacial prosthodontics, and dental oncology have been included. New to this edition are dedicated sections on nuances in pathology and diagnostic radiology, including three-dimensional imaging and computer-aided design/computer-aided manufacturing (CAD-CAM) technology in reconstruction. This edition also includes the newly published eighth edition of the staging system for head and neck cancer of the American Joint Committee on Cancer and the International Union Against Cancer. The diagnostic approaches, therapeutic decisions, and algorithmic thought process for selection of therapy

presented in this edition are a culmination of the experience of a multidisciplinary Disease Management Team (DMT), working together for over 20 years, at Memorial Sloan Kettering Cancer Center in New York. These philosophies and management strategies currently practiced by our faculty have evolved as a consensus of the multidisciplinary group of specialists working together as members of a cohesive team. Most of the outcomes presented in this book are generated from databases of patients treated by the members of the Head and Neck Disease Management Team at Memorial Sloan Kettering Cancer Center, but the treatment paradigms and information presented are relevant worldwide. Where appropriate we have added outcomes data from other global sources with stronger datasets.

Management of tumors of the head and neck has evolved into an increasingly complex specialty, demanding expertise and exposure not only in various surgical disciplines, but also in allied specialties such as radiation oncology, medical oncology, immunology, endocrinology, nuclear medicine, diagnostic radiology, pathology, and maxillofacial prosthodontics. The primary goal of contemporary management of neoplasms of the head and neck has historically been in achieving an improvement in survival. In addition, however, increasing emphasis is being placed on optimizing quality of life and limiting the sequela of treatment in the selection of treatment approaches.

The past two decades have seen major paradigm shifts in the management of tumors of the oropharynx and thyroid, as well as larynx and pharynx. The role of HPV in the genesis and management of oropharynx cancers has led to the development of new treatment strategies to minimize sequelae of treatment. Increasingly conservative approaches are applied to thyroid cancer with risk group stratification and less radical surgery and restricted use of radioactive iodine. Increasing use of minimally invasive and endoscopic laser resections has replaced open surgical procedures for conservation of voice. Failures of nonsurgical larynx preservation approaches have opened up new challenges for the surgeon in salvage surgery, with the goal of minimizing complications and improving survival. The chapter on systemic therapy includes the pharmacology of currently used drugs and evidence-based treatment recommendations from randomized clinical trials of chemotherapy, chemoradiotherapy, targeted therapy, and immunotherapy. Availability of intensity-modulated radiation therapy (IMRT) and proton beam radiation has completely changed the spectrum of radiotherapy techniques and the short- and long-term sequelae of external radiation therapy. The increasing use of IMRT and proton beam therapy is emphasized, and fundamental principles of radiation oncology essential for the surgeon are enumerated in the chapter on radiation therapy.

Surgery for neoplasms at the cranial base has reached a state of maturity, and long-term outcomes of open craniofacial surgery

have remained stable over the past three decades. In the past two decades, however, there has been increasing use of endonasal endoscopic surgery for anterior skull base lesions. These techniques are included in the current edition, and its applications and limitations are defined. Widespread application of microvascular free tissue transfer, routinely practiced for over 25 years, has matured to the state of finesse where functional restoration and aesthetic considerations are now prioritized in reconstructive techniques. These are amply demonstrated with the utility of local, regional, and free flaps. Introduction of CAD-CAM technology to facilitate accurate bone reconstruction is included with examples of mandible and maxillary reconstruction. The aesthetic impact of ablative surgical procedures has been a matter of concern for a long time. Refinements in surgical techniques have minimized the aesthetic sequelae of ablative surgery, as demonstrated in several operative procedures.

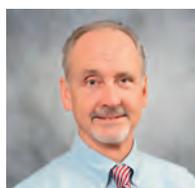
Surgical techniques demonstrated here with sequential operative photographs of actual operations performed by our faculty have evolved over the years and are continuously refined. The operative photographs taken by the authors maintain the “surgeon’s view” of the operative field. Where necessary, the operative photographs are supplemented with color artwork to demonstrate the anatomic relationships and enhance the technical details of a complex surgical field. The addition of Diagnostic Radiology and Pathology to each chapter complements the comprehensive coverage of each topic by presenting the selection of a particular imaging study and the salient histologic features of tumors.

It is impossible for a surgical book of this nature to remain “up to date” for a prolonged period. Undoubtedly, improved

understanding of the molecular mechanisms of oncogenesis; introduction of new technology in the operating room; newer modalities of imaging; newer techniques of delivering ionizing radiation; and the introduction of new drugs for chemotherapy, targeted therapy, and immunotherapy will change management strategies in the future. New surgical procedures, developed as a result of new technology, will be introduced to challenge old and established operations. The focus will be to minimize surgical trauma, preserve form and function, and leave minimal impact from surgical intervention. Similarly, complex multidisciplinary nonsurgical treatment programs will be aimed at reduction of morbidity, acute toxicity, and long-term sequelae of therapy in the future. The contents of this edition, though, reflect the state of the art in head and neck oncology and the craft of head and neck surgery as practiced today. The book is primarily aimed at the young head and neck surgeon who has completed basic surgical training in otolaryngology, general surgery, plastic surgery, or maxillofacial surgery. This book may also be of use to practicing surgeons in the specialty of head and neck surgery and oncology to become familiar with the current philosophies in the surgical management of tumors of the head and neck and the role of multidisciplinary approaches to certain tumors with an emphasis on optimizing oncologic and functional outcomes.

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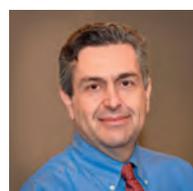
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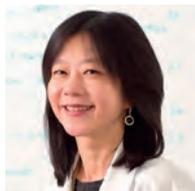
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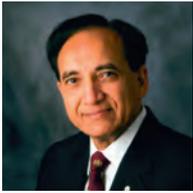
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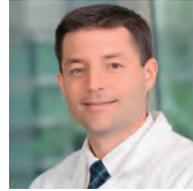
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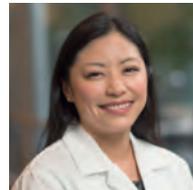
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We would like to express our sincere appreciation to our teachers, peers, and colleagues from whom we have learned and continue to learn. Every one of these individuals has contributed to our knowledge, understanding, and experience in head and neck surgery and oncology.

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**Jatin P. Shah**  
**Snehal G. Patel**  
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**Richard J. Wong**

*Dedicated to*

***Our Patients**, who have endured the suffering from cancer. These extraordinary individuals put their lives in our hands, in the quest for a life worth living. Their exemplary courage and resilience have taught us the meaning of perseverance and hope. They have a special place in our hearts.*

***Our Trainees**, whose thirst for knowledge has been a constant source of inspiration and encouragement for us to remain at the forefront of our specialty.*

*and*

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# Introduction



Anatomically and histologically, the head and neck region is one of the most diverse and complex parts of the human body. This diversity gives rise to a myriad of neoplastic processes with diverse behaviors and outcomes. The combination of anatomic and functional intricacies combined with the neoplastic spectrum necessitates a basic understanding of cancer biology, in addition to a working knowledge of all therapeutic options for delivering optimal care to patients with head and neck neoplasms. Moreover, the head and neck surgeon must appreciate and optimize the anatomic (esthetic) and physiologic (functional) impact of treatment. The vast majority of head and neck neoplasms arise from the mucosa of the upper aerodigestive tract, including the oral cavity, pharynx, larynx, nasal cavity, and sinuses, but neoplasms also can originate from the salivary glands, thyroid and parathyroid glands, soft tissue, bone, and skin. The most common malignant neoplasms of the head and neck are squamous cell carcinoma and papillary thyroid carcinoma. Salivary gland cancers and sarcomas of the soft tissue and bone are relatively infrequent.

Surgery has been the mainstay of therapy for tumors in the head and neck for more than a century. With the introduction of ionizing radiation in the latter half of the 20th century, radiotherapy became an important modality used either independently or in combination with chemotherapy as primary treatment or as an adjuvant to surgery. Although initially chemotherapy was used primarily as palliative treatment, it is now used as a component of curative treatment approaches when combined with radiation, producing significant improvements in outcomes in patients with squamous cell carcinomas of the head and neck at certain sites. Similarly, biological or targeted agents also are evolving to become part of standard therapy. Immunotherapy also has a role in the treatment of head and neck cancers and is expected to play an increasing role in the future. Accordingly, understanding and implementing multidisciplinary management strategies are cornerstones for achieving optimal therapeutic outcomes.

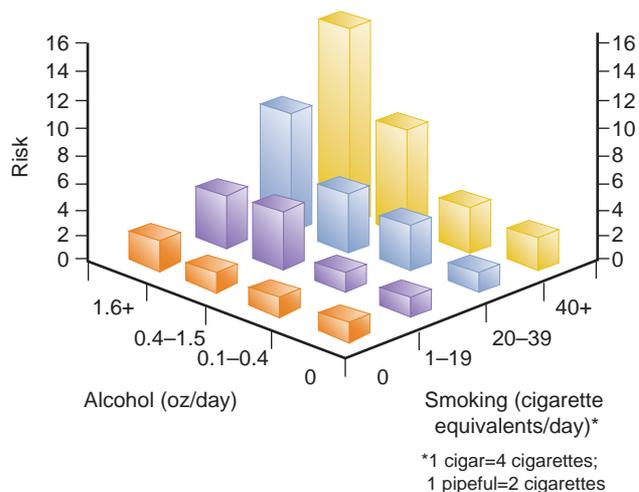
## ETIOLOGY

Most cancers result from a complex interplay between host and environmental factors. Environmental carcinogenic signals that promote the development of most human cancers remain ill-defined. In contrast, correlative studies have shown that alcohol and tobacco exposure are key causative factors for carcinomas of the mucosa of the upper aerodigestive tract. Head and neck cancers are typically tobacco-related cancers, with initial risk for the development of cancer and subsequent risk for additional primary cancers directly attributable to the

duration and intensity of tobacco use. Similarly, the chronic consumption of alcohol is estimated to increase the risk for upper aerodigestive tract cancers by two-fold to three-fold in a dose-dependent manner. Moreover, persons who both smoke and consume alcohol regularly have a multiplicative increase in risk that is up to 10 to 20 times higher than that of nonsmokers/nondrinkers, as reflected by a geometric rise in the incidence with increasing use of tobacco and increasing consumption of alcohol (Fig. 1.1). It is now well established that human papilloma virus (HPV) is associated with the development of oropharyngeal carcinomas. Genetic predisposition to the development of head and neck cancers in patients with Fanconi anemia is thought to be related to HPV infection. Similarly, immune-compromised patients with human immunodeficiency virus infection and patients undergoing chronic immunosuppressive treatment after organ transplantation have an increased risk for the development of head and neck cancers. Several other factors also are known to play a role in the pathogenesis of tumors in the head and neck region. For example, exposure to ionizing radiation increases the risk for the development of primary malignant tumors of the thyroid gland and salivary glands as well as for cancers of the skin, soft tissues, and bone. Similarly, Epstein-Barr virus infection is thought to promote the development of nasopharyngeal cancer.

## GLOBAL EPIDEMIOLOGY

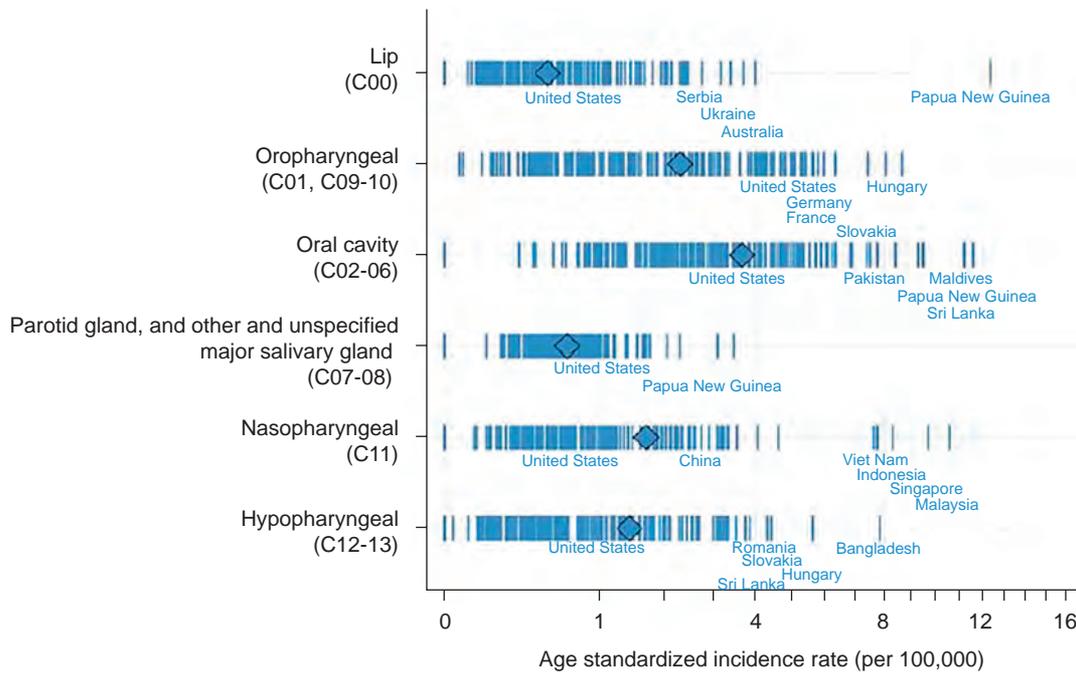
Head and neck cancers form the sixth most common cancer type and cause for cancer-related deaths worldwide. Significant



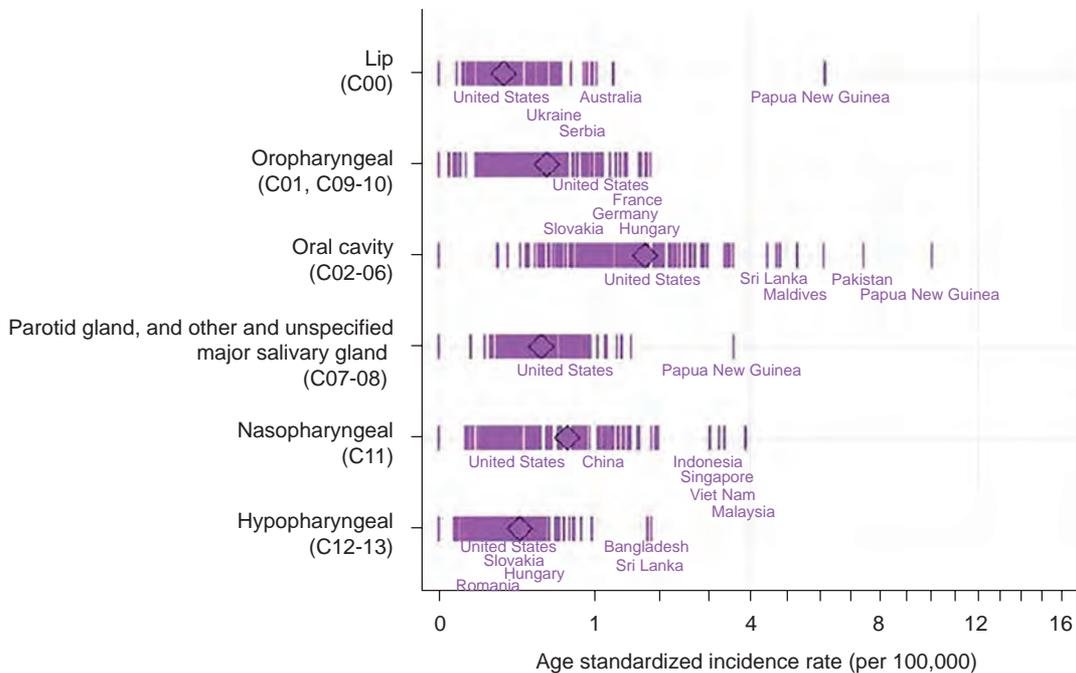
**Figure 1.1** Risk of development of squamous cell carcinoma of the head and neck with alcohol and tobacco consumption.

geographic variation exists in the incidence of squamous cell carcinomas of the head and neck. The highest incidence of carcinomas of the oral cavity and hypopharynx are reported in Southeast Asia, and particularly in India, where chewing tobacco with betel quid (“paan”) is a common practice. High rates of oral cancer are also reported in Brazil. The global incidence of squamous carcinomas of the oral cavity is shown in Figs. 1.2 and 1.3. Lip cancer had the highest incidence in Australia and central and eastern Europe, and rising incidence of oropharyngeal cancers in North America and Europe, especially in Hungary, Slovakia, Germany, and France, is associated with

alcohol use, tobacco smoking, and HPV infection. Nasopharyngeal cancers are most commonly reported from Northern Africa and Eastern and Southeast Asia, suggestive of genetic susceptibility combined with Epstein-Barr virus (EBV) infection. On the other hand, significantly higher rates of laryngeal and hypopharyngeal carcinomas are reported in Italy, France, and Spain as a consequence of higher rates of alcohol consumption and smoking. In the past two decades a rising incidence of head and neck cancer has been reported in Eastern European countries, particularly in Hungary; the exact reasons for this phenomenon remain unclear. The global incidence of lip, oral



**Figure 1.2** Age Standardized Incidence Rates (per 100,000) of Lip, Oral Cavity, and Pharyngeal Cancers by Subsite in 2012 Among Men. International Classification of Diseases 10<sup>th</sup> Revision codes are indicated for each subsite. (With permission from Shield KD, Ferlay J, Jemal A et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. *CA Cancer J Clin* 2017;67(1):51–64.)



**Figure 1.3** Age Standardized Incidence Rates (per 100,000) of Lip, Oral Cavity, and Pharyngeal Cancers by Subsite in 2012 Among Women. International Classification of Diseases 10<sup>th</sup> Revision codes are indicated for each subsite. (With permission from Shield KD, Ferlay J, Jemal A et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. *CA Cancer J Clin* 2017;67(1):51–64.)

cavity, and pharyngeal cancers of approximately 530,000 corresponds to 3.8% of all cancers. However, it is predicted to rise by 62% to 856,000 cases by 2035.

An increased incidence of differentiated carcinoma of the thyroid gland in children has been reported in Belarus and the Ukraine following the Chernobyl accident in 1986. Although initially the adult population in these areas did not show an increase in thyroid cancer, the adult population exposed to the Chernobyl accident is now manifesting an increase in thyroid cancer. It is anticipated that a similar rise in thyroid cancers may occur following the Fukushima nuclear accident in Japan. In addition, during the course of the past two decades, a rising incidence of differentiated carcinoma of the thyroid gland has been reported worldwide, likely due to the early increased diagnosis of clinically occult tumors resulting from increasing awareness and frequent utilization of routine sonography of the neck and other imaging studies.

## HEAD AND NECK SQUAMOUS CELL CANCER BIOLOGY: OVERVIEW

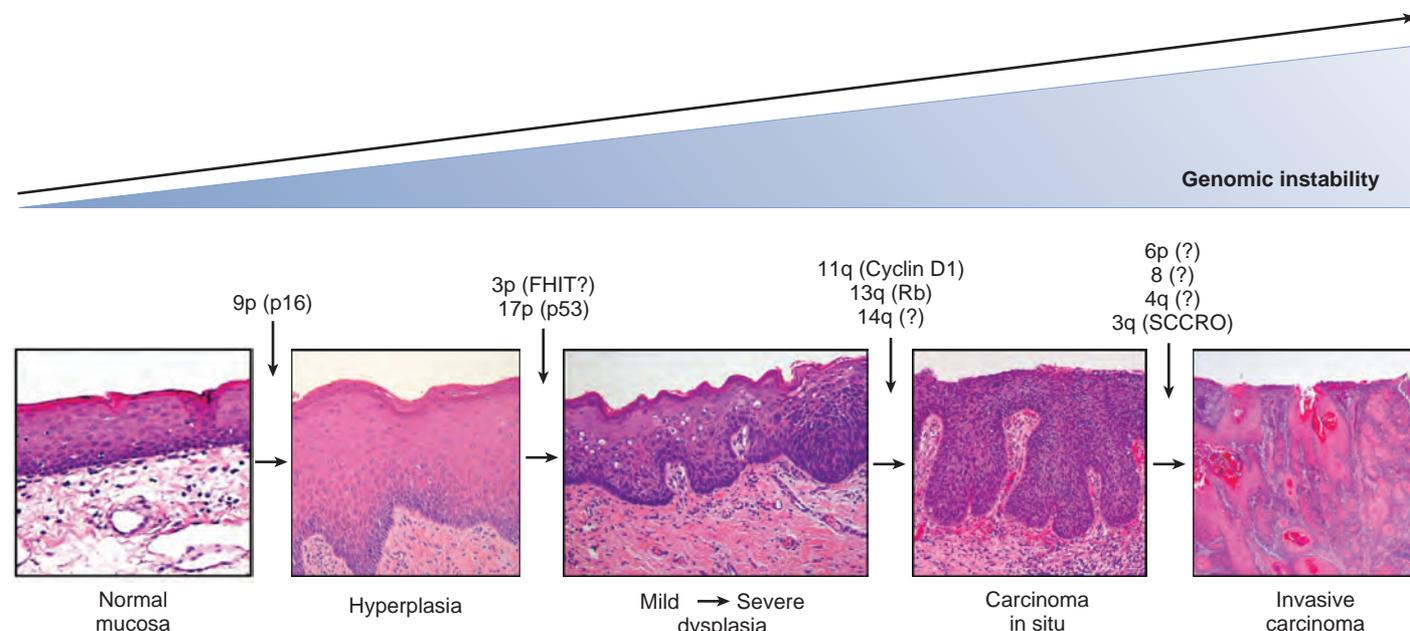
Despite its anatomic and histologic diversity, head and neck squamous cell carcinoma (HNSCC), like all human cancers, is a genetic malady in which genetic aberrations accumulate in cells consequent to an imbalance between mutagenic signals and inherent protective mechanisms. In some cases, the development of head and neck cancer may be subject to inherited predispositions, with the strongest association observed for patients with Fanconi anemia, a disease that results from mutations in a group of genes that mediate DNA damage repair. In some patients, head and neck cancers of mucosal origin are associated with exposure to mutagens, chief among which is tobacco. Tobacco use is a strong risk factor for the development of head and neck squamous cell cancer, with alcohol use representing a comparatively smaller level of risk, but the two agents appear to work synergistically and are likely responsible for up to 75% of cases. In parts of Asia, betel quid chewing also plays a significant role in the development of squamous cancer.

More recently, in the United States and developed world, oncogenic strains of the HPV (mainly HPV-16) have been linked

with the development of squamous cell cancer arising in the oropharynx; specifically, the lymphoid-rich regions of the tonsil and base of tongue. Most HPV-positive cancers occur in non-smokers and nondrinkers and are instead associated with sexual behavior as a means of transmitting the virus. In the developed world, the incidence of HPV-associated head and neck cancer is rising, while the incidence of tobacco-associated HPV-negative cancer is declining. HPV-associated cancers differ significantly from HPV-negative cancers in their genetic complexity and content, natural history, response to treatment, and outcomes. Due to these substantial differences, HPV-positive and HPV-negative cancers are best thought of as biologically distinct entities. The differences in the behavior of these two entities has led to the development of a different and separate staging system for HPV-positive oropharynx cancers.

Finally, many patients have no history of either an inherited cancer syndrome or exposure to tobacco or alcohol. The exact cause for the development of head and neck cancer in these patients remains to be defined. Although genetic aberrations appear to develop randomly, those directly contributing to carcinogenesis are selected for in a darwinian manner through the process of clonal selection. As such, cancers are a model for cellular evolution in that they constantly adapt to environmental stimuli through alterations in their genetic complement. As genetic events accumulate, these malignancies progress through several stages, ultimately resulting in invasive cancer. Head and neck cancers, especially head and neck squamous cell carcinomas and thyroid carcinomas, represent a prototypic model for cancer progression (Fig. 1.4). Moreover, with diffuse exposure to tobacco carcinogens, it is not uncommon to see multiple lesions at varying stages of progression within the upper aerodigestive tract, representing a process of field cancerization. Preclinical changes in the cellular structure of the exposed mucosa occur several years before the manifestation of clinical features suspicious for carcinoma, making field cancerization much more common than is appreciated clinically.

Given that the behavior of a cancer is directly attributable to its genetic content, the study of cancer genetics offers an opportunity to predict cancer behavior and direct targeted therapy. The study of cancer genetics has been bolstered in



**Figure 1.4** Progression model for squamous cell carcinoma of the head and neck showing increasing genomic instability from histologically normal mucosa to invasive carcinoma.

recent years by the completion of, first, the Human Genome Project and, subsequently, the large-scale tumor-sequencing studies of the Cancer Genome Atlas project. Despite these advances, the direct application of genetic information to head and neck cancer prognostication and treatment remains limited. Buoyed by successes such as anti-epidermal growth factor receptor targeting and, more recently, immunotherapy in head and neck squamous cell carcinomas and the promise of more significant contributions, the field of head and neck cancer genetics continues to advance and likely will influence cancer treatment in the years to come.

### GENETIC PREDISPOSITION TO HEAD AND NECK SQUAMOUS CELL CANCER

Only a small fraction of cases are familial in nature. The clearest link is observed in patients with Fanconi anemia, an autosomal recessive genomic-instability syndrome associated with bone marrow failure, leukemia, congenital defects, and sensitivity to cross-linking chemotherapy agents. The risk of developing head and neck cancer is elevated several hundred-fold, and most patients develop a solid tumor by age 45 years. Treatment of these patients is clinically challenging, because these patients have significant hypersensitivity to chemotherapy and radiation therapy.

It is not clear whether there is any clear genetic predisposition for head and neck cancer, apart from syndromic families. While initial studies seemed to show a genetic predisposition was common in first-degree relatives, more recent analyses now demonstrate that the association is mild. It is quite possible that inherited differences in relevant cellular pathways such as DNA repair, carcinogen metabolism, and cell cycle control may modulate the risk of cell sensitivity to carcinogen exposure.

### MOLECULAR SUBTYPES OF HEAD AND NECK SQUAMOUS CELL CANCER

The first analyses performing a broad molecular characterization of head and neck cancer utilized high throughput gene expression arrays. These first identified four distinct subgroups of HNSCC, which have been termed basal, atypical, mesenchymal, and classical. The “atypical” tumors are mostly HPV-associated, but the other subtypes do not have any clear association with patient factors such as age or smoking history. Of interest, however, is that these subtypes resemble similar subtypes in lung cancer, suggesting that there may be shared biology that is relevant for future research into factors that are prognostic or predict response to certain treatments.

### GENETIC ALTERATIONS IN HEAD AND NECK SQUAMOUS CELL CANCER

More recently, several large-scale projects have performed DNA sequencing of the exomes (the parts of the genome that are transcribed into RNA), in order to identify genes that are mutated in HNSCC. These studies have included large studies drawing tumors from multiple international centers, carried out by the Cancer Genome Atlas and the International Cancer Genome Consortium. Overall, HNSCC has the ninth highest mutational load of the 30 tumor types studied, with an average of 5 (range of 1–100) mutations per megabase. HPV-positive tumors tend to have lower mutation rates, and smoking-related tumors tend to have higher mutation rates.

HPV-negative tumors are predominantly characterized by multiple mutations in tumor suppressor genes (genes that normally function to protect cells from developing cancer), rather than oncogenes (genes that have the potential to cause cancer if altered). It has long been recognized that the most commonly altered gene in HNSCC is *TP53*, the gene that encodes the p53 protein, a protein that normally triggers cell cycle arrest in response to DNA damage or oncogenic stress. Mutations in *TP53* can be observed early in the formation of HNSCC, for example in premalignant lesions, or in histologically normal-appearing mucosa on the margin of a tumor resection. *TP53* mutations are present in 70% to 80% of HNSCC and are associated with poorer prognosis. Other commonly altered tumor suppressor genes in HNSCC include the cell cycle gene *CDKN2A* and genes involved in the differentiation and development of squamous cells, such as *NOTCH1*, *TP63*, and *FAT1*. The chief oncogenes that are altered in HNSCC include *EGFR*, which encodes the epidermal growth factor, driving downstream signaling that promotes cellular growth, invasion, and metastasis and is the target of *EGFR*-inhibiting therapeutic drugs such as cetuximab. Unlike in lung cancer, *EGFR* is rarely mutated in HNSCC but is often amplified, leading to overexpression. *PIK3CA*, a kinase gene that is the second-most commonly mutated gene in human cancer, is also mutated in up to 30% of HNSCC and plays an important role in promoting cellular growth and metabolism.

### BIOLOGY OF HUMAN PAPILLOMA VIRUS–ASSOCIATED HEAD AND NECK CANCERS

HPV-positive HNSCCs have a completely distinct molecular profile from HPV-negative HNSCC. The HPV family of genes include both low-risk and high-risk strains, based on the ability of a strain to lead to malignant progression of an infected cell. HPV has long been known to induce malignancies such as cervical, anal, and vulvar cancers. Definitive evidence linking HPV as a causative agent in oropharyngeal cancer only began to emerge in the early 2000s. It is now clear that HPV-related oropharyngeal cancers are a distinct entity that have a better prognosis than traditional smoking- and alcohol-related HNSCC. In the United States and the developed world, where smoking rates have declined, HPV is now the cause of up to 80% of oropharyngeal cancers. HPV16 is the main subtype associated with HNSCC.

HPV chiefly causes HNSCC through its two viral oncogenes, E6 and E7, that inactivate tumor suppressor genes in the host cell. E6 inactivates p53 (described previously), and E7 inactivates Rb (the retinoblastoma tumor suppressor gene). As a result of these driving events, HNSCCs caused by HPV tend to require far fewer other mutations to develop into cancer.

### PRECISION MEDICINE AND IMMUNOTHERAPY

The only molecularly targeted therapy currently used in HNSCC targets *EGFR*. Cetuximab, one of these drugs, is approved by the Food and Drug Administration (FDA) in the United States and has a 10% to 15% response rate as a single agent in advanced HNSCC. There is significant interest in exploring other targeted therapies, but our molecular understanding of HNSCC reveals that these approaches are most likely to be effective when matched to cancers with a corresponding alteration.

In recent years, a “precision” or “personalized” molecular oncology approach to advanced cancer has begun to be practiced



in several large cancer centers. The premise of such an approach is that clinicians could use molecular or genetic approaches to comprehensively profile a patient's tumor and identify targets of vulnerabilities that could be matched with a specific therapy. These approaches are currently the subject of intense investigation to determine whether in-depth molecular profiling of advanced cancer can lead to successful matching of tumors to new therapies and improved patient outcomes.

The most recent FDA-approved drugs for HNSCC are immunotherapies, specifically drugs that target checkpoints on T cells. In HNSCC, these drugs target the PD-1 (programmed cell death-1) protein, which is a receptor expressed on T cells that suppresses T cell activity. PD-1 binds to PD-L1, a protein that can be expressed (and upregulated) by cancer cells as a means of allowing tumors to evade the immune system. By inhibiting PD-1, these drugs are able to release the brakes on the immune system and unleash adaptive immunity targeting cancer cells. Current research seeks to improve the response rates of these immune checkpoint therapies against HNSCC and understand why some tumors respond and some are resistant to these treatments.

## EVALUATION

A detailed history and physical examination form the basis for initial diagnosis. In addition to tumor parameters, a complete history should include evaluation of factors that may influence the management of the primary neoplasm, including a detailed family history, lifestyle habits (including smoking and alcohol consumption), sexual behavior, and occupational exposures. The patient's comorbid conditions, such as nutritional status, chronic obstructive pulmonary disease, liver functions, and general medical condition, should be assessed carefully.

Clinical examination should be performed with the patient sitting upright. A headlight and simple instruments such as a tongue depressor should be used to facilitate examination of the oral cavity, along with a flexible fiberoptic laryngoscope to allow adequate assessment of the nasal cavity, nasopharynx, oropharynx, hypopharynx, and larynx. The examination begins with evaluation of the skin of the scalp, face, and neck, followed by palpation of the neck for masses, especially in the cervical nodal basins, and palpation of the thyroid and parotid glands. Evaluation of the external auditory canals and eardrum and anterior rhinoscopy also should be routine. Assessment of cranial nerve functions is integral and should be performed systematically. Examination of the oral cavity and oropharynx should include not only visual inspection but also palpation of the mucosa and underlying soft tissues of the tongue, floor of mouth, buccal mucosa, palate, tonsil, and base of the tongue. Flexible fiberoptic endoscopic examination should include visualization of the nasal cavity, nasopharynx, oropharynx, hypopharynx, and larynx, not only to look for mucosal and submucosal lesions but also to assess the soft palate and vocal cord function.

If a primary tumor is identified, its site of origin, visual characteristics, palpatory findings, and physical signs of local extension and invasion of adjacent structures should be meticulously assessed and documented to allow for staging and treatment planning. Adequate palpation, preferably bimanual palpation of the lesion when feasible, is necessary to assess the depth of invasion (DOI), since that is required to assign appropriate T staging of oral cancer. All malignant tumors of the head and neck region must be staged according to the staging system developed by the American Joint Committee on Cancer (AJCC)

and the International Union Against Cancer (UICC), published in the eighth edition of the *AJCC Cancer Staging Manual*.

## STAGING OF HEAD AND NECK CANCER

Cancers of the head and neck are staged according to their site of origin. Seven major sites are described in the AJCC/UICC (International Union Against Cancer) staging system. The seven major sites are (1) oral cavity; (2) pharynx; (3) larynx; (4) nasal cavity and paranasal sinuses; (5) thyroid gland; (6) salivary glands; and (7) skin cancers, including melanoma. The most recent revisions in the staging criteria for common tumors and the regional lymph nodes were published in the eighth edition of the AJCC staging manual and are shown in [Tables 1.1 to 1.9](#). Because of a different biological behavior, p16+ (HPV-positive) oropharyngeal carcinomas have a separate nodal staging system (see Chapter 11).

## RADIOGRAPHIC IMAGING

Imaging plays an integral role in the evaluation of head and neck tumors. Imaging can help define the extent of the primary tumor as well as the presence, volume, and location of regional and distant metastases. In addition, imaging is helpful in detecting synchronous or metachronous primary tumors that may not be evident clinically and for assessing treatment response, performing posttreatment surveillance, and obtaining tissue diagnosis by image-guided biopsy. In certain specific situations, such as paragangliomas or neurogenic tumors, a reliable diagnosis can be made on the basis of imaging alone without the need for tissue diagnosis. Imaging is able to define several salient features of the tumor that can have important implications in treatment selection, the extent of surgery, and planning of

**Table 1.1 Staging for Carcinoma of the Lip and Oral Cavity**

### Definitions of AJCC TNM

#### Definition of Primary Tumor

T CATEGORY	T CRITERIA
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor $\leq 2$ cm, $\leq 5$ mm depth of invasion (DOI) DOI is depth of invasion and not tumor thickness
T2	Tumor $\leq 2$ cm, DOI $> 5$ mm and $\leq 10$ mm or tumor $> 2$ cm but $\leq 4$ cm, and $\leq 10$ mm DOI
T3	Tumor $> 4$ cm or any tumor $> 10$ mm DOI
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease Tumor invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face) Note: Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4
T4b	Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

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Table 1.2 Staging for Carcinoma of the Major Salivary Glands

**Definitions of AJCC TNM****Definition of Primary Tumor (T)**

TX	T CRITERIA
T0	Primary tumor cannot be assessed
Tis	No evidence of primary tumor
T1	Carcinoma in situ
T2	Tumor 2 cm or smaller in greatest dimension without extraparenchymal extension*
T3	Tumor larger than 4 cm and/or tumor having extraparenchymal extension
T4	Moderately advanced or very advanced disease
T4a	Moderately advanced disease Tumor invades skin, mandible, ear canal, and/or facial nerve
T4b	Very advanced disease Tumor invades skull base and/or pterygoid plates and/or encases carotid artery

\*Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

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Table 1.3 Staging for Carcinoma of the Larynx

**Definitions of AJCC TNM****Definition of Primary Tumor (T)**

T CATEGORY	T CRITERIA
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx
T3	Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage
T4	Moderately advanced or very advanced
T4a	Moderately advanced local disease Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

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Table 1.4 Staging for Carcinoma of the Nasal Cavity and Paranasal Sinuses

**Definitions of AJCC TNM****Maxillary Sinus**

T CATEGORY	T CRITERIA
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone
T2	Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
T3	Tumor invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor of medial wall of orbit, pterygoid fossa, ethmoid sinuses
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
T4b	Very advanced local disease Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

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**Box 1.1 Critical Radiologic Features of the Tumor That Can Affect Selection of Treatment**

1. Submucosal/deep extension of tumor
2. Involvement or encasement of major vessels
3. Bone invasion
4. Perineural spread of disease
5. Detection of subclinical neck nodal disease
6. Lateral retropharyngeal lymphadenopathy and mediastinal lymphadenopathy

radiation therapy (Box 1.1). Selection of the appropriate imaging modality is critical for complete assessment in individual cases. Therefore the head and neck surgeon should be familiar with the strengths and weakness of each imaging modality. In addition, it is important to discuss the clinical problem with the radiologist so the investigation can be tailored to provide the desired information.

Computed tomography (CT) and magnetic resonance imaging (MRI) are the mainstay of imaging assessment of most head and neck tumors. Given their unique strengths and weaknesses, CT and MRI can complement each other to enhance the anatomic definition of selected tumors. Contrast-enhanced CT is widely used because it is readily available, less expensive than MRI, and can be performed rapidly, especially with multidetector scanners that can complete actual imaging in less than a minute. In addition, thin-section images obtained with modern scanners

Table 1.5 Staging for Carcinoma of the Pharynx

**Definitions of AJCC TNM****Definition of Primary Tumor (T)***Oropharynx (p16-)*

T CATEGORY	T CRITERIA
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible*
T4b	Very advanced local disease Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery

\*Note: Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

*Hypopharynx*

T CATEGORY	T CRITERIA
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor limited to one subsite of hypopharynx and/or 2 cm or smaller in greatest dimension
T2	Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures larger than 2 cm but not larger than 4 cm in greatest dimension without fixation of hemilarynx
T3	Tumor larger than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophagus mucosa
T4	Moderately advanced and very advanced local disease
T4a	Moderately advanced local disease Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, central compartment soft tissue, or infiltration muscle of esophagus*
T4b	Very advanced local disease Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

\*Note: Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

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can be reconstructed in sagittal and coronal planes to allow multiplanar viewing for comprehensive definition of the extent of the primary lesion and regional metastasis. Bone and soft tissue algorithms (windows) are used to provide specific details. CT is superior to MRI in evaluating cortical bone involvement, demonstrating calcification in tumors, and detecting clinically occult nodal metastasis and early extracapsular spread. However,

Table 1.6 Staging for Metastatic Carcinoma of the Cervical Lymph Nodes

**Definition of Regional Lymph Node***Clinical N (cN)*

N CATEGORY	N CRITERIA
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)
N2	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension, ENE(-); or in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension, ENE(-)
N2a	Metastasis in single ipsilateral or contralateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
N2b	Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); or metastasis in a single ipsilateral node ENE(+) or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+)
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)
N3b	Metastasis in a single ipsilateral node ENE(+) or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathologic ENE should be recorded as ENE(-) or ENE(+).  
ECS, extracapsular spread; Eg, gross; Em, microscopic; En, not present; E-, absent; E+, present.

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beam hardening artifact from dental work can limit evaluation of certain portions of the oral cavity, although modern multi-detector scanners generally can overcome this limitation. The anatomic resolution of CT is limited if the patient cannot receive iodinated intravenous contrast dye for medical reasons (e.g., renal disease or severe contrast allergy) or therapeutic reasons (e.g., planned use of radioactive iodine for thyroid cancer).

MRI is based on energy emittance from nuclei placed in a strong magnetic field. The computer-based detection and spatial localization of the released energy allows generation of an image, which is dependent on multiple factors, including the proton concentration, proton flow in vessels, and time required for stimulated nuclei to return to the basal state. The images generated by MRI are T1-weighted (based on the physical state of the material or proton density) or T2-weighted (based on loss of coherent resonance of protons). Fluid (e.g., cerebrospinal fluid and the vitreous in the eye) is bright and fat is dark on T2 images, whereas fat is bright on T1 images. Because of differences in tissue characteristics on T1 and T2 images, MRI is

Table 1.7 Staging for Carcinoma of the Thyroid Gland

**Papillary, Follicular, Poorly Differentiated, Hurthle Cell, and Anaplastic Thyroid Carcinoma**

<b>T CATEGORY</b>	<b>T CRITERIA</b>
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor <2 cm in greatest dimension limited to the thyroid
T1a	Tumor <1 cm in greatest dimension limited to the thyroid
T1b	Tumor >1 cm but <2 cm in greatest dimension limited to the thyroid
T2	Tumor >2 cm but <4 cm in greatest dimension limited to the thyroid
T3	Tumor >4 cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a	Tumor >4 cm limited to the thyroid
T3b	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing the carotid artery or mediastinal vessels from a tumor of any size

\*Note: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).

**Definition of Regional Lymph Node (N)**

<b>N CATEGORY</b>	<b>N CRITERIA</b>
NX	Regional lymph nodes cannot be assessed
N0	No evidence of locoregional lymph node metastasis
N0a	One or more cytologically or histologically confirmed benign lymph nodes
N0b	No radiologic or clinical evidence of locoregional lymph node metastasis
N1	Metastasis to regional nodes
N1a	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes

**Definition of Distant Metastasis (M)**

<b>M CATEGORY</b>	<b>M CRITERIA</b>
M0	No distant metastasis
M1	Distant metastasis

**Differentiated**

<b>WHEN AGE AT DIAGNOSIS IS...</b>	<b>AND T IS...</b>	<b>AND N IS...</b>	<b>AND M IS...</b>	<b>THEN THE STAGE GROUP IS...</b>
<55 years	Any T	Any N	M0	I
<55 years	Any T	Any N	M1	II
>55 years	T1	N0/NX	M0	I
>55 years	T1	N1	M0	II
>55 years	T2	N0/NX	M0	I
>55 years	T2	N1	M0	II
>55 years	T3a/T3b	Any N	M0	II
>55 years	T4a	Any N	M0	III
>55 years	T4b	Any N	M0	IVA
>55 years	Any T	Any N	M1	IVB

Table 1.7 Staging for Carcinoma of the Thyroid Gland—cont'd

<b>Anaplastic</b>	<b>WHEN T IS...</b>	<b>AND N IS...</b>	<b>AND M IS...</b>	<b>THEN THE STAGE GROUP IS...</b>
	T1-T3a	NO/NX	M0	IVA
	T1-T3a	N1	M0	IVB
	T3b	Any N	M0	IVB
	T4	Any N	M0	IVB
	Any T	Any N	M1	IVC

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Table 1.8 Staging for Nonmelanoma Skin Cancer

<b>Definitions of AJCC TNM</b>	
<i>Definition of Primary Tumor (T)</i>	
<b>T CATEGORY</b>	<b>T CRITERIA</b>
TX	Primary tumor cannot be identified
Tis	Carcinoma in situ
T1	Tumor smaller than 2 cm in greatest dimension
T2	Tumor 2 cm or larger, but smaller than 4 cm in greatest dimension
T3	Tumor 4 cm or larger in maximum dimension or minor bone erosion or perineural invasion or deep invasion*
T4	Tumor with gross cortical bone/marrow, skull base invasion and/or skull base foramen invasion
T4a	Tumor with gross cortical bone/marrow invasion
T4b	Tumor with skull base invasion and/or skull base foramen involvement

\*Deep invasion is identified as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumor); perineural invasion for T3 classification is defined as tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber, or presenting with clinical or radiographic involvement of named nerves without skull base invasion or transgression.

SCC, squamous cell carcinoma.

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excellent at delineating the interface between normal soft tissue and a tumor. Paramagnetic substances, such as gadolinium, can alter the MRI signal and are used as a contrast agent to enhance the definition of soft tissues.

Direct multiplanar imaging can be performed on an MRI scanner without the need for computer reformatting, which allows better anatomic definition and spatial resolution. In general, MRI is also superior to CT in identifying perineural spread of disease, differentiating tumor from postobstructive mucosal disease in the paranasal sinuses, and detecting the presence of intracranial extension by tumor. MRI is therefore ideal for the evaluation of tumors of the nasopharynx, skull base, parapharyngeal space, and soft and hard palate. However, MRI is inferior to CT in delineating bony detail, and it also can give a false-positive impression of bone invasion, particularly in the maxilla and mandible in patients with underlying odontogenic disease. On the other hand, MRI is superior in showing early invasion of

Table 1.9 Staging for Melanoma of the Skin

<b>T CATEGORY</b>	<b>THICKNESS</b>	<b>ULCERATION STATUS</b>
TX: Primary tumor thickness cannot be assessed (e.g., diagnosis by curettage)	Not applicable	Not applicable
T0: No evidence of primary tumor (e.g., unknown primary or completely regressed melanoma)	Not applicable	Not applicable
Tis (melanoma in situ)	Not applicable	Not applicable
T1	≤1.0 mm	Unknown or unspecified
T1a	<0.8 mm	Without ulceration
T1b	<0.8 mm 0.8-1.0 mm	With ulceration With or without ulceration
T2	>1.0-2.0 mm	Unknown or unspecified
T2a	>1.0-2.0 mm	Without ulceration
T2b	>1.0-2.0 mm	With ulceration
T3	>2.0-4.0 mm	Unknown or unspecified
T3a	>2.0-4.0 mm	Without ulceration
T3b	>2.0-4.0 mm	With ulceration
T4	>4.0 mm	Unknown or unspecified
T4a	>4.0 mm	Without ulceration
T4b	>4.0 mm	With ulceration

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marrow space of the mandible, without cortical destruction. Because of the high fat content of the marrow, the medullary space is bright white on T1 sequence. When involved by tumor, the fat signal is lost, and the marrow space appears grey, indicating tumor infiltration. MRI cannot be used in patients with ferromagnetic objects embedded in the body, which precludes safe scanning. In addition, because of the limited confines of the bore of the magnet, MRI may not be suitable for patients with

claustrophobia or those with a large body habitus. "Open" MRI can overcome this limitation, but the image quality is inferior in the currently available equipment. MRI requires 30 to 45 minutes for image acquisition and therefore is susceptible to degradation of image quality from any movement by the patient during the study, including swallowing.

Ultrasound is particularly useful in the head and neck for evaluation of superficial soft tissue lesions in sites such as the parotid and thyroid gland. Ultrasound allows imaging in real time and assessment of vascularity and punctate calcification, which is especially useful in characterizing thyroid disease. Although ultrasound is the modality of choice for evaluating most thyroid lesions, it cannot detect tumor extension into bone or the airway, because ultrasound waves cannot penetrate these two media. Therefore CT or MRI is useful in evaluating more advanced disease of the thyroid gland when local invasion into the central compartment viscera or the spine is a cause for concern. Ultrasound is also sensitive in detecting nodal metastases in small lymph nodes in patients with thyroid cancer. At many institutions, ultrasound is routinely used for evaluation of cervical lymph nodes for metastatic disease and has become the standard of care for posttreatment surveillance of the neck.

Functional imaging with use of 18F-fluorodeoxyglucose positron emission tomography (PET) and particularly PET/CT adds yet another dimension that enhances and complements the anatomic information gained from CT or MRI. PET imaging is particularly helpful in evaluating patients with advanced head and neck cancers for distant metastases and posttherapy recurrence. The 18F-fluorodeoxyglucose avidity reflects metabolic activity in the lesion but is unable to differentiate between inflammation, infection, or tumor as the cause of increased metabolic activity. Whereas some nuclear medicine studies such as bone scans, gallium scans, and octreotide scans have limited use in head and neck imaging, other studies that use radioisotopes such as radioactive iodine, sestamibi, and metaiodobenzylguanidine (MIBG) have specific applications in thyroid and parathyroid disease.

Interventional applications of radiology of the head and neck include angiography and image-guided biopsy. Conventional diagnostic angiography has been essentially replaced by CT and MR angiography, and diagnosis of vascular tumors can be reliably achieved without invasive angiography. Invasive angiography is now primarily reserved for specific situations such as evaluation of the adequacy of cerebral perfusion when carotid sacrifice is a possibility, balloon occlusion testing (BOT), preoperative embolization of vascular tumors such as juvenile nasopharyngeal angiofibroma, control of hemorrhage, or delivery of intraarterial chemotherapy.

Image-guided biopsy of head and neck tumors greatly aids diagnosis and subsequent treatment in the appropriate clinical setting. Image-guided biopsy can be the least invasive approach to diagnosis, and in experienced hands it is a low-risk procedure that often obviates the need for general anesthesia and a more complicated open surgical procedure for tissue diagnosis. Obviously, the clinician or cytopathologist can obtain samples of palpable lesions easily by fine-needle aspiration (FNA). Superficial lesions such as thyroid nodules, superficial parotid gland lesions, and small lateral cervical lymph nodes are readily accessible with use of real-time ultrasound guidance, and thus accurate and expeditious FNA of suspicious lesions as small as 4 to 5 mm is feasible. Lesions that are located more deeply within the head and neck require CT or MR guidance to negotiate bone and the air-tissue interface. MR is used infrequently because it

requires special nonferromagnetic MR-compatible equipment, apart from its other disadvantages compared with CT, as previously described.

Our ability to specifically image cancer cells in relation to normal tissue or posttherapy effects in tissue can be expected to improve with enhanced understanding of the biological and molecular mechanisms of cancer. In addition, the role of imaging in the management of head and neck cancer will continue to evolve with new technologic developments, newer contrast agents, and three-dimensional real-time imaging as well as in vivo confocal microscopy.

## BIOPSY AND TISSUE DIAGNOSIS

Tissue diagnosis is mandatory before treatment for any malignant tumor. Diagnosis can be achieved by performing a biopsy or a fine needle aspiration cytology (FNAC) of superficial tumors or by performing a core needle or open biopsy of deeper tumors. A sufficient quantity of representative viable tissue from the tumor should be obtained to enable the pathologist to render an accurate tissue diagnosis. Obtaining a superficial biopsy specimen from an exophytic tumor, a biopsy specimen of necrotic tissue from an extensive tumor, or a biopsy specimen from tissue adjacent to the tumor that is not representative of the true nature of the lesion will result in inaccurate tissue diagnosis. If the index of suspicion for malignancy of a tumor is high and the initial biopsy is not confirmatory, then a repeat biopsy is warranted.

Deeper tumors that are not accessible for surface biopsy, such as submucosal tumors, soft tissue tumors, or tumors of the thyroid and salivary glands, as well as enlarged cervical lymph nodes, are best assessed by an FNA biopsy for cytologic diagnosis. FNA can be performed directly with palpation or under the guidance of imaging (i.e., ultrasound or CT). Whereas histopathologic diagnosis is based on tissue architecture (i.e., the relationship of cells to one another and the context in which they coexist), cytologic diagnosis is based on evaluation of characteristics of individual cells in suspension, including nuclear features. The tissue that has been aspirated is smeared onto several slides and stained, and some material may be centrifuged, fixed in formalin, and processed into a paraffin block. This "cell block" allows for hematoxylin and eosin staining and additional studies, such as immunohistochemistry or flow cytometry. FNA is highly accurate for diagnosis of most head and neck cancers, but it is important to understand that a negative cytologic diagnosis does not rule out the presence of a malignant tumor. If FNA is not conclusive, either a core or an open biopsy should be performed. A core biopsy usually provides sufficient tissue for histopathologic analysis. An open biopsy is indicated if a core biopsy is unsafe or nondiagnostic.

## FROZEN-SECTION ANALYSIS

The indications for frozen-section analysis include confirmation of tissue diagnosis (e.g., parathyroid), diagnosis of malignancy, determination of the type of malignancy, evaluation of the margins, and adequacy of the tissue for further studies. Accuracy of the margins is dependent on the surgeon's judgment in sampling and the quality of the tissue submitted. Margins of surgical resection may be obtained from the specimen or from the surgical defect.

The accuracy of a frozen section is dependent on the context in which it is used. Limitations include assessment of bone, assessment of irradiated tissue (e.g., radiation-induced metaplasia

versus carcinoma), diagnosis of thyroid adenoma versus carcinoma (follicular and Hürthle cell neoplasms), differentiation of salivary tumors, and differentiation of necrotizing sialometaplasia and pseudoepitheliomatous hyperplasia from carcinoma. Lymphovascular invasion also cannot be assessed adequately with a frozen section. Other limitations include sampling error and electrocautery artifact.

## TISSUE PROCESSING AND PATHOLOGY

Tissue can be submitted to the pathologist unprocessed or fixed in formalin. Most tissues can be fixed in 10% neutral-buffered formalin for routine processing. Fresh tissue is required for cytogenetic or diagnostic molecular tests. The specimen should be kept sterile for cultures for cytogenetics or for microorganisms. Banking of fresh, frozen tissue is desirable to facilitate study of tumor biology.

The patient's pertinent clinical details should be provided to the pathologist for accurate tissue processing and diagnosis. Orientation and gross description of the specimen requires communication between the surgeon and the pathologist. The gross description of the tumor is an essential component of the pathology report. Assessment of the margins of surgical resection is aided by the use of colored inks on the specimen. Decalcification is required for specimens that contain bone to

allow processing. The prosector must determine the location and number of sections depending on the type of tumor for accurate histopathologic analysis.

The capsule (pseudocapsule, formed by compression of contiguous tissue) of tumors of the thyroid, salivary glands, and soft tissues should be assessed completely. Neck dissection specimens should be specifically studied, with a description of the location (levels) and number of lymph nodes. This description should be performed by the surgeon in the operating room by either pinning the specimen on a foam board with a diagram or prosecting the specimen according to designated levels. The number of lymph nodes in the neck dissection specimen depends on several factors, including the completeness of the neck dissection by the surgeon, previous radiation therapy to the neck, and the diligence of the prosector. Accurate reporting of the extent of nodal metastases requires reporting of extranodal extension (ENE), which is essential for N staging of tumors. The pathology report must also indicate whether the ENE is macroscopic (ma) or microscopic (mi).

After formalin fixation, paraffin blocks are prepared and sections that are at a thickness of 4 to 5 microns are fixed to glass slides. Hematoxylin and eosin is the gold standard for tissue diagnosis, and it is supplemented with immunohistochemistry and molecular techniques such as in situ hybridization under select circumstances (Table 1.10).

**Table 1.10 Immunohistochemistry and Molecular Techniques Can Supplement Hematoxylin and Eosin Diagnosis in Certain Tumors.**

ANTIBODY		SCC	PAPILLARY THYROID CARCINOMA	MEDULIARY THYROID CARCINOMA	MALIGNANT MELANOMA	ONB	CARCINOID	LYMPHOMA
34BE12	High-molecular-weight cytokeratin	++	–	–	–	–	–/–	–
Cam 5.2		+	+	+	–	–	–	–
AE1:AE3		+	+	+	–	–	–	–
4a4/p63	Basal cell or myoepithelial cell marker	++	–	–	–	+/-	–	–
CK7		–	+	+	–	–	–/–	–
CK20		–	–	–	–	–	–/–	–
LCA (CD45)	Leukocyte common antigen	–	–	–	–	–	–	+
CD20	B cells	–	+	–	–	–	–	+
CD5	T cells	–	–	–	–	–	–	–
HMB45		–	–	–	+/-	–	–	–
A103		–	–	–	+/-	–	–	–
MART-1 (MELAN A)		–	–	–	+/-	–	–	–
s-100		+/-	–	–	+/-	+	–	–
Thyroglobulin		–	+	–	–	–	–	–
TTF-1	Thyroid transcription	–	+	+	–	–	+/-	–
PAX B		–	+	+/-	–	–	–	–
HMBE		–	+	–	–	–	–	–
Calcitonin		–	–	+	–	–	–	–
Chromogranin		–	–	+	–	+/-	+	–
Synaptophysin		–	–	+/-	–	+	+	–
CEA		+/-	–	+/-	–	–	+/-	–
Mib-1 (Ki 67)	Proliferation marker	**	**	**	**	**	**	**

\*Variable

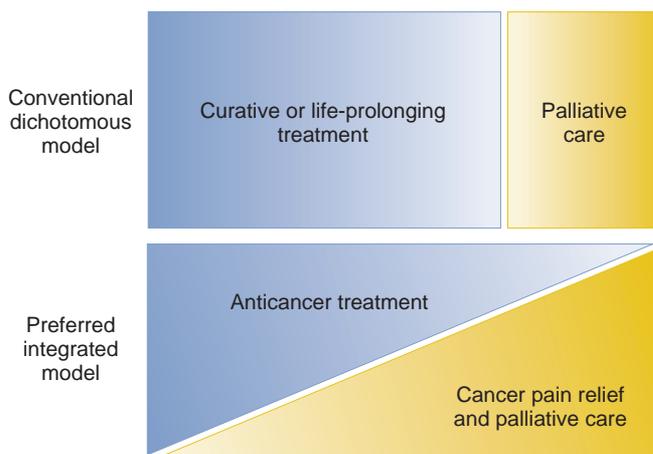
Epithelial markers Lymphoid markers Melanoma markers Thyroid markers  
ONB, Olfactory neuroblastoma; SCC, squamous cell carcinoma.

A wide variety of chromosome analysis techniques are available, ranging from basic G-banded karyotyping to 24-color spectral karyotyping as well as fluorescence in situ hybridization mapping of cloned deoxyribonucleic acids. Chromosomal translocation analysis by fluorescence in situ hybridization has become the mainstay in diagnosis of Ewing's sarcoma and rhabdomyosarcoma.

**SELECTION OF THERAPY**

Treatment of head and neck cancers can be divided into two broad categories: curative and palliative. With progression of the disease, curative treatment becomes less effective and integration of palliative therapy becomes increasingly important. Conventionally palliative treatment has only been used in patients with advanced tumors toward the end of their lives. On the other hand, it is preferable to integrate symptomatic palliation and pain relief early in the course of curative treatment (Fig. 1.5).

The selection of initial definitive treatment is dependent on the histologic diagnosis and the site and stage of the primary tumor as well as on its biological behavior and expected response to therapy. In general, early-stage tumors (i.e., stages I and II) are managed by a single-modality treatment such as surgery or radiotherapy. Selection of either surgery or radiotherapy depends on the site, size, and stage of the primary tumor as well as its proximity to bone and its depth of infiltration into the underlying soft tissues. In addition, the histologic features of the primary tumor and the history of any previous treatment also will affect the selection of therapy. Additional factors influencing the choice of initial treatment are complications and sequelae of treatment, the patient's compliance with treatment, convenience of the recommended therapy for the patient, the cost of treatment, and the competency of the treatment delivery team in executing the recommended therapy. In general, outcomes of therapy for early-stage tumors using single-modality treatment are comparable for either surgery or radiotherapy. On the other hand, advanced-stage tumors (i.e., stages III and IV) require multidisciplinary treatment with a combination of surgery and adjuvant radiotherapy or chemoradiotherapy. Thus in advanced-stage tumors, multidisciplinary input from all disciplines is necessary to develop an optimal therapeutic program. When a cure is not likely, attention turns to palliative treatment to control or prevent symptoms or to slow down



**Figure 1.5** Integrating life-prolonging and palliative treatment in patients with head and neck cancer.

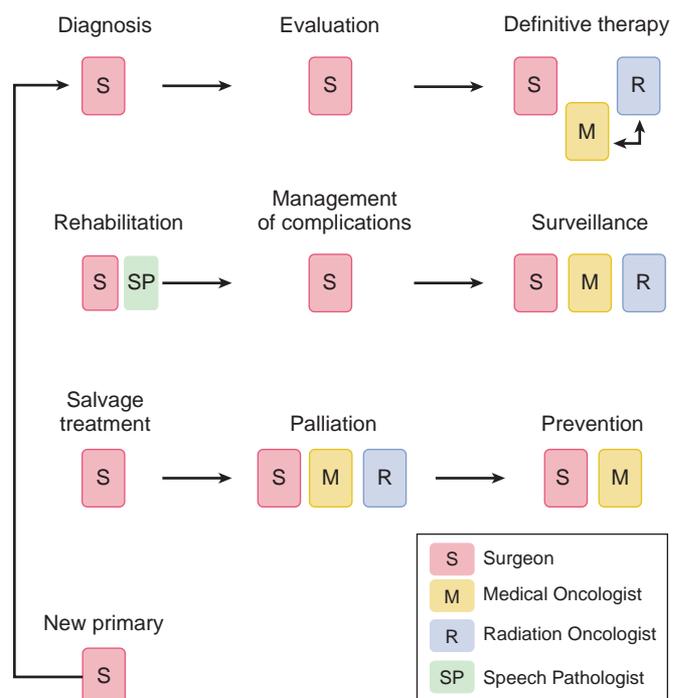
progression of the disease. Surgery may be employed for palliation in select circumstances, including resection of fungating or bleeding tumors or resection of central compartment tumors to prevent airway compromise. Similarly, radiation can be used for palliative benefit, for example, to control effects of spinal cord compression from vertebral metastasis. Chemotherapy has an important role as a “radiation booster” when employed concurrently, or as an in vivo drug sensitivity test when employed in a neoadjuvant fashion. It also has an essential role in palliative treatment, with agents selected on the basis of risk/benefit profiles and response.

**SURGERY**

The surgeon plays a pivotal role in the management of patients with head and neck tumors. Involvement of the surgeon begins with the initial diagnosis, assessment of the extent of disease, selection of optimal treatment, and during delivery of definitive treatment and continues with rehabilitation, follow-up care, surveillance, and diagnosis and management of recurrent and new primary tumors as well as palliative and terminal care (Fig. 1.6). Surgery remains the most effective curative treatment for most head and neck neoplasms. In tumors of the salivary glands, thyroid, nasal cavity and paranasal sinuses, oral cavity, soft tissues, bone, and skin, it is the treatment of choice. In select patients with squamous cell carcinoma of the oropharynx and larynx, primary surgical resection is preferred. Surgery also becomes necessary for salvage of persistent or recurrent tumors after radiotherapy or chemoradiotherapy.

**RADIATION THERAPY**

Radiation therapy results in deoxyribonucleic acid (DNA) damage, leading to death during subsequent cell division. The benefits of radiotherapy include coverage of a wider area



**Figure 1.6** Role of the various specialists in the multidisciplinary management of patients with head and neck cancer. *M*, medical oncologist; *R*, radiation oncologist; *S*, surgical oncologist; *SP*, speech pathologist.



around the primary tumor compared with surgery, applicability to surgically inaccessible or incurable tumors or to patients who, for medical reasons, cannot undergo an operation, and the potential for anatomic organ preservation. Although radiation therapy is highly effective in the treatment of tumors such as those of Waldeyer's ring and early larynx cancer, application of radiation therapy often is limited by the sensitivity of adjacent normal tissues. Several factors need to be considered when choosing radiation as part of the treatment program. First, radiation damage to normal tissues within the field is permanent. As such, long-term sequelae are quite common. Tissues with the lowest radiation tolerance, such as the salivary glands and neural tissues, show the most profound and lasting changes, resulting in xerostomia, changes in taste and dentition, and related sequelae. Moreover, reirradiation in previously treated areas may overwhelm normal tissue tolerance, limiting use of radiation for subsequent treatment. This consideration is significant given that the overall lifetime risk for additional primary tumors approaches 30% in patients cured of the index primary head and neck cancer and who continue the life style or habits of tobacco and alcohol consumption. In addition, radiation can have mutagenic effects on normal structures, leading to the development of radiation-induced malignancies. Finally, radiation may make surgical salvage more complicated, often leading to more extensive procedures. Advances in technology such as intensity-modulated radiation therapy and the availability of proton therapy are allowing improved targeting of the primary tumor volume while limiting exposure of surrounding tissues to the damaging effects. The combination of chemotherapy with radiation has improved the therapeutic outcomes in several primary sites in the head and neck.

## CHEMOTHERAPY

In the past, the role of chemotherapy in the management of head and neck cancers was primarily for palliation. With improved understanding of the impact of multimodality treatment, chemotherapy is now used as part of both definitive and adjuvant treatment regimens in conjunction with radiation therapy. For head and neck squamous cell carcinomas, platinum-based compounds are the most commonly used agents because they have shown the best responses either alone or in combination with other drugs. Platinum compounds, including cisplatin and carboplatin, traditionally have been used in combination with antimetabolites such as 5-fluorouracil and taxanes such as paclitaxel. Chemotherapy may be combined with radiation in one of several sequences, including neoadjuvant, concurrent, or induction, followed by concurrent chemoradiation therapy. Chemotherapy also is used as concurrent treatment with postoperative radiation therapy in high-risk patients.

Initially, chemotherapy was given before radiation, on the basis of the results of the Veteran's Administration larynx preservation trial. Since then, several prospective trials and metaanalyses have shown advantages of concomitant chemoradiation over sequential treatment. However, the benefits from concomitant chemoradiotherapy are tempered by higher rates of acute and long-term treatment-related sequelae. This issue is of particular concern for patients who fail to respond and who must unnecessarily endure the adverse effects of treatment and require salvage surgery. On the basis of observations that response to chemotherapy predicts radiation response, there is now renewed interest in the use of induction chemotherapy

to select patients for subsequent concomitant chemoradiotherapy. The role of biological agents is evolving. Biological agents that target epidermal growth factor receptors have shown promise in combination with radiation therapy, because this approach enhances treatment response without increasing severe adverse effects.

Introduction of immunotherapeutic agents has opened a new vista in systemic therapy of many cancers. In the head and neck cancers, immune checkpoint inhibitors, including PD 1, PDL 1, and MAP kinase inhibitors are currently being tested in clinical trials.

## POSTTREATMENT MANAGEMENT

### Rehabilitation and Lifestyle Modification

Rehabilitation of the patient after initial definitive treatment is focused on functional, psychological, and vocational restoration. Postsurgical sequelae require intervention by physical and rehabilitation specialists (e.g., neck and shoulder exercises and speech and swallowing therapy). In addition, rehabilitation of a paralyzed face or vocal cord, stricture of the pharynx, and obstruction of the nasolacrimal duct require specific interventions. Esthetic restoration of the face is crucial to psychological rehabilitation. Postradiation sequelae require management of xerostomia, dental care, and prevention of fibrosis-related complications such as trismus and frozen shoulder. Postchemotherapy sequelae require management of renal function, hearing, and peripheral neuropathy. Support services and counseling are important for vocational rehabilitation.

Modification of lifestyle to reduce the risk of recurrence and to prevent development of new primary tumors is an integral component of posttreatment management. Involvement of psychosocial specialists for cessation of smoking and alcohol use is of great benefit. Appropriate pharmacologic and behavioral interventions are necessary to achieve this goal. Genetic counseling and screening of family members should be provided in the event of certain diseases such as medullary carcinoma of the thyroid and paragangliomas.

### Posttreatment Surveillance

The patterns of tumor recurrence and risk of subsequent new primary tumors influence the frequency and intensity of surveillance. For tobacco-related cancers (such as squamous cell carcinoma of the upper aerodigestive tract), the highest risk for local/regional recurrence is within the first 2 years. Therefore regular head and neck examination at 2- to 3-month intervals is recommended for the first 2 years. Thereafter this risk diminishes gradually, but the risk of developing a new primary cancer increases at a rate of about 2% per year, reaching a lifetime cumulative risk of 35%. Long-term follow-up is therefore recommended semiannually for the first 5 years and annually thereafter. More stringent surveillance should be performed in high-risk patients such as those with field cancerization or those who continue to smoke and/or drink alcohol.

Increasing use of radiation and chemotherapy in patients with advanced-stage disease has influenced the patterns of failure with improved local/regional control but higher risk for distant metastasis. Surveillance for detection of distant metastases and new primary tumors at other locations should include annual chest imaging and/or a PET scan. Ultrasonography and biochemical surveillance (with thyroglobulin and calcitonin) is applicable in patients with thyroid cancer.

## OUTCOMES

The only available registry-based data on outcomes of therapy for head and neck cancer in the United States come from the National Cancer Database of the American College of Surgeons. The AJCC has regularly published outcomes data from the

National Cancer Database in each successive edition of its cancer staging manual. Therefore the outcomes data presented in each chapter are from the eighth edition of the *AJCC Cancer Staging Manual*. Single-institution data from Memorial Sloan-Kettering Cancer Center are also presented where appropriate, to highlight the differences in outcomes from a tertiary care cancer center.

# Basic Principles of Head and Neck Surgery



Because most patients with tumors of the head and neck initially present to the surgeon, it is the surgeon's responsibility to do a comprehensive examination of the head and neck area, accurately assess the tumor and assign the stage of the disease, discuss treatment options, obtain appropriate multidisciplinary input, and initiate treatment planning. Accordingly, the head and neck surgeon must have a basic understanding of the biology of the disease and the factors involved in cancer management, including tumor and host factors as well as the principles and effectiveness of available treatment modalities. If surgery is selected as the initial definitive treatment, the surgeon should focus on thorough preparation of the patient for surgery. This process includes patient education, a preoperative medical evaluation as well as a dental evaluation if required, speech and swallowing assessment, and psychological consultation as required. This is essential to obtain an informed consent from the patient.

## PREOPERATIVE EVALUATION AND PREPARATION

### Patient Education and Informed Consent

Before proceeding with surgery, it is essential to have a detailed discussion with the patient and provide counseling regarding the nature and severity of the disease, its impact on the selection of therapy, the treatment options available, the pros and cons of each approach, and the details of the operative procedure if surgery is recommended as the preferred choice of treatment. The sequelae and morbidity of surgery and possible complications should be discussed with the patient and appropriately documented as part of the informed consent process. Central to this discussion is the understanding and realistic expectations by the patient and family members. In addition, the patient should be informed about what to anticipate in the postoperative period. This discussion should stress the need for breathing exercises and early ambulation to prevent complications. Patients undergoing laryngectomy require specific preoperative counseling, including consultation with a speech pathologist, review of voice rehabilitation, and video education regarding expected sequelae. Similarly, patients who are expected to have significant functional or aesthetic sequelae after surgery also require specific counseling and access to support services.

### Initiation of Preventive Measures

A key factor contributing to perioperative morbidity is current tobacco use. Smoking causes changes in cardiopulmonary function that can have unfavorable implications for patients undergoing prolonged anesthesia. Smokers are at an increased risk for postoperative pulmonary complications as well as free flap

failure. Smoking-induced changes in cardiopulmonary function can be minimized by preoperative abstinence from smoking. Accordingly, appropriate counseling for cessation and support services are an essential part of preoperative preparation. The period before surgery is also an excellent time to initiate efforts at permanent smoking cessation. Similarly, perioperative  $\beta$ -blockade has been shown to reduce the incidence of myocardial ischemia, myocardial infarction, and long-term overall mortality related to cardiac events after surgery in patients at high cardiac risk. It is believed that the beneficial effects of  $\beta$ -blockers result from a positive balance of myocardial oxygen supply and demand. The current recommendations for perioperative  $\beta$ -blockade for patients at high risk for a perioperative cardiac event are to begin use of a  $\beta$ -blocker several weeks before a planned operation, titrate the dose to achieve a heart rate of 60 to 70 beats per minute, and taper the dose in the postoperative period.

### Medical Optimization

The basic preoperative assessment includes a detailed history and physical examination, a complete blood cell count, routine biochemistry tests, urinalysis, an electrocardiogram, and a chest radiograph. In addition, overall poor general medical status and the presence of comorbid conditions warrant the need for a preoperative medical or cardiology consultation. Although advanced age by itself is not a contraindication for surgery, comorbidities that are more common in older patients may require specific preoperative evaluation and optimization. In advanced tertiary care centers, special Geriatric Services are available. If such resource is available, then a preoperative geriatrics consultation should be obtained. In general, most medications can be continued until the day of surgery with the exception of anticoagulants, such as aspirin, warfarin (Coumadin), and any other antiplatelet agents, which should be stopped 5 days before surgery if medically acceptable. For patients in whom anticoagulants cannot be stopped, warfarin should be switched to short-acting anticoagulants that can be withheld on the day of surgery. Because antihypertensive agents that target angiotensin-converting enzyme can cause severe hypotension during anesthesia, they also should be discontinued before surgery.

### Preoperative Considerations for Postoperative Management

In addition to medical optimization, postoperative management issues also should be addressed before surgery. If significant or prolonged pain is expected, a pain management specialist should be consulted preoperatively. Psychological consultation and

counseling also may be considered preoperatively if a patient (or family member) is having significant problems with stress or coping. In addition, a history of heavy alcohol use warrants prophylaxis for delirium tremens, which should be instituted in collaboration with a psychiatrist. Effective treatment of delirium tremens relies on early identification of patients at risk before symptoms develop, use of benzodiazepines (e.g., lorazepam) for withdrawal prophylaxis, and then gradual tapering for detoxification.

## INTRAOPERATIVE MANAGEMENT

### Hair Removal

Traditionally, the preparation of patients for surgery has included shaving of hair from the intended surgical site the night before the operation. It is now recognized that shaving in advance of surgery can lead to hair follicle irritation and infection, and accordingly it is no longer recommended. When necessary, hair removal should be performed in the operating room with use of electric clippers. The use of sharp razors (even safety razors) is discouraged.

### Operating Room Setup

The design of the operating room should accommodate all the required equipment and yet provide easy access to the patient. To facilitate the free flow of personnel and equipment, a minimum of 800 square feet of floor space is desirable. The operating room setup for head and neck surgery requires at least two overhead operating lights and an operating table with the flexibility to position the patient as required. Procedures that require two surgical teams working simultaneously are ideally performed in an operating room with two sets of overhead operating room lights. In contemporary operating rooms, digital imaging, operative endoscopy and microscopy, electrocautery, various energy devices for coagulation, and other basic surgical instruments should be available. A typical setup of a contemporary head and neck operating room is shown in Fig. 2.1.

Standardized operating room setup allows operations to be conducted smoothly. Most head and neck surgical procedures can be performed with a single surgical team consisting of the operating surgeon, the first and second assistant surgeons, and a scrub nurse. Complex operations of the skull base, mediastinum, or thorax and free flap procedures require more than one surgical team. Some select situations require two teams to work

simultaneously. When multiple surgical teams are involved, the surgical plan and sequence should be discussed with the entire team, which includes the anesthesiologist and operating room personnel. Similarly, for robotic surgery, the setup requires specific positioning of the patient, the operating table, and the robotic console.

### Setup for General Open Head and Neck Operations

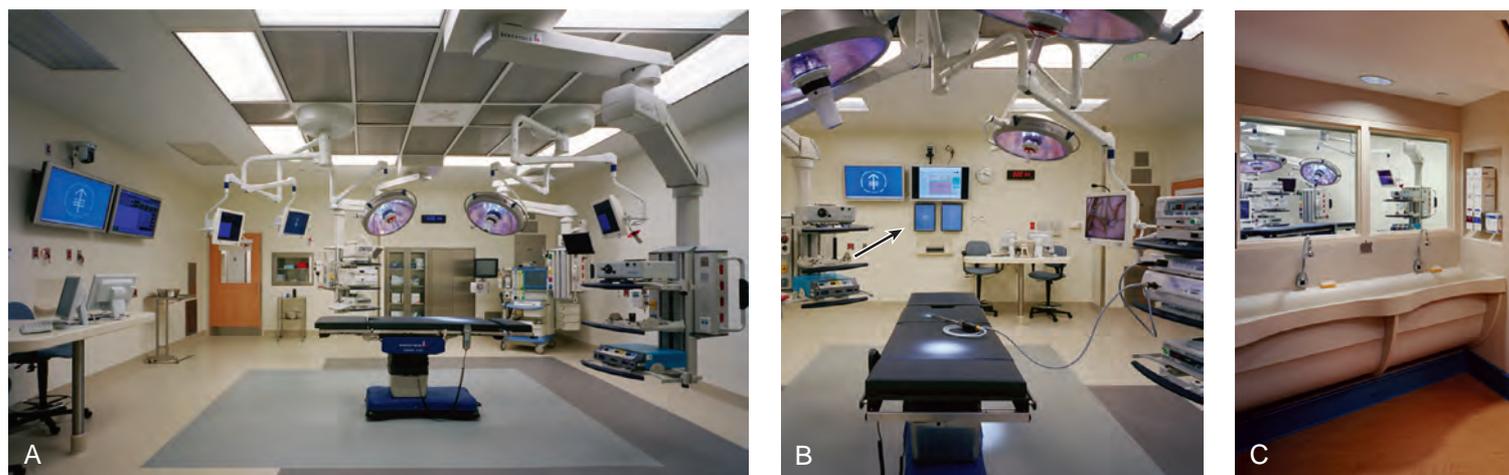
As a general rule the operating surgeon stands on the side of the operative field, with the first assistant at the head end of the table and the second assistant directly across on the opposite side of the surgeon. The endotracheal tube and the anesthesia circuit are directed diagonally away from the operative field at the head end, to be connected to the anesthesia machine. In general, the scrub nurse should stand on the same side as the surgeon, with the Gerhardt instrument table brought over the operating table and up to the level of the umbilicus of the patient (Fig. 2.2). The electrocautery cords and suction tubing are directed into the operative field between the scrub nurse and the surgeon and are secured to the drapes. Wastebaskets are positioned for easy access by the surgeon and in sight of the scrub nurse so that the contents are readily visible.

### Setup for Endoscopic Surgery

A sterile field generally is not required for endoscopic surgical procedures. The procedure is performed with the use of either endoscopes or an operating microscope. If a carbon dioxide laser is used, the appropriate laser precautions should be in place. Transnasal and transoral endoscopic surgery requires a full complement of endoscopes as well as specialized insulated instruments and suction coagulators. The setup and positioning of the operative equipment and personnel are shown in Fig. 2.3.

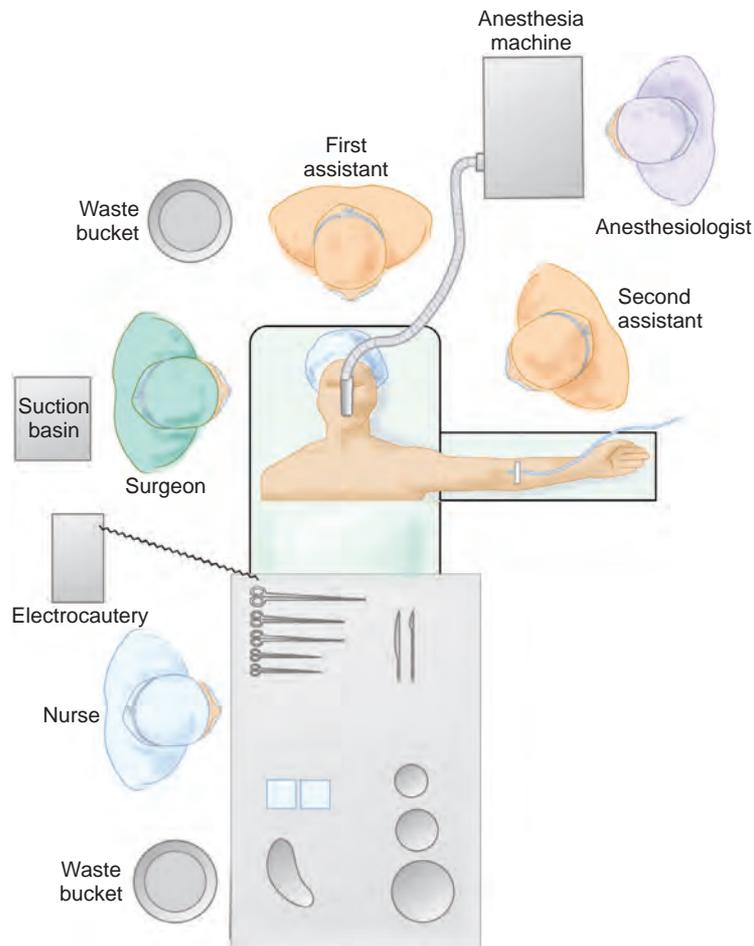
### Setup for Robotic Surgery

Setup for robotic surgery requires generally a larger operating room to accommodate the robotic console and the robot itself (Fig. 2.4). The robotic console may be located in a convenient location in the room away from the operating table and anesthesia equipment. In addition, to position the robot for transoral surgery, adequate space is necessary at the head end of the table, with space for the assistant to sit and work in the oral cavity to assist the surgeon operating the robotic arms. The



**Figure 2.1** A modern operating room showing (A) an overview; (B) a “wall of knowledge” that displays surgical video images, continuous vital signs, and imaging studies (arrow); and (C) the surgical scrub area with visual access to the operating room. (Images of MS Surgery Suite from Chuck Choi, Brooklyn, NY.)

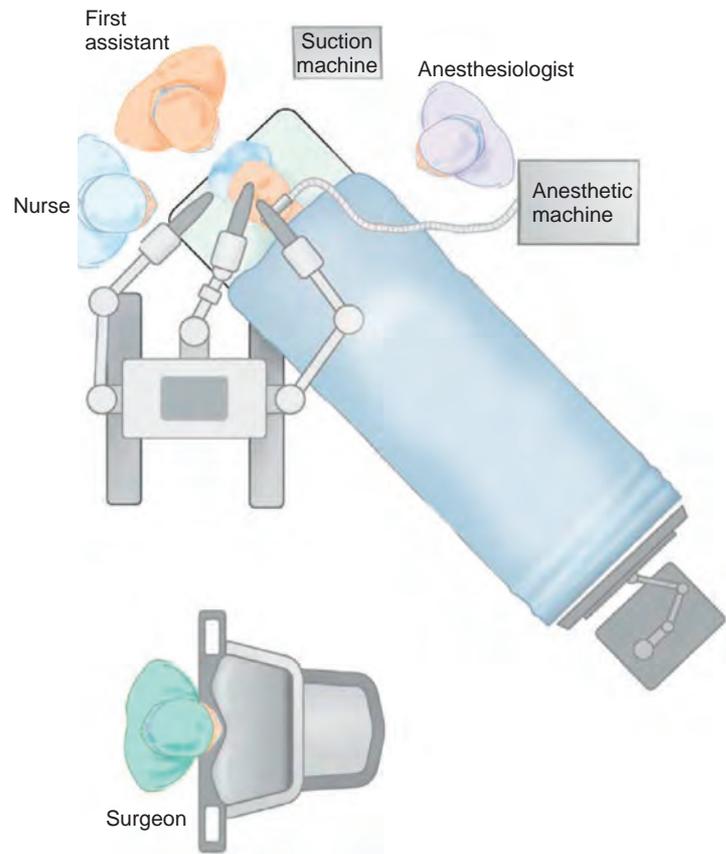
assistant may need to use the suction machine or may be required to provide additional retraction or to apply vascular clips for hemostasis. Thus, by necessity, the anesthesia tubing and circuit are extended to have the anesthetic equipment at a distance from the endotracheal tube.



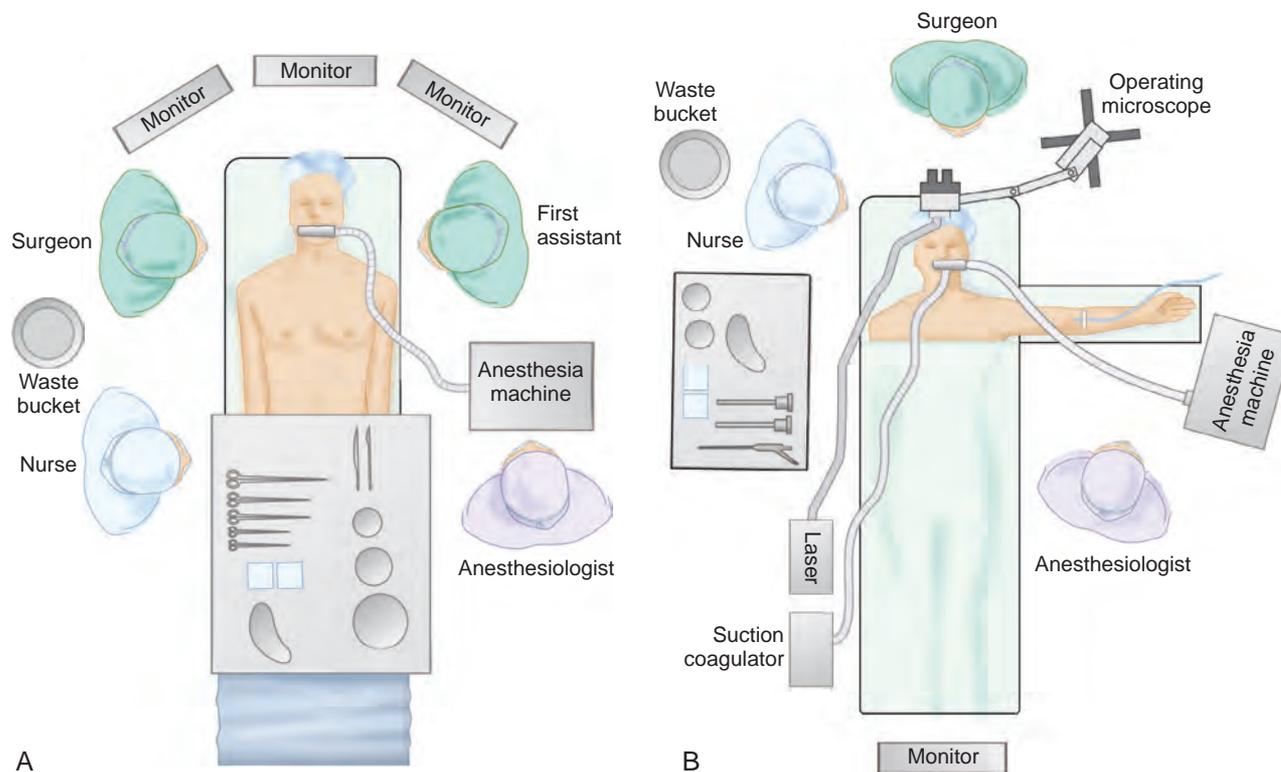
**Figure 2.2** Positioning of personnel and equipment for most open head and neck procedures.

**Setup for Two-Team Craniofacial Surgical Procedures**

Craniofacial surgery for tumors involving the skull base requires planning of the operating sequence to prevent confusion and crowding at the operating table. The patient is prepared and draped for simultaneous access by both the neurosurgical



**Figure 2.4** Positioning of personnel and equipment for transoral robotic surgery.

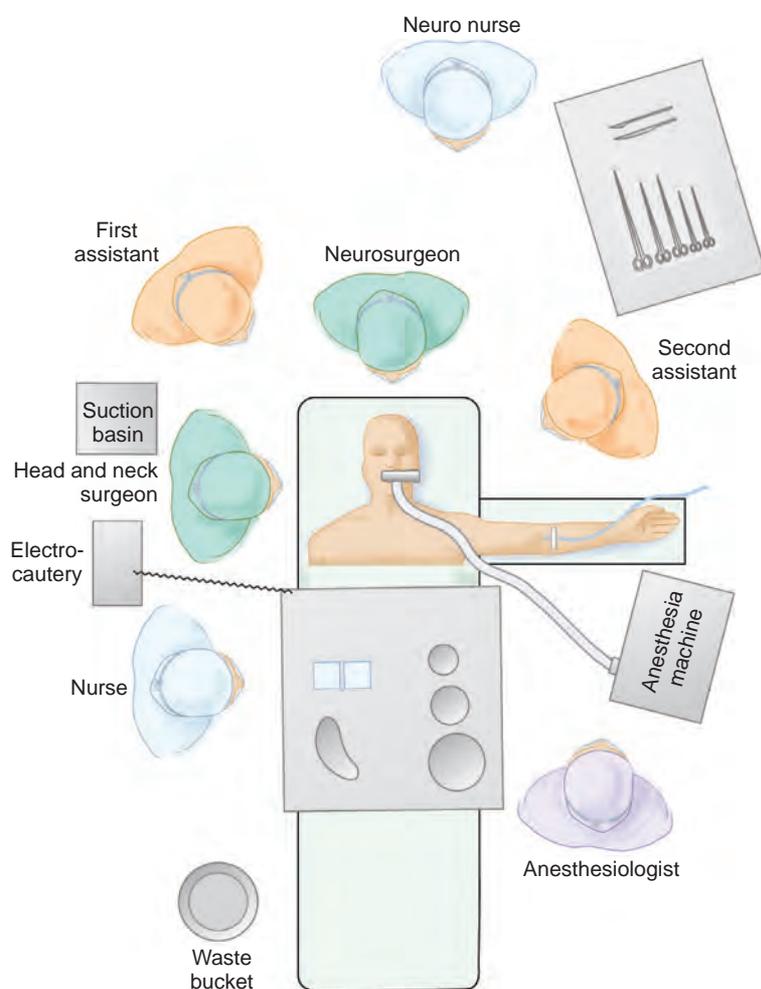


**Figure 2.3** Positioning of personnel and equipment for (A) transnasal and (B) transoral endoscopic procedures.

and the head and neck teams, even though many stages of the operation are performed sequentially by one team at a time. When both teams are working simultaneously, the head and neck surgeon works from the same side as the lesion, with the first assistant between the head and neck surgeon and the neurosurgeon, who works from the head end of the table. The operative setup is depicted in Fig. 2.5. Two sets of powered instrumentation including the appropriate drills, saws, and electrocautery and suction equipment are necessary for this complex operative procedure.

### Setup for Simultaneous Operations for Resection and Reconstruction With Two or More Surgical Teams

When a head and neck tumor resection is planned simultaneously with harvest of a microvascular free flap, two surgical teams need to work independently and often simultaneously, to save time, with their own separate scrub nurse. While the head and neck team is resecting the tumor, the reconstructive team can harvest the free flap in selected situations. Similarly, harvest of the jejunal graft or mobilization of the stomach for gastric transposition for reconstruction of a pharyngolaryngo-esophagectomy defect may be possible simultaneously. Proper positioning of operating room personnel and equipment is especially important in these situations (Fig. 2.6).



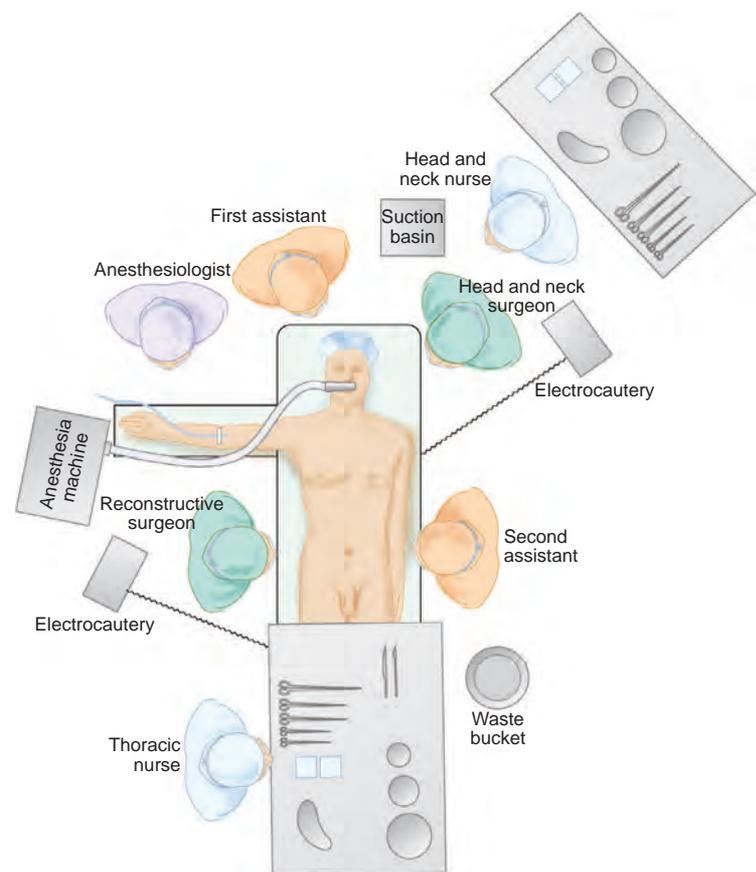
**Figure 2.5** Positioning of personnel and equipment for craniofacial surgery requiring two teams.

### Intravenous Access

A large-bore peripheral venous catheter should be in place for most head and neck surgical operations. As a general rule, the intravenous line should be placed in the arm opposite the side of the tumor resection so the anesthesiologist can have unimpeded access to it. However, if microvascular free tissue transfer is planned, the arm used for the intravenous line should be selected in consultation with the reconstructive surgeon so that harvest of a radial forearm flap, if such is planned, is not compromised.

### Intraoperative Monitoring

Peripheral monitoring equipment, including the blood pressure cuff and pulse oximeter, generally should be placed on the arm on the side opposite the operative field. For more complex and prolonged operations, an arterial line is desirable to monitor the hemodynamic status of the patient. As with intravenous access, the arterial line should also be planned in consultation with the reconstructive surgeon. The use of an esophageal temperature probe does not interfere with the surgical field for most operations on the neck, but a rectal probe should be inserted if the operation involves the upper aerodigestive tract. A Foley catheter helps monitor urine output during prolonged operations. Proper monitoring is crucial during the operation to avoid overloading the patient's cardiovascular system with intravenous fluids, especially if there is significant blood loss that needs to be replaced with blood or blood products. Fluid balance is particularly important in older and physiologically compromised patients undergoing prolonged operations, because fluid overload can result in significant postoperative cardiopulmonary complications.



**Figure 2.6** Positioning of personnel and equipment for resection and reconstructive surgery requiring two teams.

## Antibiotics

Prophylactic perioperative antibiotics are administered for specific indications. In clean cases, such as thyroidectomy, parotidectomy, or neck dissection without simultaneous resection of a mucosal primary tumor, antibiotic coverage is not required. Because most operations on the upper aerodigestive tract and paranasal sinuses are considered *clean-contaminated*, appropriate antibiotic coverage should be provided before skin incision. The choice of antibiotic regimen is dictated by the type of the operation being performed. As a general rule, prophylactic use of a cephalosporin with metronidazole is preferred for most operations on the upper aerodigestive tract. Clindamycin may be used for patients who are allergic to penicillin. A combination regimen of ceftazidime, metronidazole, and vancomycin is recommended for patients undergoing craniofacial surgery. The first intravenous dose of antibiotics is given before the induction of anesthesia, and the dose should be repeated at appropriate intervals for prolonged procedures.

## Anesthesia

An anesthesiologist familiar with head and neck surgery is preferred as a member of the operating team, because his or her role is critical for the smooth conduct of head and neck operations. Discussion of the operative procedure between the operating surgeon and the anesthesiologist is essential to allow for safe and expeditious surgery. The mode of anesthesia induction, type and route of intubation, need for muscle relaxation, maintenance of a desired level of blood pressure, anticipated blood loss, and the need for blood transfusion and the rate of fluid administration should be discussed before surgery.

The key anesthesia issue in head and neck surgery involves airway management. Unlike surgical operations at other sites in the body, management of the airway must be a collaborative effort between the anesthesiologist and the head and neck surgeon. Preoperative identification of a potentially difficult airway is the responsibility of the head and neck surgeon. The anesthesiologist should be alerted so that the induction of anesthesia and endotracheal intubation is accomplished safely. Moreover, it is also incumbent upon the surgeon to be proficient in endotracheal intubation techniques, because in select circumstances the head and neck surgeon should take charge and intubate the patient in collaboration with the anesthesiologist.

The surgeon should be familiar with various endotracheal tubes that are available and their applicability to the planned head and neck surgical procedures. As a general rule, the smallest size endotracheal tube that permits satisfactory ventilation should be used, especially for endoscopic surgery for laryngopharyngeal tumors. A wire-reinforced flexible endotracheal tube rather than a simple flexible plastic tube is preferred so that kinking is prevented.

## Endotracheal Intubation

The mode of intubation should be planned in advance. Although transoral intubation is appropriate for most head and neck procedures, operations in the oral cavity and oropharynx are best performed with nasotracheal intubation. Similarly, nasotracheal intubation is also helpful in allowing complete excursion of the mandible during operations on the deep lobe of the parotid gland and other tumors in the parapharyngeal space. For nasotracheal anesthesia, special tubes that conform to the

curve of the nasal air passage into the larynx are available. Nasotracheal tubes require flexible connections to prevent kinking between the tip of the nose and the anesthesia circuit. Moreover, transoral endoscopic procedures using the CO<sub>2</sub> laser require the use of a “laser safe” endotracheal tube and isolation of the endotracheal tube away from the operative field with moist patties to prevent injury to the tube or cuff and laser-induced fire. High-frequency jet ventilation via a catheter is useful in select circumstances for transoral procedures. Finally, if neuromonitoring of the recurrent laryngeal or vagus nerves is planned during thyroid surgery, an electrode-embedded endotracheal tube is required.

An airway that is difficult to manage should be approached cooperatively. Endotracheal intubation may be difficult in patients with trismus; bulky tumors that preclude a clear view of the laryngeal introitus; or a fibrotic, contracted neck resulting from chemoradiation. In these situations, flexible fiberoptic endoscope-guided nasal intubation should be considered. An elective tracheotomy performed with the patient under local infiltration anesthesia to secure the airway preoperatively may be necessary in select circumstances, such as when a bulky and friable tumor obstructs the laryngeal introitus. If the tracheotomy site is within the sterile operative field, a wire-reinforced endotracheal tube is used intraoperatively, because it is flexible enough to conform to the contour of the patient's chest during surgery. If the tracheotomy site is not within the operative field, a regular cuffed Silastic tracheotomy tube is used and secured with silk sutures. A flexible “accordion” type plastic or metallic connector is used to connect the tracheotomy tube to the anesthesia circuit.

## Nerve Monitoring

Recurrent laryngeal nerve monitoring has become an important tool in modern-day surgery on the thyroid gland. Specialized electrode-impregnated endotracheal tubes are available for this purpose. It is important for the anesthesiologist and the surgeon to ensure that the endotracheal tube is accurately positioned to have proper contact of the electrodes with the vocal cords. Inadequate placement of the tube (electrodes distal to vocal cords or above the vocal cords) will give false signals and inaccurate response to stimulation of the recurrent laryngeal nerves.

## Blood Pressure Maintenance

Most head and neck surgical procedures are best conducted with a systolic pressure of approximately 90 mm of mercury. Hypertensive episodes during surgery cause unnecessary blood loss and impede smooth conduct of a safe surgical procedure. A thorough understanding between the surgeon and the anesthesiologist is crucial for maintaining systolic pressure at this level throughout the surgical procedure. Hypotensive anesthesia is particularly indicated in patients requiring craniotomy and major skull base resection. Appropriate use of hypotensive agents should be discussed with the anesthesiologist before starting the surgical procedure.

## Muscle Relaxation

Most surgical procedures in the head and neck are best conducted with the patient fully relaxed and paralyzed with appropriate use of short-acting or long-acting muscle relaxants. Thus patients requiring prolonged endoscopic surgical procedures, such as endoscopic laser resections of laryngopharyngeal tumors, require complete

paralysis to achieve optimal positioning of instrumentation for ease of the operative procedure. On the other hand, muscle relaxants should be avoided during surgical procedures in which neuromonitoring is used, such as surgery of the facial nerve, and for monitoring recurrent laryngeal nerves during thyroid surgery.

### Position and Draping

For head and neck surgical procedures, the patient is placed on the operating table so that extension of the neck in a partially propped-up position is possible. Preferably the operating table should be electrically controlled, and it should be able to hinge in two sections. The standard position recommended for most head and neck surgical procedures requires the table to hinge at approximately 30 degrees at the patient's waist, with the headboard dropped at least 35 degrees to provide extension of the neck (Fig. 2.7). The patient is essentially in a semisitting position, and elevation of the head serves the purpose of reducing bleeding from minor blood vessels. If possible the patient should be supported with a footboard, and all pressure points, including the heels and elbows, should be padded and protected. The arm on the side of the lesion is tucked by the patient's side so that the shoulder is drawn down, exposing the neck. A surgical hat covers the patient's hair, and a paper tape is used to secure the hat to the patient's skin along the hairline. The pinna on the surgical side is exposed, whereas the contralateral pinna is covered by the hat. The patient's head is supported by a donut cushion to prevent it from rolling from side to side during the operation.

### Eye Care

Protection of the cornea during surgery is important for obvious reasons. The patient's eyes are generally not included in the operative field for most head and neck operations. In such instances, the eyes are protected with instillation of an ophthalmic methylcellulose lubricant and are taped shut with the use of a transparent plastic adhesive sheet such as Tegaderm (Figs. 2.8 and 2.9). For surgical procedures on the face that include the eye in the operative field, a 60 nylon suture through the skin of the upper and lower eyelids is recommended to keep the eyelids closed to protect the cornea. Alternatively, a ceramic corneal shield is inserted in the conjunctival sac to protect the cornea. The corneal shield rests on the sclera, and thus protects the cornea, but allows access to the eyelids and

conjunctival sac. This is particularly necessary for surgery on facial skin or eyelids.

The skin at the surgical site is prepared with a bacteriostatic solution such as Betadine or chlorhexidine. In patients who are allergic to iodine, alcohol may be used for skin preparation. In general, the area prepared should include not only the immediate field of surgical intervention but also any possible extensions of the procedure. For example, the skin from the hairline of the forehead (including the skin in front of and behind the pinna) and the ipsilateral side of the face, and the neck up to the clavicles, should be prepared for a parotidectomy. In addition, the entire neck and upper chest on the surgical side should also be prepared in the event that the surgical procedure needs to be extended for a neck dissection. For surgery of facial lesions and surgery on the paranasal sinuses, the entire face on both sides is prepared from the hairline down to the clavicle. The skin of the face and neck from a line joining the tragus to the ala of the nose at the upper end and down to the nipples at the lower end should be prepared for operations on the oral cavity, pharynx, and neck. If a pectoralis major myocutaneous flap is anticipated, the skin preparation should extend down to the umbilicus. Other donor sites for harvest of skin grafts or free flaps, such as the arm, abdomen, thigh, or leg, should be prepared as necessary depending on the reconstructive plan.



**Figure 2.7** Position of the table for most open head and neck procedures.



**Figure 2.8** Adhesive plastic protective eye covering.



**Figure 2.9** The eyes are taped shut after instillation of Lacri-Lube ointment.



Once the skin is prepared, draping of the surgical field begins. Isolation of the head with a head drape requires the use of two folded sheets, placed one over the other with a margin of approximately 10 cm between the folded edges of the two drapes. This method allows the lower drape to rest on the table while the upper drape is wrapped around the patient's head alongside the paper tape that holds the surgical hat in place (Fig. 2.10). The patient's head is lifted and the two sterile drapes are tucked under the head and down to and under the shoulders (Fig. 2.11). The anesthetic tubing must be held up in the air while this draping is taking place. The patient's head is then placed back on the drapes, and the upper drape is wrapped around the patient's head. A towel clip is applied to hold the folded drape in position over the patient's forehead (Fig. 2.12). The anesthesiologist now places the anesthetic tubing over the folded head drape and secures it in place without kinking by folding over the ends of the head drape and securing them with another towel clip (Fig. 2.13). With the head draping completed, a split sheet is placed over the anterior surface of the patient's body and is secured in place. The exposed anesthetic tubing and the upper part of the head are now isolated with a sterile transparent plastic drape, which provides easy view of the endotracheal tube and anesthesia circuit and the eyes during the operation (Fig. 2.14).



**Figure 2.12** The top sheet is used to fold over the head while the bottom sheet rests on the operating table under the head.



**Figure 2.10** Two flat sheets are held together for draping of the head.



**Figure 2.13** The anesthesia tubing is held in the head drape with a towel clip.



**Figure 2.11** Both flat sheets are placed under the head.



**Figure 2.14** A sterile, transparent plastic drape is used to isolate the upper part of the head and anesthesia tubing out of the sterile field.

## BASIC SURGICAL TECHNIQUE

### Surgical Incision

The surgical incision for any procedure in the head and neck is planned to provide maximum exposure while allowing for the best aesthetic and functional outcome. Most incisions for head and neck surgery should be planned to respect natural skin creases (Langer's lines) to minimize unpleasant scarring. When the initial surgical incision is planned, the possible need to extend the surgical procedure intraoperatively should be considered, and any future surgical procedures that may be required should be thought of. An ill-placed incision can significantly compromise a subsequent surgical procedure (Fig. 2.15). Issues related to the planning of surgical access and incisions are addressed in detail where applicable for each operation in its respective chapter.

### Surgical Procedure

The initial skin incision is made thru the epidermis into the dermis with a scalpel. The remainder of the operative procedure is performed with electrocautery, which allows safe and controlled surgical dissection with minimal blood loss. Because each electrocautery unit is unique, an appropriate wattage setting should be selected and standardized by the operating surgeon for each unit based on his or her level of comfort. Electrocautery does not work well in loose and lax tissue or in a surgical field flooded by blood or fluids. Therefore the surgical field should be dry and tense under traction or retraction for the effective use of electrocautery.

Cutting current is used to divide the dermis up to the subcutaneous tissue to prevent charring of the skin edges, after which coagulating current or a blend of cutting and coagulating current can be used for dissection. Electrocautery should be used to facilitate surgery that allows dissection in tissue planes exposed by properly applied traction and countertraction. Only the tip of the instrument should be used at an angle of 15 to 30 degrees to the tissue rather than at right angles. When used correctly, tissues undergoing electrocautery dissection should show clean, healthy cut edges without any "black" charred tissue. With appropriate use of electrocautery, nearly all surgical procedures in the head and neck can be conducted safely with minimal blood loss. Although monopolar cautery can be used near neurovascular structures, bipolar cautery is preferred to avoid the risk of thermal or conduction injury. In addition, harmonic devices are available to seal and divide blood vessels and tissues. These devices are products of new technology that function at lower temperatures than electrocautery and use ultrasonic waves rather than an electrical current, thus lowering the risk for thermal or conduction injuries.

### Energy Devices

Use of energy devices for control of bleeding has entered the arena of head and neck surgery. Commercial devices include the Harmonic scalpel, Ligasure, etc. These instruments are effective in control of bleeding and securing hemostasis and do save some time during surgery. However, the tips of these devices are quite blunt and do not permit meticulous delicate dissection of tissues. In addition the "jaws" of these instruments generate heat and pose a risk of thermal injury to delicate neurovascular structures. Thus caution should be exercised when using energy devices near important nerves.

### Wound Closure

Mucosal wounds are closed with interrupted sutures using chromic catgut or synthetic absorbable sutures such as Vicryl. Wound closure should not be under tension, and the sutures should be placed only a few millimeters apart to avoid large gaps in the suture line to prevent fistula formation. The skin wound is closed in layers, using absorbable material for the platysma and subcutaneous tissue and fine nylon for subcuticular tissue or sutures through the skin.

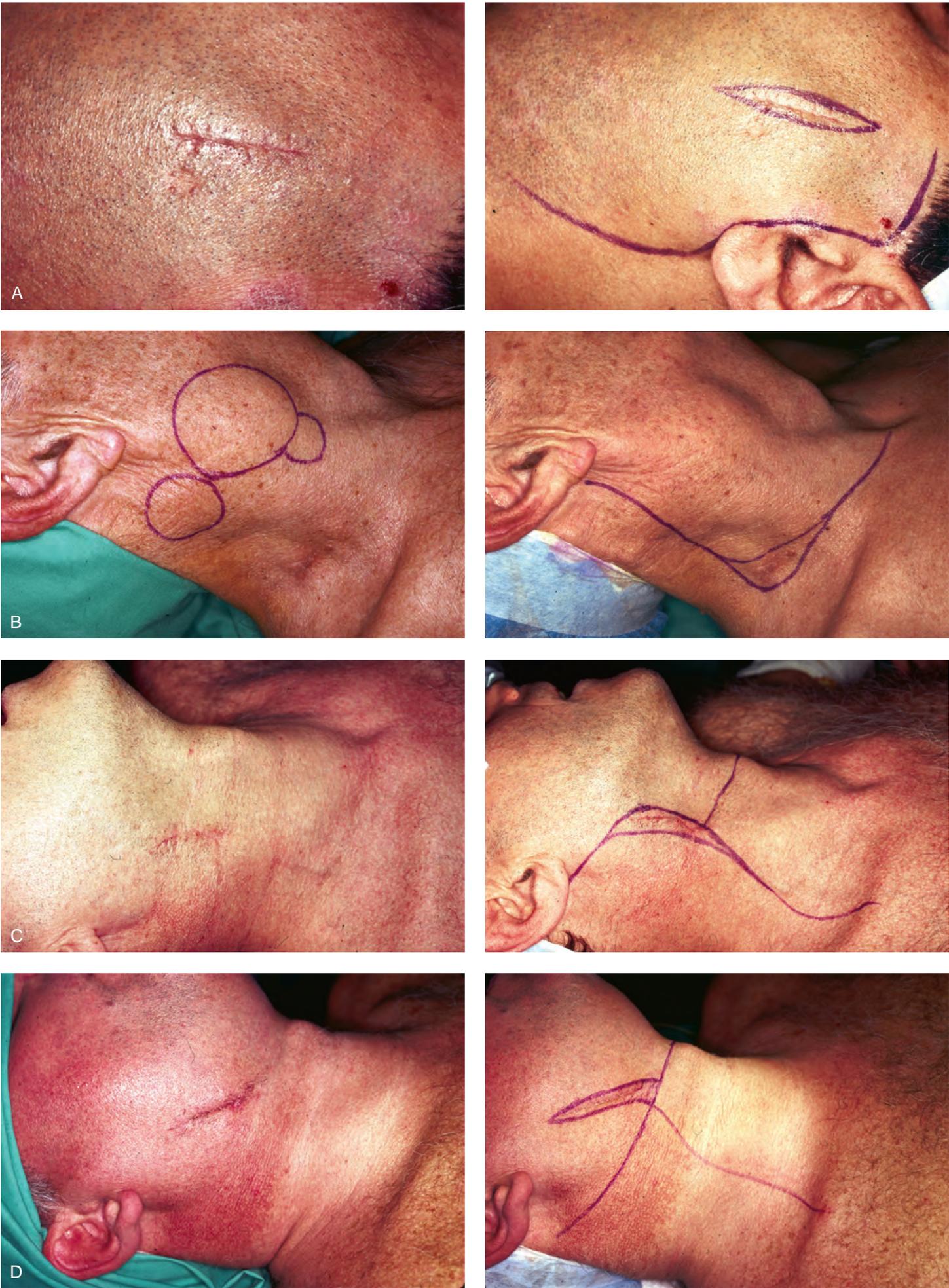
### Salvage Surgery

With increasing use of chemoradiotherapy treatment protocols, employed for tumors of the larynx and pharynx, a new treatment paradigm has been established for these tumor sites. However, approximately 20% to 60% of patients being treated with chemoradiotherapy fail to respond and require salvage surgery. Embarking upon surgery in a previously treated field with chemoradiotherapy poses a significant risk of failure to heal, leading to major wound complications. Therefore special preoperative and intraoperative treatment planning is required to avoid and prevent such disastrous complications. Patients must be nutritionally adequate to undergo surgery, and are thus brought into positive nitrogen balance with preoperative nutritional supplements. Their hematocrit is optimized. Nonradiated well-vascularized regional or distant free flaps are generously employed on mucosal suture lines as a buttress to bring in new blood supply to promote healing. In spite of such measures, wound complications occur due to skin necrosis. In a situation where there is significant radiation damage to the skin, manifested by thinning of skin with lack of elastic tissue, and dermal telangiectasia, consideration should be given to excising such compromised skin and replacing it with a local, regional, or distant free flap.

### Surgical Drains

The decision to place a drain and the type of drain to be used in a wound depends on the operation performed and the status of the surgical bed at the time of closure. Most procedures with dry fields, absence of large dead spaces, and no anticipated lymphatic fluid accumulation, such as thyroidectomy, do not require drain placement. A Penrose drain is used for small, superficial wounds where only a minimal amount of serosanguineous drainage is anticipated; it also is preferred for drainage after parotid surgery, because suction drain has the potential to injure the underlying facial nerve. The drainage from a Penrose drain is collected in sterile gauze dressing held in place with a stockinette. The gauze should be changed as often as required to prevent maceration of the skin.

Suction drains should always be used for patients who have had operations such as neck dissection, where draining of a larger volume of serum or serosanguinous fluid is anticipated. The perforated inner ends of the suction tubes are carefully positioned in the wound away from nerves and major vessels. A loose loop of chromic catgut suture can be used to hold the distal end of the drain in position. The drains are brought out through separate incisions in the skin of the neck and sutured in place with silk sutures. The patency of the suction drains should be checked carefully during the final stages of wound closure, and clots in the drainage tubes should be cleared. The wound should be irrigated with saline solution to verify that



**Figure 2.15** Examples of ill-placed incisions for biopsy. This requires modifications of standard incisions for subsequent definitive surgery. **A**, Parotidectomy. **B**, **C**, and **D**, Neck dissections.

the suction drains work. At the end of the operation, the skin flaps should be completely flat and the drains should be able to maintain negative pressure with suction. Any air leaks leading to loss of suction should be rectified before reversal of anesthesia. Prevention of clogging of the suction drains is crucial, because close apposition of the undersurface of the skin flaps to the raw area in the neck plays an important role in minimizing oozing. Loss of suction allows the skin flaps to lift off the surgical bed, leading to oozing and ultimately hematoma formation. Therefore the suction drains should be connected to a "high negative pressure" suction source for at least 24 to 48 hours, at which point they may be transferred to the self-suctioning canister.

## POSTOPERATIVE MANAGEMENT

To minimize complication rates and recovery time, postoperative care for patients undergoing major head and neck surgery should proceed in an organized manner with established protocols. Key issues include infection control, management of the surgical site and drains, free flap monitoring, pain control, airway management, and nutrition.

### Infection Control

Infection is a major risk for patients in the postoperative period. Several measures should be instituted to minimize infection risks. Early ambulation and respiratory therapy with an incentive spirometer are crucial to prevent atelectasis, pneumonia, and thromboembolic phenomena. If a Foley urinary catheter was placed, it should be removed as soon as the patient is ambulatory. Intravenous lines and narcotic analgesic drugs also should be discontinued as early as possible in the postoperative period. Perioperative antibiotics are usually discontinued within 24 to 48 hours. Longer use of prophylactic antibiotics is indicated in select circumstances such as craniofacial surgery and surgical procedures where "packing" is used, creating a contaminated "closed space," for example, for a defect after a maxillectomy.

### Management of the Surgical Site and Drains

Most surgical wounds in the head and neck region do not require a dressing and can be kept open to the air. These surgical sites must be kept meticulously clean to prevent infection. Blood clots and crusting around the suture line are cleaned daily, and Bacitracin ointment is applied to keep the wound free from superficial infection. Intraoral suture lines should be cleaned beginning 2 to 3 days after surgery with hydrostatic power sprays of saline solution, with or without hydrogen peroxide. A dilute solution of hydrogen peroxide and saline is sprayed using powered equipment at least twice daily in the oral cavity to keep the area mechanically clean. In addition, the patient is taught self-care using frequent gravity-controlled oral irrigations. The surgical drain site should be kept clean, with frequent sterile dressing changes if a Penrose drain is used. Output from surgical drains should be monitored and the drain removed when output is less than 25 mL in 24 hours for closed suction drains and when output is minimal for Penrose drains.

### Pain Control

Intravenous analgesic drugs are administered for pain control in the first 24 hours following surgery. For most head and

neck procedures, the use of intravenous analgesic agents should be terminated as soon as the patient is able to take oral analgesic medications. In selected cases, patient-controlled analgesia (PCA) may be initiated if intense pain is anticipated or in situations in which a patient is not able to communicate analgesic needs. This system allows the patient to self-administer intravenous analgesics as required on demand and can be adjusted until pain is properly controlled. Management of prolonged pain following surgery requires consultation with a pain specialist.

### Airway Management

Humidification of the airway is essential for smooth recovery from anesthesia in the immediate postoperative period. If the patient is breathing through his or her mouth or nose, humidity is delivered with the use of a face tent. The use of nasal catheters to deliver oxygen should be discouraged, because they are prone to cause drying of the nasal cavity, increasing the risk for epistaxis. If a tracheotomy is performed, humidity is delivered via a tracheotomy collar to maintain moisture in the air delivered to the lungs. The nursing staff should be familiar with the care of the tracheotomy site and the tube. The cuff of the tracheotomy tube should remain deflated if the patient is breathing spontaneously. Regular gentle suctioning of the airway is generally required for the first few days, and the patient should be encouraged to cough out secretions. The cuffed tracheotomy tube generally should be exchanged for a cuffless tube when mechanical ventilatory support is no longer required. Ties around the neck to secure the tracheostomy tube should be avoided in patients who have undergone reconstruction with a pedicled or free flap to prevent pressure on the vascular pedicle of the flap. In such instances the tracheostomy tube is secured with sutures to the skin of the neck. When the patient is able to tolerate plugging of the tracheotomy tube for 24 to 48 hours, it may be removed safely. Downsizing of the tracheotomy tube in anticipation of decannulation is not necessary. The sequence of decannulation of the tracheotomy tube in relation to the nasogastric tube depends on several factors; this issue will be addressed with each surgical procedure as applicable. Following decannulation, an occlusive dressing is applied to the tracheotomy site. The patient is instructed to apply digital pressure on the dressing when he or she coughs and phonates for the first few days. Most temporary tracheotomy wounds heal within a few days, and no special wound care is required. If a long-term tracheotomy is anticipated, the patient and the family should be educated and instructed about tracheostomy care as soon as the patient is stable.

### Nutrition

Maintenance of adequate nutrition is necessary for satisfactory wound healing. An average daily intake of 2000 calories is satisfactory for most patients. Intravenous alimentation is seldom required, because the alimentary tract is physiologically intact in nearly all patients undergoing head and neck surgery. For most uncomplicated procedures in the oral cavity, oral intake can begin on the first postoperative day, starting with liquids and advancing to a full diet as tolerated. In cases in which a short restriction in oral diet is anticipated, a nasogastric feeding tube should be placed at the time of the operation. The tube should be sutured in place to the ala of the nose to minimize

risk for accidental removal. The position of the tube should be confirmed radiographically with a chest x-ray, before starting tube feedings. If prolonged use of nasogastric feeding is anticipated, placement of a percutaneous endoscopic gastrostomy (PEG) tube should be considered. Oral intake can start 7 to 10 days after most uncomplicated laryngopharyngeal surgical procedures, even when free tissue transfer is used for reconstruction. The timing of oral intake may be delayed in patients who have previously received radiation or when fistula formation is a concern. Consultation with a speech and swallowing pathologist should be considered in cases in which dysphagia or aspiration is a concern before starting an oral diet.

### **Rehabilitation**

Successful outcome after head and neck surgery depends on multidisciplinary involvement in preoperative assessment and thorough preparation of the patient, intraoperative management,

and postoperative care. Participation by the patient in understanding the disease, its natural history, and self-care after recovery from surgery are also crucial to a successful outcome. As the patient recovers from the operation, the emphasis of care should transition to education of the patient and his or her family regarding self-care and early rehabilitation. Rehabilitative measures, including speech and swallowing and physical and occupational therapy, should be initiated in the hospital and continued until satisfactory goals are achieved. Psychosocial issues often surface after treatment and should be anticipated, identified, and addressed as required. Long-term preventative measures also should be instituted in the perioperative period, including smoking and alcohol cessation with involvement of dedicated personnel if possible. Finally, lifelong follow-up is necessary for patients undergoing head and neck surgery for cancer so that they can be monitored for recurrence and new primary cancers and their psychosocial needs can be addressed.



# Scalp and Skin



The skin, by surface area, is the largest organ in the human body. In its role as a barrier to the outside environment, the skin is continuously exposed to putative carcinogens; thus it is not surprising that skin cancer represents the single most common human malignancy. The diversity of embryologic origins of the skin and its adnexal structures leads to a wide range of malignancies. Although their true incidence is difficult to determine, it is well established that basal and squamous cell carcinomas represent the most common human malignancies, accounting for more than 3 million new cases annually in the United States (Table 3.1). Melanomas are the third most common cutaneous malignancy, with approximately 73,000 new cases annually. Nonepithelial skin cancers such as adnexal carcinomas account for an additional 5000 cases. Moreover, the rates of both melanoma and nonmelanoma skin cancers are rising in the United States. The increase is most pronounced for melanoma. The precise cause for this increase is unknown, but it may be related to increased sun exposure and an increased rate of detection. In spite of the rising rates of skin cancers, mortality rates have remained relatively stable. Overall, the clinical behavior of these tumors ranges from low-risk basal cell carcinoma to the more aggressive melanoma and adnexal tumors, with squamous cell carcinoma holding an intermediate position.

Excessive and/or cumulative sunlight exposure occurring at a younger age in fair-skinned persons contributes to skin cancer pathogenesis. Ultraviolet (UV) radiation, specifically UV-B radiation in sunlight, promotes oncogenesis through deoxyribonucleic acid (DNA) damage. Innate defense mechanisms against UV-B-induced oncogenesis include melanin synthesis and active DNA repair mechanisms. Therefore fair-skinned persons with low levels of melanin or those with compromised DNA repair are at highest risk for development of skin cancers. Patients with an immune dysfunction such as acquired immunodeficiency syndrome or medical immunosuppression related to

transplantation or lymphoma also have a significantly higher risk of cutaneous squamous cell carcinomas, Merkel cell carcinoma, and possibly melanomas. Moreover, heritable factors are known to play a role in skin cancer pathogenesis. For example, a family history of melanoma is associated with a twofold to eightfold increased risk for developing melanoma. In addition, several genetic syndromes predispose some persons to skin cancer, including xeroderma pigmentosum (*XPC* mutation; basal cell carcinoma and melanoma), nevoid basal cell carcinoma syndrome (*PTCH1* mutation; basal cell carcinoma), Bazex syndrome (basal cell carcinoma), and basal cell nevus syndrome (melanoma).

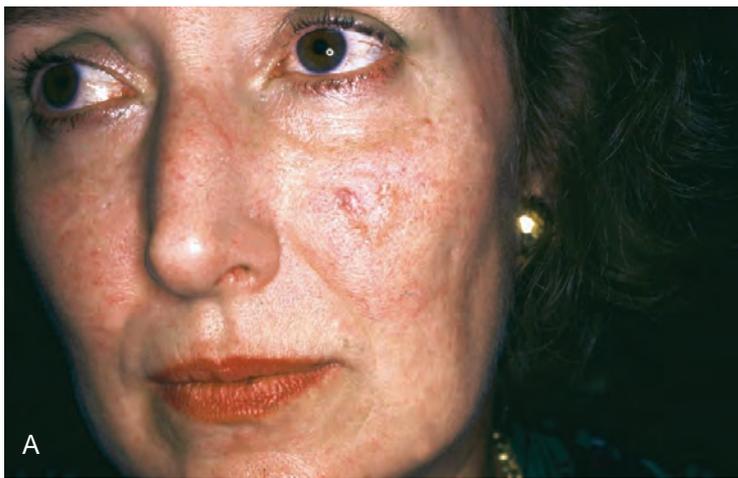
A wide range of genetic changes occur in human skin cancers. Mutations in specific pathways known to contribute to skin carcinogenesis include hedgehog signaling and the mitogen-activated protein kinase pathway. Mutations in the patched gene (*PTCH1*), which is the receptor for the sonic hedgehog (*SHH*) gene, have been identified both in patients with sporadic basal cell carcinomas and in patients with nevoid basal cell carcinoma syndrome. Germline mutations in cell cycle regulatory genes (*CDKN2A*, cyclin-dependent kinase 4, and the melanocortin 1 receptor gene) have been associated with melanoma development. Inactivation of *CDKN2A* by methylation and of cyclin-dependent kinase 4 by amplification is common in sporadic cases. The identification of activating somatic mutations in the *BRAF* gene in patients with melanoma has had a significant impact on our understanding of this disease and on development of novel treatment approaches. Although activation of *BRAF* mutations is common in melanomas (>50%), it also is found in high frequency in patients with benign nevi, suggesting it may be an early event in carcinogenesis. No pathognomonic or highly characterized abnormalities have been identified in other cutaneous malignancies.

## EVALUATION

Most cutaneous malignancies present as surface lesions (Fig. 3.1). In contrast, adnexal tumors typically present as subepithelial lesions (Fig. 3.2). In most cases, a thorough clinical examination including palpation of the lesion and surrounding tissue and draining the lymph node basin is sufficient to define the extent of the tumor. Optical aids such as dermoscopy (epiluminescence microscopy) and Wood light may be used to enhance clinical evaluation. Technologic advancements, such as confocal microscopy and computer-assisted image analysis, likely will provide clinicians with additional diagnostic tools in the future. Although selected indeterminate lesions can be followed clinically and/or with photodocumentation, biopsy is the cornerstone of diagnosis of skin malignancy.

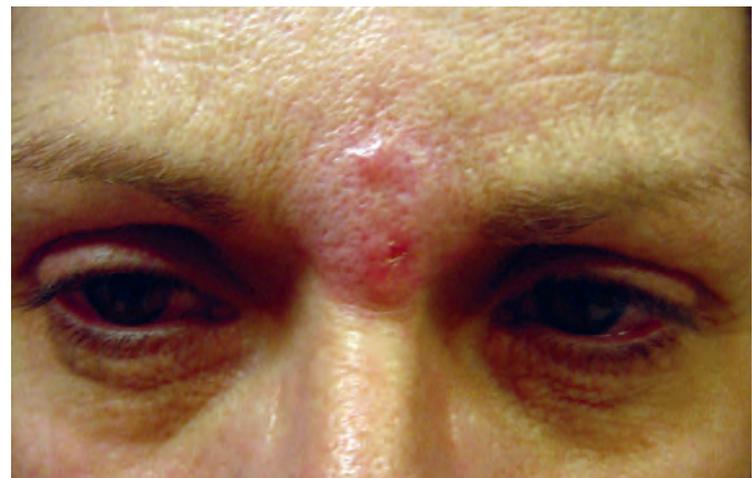
**Table 3.1 Annual Incidence and Mortality From Cutaneous Malignant Tumors in the United States**

HISTOLOGY	ANNUAL INCIDENCE (US)	ANNUAL MORTALITY (US)
Basal cell and squamous cell carcinoma	>3 million	<5000 (<0.1%)
Melanoma (all)	135,000	
Invasive (2015 American Cancer Society estimates)	73,870	9490 (12.8%)



**Figure 3.1** Clinical appearance of (A) basal cell carcinoma, (B) squamous cell carcinoma, and (C) malignant melanoma.

Radiologic evaluation is helpful in selected cases. Local extension of disease in the dermis, subcutaneous plane, and satellite nodules, along with bone erosion, can be defined by computed tomography (CT) (Fig. 3.3) or magnetic resonance imaging (MRI). Several skin malignancies can be neurotropic and manifest perineural extension. The cranial nerve most commonly at risk is the trigeminal nerve, which provides the sensory supply to the majority of the face (Fig. 3.4). MRI is useful in demonstrating the presence and extent of perineural spread of disease (Fig. 3.5). The role of positron emission



**Figure 3.2** Typical appearance of an adnexal tumor.

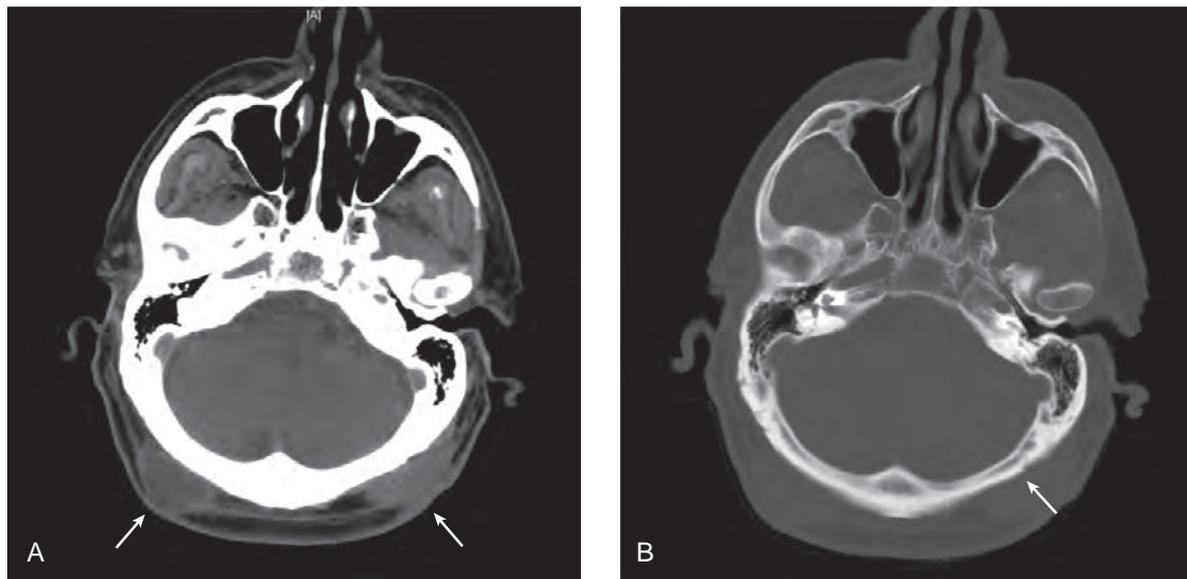
tomography scanning is evolving, but this type of scan appears to be a valuable adjunct for assessing the extent of disease.

### Basal Cell Carcinomas

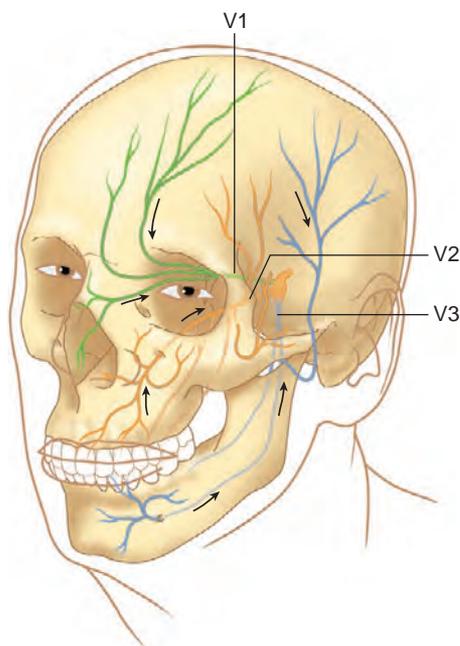
Approximately 80% of basal cell carcinomas occur in the head and neck region. These tumors classically present as pearly papular lesions that can ulcerate and invade local tissues, earning them the nickname of “rodent ulcer.” Because basal cell carcinomas also can be pigmented, malignant melanoma may be a consideration in the differential diagnosis. Morpheiform basal cell carcinoma can present as a flat atrophic lesion with poorly defined borders similar to a scar appearance, making clinical diagnosis challenging (Fig. 3.6). After diagnosis of a basal cell carcinoma, there is substantial risk of developing a subsequent basal cell carcinoma within a few years. These tumors rarely metastasize (only in 0.01% of cases) but can cause significant tissue destruction and disfigurement if not diagnosed and treated appropriately. Metastasis is associated with a poor clinical outcome with an expected survival of <10% at 5 years. Recent advances in hedgehog pathway inhibitor drugs offer patients with locally advanced or metastatic basal cell carcinoma another treatment option when further surgery or radiation is no longer possible. Basal cell carcinomas are derived from basal progenitor cells of the epidermis. Histologically these tumors are composed of dark, elongated cells aligned side by side with peripheral palisading and retraction from the adjacent stroma, producing a cleftlike space. This space may contain prominent stromal mucin (hyaluronic acid). The histologic growth patterns include superficial, nodular, infiltrative, morpheiform, and metatypical (Fig. 3.7), and frequently more than one pattern is present in a tumor. Infiltrative, morpheiform, and metatypical (or basosquamous) types are considered more aggressive with greater invasion and increased risk for recurrence. While immunohistochemical studies are not typically required in diagnosis, these tumors are known to be immunoreactive for Ber-EP4 and pankeratin and may even show carcinoembryonic antigen (CEA) positivity.

Although there is no formal staging system for basal cell carcinoma, the National Comprehensive Cancer Network has developed guidelines for treatment based on evidence and consensus expert opinion. The guidelines divide basal cell carcinoma into low and high risk for local recurrence based on clinical and histologic tumor features. The “mask-area” of the face (around eyes, nose, lips, ears, temple, mandible) represents





**Figure 3.3** Computed tomography scan of a patient with squamous cell carcinoma of the scalp show (A) satellite nodules on soft tissue window (arrows) and (B) erosion of the calvarium on the bone window (arrow).

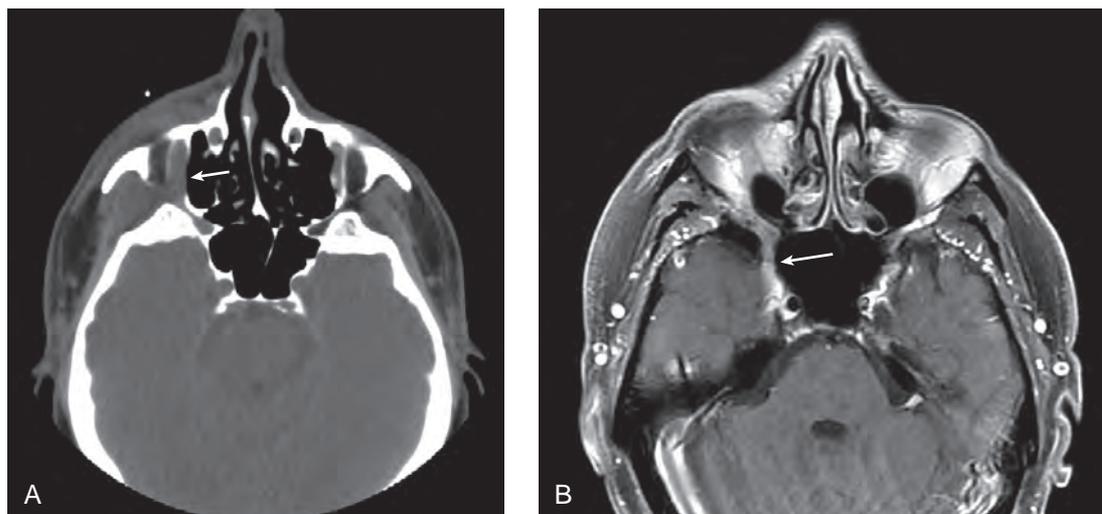


**Figure 3.4** Pathways of perineural spread of cutaneous malignancies along the trigeminal nerve.

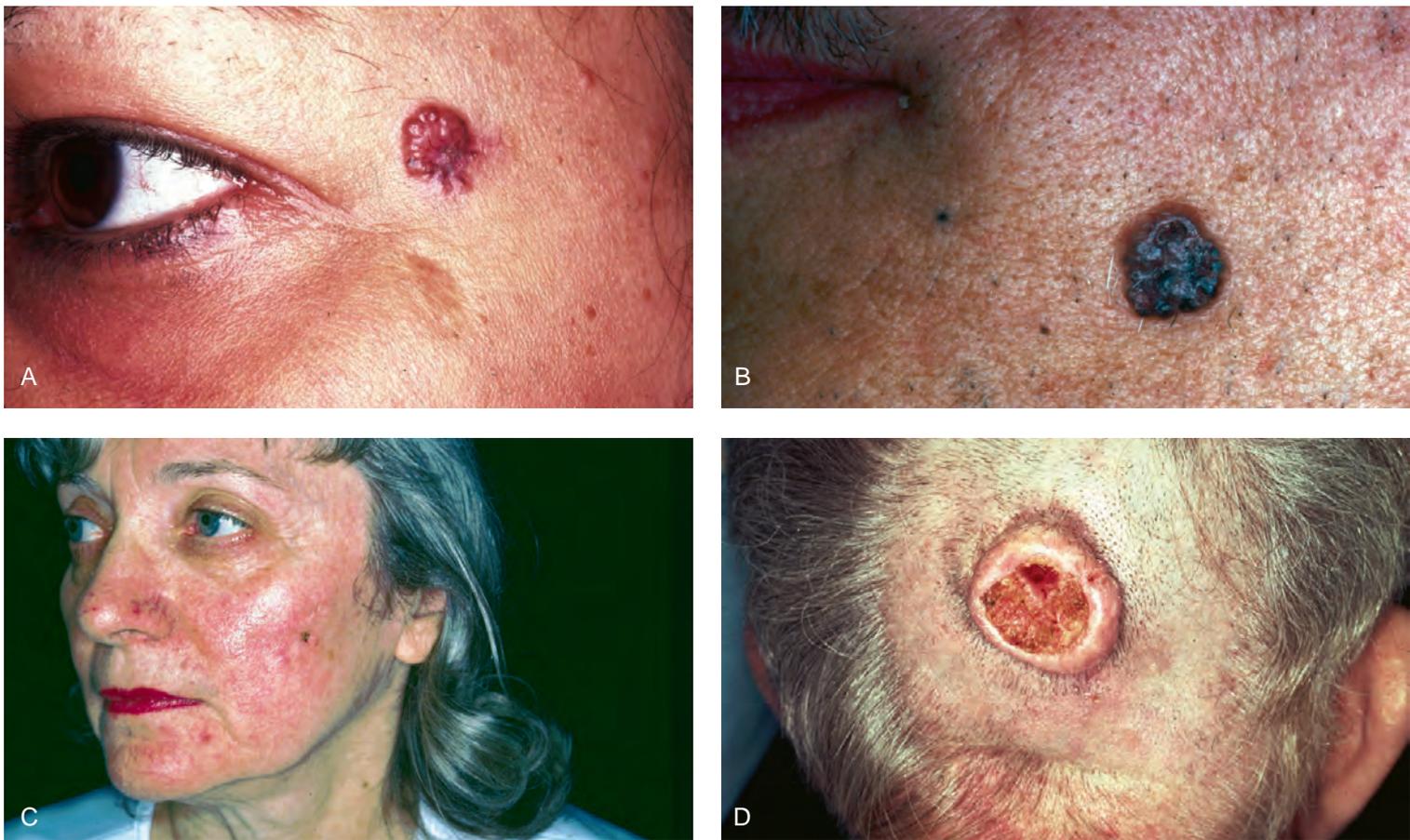
a higher risk location for skin cancer extension and recurrence. High-risk features include large size, location in “mask area,” poorly defined clinical borders, recurrence, site of prior radiation, aggressive histologic subtype, and immunosuppression.

### Squamous Cell Carcinomas

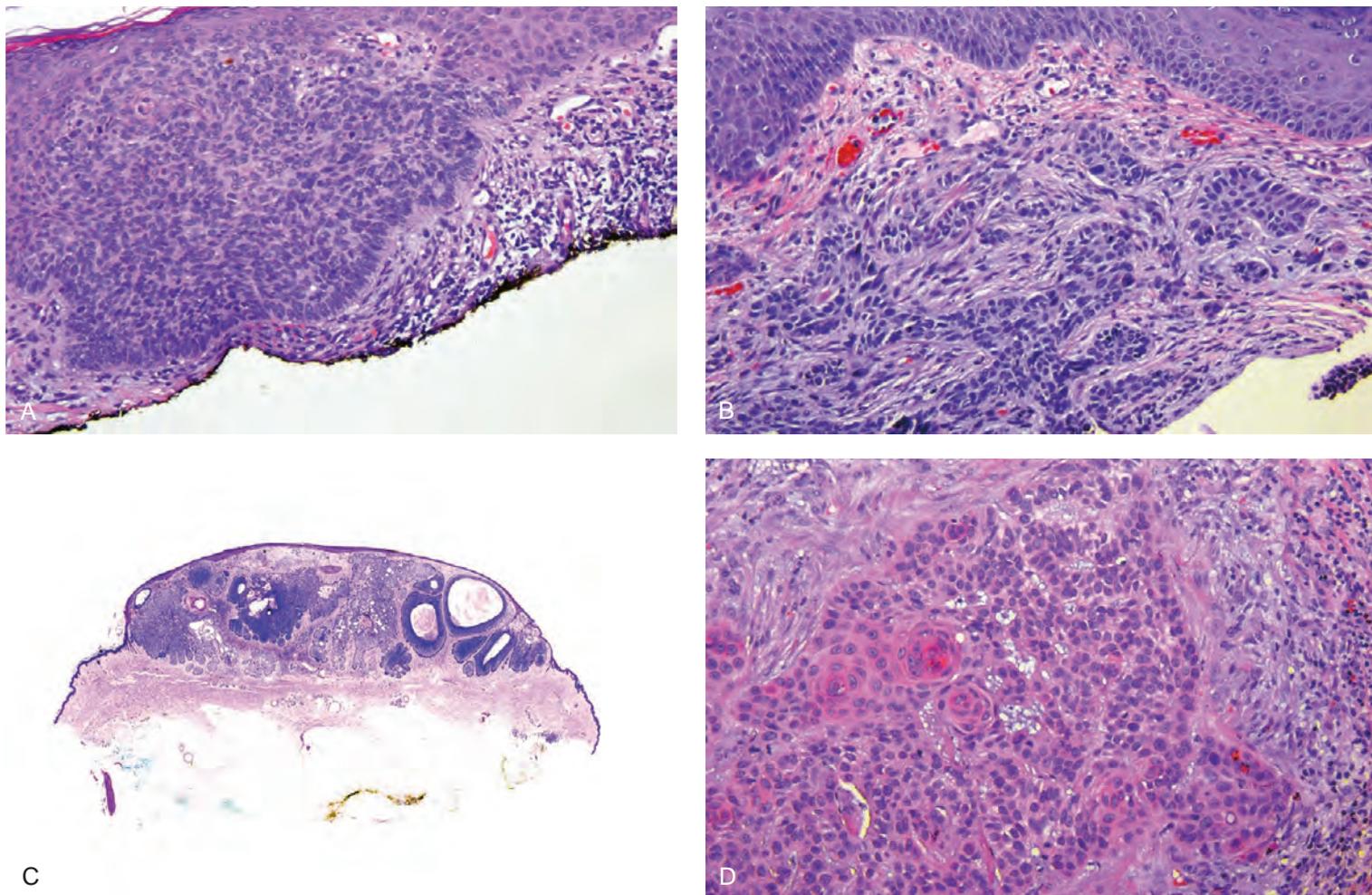
Squamous cell carcinomas can be variable in their presentation, ranging from erythematous scaly lesions to highly infiltrative aggressive tumors. Dermal lymphatic permeation presents as distinct intradermal nodules and have an aggressive behavior (Fig. 3.8). More than 70% of all cutaneous squamous cell carcinomas arise in the head and neck region in sun-exposed areas primarily on the ear and upper face. A small proportion of these tumors arise from preexisting actinic keratoses. Although progression has been reported to occur in as many as 25% of untreated cases, the true progression rate for actinic keratoses to squamous cell carcinoma is closer to 0.01% to 0.2% per lesion per year. When actinic damage develops on the lower lips, the term *actinic cheilitis* is used. Other causes of squamous cell carcinoma include ionizing radiation exposure, chronic nonhealing wounds, and human papilloma virus.



**Figure 3.5** Perineural extension of a skin cancer along the second division of the trigeminal nerve. A, Computed tomography scan showing involvement of the infraorbital nerve (arrow). B, Magnetic resonance imaging scan showing extension into Meckel's cave (arrow).



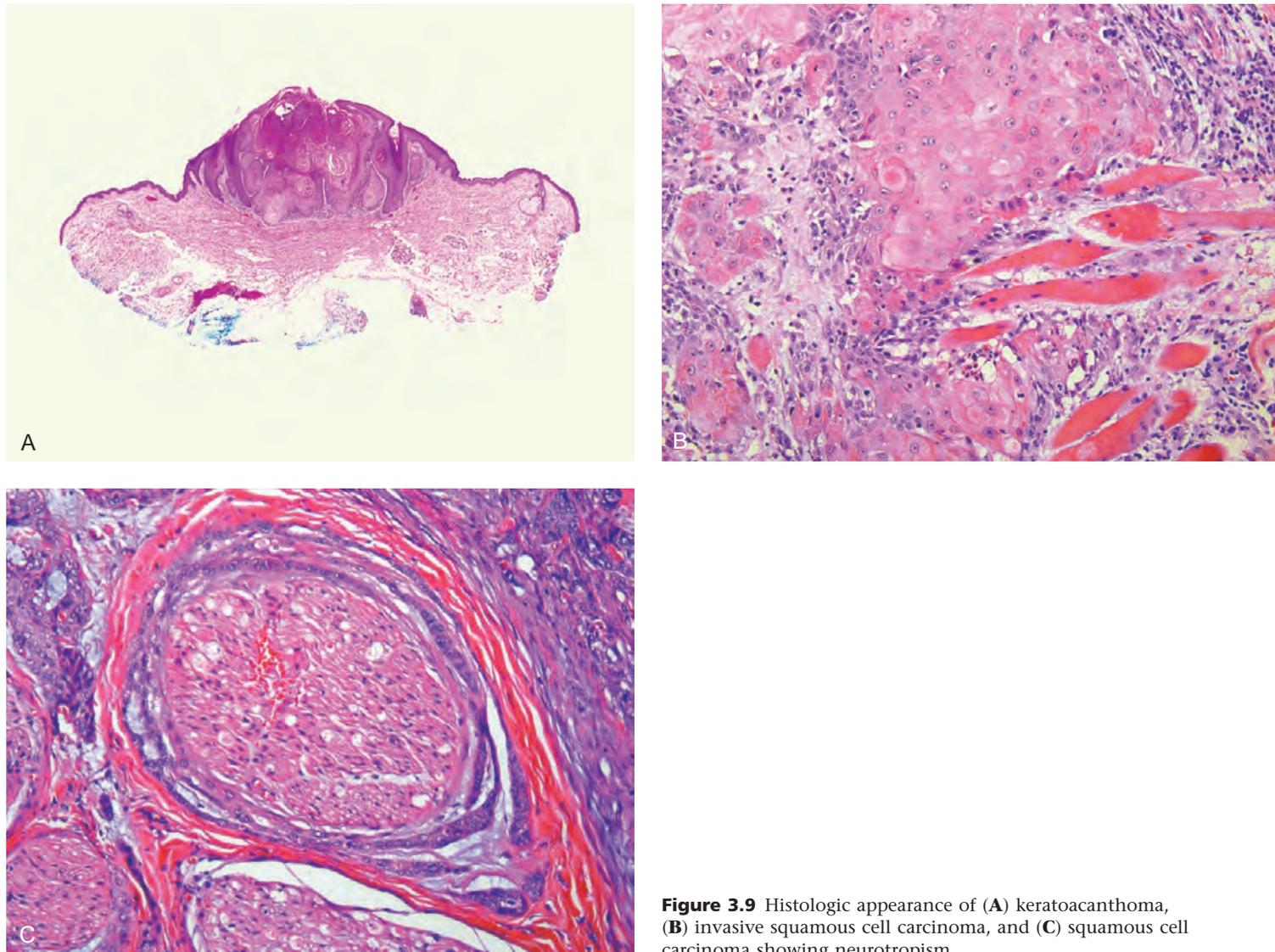
**Figure 3.6** Clinical variants of basal cell carcinoma. **A**, Classic. **B**, Pigmented. **C**, Morpheaform.



**Figure 3.7** Histologic subtypes of basal cell carcinoma showing low to high risk types. **A**, Superficial. **B**, Nodular. **C**, Infiltrative. **D**, Metatypical.



**Figure 3.8** Clinical appearance of squamous cell carcinoma. **A**, Multiple superficial lesions. **B**, Infiltrative. **C**, Extensive squamous cell carcinoma of the scalp with dermal nodules.



**Figure 3.9** Histologic appearance of **(A)** keratoacanthoma, **(B)** invasive squamous cell carcinoma, and **(C)** squamous cell carcinoma showing neurotropism.

Bowen disease (also known as *intraepithelial squamous cell carcinoma*) and keratoacanthoma are unique variants of squamous cell carcinoma. Bowen disease is essentially an in situ squamous cell carcinoma that can progress to invasive cancer if left untreated. Keratoacanthomas are unusual neoplasms that often display rapid growth over a 2- to 4-week period, followed by involution. The precise classification of keratoacanthomas as a variant of squamous cell carcinoma or as a unique entity remains a topic of debate. Histologically, squamous cell carcinomas

show a “mosaic” or tile-like pattern of cells with anastomosing intracellular bridges, or desmosomes. Tumors may grow in nests, islands, or single cells and can show variable degrees of intracytoplasmic keratinization, with keratin pearl formation in well-differentiated carcinomas (Fig. 3.9).

Overall, small squamous cell carcinomas (<2 cm) rarely metastasize (metastasis occurs in <5% of cases), but when metastasis does occur, it portends a dismal outcome. Other negative prognostic features include a size larger than 2 cm, prior

treatment, immunosuppression, tumor invasion into subcutis or greater (>6 mm), poor differentiation, and neurotropism (perineural invasion). Microscopic perineural invasion does not portend the same poor prognosis as invasion of named nerves such as the trigeminal and facial nerves. Peripheral nerve involvement is indicated by pain, paresthesia, and numbness along sensory nerves and by fasciculation or weakness of muscles of expression, denoting involvement of the facial nerve. Several staging systems have been proposed for squamous cell carcinoma using high-risk features for local recurrence and metastasis, including American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC; eighth edition). The most recent staging criteria include histologic criteria such as depth of invasion (DOI; >6 mm) and perineural invasion.

## Melanoma

Melanomas originate from junctional or dermal melanocytes that frequently involve the skin of the head and neck. In addition to skin type and a history of sun exposure, the presence of dysplastic nevi, family history, and immune dysfunction raise the risk for melanoma. Nearly half of all melanomas occur de novo in normal skin, and the remaining ones arise from preexisting nevi. A change in the size or appearance of a preexisting nevus with itching, variegated appearance, ulceration, and bleeding should prompt examination of a biopsy specimen.

Melanomas typically present as an irregularly pigmented lesion with a macular or papular appearance. They can be amelanotic or scarlike (i.e., desmoplastic melanomas), but this presentation is rare. These nonpigmented lesions can be mistaken for the more common basal or squamous cell carcinomas. The four main subtypes of melanoma are (1) superficial spreading melanoma (70% of cases) and has a characteristic horizontal growth pattern; (2) lentigo maligna, which occurs in heavily sun-exposed regions with potential for unpredictable subclinical horizontal extension; (3) acral lentiginous melanoma, which typically occurs in the nail beds, palms, and soles of the feet and is more common in African Americans and Asians; and (4) nodular melanoma, which usually is invasive at presentation and has a predilection for the extremities and trunk, with the scalp being the most common site in the head and neck (Fig. 3.10).

The clinical behavior of melanoma typically is defined by its depth of infiltration, which is assessed microscopically by direct measurement (Breslow's thickness) and is used to define the T stage (except for T1 tumors) by the AJCC. In the past, Clark's Level of Depth of Invasion was used for staging of cutaneous melanoma. However, Breslow thickness is more accurate in prediction of prognosis for melanoma and is currently used in staging. Comparative depth of invasion between Clark's Levels and Breslow thickness are shown in Fig. 3.11. Other factors included in the staging system are ulceration, mitotic rate, nodal metastasis (i.e., number and size), and distant metastasis (i.e., location and the serum lactate dehydrogenase level). Whereas thin melanomas rarely metastasize, intermediate-thickness melanomas show a high propensity for regional nodal metastasis, and thick melanomas have equal predilection to metastasize to both regional and distant sites. Moreover, melanomas also can produce "in transit" or "satellite" metastases.

Histologically, melanomas may or may not be pigmented and are composed of round to oval or fusiform tumor cells with nuclear pleomorphism and large, cherry-red, prominent nucleoli. These cells generally are located in rounded nests or

as solitary units at the dermal-epidermal junction. Within the epidermis, tumor cells may migrate upward to the surface of the epidermis (pagetoid spread). Invasive melanoma may infiltrate the dermis as single cell units or in groups of cells. In some instances the malignant cells may appear epithelioid, whereas in other instances they may appear to be elongated and spindle (fusiform). Hence numerous histologic phenotypes of melanoma exist (e.g., conventional epithelioid, spindle cell, signet ring cell, or balloon cell). Immunohistochemical staining for S-100 protein, Sox 10, Melan-A (MART-1; A103), HMB-45, tyrosinase, and microphthalmia transcription factor can help differentiate melanomas from other nonmelanotic malignant tumors. S-100 protein and Sox 10 also stain myoepithelial and dendritic cells and are found in nevi but are valuable markers for the diagnosis of desmoplastic melanomas. Melanomas are usually negative for epithelial markers. HMB-45 and Melan-A are highly specific for melanocytes, although Melan-A also can label adrenocortical carcinoma and sex cord stromal tumors of the ovary. Molecular diagnosis also may play a role in assessment of melanocytic tumors and help with treatment selection by identifying the presence or absence of a targetable mutation such as *BRAF V600E*.

## Adnexal Tumors

Adnexal tumors in the head and neck region present as intradermal or subcutaneous nodules and represent a wide range of neoplasms that vary in behavior and malignant potential. Nevus sebaceous is a congenital hamartoma that probably arises from basal cells and has a small propensity for transformation to basal cell carcinoma. Cyndromas (turban tumors) can be of either apocrine or eccrine origin and typically arise in the scalp or facial region of young adults. These lesions can occur de novo or may be inherited in an autosomal-dominant pattern. The *CYLD1* tumor suppressor gene is inactivated in both sporadic and familial forms. These tumors have a small propensity for malignant transformation to sweat gland carcinomas. Head and neck syringomas are tumors of eccrine origin that typically arise from the facial skin and eyelids. These lesions are usually multiple, yellowish in color, and have a fleshy covering. Eccrine spiradenomas usually are seen in younger patients and have a small propensity for malignant degeneration. These lesions present as expanding solitary nodules that are painful. Other benign tumors originating in adnexal structures include trichoepitheliomas and pilomatrixomas, but they are relatively rare.

Sweat gland carcinomas are skin appendage tumors derived from eccrine or apocrine glands. Unlike other skin cancers, these tumors do not have a racial predilection. These tumors typically present as 1- to 2-cm, firm, fixed, intradermal, or subcutaneous nodules that may ulcerate and become necrotic (Fig. 3.12). As they grow, they may coalesce and form larger subcutaneous lesions. Apocrine gland carcinomas are less common and occur most often in the axilla of elderly persons. In the head and neck, apocrine gland carcinomas can arise from various sites, including in the eyelid from Moll's gland, a modified apocrine gland. Apocrine gland carcinomas are highly aggressive neoplasms with a mortality rate over 50%. Metastases occur most frequently in regional lymph nodes, and local recurrence after resection is common. Eccrine gland carcinomas arise either de novo or from preexisting benign lesions. Histologic variants of sweat gland carcinomas include primary cutaneous, mucinous carcinoma, eccrine duct carcinoma, porocarcinoma, microcystic adnexal/sclerosing sweat duct carcinoma, endocrine



**Figure 3.10** Clinical variants of cutaneous melanoma. **A**, In-situ. **B**, Superficial spreading. **C**, Lentigo maligna melanoma. **D**, Acral lentiginous melanoma. **E**, Nodular melanoma with satellitosis.

mucin-producing sweat gland carcinoma, cribriform adenocarcinoma, and adenocarcinomas arising in association with a cylindroma or spiradenoma. Eccrine gland carcinomas typically arise from the ocular adnexa, including the meibomian glands, Zeis' glands, or pilosebaceous glands in older women. Salivary gland-type adenocarcinoma, or a metastasis of breast, pulmonary, or even prostate origin, may come into consideration in the differential diagnosis of eccrine carcinoma such as adenoid cystic carcinoma.

### Merkel Cell Carcinoma

Merkel cell carcinoma is a neuroendocrine neoplasm of the skin. The majority of these tumors in North America (80%) are

caused by infections with Merkel cell polyomavirus (MCPV), a double-stranded DNA virus. Nearly half of all Merkel cell carcinoma lesions occur in the head and neck region. The cheek is the most common site, followed by the upper neck and nose. These lesions typically occur in elderly white persons and appear as a red to violaceous, smooth, dome-shaped lesion with telangiectasias (Fig. 3.13). These tumors have a high propensity for metastatic spread to regional lymph nodes as well as distant sites. Histologically they are composed of basophilic cells with scant cytoplasm and dark powdery chromatin, and they may be morphologically similar to other neuroendocrine carcinomas. Hence metastatic small cell carcinoma, malignant melanoma, or primary neuroendocrine (or "small cell") carcinoma of the parotid gland may be considerations in the differential diagnosis.