Chapter 5: Oral Health and Oral Pharyngeal Cancers

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Learning objectives

- Define the term oral health.
- Study the parts of the mouth affected by oral cancer.
- Review the different types of cancer, benign and malignant.
- List the major risk factors of oral cancer.
- Identify the signs and symptoms.
- Describe the possible treatments and side effects.

Introduction

In 2008, in the United States alone, about 34,000 individuals were diagnosed with oral cancer. Statistics show that 66 percent of the time, these will be found as a late stage three or four disease. The term oral cancer includes cancers of the mouth and the pharynx, part of the throat. About two-thirds of oral cancers occur in the mouth and about one-third are found in the pharynx. Oral cancer will be diagnosed in an estimated 35,000 Americans this year and will cause approximately 7,500 deaths. Oral cancer can spread quickly. On average, 60 percent of those with the disease will survive more than five years. Oral cancer most often occurs in people over the age of 40 and affects more than twice as many men as women. Low public awareness of the disease is a significant factor, but these cancers could be found at early, highly survivable stages through a simple, painless, five-minute examination by a trained medical or dental professional.

Scientists are studying oral cancer to learn more about this disease, and doctors are exploring new ways to treat it. This research keeps increasing our knowledge about oral cancer.

Oral health means more than healthy teeth and the absence of disease. It involves the ability of individuals to carry out essential functions such as eating and speaking as well as to contribute fully to society. The meaning of oral health has developed in tandem with progress in understanding the two chief dental diseases – dental caries and periodontal diseases – which historically have been the major preoccupation of patients, providers and research investigators alike.

There is a marvelous success story here regarding the prevention of oral cancer and how it can be detected early. These investigations were complemented by studies of the tissues of the mouth and adjacent areas – the craniofacial complex.

Great progress has been made in reducing the extent and severity of common oral diseases, and recent history has seen marked improvements in the nation’s oral and dental health, thanks to successful prevention measures adopted by communities, individuals and oral health professionals. However, not everyone is experiencing the same degree of improvement. What amounts to a silent epidemic of dental and oral diseases is affecting some population groups – a burden of disease that restricts activities in school, work and home, and often significantly diminishes the quality of life.

The word oral, both in its Latin root and in common usage, refers to the mouth. The mouth includes not only the teeth and the gums (gingiva) and their supporting connective tissues, ligaments and bone, but also the hard and soft palate, the soft mucosal tissue lining of the mouth and throat, the tongue, the lips, the salivary glands, the chewing muscles and the upper and lower jaws, which are connected to the skull by the temporomandibular joints. Equally important are the branches of the nervous, immune and vascular systems that animate, protect and nourish the oral tissues, as well as provide the connections to the brain and the rest of the body. The genetic patterning of development in utero further reveals the intimate relationship of the oral tissues to the developing brain and to the tissues of the face and head that surround the mouth, structures whose location is captured in the word craniofacial.

A major theme of this course is that oral health means much more than healthy teeth. It means being free of chronic oral-facial pain conditions, oral and pharyngeal (throat) cancers, oral soft tissue lesions, birth defects such as cleft lip and palate, and scores of other diseases and disorders that affect the oral, dental and craniofacial tissues, collectively known as the craniofacial complex. These are tissues whose functions we often take for granted, yet they represent the very essence of our humanity. They allow us to speak and smile; sigh and kiss; smell, taste, touch, chew and swallow; cry out in pain; and convey a world of feelings and emotions through facial expressions. They also provide protection against microbial infections and environmental insults.

The craniofacial tissues also provide a useful means to understanding organs and systems in less accessible parts of the body. The salivary glands are a model of other exocrine glands, and an analysis of saliva can provide telltale clues of overall health or disease. The jawbones are examples of other skeletal parts. The nervous system apparatus underlying facial pain has its counterpart in nerves elsewhere in the body.

A thorough oral examination can detect signs of nutritional deficiencies as well as a number of systemic diseases, including microbial infections, immune disorders, injuries and some cancers. Indeed, the phrase “the mouth is a mirror” has been used to illustrate the wealth of information that can be derived from examining oral tissues.

New research is pointing to associations between chronic oral infections and heart and lung diseases, stroke, and low birth-weight and premature births. Associations between periodontal disease and diabetes have long been noted. This course assesses these associations and explores mechanisms that might explain these oral-systemic disease connections.

In parallel with the broadened meaning of oral health, the meaning of health has evolved. The standard definition of health, “freedom from disease, defect, or pain,” defines what health is not, rather than what it is. A more positive definition, one that the World Health Organization established in 1948, states that health is a complete state of physical, mental, and social well-being, and not just the absence of infirmity.
The broadened meaning of oral health parallels the broadened meaning of health. In 1948, the World Health Organization expanded the definition of health to mean “a complete state of physical, mental and social well-being, and not just the absence of infirmity.” It follows that oral health must also include well-being. Just as we now understand that nature and nurture are inextricably linked, and mind and body are both expressions of our human biology, so, too, we must recognize that oral health and general health are inseparable. We ignore signs and symptoms of oral disease and dysfunction to our detriment.

Consequently, a second theme of the report is that oral health is integral to general health. You cannot be healthy without oral health. Oral health and general health should not be interpreted as separate entities. Oral health is a critical component of health and must be included in the provision of health care and the design of community programs.

The wider meanings of oral and health in no way diminish the relevance and importance of the two leading dental diseases, caries (tooth decay) and the periodontal diseases. They remain common and widespread, affecting nearly everyone at some point in the life span. What has changed is what we can do about them.

At the start of the 20th century, most Americans expected to be toothless by age 45, and most were. Expectations have changed, and most people now assume that they will maintain their teeth over their lifetime and take active measures to do so. Researchers in the 1930s discovered that people living in communities with naturally fluoridated water supplies had fewer dental caries than people drinking unfluoridated water. But not until the end of World War II were the investigators able to design and implement the community clinical trials that confirmed their observations and launched a better approach to the problem of dental caries: prevention. Soon after, adjusting the fluoride content of community water supplies was pursued as an important public health measure to prevent dental caries.

Although this measure has not been fully implemented, the results have been dramatic. Dental caries began to decline in the 1950s among children who grew up in fluoridated cities, and by the late 1970s, declines in decay were evident for many Americans. The application of oral science to improved diagnostic, treatment and prevention strategies has saved billions of dollars per year in the nation’s annual health bill. Even more significant, the result is that far fewer people are edentulous (toothless) today than a generation ago.

The theme of prevention gained momentum as pioneering investigators and practitioners in the 1950s and 1960s showed that not only dental caries but also periodontal diseases are bacterial infections. The researchers demonstrated that the infections could be prevented by increasing host resistance to disease and reducing or eliminating the suspected microbial pathogens in the oral cavity. The applications of research discoveries have resulted in continuing improvements in the oral health of Americans, new approaches to the prevention and treatment of dental diseases, and the growth of the science.

The significant role that scientists, dentists, dental hygienists and other health professionals have played in the prevention of oral disease and disability leads to a third theme of this report: safe and effective disease prevention measures exist that everyone can adopt to improve oral health and prevent disease. These measures include daily oral hygiene procedures and other lifestyle behaviors, community programs such as community water fluoridation and tobacco cessation programs, and provider-based interventions such as the placement of dental sealants and examinations for common oral and pharyngeal cancers. It is hoped that this surgeon general’s report will facilitate the maturing of the broad field of craniofacial research so that gains in the prevention of craniofacial diseases and disorders can be realized that are as impressive as those achieved for common dental diseases.

At the same time, more needs to be done to ensure that messages of health promotion and disease prevention are brought home to all Americans. In this regard, a fourth theme of the report is that general health risk factors, such as tobacco use and poor dietary practices, also affect oral and craniofacial health. The evidence for an association between tobacco use and oral diseases has been clearly delineated in almost every surgeon general’s report on tobacco since 1964, and the oral effects of nutrition and diet are presented in the surgeon general’s report on nutrition (1988). All the health professions can play a role in reducing the burden of disease in America by calling attention to these and other risk factors and suggesting appropriate actions.

Clearly, promoting health and preventing disease are concepts the American people have taken to heart. For the third decade, the nation has developed a plan for the prevention of disease and the promotion of health, embodied in the U.S. Department of Health and Human Services (2000) document, Healthy People 2010. As a nation, we hope to eliminate disparities in health and prevent oral diseases, cancer, birth defects, AIDS and other devastating infections; mental illness and suicide; and the chronic diseases of aging. To live well into old age free of pain and infirmity and with a high quality of life is the American dream.

Scientists today take that dream seriously in pursuing the intricacies of the craniofacial complex. They are using an ever-growing array of sophisticated analytic tools and imaging systems to study normal function and diagnose disease. They are completing the mapping and sequencing of human, animal, microbial and plant genomes, the better to understand the complexities of human development, aging and pathological processes. They are growing cell lines, synthesizing molecules and using a new generation of biomaterials to revolutionize tissue repair and regeneration. More than ever before, they are working in multidisciplinary teams to bring new knowledge and expertise to the goal of understanding complex human diseases and disorders.

The mouth

The mouth is the gateway to the body, performing dozens of functions that place high demands on its unique hard and soft tissues. The point of entry is the lips, which open into the oral cavity. The cheeks form the sides of the cavity, and the roof is formed by the palate, which separates the mouth from the nose above and the pharynx (throat) behind. The anterior palate is hard, formed by underlying bone, and serves as a shield against trauma to the face and head. The posterior palate is soft, composed of muscles and connective tissue that blend into the walls of the pharynx. Hanging from the rear of the soft palate is the uvula, a mass of muscle and connective tissue. Under the tongue is the floor of the mouth, composed primarily of muscle and salivary glands. The paired tonsils and adenoids, important components of the immune system, lie at the sides of the palate and within the nasopharynx, respectively.

The pharynx opens into channels leading either to the lungs for respiration or the esophagus for further digestion and passage to the stomach. This is a point of vulnerability, where food or other obstructions can lodge in the airway and lead to death by asphyxiation.

Externally, the oral cavity is bounded by the maxilla (the upper jaw bone), attached to the cranium, and the mandible (the lower jaw), attached to the temporal bone of the skull by the temporomandibular joint.
The oral mucosa

Except for the teeth, the oral tissues are covered by a mucous membrane called the oral mucosa, which varies in color from pink to brownish purple, depending on an individual's skin color. Like skin, the oral mucosa acts as a major barrier against chemical irritants and mechanical forces; it can even withstand temperatures that would be painful to the skin. In areas subject to chewing forces and food movements, the surface layer is relatively hard, composed of epithelial cells filled with insoluble keratin, the fibrous protein found in skin, nails, hair, and animal horn. Elsewhere – in the mucosal lining of the cheeks, for example – the surface layers are softer and more flexible, enabling the mobility we need to speak, chew and make facial expressions. To aid in their barrier function, surface mucosal cells are square-shaped and closely juxtaposed, with specialized organelles and cell products that promote cell-cell adherence. The cells can also secrete sticky molecules to plug gaps between them and further impede penetration by damaging chemicals or microorganisms. Still another type of oral mucosa forms the pebbly surface of the back and sides of the tongue. Lining the depths of these surface “papillae” are the taste buds.

Interestingly, the epithelium that lines the gingival surface completely lacks a keratin layer, yet this “naked” epithelium lies next to one of the most dense concentrations of bacteria to be found in the body. Thus there is an opportunity for infectious agents or their byproducts to penetrate the naked epithelial barrier and initiate an inflammatory response, as happens in gingival disease.

Special cells in the basal layer of the oral mucosa generate replacements for surface cells as they wear out. The painful oral ulcers and oral mucositis that may develop in patients undergoing radiation or chemotherapy for head and neck cancer occur because these cancer-killing agents attack all cells undergoing rapid turnover, whether healthy or cancerous.

The teeth

The most prominent features of the oral cavity are the teeth. The 20 primary, or deciduous, teeth erupt generally between 6 months and 2 to 3 years of age and are succeeded by the permanent teeth beginning at about age 6. The primary teeth enable infants to eat solid foods, aid speech development, and serve as placeholders for the permanent dentition. Keeping primary teeth healthy is important, not only in sparing an infant pain and disease, but also in preserving the dimensions of the dental arches and lessening the risk of dental caries in the permanent teeth. A period of mixed primary and permanent dentition occurs from about ages 6 to 13. There are 28 to 32 permanent teeth, depending on whether the four wisdom teeth (third molars), which are last to erupt, are present. Teeth are anchored in the jaws by the periodontal ligament. This ligament connects the cervix (neck) of the tooth, at the junction between the crown and root, to the gingiva. Below that, the ligament connects the outer layer of the tooth root, the cementum, to the adjacent alveolar bone (the part of the jaw bone that supports the tooth roots).

The evolutionary forces that shaped the human mouth designed an apparatus for optimal food intake. The front four upper and lower incisor teeth are chisel-shaped for biting, cutting and exerting forces of 30 to 50 pounds. The canines, or cusps, are larger and stronger and have deeper roots than the incisors; their conical cusps are effective for ripping and tearing. The premolars, or bicuspids, and the molars are designed for heavy grinding and chewing, exerting forces as high as 200-plus pounds. The temporomandibular joint, the most complex synovial joint in the body, equips the human jaw with extraordinary mobility, enabling movements in three dimensions. Its range of motion is controlled by three sets of muscles of mastication – the masseter, temporalis, and pterygoid muscles. Chewing reduces food to small particles and mixes it with saliva to form a bolus for swallowing.

The salivary glands

Saliva is the mixed product of multiple salivary glands that lie under the mucosa. The three major glands are the paired parotid, submandibular and sublingual glands. The parotids, near the ears, secrete a watery saliva into the mouth via ducts in the cheeks. The walnut-sized submandibular glands lie in the floor of the mouth and secrete a mucous fluid. The secretions of the almond-shaped sublingual glands, also in the floor of the mouth but near the front, usually join with those of the submandibular glands. Tiny minor salivary glands are scattered within the inner surfaces of the lips, cheeks and soft and hard palates; these secrete a mucous saliva directly onto the soft tissue surfaces.

Saliva moistens food and provides mucinous proteins to lubricate the bolus for ease of swallowing. The combined movements of the tongue and cheeks move the bolus to the back of the mouth. Saliva also contains the enzyme amylase, which initiates the digestion of starch. By solubilizing food components and facilitating their interaction with the taste buds on the tongue and palate, saliva also contributes to taste enhancement.

Tissue protection

The main function of saliva is not – as is commonly believed – to aid digestion, but to protect the integrity of the oral tissues. The moment a baby passes through the birth canal and takes its first breath, microbes begin to take up residence in its mouth. Later, as the teeth erupt, additional bacteria establish colonies on tooth surfaces. Nearly 500 species of microbes in all, most of which are not harmful, will colonize the oral cavity. The microbes form a biofilm, in which their numbers greatly exceed the number of human inhabitants on Earth. Millions of years before there were toothbrushes, dental floss and water irrigators, evolutionary forces generated protective mechanisms to combat potentially harmful microbes. The physical flow of saliva helps to dislodge pathogens (viruses, bacteria and yeast) from teeth and mucosal surfaces, just as tearing and blinking, sneezing and coughing and expectorating clear the eye, nose and throat. Saliva can also cause microbes to clump together so that they can be swallowed before they become firmly attached. Saliva can destroy orally shed infected white blood cells by virtue of its low salt content: the infected cells – of higher salt content – swell and burst when exposed to fluids of lower salinity.

Salivary secretions, like tears and other exocrine gland secretions, are rich in antimicrobial components. Certain molecules in saliva, such as lysozyme, lactoferrin, peroxidase and histatins, can directly kill or inhibit a variety of microbes; the histatins are particularly potent antifungal agents. Several salivary proteins exhibit antiviral properties, including secretory leukocyte protease inhibitor (SLPI), recently discovered to have the ability to inhibit HIV from invading cells.

The ability of saliva to limit the growth of pathogens, in some instances even preventing them from establishing a niche in the
biofilm community in the first place, is a major determinant of general as well as of oral health. When salivary flow is compromised, the

**Barrier and buffering properties**

Salivary components protect oral tissues in other ways as well. Mucins have unique properties that enable them to concentrate on mucosal surfaces and provide an effective barrier against drying and physical and chemical irritants. They act as natural waterproofing, control the permeability of the tissue surfaces and help limit penetration of potential irritants and toxins in foods and beverages, as well as toxic chemicals and potential carcinogens in tobacco and tobacco smoke and from other sources. This barrier function complements the barrier formed by the oral mucosa itself. The mucosa has a specific permeability coefficient that can change under various conditions of stress, nutritional status, and other challenges.

Saliva contains several effective buffering systems that can help maintain a normal pH when acidic foods and beverages are introduced, thereby protecting oral tissues against acidic attack. When swallowed, these buffers protect the esophagus, helping neutralize the reflux acids of conditions such as heartburn and hiatal hernia.

**Wound healing**

Saliva also contains molecules that nurture and preserve the oral tissues, even helping them to repair and regenerate. Experimental studies have shown that wound healing is significantly enhanced by saliva, in part because of the presence of a potent molecule, epidermal growth factor (EGF). When swallowed, EGF can also protect the tissue surfaces of the esophagus. Vascular endothelial growth factor (VEGF) has also been identified in saliva. VEGF stimulates blood vessels and may contribute to the remarkable healing capacity of oral tissues.

**Caries protection**

Saliva also guards against dental caries (tooth decay), the disease that has been the greatest threat to teeth. Caries is caused by bacteria that generate acids that attack tooth mineral. The buffering systems in saliva, augmented by the neutralizing components urea and ammonium, counter the acid formation. The physical flow of saliva also helps flush out sugars and food particles that are the bacterial food source. Mineral salts in saliva – calcium and phosphate – can remineralize tooth enamel, effectively reversing the decay process. This regenerative function is greatly enhanced by the presence of fluoride in saliva. Finally, saliva forms a film on teeth made up of selectively adsorbed proteins that have a high affinity for tooth mineral. This acquired pellicle is insoluble and limits the diffusion of acids into the teeth and the dissolution of tooth mineral.

**The immune system**

The salivary glands and the oral mucosa, along with the body’s other mucosal linings and the lymphatic circulation, constitute a major component of the body’s defense system – the mucosal immune system. When the area of the oral mucosa is combined with the areas of the mucosal linings and passageways of the respiratory, gastrointestinal, urinary, and genital tracts, the total represents the largest surface area of the body – nearly 400 square meters, or 200 times larger than the total skin area.

The great majority of infectious diseases affect or are acquired through mucosal surfaces. Immune cells that line the mucous membranes throughout the body secrete antibodies targeted to specific disease-causing microbes. The mucosal immune system works in concert with the blood-borne immune system to detect and dispose of foreign substances and invading microbes.

The two components of the immune system consist of molecules and cells that provide both broad and specific defense mechanisms. In the broad group are some circulating white blood cells (monocytes and granulocytes) associated with the inflammatory response. These cells migrate to a site of injury or infection and move into damaged tissues manifesting the four signs of inflammation: swelling, heat, redness and pain. The cells promote an increase in blood flow to begin the healing process, and they recruit other cells able to engulf and dispose of the offending organism.

The specific immune system is associated with two major classes of immune cells: T cells and B cells. T cells react to antigens (proteins associated with microbes or irritants) and can stimulate B cells to make antigen-specific antibodies. These are the Y-shaped molecules called immunoglobulins.

T cells are the instruments of cell-mediated immunity; they are able to detect telltale surface markers on diseased or foreign cells that distinguish them from normal body cells. Some T cells can kill infected cells and cancer cells directly. T cells are also involved in the rejection of organ transplants.

Certain T cells are memory cells, preserving the information from earlier encounters with specific pathogens. Thus they are able to initiate more rapid and effective responses in the event of a repeat encounter with the pathogen. Helper T cells assist in activating killer T and B cells. It is the loss of helper T cells that leads to the many infections that cause illness and death in HIV disease. Still another group of T cells, suppressor T cells, moderates the activities of both B and T lymphocytes.

Activated T cells generate and release cytokines – potent families of proteins, such as the interleukins, that can stimulate immune cells to divide, migrate, attack and engulf invaders or participate in the inflammatory response. Other cytokines include varieties of tumor necrosis factor and adhesins (proteins that facilitate the binding of immune cells to each other or to blood vessel linings). Feedback mechanisms provide a system of checks and balances to regulate cytokine production.

The immune system interacts with the nervous and endocrine systems. For example, immune cytokines secreted into the brain can induce the fever associated with infection: the high temperature may help destroy the infectious agent. The brain’s response to stress also has repercussions for the immune system. The hypothalamus-pituitary-adrenal axis is a major pathway activated in response to stress, which results in the secretion of cortisol, the stress hormone, from the adrenal glands. Cortisol promotes the body’s fight-or-flight mechanisms, but via feedback loops, cortisol acts to depress immune reactions.

Much of what we know about the immune system has come from studies of serum factors, but research in the last two decades has generated much new information about mucosal immunity. The mucosal immune system can be divided into inductive and effector compartments. The nasal-associated lymphoreticular tissues (NALT)
in the nasopharyngeal area (which includes the tonsils) and the gut-associated lymphoreticular tissues (GALT) in gut tissue are inductive regions where foreign invaders are encountered. If, for example, infectious bacteria are swallowed, they can stimulate immune cells in GALT to circulate T and B cells through the lymph system to various effector sites in the gastrointestinal and upper respiratory tracts and in the salivary and other exocrine glands. The B cells in the gland produce antibodies, designated S-IgA, to which is attached a secretory component. These antibodies are the dominant type found in saliva, tears, breast milk and colostrum and in the gastrointestinal and genitourinary tracts.

The uses of the mucosal immune system extend beyond its normal surveillance and defense functions. The tissues can be used as routes for delivery of oral (swallowed) or nasal (inhaled) vaccines, as sites for gene transfer to augment host defenses, and as a means of invoking oral tolerance — the suppression of overactive or inappropriate immune responses that occur in chronic inflammatory and autoimmune diseases.

### Craniofacial origins

The extraordinary successes of research in molecular genetics over the past decade, coupled with the National Institutes of Health’s project to map and sequence the human genome, have proved to be a boon in understanding craniofacial development. The use of automated gene-sequencing equipment, the Internet availability of genome databases and the ability to transfer genes or create “knockout” animals — in which a gene of interest has been eliminated — have greatly facilitated progress. The events that govern the transformation of a fertilized human egg cell into a healthy newborn with all organs and systems in place are being unfolded at the molecular level. Families of master and regulatory genes have been identified, and their role in controlling how the body’s general shape and specialized tissues and organs are formed is coming to light.

### EARLY DEVELOPMENT

#### The three-germ cell layers

By the time the face and the mouth are ready to form, the human embryo is in the third week of development. The embryo has evolved from a sphere to an oval, two-layered disk with a head-to-tail orientation. The outer layer is the epiblast and will become the ectodermal germ layer. A narrow groove, called the primitive streak, extends from the tail toward the center of the disk, where it ends in a spot surrounding a small depression called the primitive pit. Epiblast cells migrate toward the streak and pit, detach from the surface and slip downward to form the two additional germ-cell layers, the mesoderm and, below that, the endoderm.

The ectodermal layer gives rise to tissues that relate the body to the outside world: the nervous system; the sensory epithelium of the ears, nose, and eyes; skin, hair, nails, salivary glands, tonsils and tooth enamel; and the pituitary, mammary and sweat glands. At the head end, the mesodermal layer gives rise to a primitive connective tissue, called mesenchyme, which will interact with the ectoderm to form parts of the head and mouth. The remaining mesoderm develops into the muscle, cartilage, bone and subcutaneous skin tissue of the rest of the body. The mesoderm is also the origin of the vascular and urogenital systems (except for the bladder), the spleen and the adrenal cortex. The innermost, endodermal layer provides the linings of the gut, the respiratory system, bladder, liver, pancreas, thyroid and parathyroid glands, and parts of the middle ear.

#### Neural tube and neural crest

Further migrations and descending movements of cells result in the formation of the notochord, a solid cord of cells along the midline that will become the backbone. The ectoderm above the notochord next thickens to form a neural plate. The sides of the plate curve up and inward to form a neural tube, beginning at the head, with fusion completed by the end of the fourth week. The tail end of the tube will form the spinal cord; the head end differentiates into the three parts of the primitive brain: the forebrain, midbrain and hindbrain.

What happens next is of central importance to the craniofacial complex: Cells that were at the edges of the neural plate break away to form neural crest cells, which migrate to the forebrain area and to the nearby branchial arches, a series of swellings on either side of the embryo adjacent to the hindbrain. The hindbrain becomes organized into eight rhombomeres, segments of future nerve tissue arranged in an orderly fashion so that the first two rhombomeres innervate branchial arch 1, and so on.

During the formation of the midbrain and hindbrain, cranial neural crest cells migrate into the developing facial areas and differentiate into neuronal and nonneuronal tissues. The neuronal tissues include the clusters of nerve cells (ganglia) that lie adjacent to the spinal cord, parts of the ganglia of four cranial nerves, and two of the meningeal layers of the brain. The nonneuronal tissues include major bones, cartilage, the dentin and cementum of teeth, and the various types of connective tissues of the craniofacial complex, as well as the muscles of the eye. The branchial arches give rise to the bones, cartilage, nerves, muscles, and blood supply of successive segments of the head and neck.

#### The face and mouth

The branchial arches play a key role in the formation of the facial structures. Toward the end of the fourth week of gestation, a primitive mouth appears. This “stomadeum” is flanked by a series of swellings, or prominences, derived from the first pair of branchial arches. A single frontonasal prominence forms the upper border of the stomadeum. On either side of this prominence are two thickened regions of ectoderm — the nasal placodes. At the sides of the stomadeum and below it are pairs of maxillary and mandibular prominences.
forms from shelflike outgrowths of the maxillary prominences. These
growths appear in the sixth week, and in the following week fuse along
the midline above the tongue. (The tongue appears at approximately
four weeks, the front two-thirds forming from the first branchial
arch and the posterior third from parts of the second, third and fourth
branchial arches.) The palatal shelves also fuse with the primary palate
along a triangular border called the incisive foramen. This border is
considered the line of division among clefting abnormalities. Lateral
cleft lip, cleft upper jaw, and clefts between the primary and secondary
palates are associated with defects anterior to the incisive foramen.
Cleft palate and cleft uvula occur because of defects affecting closure
of the palatal shelves posterior to the foramen.

The teeth

Tooth development begins in the sixth week with the appearance of
an epithelial band lining the upper and lower jaws. A part of the band
develops into a dental lamina, which forms a series of projections
into the jaw. These are the tooth buds and correspond to the sites of
deciduous teeth. The epithelial tissue of the bud develops into an enamel
organ that forms a cap over tissue that is differentiating in the jaw to
become the dental papilla. The two structures – the enamel organ,
derived from the epithelium, and the dental papilla, derived from neural
crest mesenchyme – constitute the tooth germ.

With further development, the tooth germ assumes a bell shape and
separates from the oral epithelium. At the same time, the internal
epithelial layer of the enamel organ undergoes a series of infoldings
that will shape the future crown of the tooth.

Genetic controls

Only in the last decade have scientists begun to understand how
certain genes and gene families control embryonic development. Their
findings have come from detailed studies of species ranging from
fruit flies, nematodes and zebrafish to frog, chick, mouse and human
embryos. In many cases, the simpler organism has been the source
of discoveries of genes or developmental processes that are highly
conserved in the course of evolution.

Research on the fruit fly, for example, has revealed that particular
families of genes are responsible for the fundamental head to thorax
to tail patterning of the fly’s body. Another set of genes determines
the back-to-front positioning of organs, and a third set subdivides
this general body plan into a series of discrete segments. With
further development, yet another family of genes confers a positional
memory on the cells within a segment. These “homeotic selector”
genesis ensure that cells in one part of a particular segment “know”
that they are destined to be wings and not legs, or to be eyes and not
antennae. In flies the homeotic genes are known as hom genes. Their
arrangement on the fly chromosome is ordered with genes at one end
of the chromosome specifying the developmental destiny of cells in
the most anterior segments of the fly’s body and genes at the other end
specifying the fate of cells in the most posterior segments.

In the course of evolution, mammals have developed four overlapping
sets of positional memory gene clusters homologous to the fly’s single
hom complex. The four mammalian hom gene families are ordered in
a similar anterior-posterior fashion along four different chromosomes.
The mammalian genes appear to operate like the hom genes: they code
for DNA-binding proteins that control gene expression. The similarity
from fly to human is particularly evident when maps of the expression
domains of hom genes in anterior segments of the fly embryo are
compared to maps of hox gene expression as seen in the rhombomeres
and branchial arches of mammals.

Molecular genetic studies of flies and other nonmammalian species
show some variation in how and when the basic body patterns and
repeating segments are formed. Sometimes the head-to-tail pattern
is laid down in the egg cell before fertilization – dictated by egg
polarity genes. Although egg polarity genes do not operate in humans,
mutations have been found in a human gene homologous to the fly egg
polarity gene and account for serious syndromes in which there are
defects in anterior organs, such as the pituitary gland and heart.

None of these developmental controls work in isolation. Much
remains to be understood about the genetic clock that determines
when and where developmental genes act, how they interact, and what
mechanisms are used to sustain as well as terminate their function. The
systems that govern programmed cell death are also important: normal
development depends as much on the elimination of cells as it does on
the orderly movement, proliferation and differentiation of cells.

When it comes to processes that control the development of particular
tissues or organs – bones, skin or heart – developmental biologists
observe that there is often an “organizer,” that is, a cell or set of
cells that initiates the process. The organizer induces changes in the
behavior of neighboring cells through cell-cell interactions, so that
these cells develop into the specified type – bone or skin or heart
muscle. The interaction with the neighboring cell is often in the form
of a signaling molecule, such as a growth factor (e.g., transforming
growth factor beta, epidermal growth factor, fibroblast growth factor)
that attaches to a receptor on the surface membrane of the recipient
cell. This interaction is translated to the interior of the cell, where a
chain of molecular interactions eventually reaches the cell nucleus
effect gene expression. One of the more startling discoveries of
the past decade has been the finding that a series of mutations, each
associated with a change in only one nucleotide of the gene for
the fibroblast growth factor receptor – also called point mutation –
accounts for a range of organ defects seen in at least a half dozen
craniofacial syndromes. Interestingly, all these syndromes include
craniosynostosis, a premature closure of the bones that form the skull.

The aging of craniofacial tissues

Normal aging describes the developmental processes that begin at
conception, continue in childhood and merge gradually into maturation
and senescence. The milestones of development such as the age when
children teeth, begin to walk, talk, enter puberty, attain their full
height and so on, are under genetic and hormonal controls, subject to
important environmental factors such as nutrition and exercise. Despite
the complexity and interrelationships of the variables involved, a
reasonably accurate picture of normal age-related changes in the craniofacial complex is emerging.

Barring major illness or injury, destructive behaviors or severe or unusual environmental circumstances, the cells, tissues and fluids of the face and mouth are hardy survivors, eminently durable and functional over a long life span. For any given individual the combination of life experience and lifestyle (including medical and dental history) creates a unique craniofacial portrait, one that inspired George Orwell to remark, “By the age of 50, a man gets the face he deserves.”

The teeth
One of the more dramatic discoveries in biomedical science in the 20th century has been the realization that tooth loss is not an inevitable consequence of aging, but the result of disease or injury. Aging does produce a number of other dental changes, however. Teeth change in form and color with age. Wear and attrition alter the biting and chewing surfaces, as do food choices and oral habits. The altered surface structure produces a different pattern of light reflection in older teeth, resulting in some yellowing and a general loss of translucency. Fully formed enamel is acellular, hence there is no metabolic activity or turnover as occurs in skin, for example. Dentin and cementum have limited cellular activity. In contrast, tooth pulp and periodontal ligament undergo relatively high levels of tissue turnover.

Tooth surfaces can be eroded by chemical dissolution from fruit acids and from acids from sugars in foods such as soft drinks and candies. This destructive process can occur at any age, resulting in loss of translucency as well as some tissue loss from demineralization. Countering the erosive forces are the natural components in saliva that help re-mineralize the enamel surface, a process that is enhanced when fluoride is present.

The cementum increases in thickness with age. Gingival recession caused by normal aging exposes the cementum to the oral environment (and is the origin of the expression “long in the tooth”). The exposed cementum can often be worn away mechanically, exposing the underlying dentin, which can then become hypersensitive. Dentin responds through a series of protective changes that work to close off the connections between dentin and nerves in the pulp, reducing transmission of painful stimuli.

The jaws
The bones of the maxilla and mandible that support the teeth, called the alveolar processes, are, like bone elsewhere in the body, subject to cellular turnover in a coordinated process of bone resorption and formation. Alveolar bone is well adapted to mechanical stresses and changes continuously during facial growth, tooth eruption, tooth wear and tooth loss. This lifelong adaptation makes orthodontic treatments to reposition teeth in adults possible.

Because the primary function of alveolar bone is to support the teeth, the loss of teeth will lead to bone atrophy, making prosthetic replacements difficult. The rate of bone loss is affected by both local disease such as periodontal disease and systemic conditions such as osteoporosis.

The oral mucosa
The high density of sensory nerve endings in the craniofacial tissues and their functional abilities are well-preserved in aging. There may be minor increases in threshold detection levels or in judgments of intensity, but, for the most part, sensory cells can turn over or have a built-in reserve capacity that allows for near-optimal functioning in aging. The exception is olfaction, which declines in both men and women with age. This decrement in smell may lead to some dissatisfaction with how foods taste and increased use of flavor enhancers to compensate. But for most people, the ability to enjoy food is not appreciably diminished as time goes by. Any dramatic change in sensory function – complaints of a continued unpleasant taste or smell or the sudden complete loss of a sensory modality – should be taken seriously as a sign of possible oral or systemic disease or a side effect of medication and not dismissed as a natural byproduct of aging.

The distribution of motor fibers in the craniofacial tissues is also abundant and sufficiently fine-tuned to allow for a full range of movement of the tongue, jaws and oral-facial muscles. There is some loss of muscle tone in aging, along with changes in tongue shape and function in articulating specific speech sounds. Subtle changes may also occur in preparing food for swallowing. As with sensory changes, these developments do not seriously interfere with motor function in healthy older adults.
Findings

Natural selection has served Homo sapiens well in evolving a craniofacial complex with remarkable functions and abilities to adapt, enabling the organism to meet the challenges of an ever-changing environment. An examination of the various tissues reveals elaborate designs that have evolved to serve the basic needs and functions of a complex mammal as well as those that are uniquely human, such as speech. The rich distribution of nerves, muscles and blood vessels in the region as well as extensive endocrine and immune system connections is an indication of the vital role of the craniofacial complex in adaptation and survival over a long life span. In particular, genes controlling the basic patterning and segmental organization of human development, and specifically the craniofacial complex, are highly conserved in nature. Mutated genes affecting human development have counterparts in many simpler organisms.

There is considerable reserve capacity or redundancy in the cells and tissues of the craniofacial complex, so that if they are properly cared for, the structures should function well over a lifetime.

The salivary glands and saliva subserve tasting and digestive functions and also participate in the mucosal immune system, a main line of defense against pathogens, irritants, and toxins. Salivary components protect and maintain oral tissues through antimicrobial components, buffering agents and a process by which dental enamel can be remineralized.

Oral and pharyngeal cancers and precancerous lesions

In 2000, oral or pharyngeal cancer was diagnosed in an estimated 30,200 Americans and caused more than 7,800 deaths (Greenlee et al. 2000). Over 90 percent of these cancers are squamous cell carcinomas – cancers of the epithelial cells. The most common oral sites are on the tongue, the lips and the floor of the mouth. Oral cancer is the sixth most common cancer in U.S. males and takes a disproportionate toll on minorities; it now ranks as the fourth most common cancer among African American men. The prominent role of tobacco use, especially in combination with alcohol, in causing these cancers is a major incentive to develop effective health promotion and disease prevention efforts.

This course is about cancers that occur in the mouth (oral cavity) and the part of the throat at the back of the mouth (oropharynx).

Heightening the risk

Oral cancer develops as a clone from a single genetically altered cell. It generally has a long latency period and invariably develops from a precancerous lesion on the oral mucosa, such as a white leukoplakia, or more commonly, a reddish erythroplakia. Both kinds of lesions are usually induced by tobacco use alone or in combination with heavy use of alcohol. The development of squamous cell carcinoma from initial erythroplakia lesions has been well demonstrated experimentally. Reported rates of malignant transformation for leukoplakias are between 0.13 and 17.5 percent. However, there is considerable debate as to the actual malignant potential of the leukoplakia lesion associated with the use of smokeless (spit) tobacco. Meaningful data for determining a specific malignant transformation rate or relative risk of oral cancer due to smokeless tobacco use are difficult to obtain because of the confounding effects of other habits such as concurrent smoking and alcohol consumption and because of the variations in smokeless (spit) products and how they are used.

Another oral precancerous lesion that has received attention is submucous fibrosis. It is commonly seen in India and Southeast Asia and is related to betel nut use.

Tobacco and alcohol

Tobacco and alcohol are the major risk factors for oral cancers, and their effects have been studied for many years. Tobacco contains substances that are frankly carcinogenic or act as initiators or promoters of carcinogenesis. Among these are N-nitrosornericotine, 4-nitroquinolone-N-oxide and benzpyrene. The most damaging carcinogens are found in the tars of tobacco smoke, but many forms of smokeless (spit) tobacco, including snuff, have been implicated in the development of mouth cancer. Other habits that have been related to oral cancer include chewing betel nut in the presence of tobacco, as is done primarily in Southeast Asia, and, more recently, using marijuana.

The role of alcohol in oral carcinogenesis has been demonstrated experimentally and appears to be related to its damaging effect on the liver. Major metabolites of alcohol, such as acetaldehyde – a known carcinogen in animals – may also be important. Alcohol is also thought to act as a solvent that facilitates the penetration of tobacco carcinogens into oral tissues. That observation may partly explain why the combined use of tobacco and alcohol produces a greater risk for oral cancer than use of either substance alone. Indeed, tobacco and alcohol, working in tandem, are thought to account for 75 to 90 percent of all oral and pharyngeal cancers in the United States.

The oral cavity and oropharynx have many parts:
- Lip
- Tongue
- Salivary glands (glands that make saliva)
- Floor of the mouth
- Hard palate
- Soft palate
- Uvula
- Oropharynx
- Tonsils
- Tongue

Pictured below are the following parts:

- Tongue
- Soft palate
- Hard palate
- Floor of the mouth
- Salivary glands
- Oropharynx
- Tongue
- Lip

Early epidemiologic studies identified behaviors such as smoking and environmental factors such as exposure to solar radiation and x-rays as causes of intraoral and lip cancers. Researchers then sought experimentally to explain the mechanisms of initiation. In the 1980s and 1990s, investigators explored the techniques of molecular biology and genetics to probe what was going on deep inside the cell. These studies revealed an abundance of systemic and local factors, including viral and fungal infections, that affect cell behavior. Some factors stimulate cell division and others inhibit it – even to the point of initiating a program of cell “suicide,” called apoptosis. How a given cell behaves at any given time in its life cycle is the net result of the signals it receives from neighboring cells and molecules, from circulating factors in the blood or immune system and from its own internal controls. The following sections provide a brief description of these factors and how they may participate in enhancing the risk for the development of oral cancers.

Pictured below are the following parts:
Viruses

The role of viruses in causing cancer in animals was established early in the century when Rous showed that a virus, later named the Rous sarcoma virus (RSV), caused tumors in chickens. The issue of whether viruses could cause cancer in humans remained unexplored until the mid-1970s, when Varmus and Bishop showed that RSV had a special gene, which they called src (for sarcoma), that could transform the cell it infected into a malignant cell. It was an oncogene, or cancer-causing gene. The researchers subsequently, and surprisingly, discovered that src was not native to the virus, but had been picked up by some ancestor virus from a chicken cell’s own genome, where src had presumably played a role in the chicken cell’s normal growth and development. Somehow RSV was able to subvert src when it infected a chicken cell to cause the cell to divide uncontrollably.

Varmus and Bishop called the normal cellular src gene a proto-oncogene, meaning that it had the potential to be converted to an oncogene. Subsequent research led to the discovery of other viruses that could cause tumors in animals and revealed the presence of proto-oncogenes in birds and mammals. These genes could also be converted to oncogenes, behaving exactly like those carried by cancer viruses. In 1982, an oncogene isolated from a human bladder cancer turned out to be virtually identical to ras, the oncogene found in a rat sarcoma virus.

Viruses that have been implicated in oral cancer include herpes simplex type 1 and human papillomavirus. Epstein-Barr virus, also growth, play a major role in cancer development. If an individual inherits or acquires a mutation in one or more tumor-suppressor genes, for example, the loss of this protective mechanism reduces the number of other deleterious changes needed for cancer to develop.

Tumor suppressor genes suspected to be mutated in oral and pharyngeal cancers include those for Rb, p16 (MTS1, CDKN2, or IN4a), and p53. Of the group of tumor suppressor genes, that coding for p53 is considered of major importance, with mutations in the p53 gene detected in many types of cancer, including oral and pharyngeal. The p53 gene has been called the “guardian of the genome” because of its ability to recognize damage to a cell’s DNA and stop the process of growth and division until the damage is repaired. If repair is not possible, p53 can trigger apoptosis. Mutations in the p53 gene in oral cancer have been linked to smoking and alcohol use.

Genetic derangements

Of the more than 50 known oncogenes, many have been reported to be present in oral cancer, and multiple oncogenes have been reported in oral and pharyngeal cancer. Some of these are Bcl-1, c-erb-B2, c-myc, ins-2 and members of the ras family.

The genetic derangements that can give rise to oral cancer, including many mutations associated with the transformation of proto-oncogenes, have received notable attention. In some instances, a change in a single nucleotide base – a point mutation – in a gene encoding a proto-oncogene is enough to transform it into an oncogene. Cancerous changes may also involve alterations, deletions and break points in chromosomes that affect the position of genes.

Mutations that disarm the cell’s DNA repair mechanisms as well as mutations in tumor suppressor genes, which inhibit abnormal cell growth, play a major role in cancer development. If an individual inherits or acquires a mutation in one or more tumor-suppressor genes, for example, the loss of this protective mechanism reduces the number of other deleterious changes needed for cancer to develop.

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Loss of immnosurveillance and control

The immune system can, as first noted by Paul Ehrlich in 1909, seek and destroy initial clones of transformed cancer cells. Ehrlich called this process immunosurveillance, and it has been confirmed in experimental animals and in humans with induced immunosuppression.

One mechanism of immunosurveillance involves stimulating cytotoxic macrophages and lymphocytes to migrate to the tumor site and release tumor necrosis factors alpha and beta. Another mechanism operative in oral cancer appears to be stimulation of Langerhans cells, a special group of immune cells, in the oral mucosa. Other immune cells implicated in tumor rejection are natural killer cells and lymphokine-activated killer cells.

There is an increased incidence of cancer in patients with AIDS or other immunodeficient conditions or with induced immunosuppression prior to organ transplantation.

In addition, there is evidence that smoking depresses the immune system, and this may be one of the ways in which smoking acts as a major risk factor in oral cancer.

Growth factors

Immune cells are potent generators of growth factors and other molecules that can stimulate other cells to migrate and proliferate. This capacity is important in normal cell growth and turnover, in wound healing and in coping with infection. Unfortunately, the release of growth factors can contribute to oral cancer by stimulating keratinocyte (oral epithelial cell) proliferation. Increased levels of transforming growth factor alpha (TGF-alpha) and epidermal growth factor have been found in oral and pharyngeal cancers and therefore could serve as markers for malignancy. Nicotine at high doses stimulates the release of growth hormones, among other endocrine effects.
Understanding cancer

Cancer begins in cells, the building blocks that make up tissues. Tissues make up the organs of the body. Normally, cells grow and divide to form new cells as the body needs them. When cells grow old, they die, and new cells take their place. Sometimes this orderly process goes wrong. New cells form when the body does not need them, and old cells do not die when they should. These extra cells can form a mass of tissue called a growth or tumor. Tumors can be benign or malignant:

- **Benign tumors:**
  - Benign tumors are not cancer:
    - Benign tumors are rarely life-threatening.
    - Generally, benign tumors can be removed, and they usually do not grow back.
    - Cells from benign tumors do not invade the tissues around them.
    - Cells from benign tumors do not spread to other parts of the body.

- **Malignant tumors:**
  - Malignant tumors are cancer.
  - Malignant tumors are generally more serious than benign tumors.
  - They may be life-threatening.
  - Sometimes they grow back.
  - Cells from malignant tumors can invade and damage nearby tissues and organs.
  - Cells from malignant tumors can spread to other parts of the body.
    - The cells spread by breaking away from the original cancer (primary tumor) and entering the bloodstream or lymphatic system.
    - They invade other organs, forming new tumors and damaging these organs.
    - The spread of cancer is called metastasis.

What are benign tumors?

There are many forms of benign (noncancerous) tumors that can appear in the oral cavity or oropharynx (in addition to other sites in/on the body), including:

<table>
<thead>
<tr>
<th>Benign Tumors</th>
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<tbody>
<tr>
<td>Lipoma</td>
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<tr>
<td>Neurofibroma</td>
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<td>Odontogenic tumors</td>
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<td>Osteochondroma</td>
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<td>Papilloma</td>
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<td>Pyogenic granuloma</td>
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<td>Rhabdomyoma</td>
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<tr>
<td>Schwannoma</td>
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<td>Verruca form xanthoma</td>
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Some benign tumors disappear on their own. Others may have to be removed surgically. Most benign tumors do not recur. Always consult your physician for a diagnosis.

What oral conditions may be precancerous?

Two conditions in the mouth — leukoplakia and erythroplakia — actually can be precursors to cancer. Often caused by smoking or chewing tobacco, these (initially) benign conditions can occur anywhere in the mouth. Only a biopsy can determine whether precancerous cells (dysplasia) or cancer cells are present in a leukoplakia or erythroplakia.

- **Leukoplakia** — a condition characterized by a whitish patch that develops inside the mouth or throat.
- **Erythroplakia** — a condition characterized by a red, raised patch that develops inside the mouth.

Treatment for leukoplakias or erythroplakias may include use of retinoids — medications related to vitamin A — to eliminate, reduce, and/or prevent dysplasia from forming.
What are malignant oral tumors?

Although there are several types of malignant oral cancers, more than 90 percent of all diagnosed oral cancers are squamous cell carcinoma.

<table>
<thead>
<tr>
<th>Malignant tumors</th>
<th>Verrucous carcinoma</th>
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<tbody>
<tr>
<td><em>Squamous cell carcinoma</em></td>
<td>Although also considered a type of squamous cell carcinoma, this low-grade cancer rarely metastasizes (spreads to distant sites). Comprising less than 5 percent of all diagnosed oral cancers, verrucous carcinoma can spread deeply into surrounding tissue, requiring surgical removal with a wide margin of surrounding tissue.</td>
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<tr>
<td><strong>Oral cancer and squamous cells</strong></td>
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<tr>
<td>Oral cancer is part of a group of cancers called head and neck cancers. Oral cancer can develop in any part of the oral cavity or oropharynx. Most oral cancers begin in the tongue and in the floor of the mouth. Almost all oral cancers begin in the flat cells (squamous cells) that cover the surfaces of the mouth, tongue, and lips. These cancers are called squamous cell carcinomas. When oral cancer spreads (metastasizes), it usually travels through the lymphatic system. Cancer cells that enter the lymphatic system are carried along by lymph, a clear, watery fluid. The cancer cells often appear first in nearby lymph nodes in the neck. Cancer cells can also spread to other parts of the body. When this happens, the new tumor has the same kind of abnormal cells as the primary tumor. For example, if oral cancer spreads to the lungs, the cancer cells in the lungs are actually oral cancer cells. The disease is metastatic oral cancer, not lung cancer. It is treated as oral cancer, not lung cancer. Doctors sometimes call the new tumor “distant” or metastatic disease.</td>
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<tr>
<td><strong>Oral cancer: Who’s at risk?</strong></td>
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| Dentists and doctors cannot always explain why one person develops oral cancer and another does not. However, we do know that this disease is not contagious. Scientists have determined that one cannot “catch” oral cancer from another person. Research has shown that people with certain risk factors are more likely than others to develop oral cancer. A risk factor is anything that increases your chance of developing a disease. The following are risk factors for oral cancer: | quitting tobacco reduces the risk of oral cancer. Also, quitting reduces the chance that a person with oral cancer will get a second cancer in the head and neck region. People who stop smoking can also reduce their risk of cancer of the lung, larynx, mouth, pancreas, bladder and esophagus. There are many resources to help smokers quit:  
- Advise patients to call The Cancer Information Service at 1-800-4-CANCER where they can talk with callers about ways to quit smoking and about groups that offer help to smokers who want to quit. Groups offer counseling in person or by telephone.  
- Help patients find a local smoking cessation program.  
- Tell them about the medicines (bupropion, Chantix) or about nicotine replacement therapy, which comes as a patch, gum, lozenges, nasal spray or inhaler.  
- Give them The “National Cancer Institute Information Resources” information about the federal government’s smoking cessation website, http://www.smokefree.gov.  
As a dental professional, you should discuss any concerns your patients share with you regarding cancer or any that you may have with them as soon as possible. Discuss an appropriate schedule for checkups. Alert your patients that not using tobacco and limiting their use of alcohol are the most important things they can do to prevent oral cancers. If they spend a lot of time in the sun, using a lip balm that contains sunscreen and wearing a hat with a brim will help protect their lips. Regular checkups can detect the early stages of oral cancer or conditions that may lead to oral cancer. Check the tissues in the mouth as part of the routine examination. |
| Tobacco: Tobacco use accounts for most oral cancers. Smoking cigarettes, cigars or pipes; using chewing tobacco; and dipping snuff are all linked to oral cancer. The use of other tobacco products (such as bidis and kreteks) may also increase the risk of oral cancer. Heavy smokers who use tobacco for a long time are most at risk. The risk is even higher for tobacco users who drink alcohol heavily. In fact, three out of four oral cancers occur in people who use alcohol, tobacco, or both alcohol and tobacco. |
| Alcohol: People who drink alcohol are more likely to develop oral cancer than people who don’t drink. The risk increases with the amount of alcohol that a person consumes. The risk increases even more if the person both drinks alcohol and uses tobacco. |
| Sun: Cancer of the lip can be caused by exposure to the sun. Using a lotion or lip balm that has a sunscreen can reduce the risk. Wearing a hat with a brim can also block the sun’s harmful rays. The risk of cancer of the lip increases if the person also smokes. |
| A personal history of head and neck cancer: People who have had head and neck cancer are at increased risk of developing another primary head and neck cancer. Smoking increases this risk. Some studies suggest that not eating enough fruits and vegetables may increase the chance of getting oral cancer. Scientists also are studying whether infections with certain viruses (such as the human papillomavirus) are linked to oral cancer. |
Symptoms

Common symptoms of oral cancer include:
- Patches inside the mouth or on the lips that are white, a mixture of red and white, or red. White patches (leukoplakia) are the most common. White patches sometimes become malignant. Mixed red and white patches (erythroplakia) are more likely than white patches to become malignant. Red patches (erythroplakia) are brightly colored, smooth areas that often become malignant.
- A sore on the lip or in the mouth that won’t heal.
- Bleeding in the mouth.
- Loose teeth.
- Difficulty or pain when swallowing.
- Difficulty wearing dentures.
- A lump in the neck.
- An earache.

Most often, these symptoms do not mean cancer. An infection or another problem can cause the same symptoms.

Diagnosis

- If your patient comes to you with symptoms that suggest oral cancer, such as red or white patches, lumps, swelling or other problems, you should explain to him or her very carefully that you are doing a special exam.
- Discuss this with the patient and explain that the exam includes looking carefully at the roof of the mouth, back of the throat and insides of the cheeks and lips.
- Let the patient know that you will gently pull out the tongue so it can be checked on the sides and underneath. Tell them that you will check the floor of the mouth and lymph nodes in the neck.
- Explain each step carefully. This is not a routine exam for you, and it is definitely not a routine checkup for your patient.
- When the exam is complete, you will need to discuss the next step with the patient.

Early diagnosis of oral and pharyngeal cancers

Dentists and primary care providers can counsel patients about lifestyle behaviors that increase the risk for oral cancers. Dental as well as medical personnel have provided successful tobacco control programs in their offices. Generally, Americans are ill-informed about the risk factors as well as the signs and symptoms of oral cancers. The mass media have paid little attention to the topic, and health education textbooks are nearly devoid of discussion. The scant attention that has been paid to oral cancers has focused on the role of spit tobacco.

At present, the principal test for oral and pharyngeal cancers is a comprehensive clinical examination that includes a visual/tactile examination of the mouth, full protrusion of the tongue with the aid of a gauze wipe and palpation of the tongue, floor of the mouth and lymph nodes in the neck. The U.S. Preventive Services Task Force concluded that there was insufficient evidence to recommend for or against routine screening for oral cancers, but noted that clinicians should remain vigilant for signs and symptoms of oral cancers and premalignancy in people who use tobacco or regularly use alcohol.

Biopsy

If the exam shows an abnormal area, a small sample of tissue may be removed. Removing tissue to look for cancer cells is called a biopsy. Usually, a biopsy is done with local anesthesia. Sometimes, it is done under general anesthesia. A pathologist then looks at the tissue under a microscope to check for cancer cells.

A biopsy is the only sure way to know whether the abnormal area is cancerous. When discussing a biopsy with patients, it is always good to be prepared to answer these questions:
- Why do I need a biopsy?
- How much tissue do you expect to remove?
- How long will it take? Will I be awake? Will it hurt?
- How soon will I know the results?
- Are there any risks? What are the chances of infection or bleeding after the biopsy?

How should I care for the biopsy site afterward? How long will it take to heal?
- Will I be able to eat and drink normally after the biopsy?
- If I do have cancer, who will talk with me about treatment? When?

If an exam shows an abnormal area, a small sample of tissue may be removed. Usually, a biopsy is done with local anesthesia. Sometimes, it is done under general anesthesia. A pathologist then looks at the tissue under a microscope to check for cancer cells.

Remember, your patients are scared, because cancer is very serious. They will not understand many things. They will need you to explain everything to them and their family. It is often a good idea to schedule a family appointment to discuss the type of cancer and the necessary treatment.

Staging cancer

Staging is the key to finding the cancer in the early development. When found early, oral cancers have an 80 to 90 percent survival rate. Unfortunately at this time, the majority are found as late-stage cancers, and this accounts for the very high death rate of about 45 percent at five years from diagnosis, and high treatment-related morbidity in survivors. Late-stage diagnosis is not occurring because these cancers are hard to discover, it is because of a lack of public awareness coupled with the lack of a national program for opportunistic screenings which would yield early discovery by medical and dental
professionals. Worldwide the problem is far greater, with new cases annually exceeding 481,000.

If the biopsy shows that cancer is present, you will need to know the stage (extent) of the disease to plan the best treatment. The stage is based on the size of the tumor, whether the cancer has spread and, if so, to what parts of the body. Staging may require lab tests. It also may involve endoscopy. This involves a thin, lighted tube (endoscope) to check the throat, windpipe and lungs. You will need to explain this procedure to the patient before scheduling the appointment and inform them that local anesthesia is used to ease the discomfort. This exam may be done in a dental office, an outpatient clinic or a hospital. At this time the dental professional may order one or more imaging tests to learn whether the cancer has spread:

- Dental x-rays: An x-ray of the entire mouth can show whether cancer has spread to the jaw.
- Chest x-rays: Images of the chest and lungs can show whether cancer has spread to these areas.
- CT scan: An x-ray machine linked to a computer takes a series of detailed pictures of the body. Depending on the type of tests, an injection of dye may be used.
- MRIs: A powerful magnet linked to a computer is used to make detailed pictures. The dentist or doctor can view these pictures on a monitor and can print them on film. An MRI can show whether oral cancer has spread.

Treatment

Many people with oral cancer want to take an active part in making decisions about their medical care. Be prepared to discuss all options with the patient. However, shock and stress after the diagnosis can make it hard to think of everything they want to ask. It often helps to make a list of questions and answers, have this ready to give to the patient before an appointment. Specialists who treat oral cancer include oral and maxillofacial surgeons, otolaryngologists (ear, nose and throat doctors), medical oncologists, radiation oncologists and plastic surgeons. There may be a team that includes specialists in surgery, radiation therapy or chemotherapy. Other health care professionals who may work with the specialists as a team include a speech pathologist, nutritionist and mental health counselor.

Surgical treatment for oral and pharyngeal cancers

Surgical treatment for oral and pharyngeal cancers can result in functional impairment as well as permanent disfigurement. Problems may include the loss of part of the tongue, loss of taste, loss of chewing ability, difficulty in speaking and pain. Furthermore, in addition to concerns about their function and their future, oral and pharyngeal cancer patients must cope with an altered appearance. In a study of patients who were disease-free from six months to eight years following surgical tumor removal, those with more pronounced disfigurement had greater changes in self-image, a worsened relationship with their partner, reduced sexuality and increased social isolation. One study noted that 30 percent of oral and pharyngeal cancer patients were still experiencing psychological distress seven to 11 years after treatment. Depression, too, is frequent in cancer patients. Patients with oral and pharyngeal cancers are at an even greater risk for depression than other cancer patients, due to surgeries that alter their appearance. Because oral and pharyngeal cancers are also frequently associated with chronic alcohol and tobacco use, depression may be related to withdrawal from these substances or to pre-existing psychopathology. Persistent pain, as noted earlier, may also be a contributing factor to depression.

A study conducted a prospective analysis of changes in quality of life over time with the aim of identifying which factors might be predictive of future improvements or declines. Participants were 186 oral and pharyngeal cancer patients, all smokers or recent former smokers, diagnosed with primary carcinomas of the oral cavity, pharynx, or larynx.

Type of procedure

Surgical excision (removal) of the tumor is usually recommended if the tumor is small enough, and if surgery is likely to result in a functionally satisfactory result. Radiation therapy is often used in conjunction with surgery or as the definitive radical treatment, especially if the tumor is inoperable. Surgeries for oral cancers include:

- Maxillectomy (can be done with or without orbital exenteration).
- Mandibulectomy (removal of the mandible or lower jaw or part of it).
- Glossectomy (tongue removal, can be total, hemi or partial).
- Radical neck dissection.

Moh’s procedure.

Combinational e.g. glossectomy and laryngectomy done together.

Owing to the vital nature of the structures in the head and neck area, surgery for larger cancers is technically demanding. Reconstructive surgery may be required to give an acceptable cosmetic and functional result. Bone grafts and surgical flaps such as the radial forearm flap are used to help rebuild the structures removed during excision of the cancer. An oral prosthesis may also be required.

Survival rates for oral cancer depend on the precise site, and the stage of the cancer at diagnosis. Overall, survival is around 50 percent at

The patients were tested at baseline, at one month after radiation and/or surgery, and one year later (for a subset of 105 patients available for follow-up). Measures used included the Karnofsky Performance Scale, which uses expert judgments of functional performance scored from 0 to 100; the Cancer Rehabilitation Evaluation System Short Form, in which patients rate their quality of life along physical, psychosocial, marital, sexual and medical interaction scales; the previously mentioned Performance Status Scale for Head and Neck Cancer Patients (which includes scales for eating and speaking); and the Profile of Mood States, in which patients rate their feelings over the previous week, yielding analyses that enable scaling along six mood states: tension-anxiety, depression-dejection, anger-hostility, confusion-bewilderment, and vigor-activity.

Results indicated that in spite of functional improvement on some scales over time, there was continued dysfunction in speech and eating. Patients also reported declines in marital and sexual functioning, as well as an increase in alcohol use. Interestingly, the best predictor of quality of life one year after treatment was the scores obtained after initial smoking cessation advice was given, while the patients were undergoing treatment and in recovery. Other predictors were treatment type (quality of life was generally poorer for radiation patients) and score on the vigor subscale of the Profile of Mood States. The investigators concluded that medical follow-up must integrate tailored psychological and behavioral interventions to achieve better quality of life for oral and pharyngeal cancer patients.
Dietary counseling

Rehabilitation may include:

- Movement, chewing, swallowing and speech. Speech and language pathologists may be involved at this stage.

Chemotherapy is useful in oral cancers when used in combination with other treatment modalities such as radiation therapy. It is seldom used alone as a monotherapy. When cure is unlikely, it can also be used to extend life and can be considered palliative but not curative care. Biological agents such as Cetuximab have recently been shown to be effective in the treatment of squamous cell head and neck cancers and are likely to have an increasing role in the future management of this condition when used in conjunction with other treatments.

Methods of treatment

Oral cancer treatment may include surgery, radiation therapy, or chemotherapy. Some patients have a combination of treatments. At any stage of disease, people with oral cancer may have treatment to control pain and other symptoms, to relieve the side effects of therapy, and to ease emotional and practical problems. This kind of treatment is called supportive care, symptom management or palliative care.

Radiation therapy

Radiation therapy (also called radiotherapy) is a type of local therapy. It affects cells only in the treated area. Radiation therapy is used alone for small tumors or for patients who cannot have surgery. It may be used before surgery to kill cancer cells and shrink the tumor. It also may be used after surgery to destroy cancer cells that may remain in the area. Radiation therapy uses high-energy rays to kill cancer cells. Doctors use two types of radiation therapy to treat oral cancer:

- External radiation: The radiation comes from a machine. Patients go to the hospital or clinic once or twice a day, generally five days a week for several weeks.
- Internal radiation (implant radiation): The radiation comes from radioactive material placed in seeds, needles, or thin plastic tubes put directly in the tissue. The patient stays in the hospital. The implants remain in place for several days. Usually they are removed before the patient goes home. Some people with oral cancer have both kinds of radiation therapy.

Chemotherapy

Chemotherapy uses anticancer drugs to kill cancer cells. It is called systemic therapy because it enters the bloodstream and can affect cancer cells throughout the body. Chemotherapy is usually given by injection. It may be given in an outpatient part of the hospital, at the dentist/doctor’s office, or at home. Rarely, a hospital stay may be needed.

Rehabilitation after oral cancer

Rehabilitation may vary from person-to-person depending on the type of oral cancer treatment and the location and extent of the cancer. Rehabilitation may include:

- Dietary counseling: Many patients recovering from oral cancer surgery have difficulty eating, so it is often recommended that they eat small meals consisting of soft, moist foods.
- Surgery: Some patients may benefit from reconstructive or plastic surgery to restore the bones or tissues of the mouth, returning a more normal appearance.

Pharmacological agents such as Cetuximab have recently been shown to be effective in the treatment of squamous cell head and neck cancers and are likely to have an increasing role in the future management of this condition when used in conjunction with other treatments. Treatment of oral cancer will usually be by a multidisciplinary team, with treatment professionals from the realms of radiation, surgery, chemotherapy, nutrition, dental professionals, and even psychology all possibly involved with diagnosis, treatment, rehabilitation, and patient care.

Complications may include:

- Postoperative disfigurement of the face, head and neck.
- Complications of radiation therapy, including dry mouth and difficulty swallowing.
- Other metastasis (spread) of the cancer.

Definitions

Benign – Not cancerous. Benign tumors do not spread to tissues around them or to other parts of the body.

Bidi – A cigarette made by rolling tobacco by hand into a dried leaf. Most bidis come from India in a variety of flavors.
Biopsy – The removal of cells or tissues for examination under a microscope. When only a sample of tissue is removed, the procedure is called an incisional biopsy or core biopsy. When an entire lump or suspicious area is removed, the procedure is called an excisional biopsy. When a sample of tissue or fluid is removed with a needle, the procedure is called a needle biopsy or fine-needle aspiration.

Bupropion – A substance that is used to treat depression and to help people quit smoking. It belongs to the family of drugs called antidepressants.

Cancer – A term for diseases in which abnormal cells divide without control. Cancer cells can invade nearby tissues and can spread through the bloodstream and lymphatic system to other parts of the body.

Cell – The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells.

Chemotherapy – Treatment with anticancer drugs.

Clinical trial – A type of research study that uses volunteers to test new methods of screening, prevention, diagnosis or treatment of a disease. The study may be carried out in a clinic or other medical facility. Also called a clinical study.

CT scan – Computed tomography scan. A series of detailed pictures of areas inside the body taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan.

Dental implant – A small metal pin placed inside the jawbone or oral tissue. Dental implants can be used to help anchor a false tooth or teeth, or a crown or bridge.

Dentist – A health professional who specializes in caring for the teeth, gums and oral tissues.

Endoscope – A thin, lighted tube used to look at tissues inside the body.

Endoscopy – The use of a thin, lighted tube (called an endoscope) to examine the inside of the body.

Erythroplasia – A patch found in the mouth that is a mixture of red and white. It can develop into cancer.

Erythroplasia – A reddened patch with a velvety surface found in the mouth. It can develop into cancer.

External radiation – Radiation therapy that uses a machine to aim high – energy rays at the cancer. Also called external-beam radiation.

Fluoride – A mineral that helps prevent tooth decay. Fluoride may be present in drinking water. It may be applied to the teeth as a gel, in toothpaste, or as a rinse.

General anesthesia – Drugs that cause loss of feeling or awareness and put the person to sleep.

Gland – An organ that makes one or more substances, such as hormones, digestive juices, sweat, tears, saliva or milk. Endocrine glands release the substances directly into the bloodstream. Exocrine glands release the substances into a duct or opening to the inside or outside of the body.

Graft – Healthy skin, bone or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body.

Hard palate – The front, bony portion of the roof of the mouth.

Head and neck cancer – Cancer that arises in the head or neck region (in the nasal cavity, sinuses, lip, mouth, salivary glands, throat or larynx [voice box]).

Human papillomaviruses – HPVs. Viruses that cause abnormal tissue growth (warts). Some types of HPV are associated with cervical and certain other cancers.

Imaging – Tests that produce pictures of areas inside the body.

Implant radiation – A procedure in which radioactive material sealed in needles, seeds, wires or catheters is placed directly into or near a tumor. Also called brachytherapy, internal radiation or interstitial radiation therapy.

Internal radiation – A procedure in which radioactive material sealed in needles, seeds, wires or catheters is placed directly into or near a tumor. Also called brachytherapy, implant radiation or interstitial radiation therapy.

Kretek – A cigarette made of a mixture of tobacco and clove spices.

Leukoplakia – A white patch that may develop on mucous membranes such as the gums, the tongue or the inside of the cheeks, and may become cancerous.

Local anesthetics – Drugs that cause a temporary loss of feeling in one part of the body. The patient remains awake but has no feeling in the part of the body treated with the anesthetic.

Local therapy – Treatment that affects cells in the tumor and the area close to it.

Lymph – The clear fluid that travels through the lymphatic system and carries cells that help fight infections and other diseases. Also called lymphatic fluid.

Lymph node – A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph (lymphatic fluid), and they store lymphocytes (white blood cells). They are located along lymphatic vessels. Also called a lymph gland.

Lymphatic system – The tissues and organs that produce, store and carry white blood cells that fight infections and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and lymphatic vessels (a network of thin tubes that carry lymph and white blood cells).

Malignant – Cancerous. Malignant tumors can invade and destroy nearby tissue and spread to other parts of the body.

Medical oncologist – A doctor who specializes in diagnosing and treating cancer using chemotherapy, hormonal therapy and biological therapy. A medical oncologist often is the main health care provider for a person who has cancer. A medical oncologist also may coordinate treatment provided by other specialists.

Mental health counselor – A specialist who can talk with patients and their families about emotional and personal matters, and can help them make decisions.

Metastasis – The spread of cancer from one part of the body to another. A tumor formed from cells that have spread is called a “metastatic tumor” or a “metastasis.” The metastatic tumor contains cells that are like those in the original (primary) tumor. The plural form of metastasis is metastases.

MRI – Magnetic resonance imaging – A procedure in which radio waves and a powerful magnet linked to a computer are used to create detailed pictures of areas inside the body. These pictures can show the difference between normal and diseased tissue. MRI makes better images of organs and soft tissue than other scanning techniques, such as CT or X-ray. MRI is especially useful for imaging the brain, spine, the soft tissue of joints, and the inside of bones. Also called nuclear magnetic resonance imaging.

Nutritionist – A health professional with special training in nutrition who can offer help with the choice of foods a person eats and drinks. Sometimes called a dietitian.

Oral cavity – The mouth.
**Oral and maxillofacial surgeon** – A dentist who specializes in surgery of the mouth, face and jaw.

**Radiation therapy** – The use of high-energy radiation from x-rays, gamma rays, neutrons and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy, irradiation, and x-ray therapy.

**Radioactive** – Giving off radiation.

**Radiotherapy** – The use of high-energy radiation from x-rays, gamma rays, neutrons and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy, implant radiation or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiation therapy, irradiation, and x-ray therapy.

**Saliva** – The watery fluid in the mouth made by the salivary glands. Saliva moistens food to aid in digestion and protects the mouth against infections.

**Side effects** – Problems that occur when treatment affects tissues or organs other than the ones meant to be affected by the treatment. Some common side effects of cancer treatment are fatigue, pain, nausea, vomiting, decreased blood cell counts, hair loss and mouth sores.

**Soft palate** – The muscular (not bony) part at the back of the roof of the mouth.

**Speech pathologist** – A specialist who evaluates and treats people with communication and swallowing problems. Also called a speech therapist.

**Squamous cell carcinoma** – Cancer that begins in squamous cells, which are thin, flat cells that look like fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body and the passages of the respiratory and digestive tracts. Also called epidermoid carcinoma.

**Squamous cells** – Flat cells that look like fish scales under a microscope. These cells cover internal and external surfaces of the body. They are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body and the passages of the respiratory and digestive tracts.

**Stage** – The extent of a cancer within the body. If the cancer has spread, the stage describes how far it has spread from the original site to other parts of the body.

**Staging** – Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. It is important to know the stage of the disease in order to plan the best treatment.

**Tumor** – A new mass of excess tissue that results from abnormal cell division. Tumors perform no useful body function. They may be benign (not cancerous) or malignant (cancerous).

**Uvula** – The soft flap of tissue that hangs down at the back of the mouth (at the edge of the soft palate).

**X-ray** – A type of high-energy radiation. In low doses, x-rays are used to diagnose diseases by making pictures of the inside of the body. In high doses, x-rays are used to treat cancer.

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**References**

- American Cancer Society
- American Surgeon General
- www.cdc.gov
<table>
<thead>
<tr>
<th>Question</th>
<th>True</th>
<th>False</th>
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</thead>
<tbody>
<tr>
<td>1. The great majority of infectious diseases affect or are acquired</td>
<td></td>
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<td>through mucosal surfaces.</td>
<td></td>
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<td>2. The canines, or cuspids, are designed for heavy grinding and</td>
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<td>chewing, exerting forces as high as 200-plus pounds.</td>
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<td>3. Two conditions in the mouth – leukoplakia and erythroplakia –</td>
<td></td>
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<td>actually can be precursors to cancer.</td>
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<td>4. If oral cancer spreads to the lungs, the cancer cells in the lungs</td>
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<td>are actually oral cancer cells. The disease is metastatic lung cancer.</td>
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<td>5. Staging is the key to finding the cancer in the early development.</td>
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Final Examination Questions
Select the best answer for each question and mark your answers on the Final Examination Answer Sheet found on page 136, or for faster service complete your test online at Dental.EliteCME.com.