DIFFERENTIAL DIAGNOSIS of

ORAL and

MAXILLOFACIAL LESIONS
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with 1343 illustrations and 120 color plates

Mosby
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The Fifth Edition is dedicated to the outstanding lifetime contributions of

PAUL W. GOAZ, B.S., D.D.S., S.M.
ORION H. STUTEVILLE, D.D.S., M.D.S., M.D.
The purposes of this book remain the same: (1) to serve as an interface textbook between oral pathology/oral medicine/oral radiology and clinical practice, (2) to simplify the classification of lesions by clinical or radiographic appearances, and (3) to help the practitioner arrive at a working (clinical) diagnosis through the differential diagnosis process.

The expanded title of this edition to include maxillofacial lesions gives a truer indication of the regions covered. Lesions of the face, neck, lips, and jawbones are covered, as well as lesions of the oral soft tissues. This also follows the trend set in recent years by oral pathology, oral surgery, and oral radiology academies and some journals.

The present edition represents a major overhaul. This is due in part to the author's other responsibilities during the preparation of the previous edition, which precluded heavy revision. Much new information has appeared during the last 5 years as well. The following housekeeping chores have been rigorously attended to: (1) redundancy has been significantly reduced; (2) more crispness of expression, simpler sentence structure, and clarity of wording has been accomplished for improved readability and understanding; (3) up-to-the-minute references have been introduced and selected older ones retained; (4) the reference style has been changed from author names to numbers for both conciseness and unhindered thought; and (5) pictures have been cropped judiciously so that the lesion is shown with just enough anatomic landmarks to identify location. This makes the lesion itself larger, clearer, and more prominent.

The following changes have been made in content. In Chapter 2, discussion of the patient history section and a detailed treatment of radiologic views have been deleted or condensed because more thorough works are available from other sources. This leaves room for deeper discussion of material more pertinent to our book. Some ranking of lesions according to frequency has been changed because of new literature and quiet reflection. Some fairly common lesions left out of former editions have been included in this edition. More rarities gathered from the monthly journals have been included in their proper place, often with references.

Chapters 35 (Oral Cancer), 36 (AIDS), and 37 (Viral Hepatitis) have been added. A variety of pulpoperiapical lesions that produce various radiographic changes in the bony and soft tissue floor of the maxillary sinus have been added to Chapter 16 (Periapical Radiolucencies). Both candidiasis and oral cancer are discussed in much greater detail and current methods of management dealt with at length.

All illustrations have been carefully reviewed. Many black and white pictures have been replaced with more characteristic examples or better quality pictures. Judicious cropping has helped also. The color plates have been much improved in quality and the numbers more than doubled. New Plates E through H are devoted to the many appearances and types of oral cancer. These are arguably among the best collections of colored pictures of oral cancer available today. Recent shifts in philosophy and specific information that appeared in literature during the past 6 years have been included throughout. A new index more suitable to the differential style of the textbook has been developed.

As in past editions, the author is indebted to many confreres who have helped with the preparation of the fifth edition. Authors and coauthors are listed at the head of chapters. Numerous colleagues have supplied excellent slides from their personal collections, and others have given permission to use previously published information, charts, tables, or pictures. In this regard, I mention the material borrowed from an article by Dr. L. Gold, et al, on the uniform use of surgical procedure terms, which we have included in the introduction to the Bony Lesions section. We have endeavored to use correct surgical procedure terms throughout discussions of the management of bony lesions. Global usage of a uniform system would make the surgical literature more meaningful and enrich assessment of various procedures.

I am indebted to Ms. Colleen Murdock, who kindly gave much assistance in printing a number of black and white glossies. I especially express my deepest gratitude to my wife Carole, who typed the manuscripts of new chapters and altered other chapters using the material provided on diskettes by the publisher.

NORMAN K. WOOD
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DIFFERENTIAL DIAGNOSIS of

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LESIONS
CHAPTER 1

Introduction

The objective of this text is to present a systematic discussion of the differential diagnosis of oral lesions based on a classification of lesions, which are grouped according to their similar clinical or radiographic appearances.

Part I consists of three preparatory chapters. Chapter 2 is devoted to a review of pertinent steps and modalities to follow in the examination of the patient. Chapter 3 explains on a functional and histologic basis the clinical and radiographic features of lesions discovered during the clinical examination. Chapter 4 outlines the diagnostic sequence we prefer, commencing with the detection of the lesion and progressing through intermediate steps until a final diagnosis is established.

Parts II and III make up the differential diagnosis section of the text, which deals with the specific disease entities. Part II is devoted primarily to the soft tissue lesions (Chapters 5 to 14), and Part III deals with lesions that originate in bone (Chapters 15 to 30). In each part the individual entities are classified into groups consisting of similar-appearing lesions, and each group forms the subject of a chapter.

Part IV is devoted to the presentation and discussion of lesions according to specific anatomic location. Thus Chapters 31 to 34 deal with masses in the neck, lesions of the facial skin, lesions of the lips, and intraoral lesions by anatomic region.

Part V deals with additional subjects. Thus Chapters 35 to 37 present oral cancer, acquired immunodeficiency syndrome (AIDS), and viral hepatitis.

Although our text is primarily for the clinician, the microscopic picture is also discussed, but this aspect is stressed only when it contributes to the recognition and comprehension of the clinical or radiologic features. This approach evolved from our observation of dental students entering the clinic and encountering great difficulty as they attempted to relate their knowledge of histopathology to the clinical features of lesions. Apparently, students experience this difficulty because, first, they are not adequately instructed in the simple but meaningful correlations between the histologic and clinical pictures. Second, they lack experience in the grouping of lesions according to clinical and radiographic appearances, which is necessary before a usable differential diagnosis can be developed.

Of course, there are several excellent textbooks of oral pathology that complement the clinical study of oral lesions, but these books classify and discuss lesions according to etiology, tissue of origin, microscopic nature, or areas of occurrence. Although such an approach has proved to be effective for presenting a course in pathology, our experience has shown it to be cumbersome. In an attempt to alleviate this problem, we group and discuss lesions according to their clinical or radiographic appearance. Regardless of etiology or area of occurrence, all similar-appearing lesions are grouped together and discussed in the same chapter.

Although some experts may object to our particular ranking of lesions, no inerrant authority is claimed. We have attempted to rank the entities in each category according to frequency of occurrence—with the discussion of the most common being first. The very rare lesions are simply listed. This particular arrangement was borne out of our personal experience, as well as from our assessment of other authors’ statistics.* It is not intended to be an authoritative statement but merely an aid to the clinician in the development of a differential diagnosis.

Our ranking of lesions must be taken in the general context of this book, since different frequency rates occur in different age groups and are modified by socioeconomics, as well as by cultural and geographic factors. Also, new journal articles may modify these rankings from time to time, but we doubt that these changes will detract significantly from the usefulness of the arrangement presented here.

Pathoses of the dental hard tissues, gingivitis, temporomandibular joint problems, and facial and oral pain

*We are particularly indebted to Drs. Charles Halstead and Dwight Weathers of Emory University, who have graciously made available to us statistical rankings from their extensive computerized study on the differential diagnosis of oral lesions.
have been excluded because they are adequately dis­
cussed elsewhere. In some cases, entire books have been
devoted to these difficult and sometimes unresolvable di­
gnostic problems.

It is important to recognize that discussions of entities
included in this text are not intended to be exhaustive de­
scriptions of any disease but only to present pertinent
points that will minimize confusion and contribute to the
development of a differential diagnosis. Specifically, we
have avoided controversial issues concerning etiology
and tissue of origin that are unresolved, since they have
been exhaustively discussed in other sources and con­
tribute little that is clinically useful to the dental practi­
tioner.

Also, the discussions of the features of particular les­
sions have not been specifically subdivided on the basis
of clinical, radiographic, and histologic characteristics.
On the contrary, these have been blended in an attempt to
illustrate how the three disciplines interrelate and to aid
in the explanation of the features found in each.

Again the primary aim of this book is to provide the
clinician with the pertinent features of relatively common
oral diseases that we consider necessary to the differenti­
ation of similar-appearing lesions.

The diagnoses that appear in the descriptions of the re­
production of the clinical pictures and radiographs have
been determined by microscopic examination in the vast
majority of cases.

REFERENCE

1. Halstead CL, Weathers DR: Differential diag­
nosis of oral soft tissue pathoses: site unit(s)-
3379: instructional materials for health pro­
fessional education, National Library of
Medicine/National Medical Audiovisual Cen­
ter, Washington, DC, 1977, US Department
PART I

GENERAL PRINCIPLES
OF DIFFERENTIAL DIAGNOSIS
CHAPTER 2

History and Examination of the Patient

NORMAN K. WOOD
PAUL W. GOAZ

Collecting the information necessary to determine the cause of a patient’s complaint is accomplished by determining the patient’s medical and dental history and performing a physical examination. Properly performed, the history and physical examination are frequently the most definitive of the diagnostic procedures. Without the information provided by the history and physical examination, the diagnostic process is reduced to hazardous speculation. These diagnostic procedures include the following:

RECORDING THE IDENTIFYING DATA
HISTORY AND PHYSICAL EXAMINATION
CHIEF COMPLAINT
PRESENT ILLNESS
PAST MEDICAL HISTORY
Family history
Social history
Occupational history
Dental history
REVIEW OF SYMPTOMS BY SYSTEM

PHYSICAL EXAMINATION
Radiologic examination
DIFFERENTIAL DIAGNOSIS
WORKING DIAGNOSIS
Medical laboratory studies
Dental laboratory studies
Biopsy
Incisional
Excisional
Fine-needle aspiration
Exfoliative cytology

Toluidine blue staining
Consultation
FINAL DIAGNOSIS
TREATMENT PLAN

HISTORY AND PHYSICAL EXAMINATION

The reader is referred to other books\(^1\sim4\) for information on history and physical examination because space does not permit an adequate description of these aspects. Oral chief complaints are detailed in Chapter 4, and physical characteristics of lesions and masses are covered in Chapter 3.

Radiologic Examination

The use of diagnostic radiology is not routinely prescribed. After completion of the history and physical examination, the examiner may order pertinent views that will most likely contribute to the further description and diagnosis of the lesion. Radiographs should never be accepted as the sole criterion for the diagnosis or selection of treatment.

Most routine examinations may require one or more of the following traditional radiographic projections whose images are produced on film:

I. Intraoral radiographic examinations; periapical, interproximal (bitewing), and occlusal projections\(^5\)

II. Extraoral radiographic examinations of oral and perioral areas
   A. Panoramic projection
PART I  General Principles of Differential Diagnosis

B. Lateral oblique projection
   1. Mandibular (anterior or posterior) body projection
   2. Mandibular ramus projection

C. Skull projections
   1. Posteroanterior (anteroposterior) projection
   2. Lateral skull (cephalometric) projection

D. Facial projections
   1. Waters’ projection
   2. Submentovertex projection
   3. Reverse Towne’s projection

E. Temporomandibular joint projection
   1. Transpharyngeal (infracranial) projection
   2. Transorbital (Zimmer) projection
   3. Facial projections

F. Conventional tomography

For a description of the structures that these technical procedures demonstrate and how they are performed, see Goaz and White.6

Panoramic radiography. The mechanics and images of panoramic radiography have been described adequately elsewhere.6-8 The finer detail obtained by intraoral radiation source machines has been described by Jensen.9

Conventional tomography (laminography) Often, images produced by the previously described techniques are obscured because of superimposition of details of the complete thickness of the anatomic region radiographed. Tomography eliminates this superimposition by selectively imaging a layer or “slice” of an object so that it may be clearly seen, while overlying and underlying structures are blurred or not imaged at all. For a description of the technology, the reader is referred elsewhere.6,10

The basic principle applied in conventional tomography is also used in computed tomography (CT), sonography, single-photon emission tomography, positron emission tomography, and magnetic resonance imaging (MRI).

In general, motion tomography finds its major application in imaging fine-detail, high-contrast objects. In dentistry, tomography is frequently used for the demonstration of the temporomandibular joint (Fig. 2-1) and for the identification and location of facial fractures. Tomograms in straight anteroposterior and lateral views assess more accurately than plain films the extent of both soft tissue disease and bony destruction of the paranasal sinuses.11

Computer-Assisted Imaging

Developments and refinements in imaging technology have appeared with the advent of scanning and digital computer techniques to supplement the information gained by traditional radiology. These developments permit discrimination between small differences in physical densities and tend to eliminate the confusion caused by superimposition. In addition, these new imaging technologies have provided access to lesions in such areas as the pharyngeal space and the pterygopalatine fossa that were not easily evaluated by conventional x-ray imaging. Some of the modern imaging procedures such as digital radiography, subtraction radiography, CT, radionuclide scanning, MRI, and ultrasound imaging are introduced here. More detailed information may be found elsewhere.6

Digital radiography Digital radiography (digital x-ray imaging) is a technique that is fundamental to CT, MRI, diagnostic ultrasound, nuclear medicine, and even film radiography. The remnant beam of x-rays is directed onto a phosphor screen instead of a film. The screen is scanned by a television type of camera whose output is directed into a data acquisition system (digital computer). The computer digitizes the image, that is, divides the image into small areas, or pixels, and assigns a number to each pixel proportional to the intensity of the light at that pixel. These numbers can be stored in the computer and used to reconstruct the original image on a TV monitor by converting the numbers to light of appropriate intensity. The computer or digital processor performs a variety of functions, including: (1) image acquisition control, (2) image reconstruction, (3) image storage and retrieval, (4) image processing, and (5) image analysis. Unlike the other techniques described here, the digital imaging equipment does not provide a cross-sectional image.

The image from a conventional radiograph can also be digitized, improved, and stored for future viewing. To improve the quality of an image, the operator manipulates its pixel numbers, thereby changing the density and contrast of selected areas or of the entire image (Fig. 2-2).

Subtraction radiography. Subtraction radiography is an extension of digital radiography. To subtract images, the computer digitizes two radiographs of the same area and electronically subtracts the numbers representing the intensity of light at each pixel of the second radiograph from the numbers in analogous locations on the first radi-
History and Examination of the Patient

CHAPTER 2

Fig. 2-2. Comparison of A, a conventional lateral cephalometric projection with B, a view of the video conversion of its digitized image, illustrating the increase in detail achieved by contrast modification. (Courtesy Peter H. Buschang, Dallas.)

CT scanning can also distinguish between tissues that differ in physical density by less than 1%, in contrast to the 10% difference required by conventional radiology. Although computer scanning of the oral cavity is not practical because of the artifacts caused by dental restorations (Fig. 2-4), it is frequently useful in determining how far a lesion may have extended from the oral cavity into the base of the skull, cervical spine, or paranasal sinuses. A more detailed image of the paranasal sinuses, the nasopharynx, or the base of the skull and surrounding area is possible with CT than with conventional tomography. CT has been described by some as the method of choice for evaluating salivary masses. It is also more reliable for the evaluation of tumor extent, but it does not image in the sagittal plane, nor does it readily distinguish between tumor and inflammatory change in the sinuses. For a detailed description of the physical principles of CT, as well as how to interpret the CT image, see Sprawls and Valvassori et al.

Radionuclide imaging Radionuclide imaging takes advantage of the propensity of particular substances to concentrate selectively in certain “target” tissues and organs. These substances can be chemically tagged with radionuclides, and in some cases the ionic form of a nuclide selectively concentrates at the “target.” The radionuclides used for this procedure are γ-ray producers with relatively...
short half-lives (a few hours to a day). These agents are injected or ingested. The γ-rays from the isotope that has concentrated at a particular area in the body are then detected by a gamma camera that converts the energy to electric impulses that are used by a computer to form an image on a cathode ray tube, transfer it to a film (Polaroid or x-ray), or store it for future viewing.13

The radionuclide imaging techniques delineate areas of increased or decreased metabolism (Fig. 2-5). To determine the cause of the altered function, the clinician must qualify this information with other diagnostic tests and clinical deductions. This technique demonstrates abnormalities in tissue and the extent of these changes even before they are demonstrable on routine radiographs.22,23

Bone resorption and formation such as bony metastases, primary bone tumors, infections, metabolic bone diseases, and stress fractures may be detected with this technique.24 Scintigraphy is a “part of the standard diagnostic program in planning the therapy of malignant tumors of the oral cavity.”25 The technique has been used as an indication of the rate of alveolar crest bone loss, and the results are verifiable by sequential radiographic examinations. This examination delivers a radiation dose of less than 0.5 rem to the individual.26

A variation of this nuclear imaging is positron emission tomography, in which the radiopharmaceuticals are labeled with positron-emitting isotopes (11C, 18F, 13N, 15O) and the gamma camera is moved around the patient. The information from the camera is analyzed by a computer, which constructs sectional images using the same mathematical models used in computed tomography.27

Magnetic resonance imaging

Chemical elements with nuclei that have an odd number of nucleons have a magnetic moment and a characteristic resonant frequency (in the FM radio range) when placed in a magnetic field. This frequency is unique to each element (nuclei) and varies with the strength of the magnetic field. If such elements are subjected to electromagnetic radiation (EMR) when they are in a magnetic field, they absorb energy and radiate it when the EMR is terminated. Since hydrogen represents at least 60% of the atoms in the body and hydrogen has the strongest MRI signal, most MRI systems are tuned to the resonant frequency of hydrogen.28 These radio signals from hydrogen are detected by an antenna (field coil[s]), and a computer constructs the MR image, which is displayed on a TV screen that is similar to that used by the CT scanner. It may also be recorded on film or magnetic tape for later interpretation.

MRI is being adapted for use in the diagnosis of almost all body organs and systems. MRI images of normal and abnormal tissues have better contrast and resolution than CT (Fig. 2-6). Because of these improved image characteristics, tumor margins in the nasopharynx, oropharynx, and base of the skull are more sharply represented. MRI has proved useful for demonstrating the oral cavity, temporomandibular joint, and salivary glands. It can also differentiate between muscles, tonsils, mucosa, and lymph nodes. In contrast to CT, there is an absence of artifact generation by dental restorations. In CT, these artifacts frequently obscure regions of the oropharynx. Also, major blood vessels can be visualized in MRI without contrast medium, and images of transverse, coronal, and sagittal sections can be produced without repositioning the patient as is necessary with CT.

A disadvantage of MRI is its poor visualization of air spaces, subtle osseous abnormalities, and bone in general. The low concentration of magnetic nuclei in air and the rigid fixation of hydrogen in the bony matrix (pre-
History and Examination

Fig. 2-5. Right and left radionuclide image of head showing more intense uptake in right parotid caused by chronic parotitis with accompanying abscess formation in this gland. The accumulation of activity in oral cavity is due to gingival inflammation and the appearance of the isotope in the saliva. (Courtesy Byron W. Benson, Dallas.)

including resonance) cause MRI to produce weak signals and poor images. However, with improved soft tissue contrast and the capacity to image exact tumor borders (Fig. 2-7), this disadvantage is minimal.

For a detailed description of the physical principles of MRI, and for interpreting the MR image, see Sprawls and Mills et al.

Sonography

Ultrasonic examination does not use any form of electromagnetic radiation. Instead high-frequency sound pulses (approximately $1 \times 10^{-6}$/sec) are directed into the body (500 pulses/sec) from a handheld transducer in contact with the skin. The sound is reflected by tissue interfaces, and the resulting echoes are detected by the same transducer, which then converts them to electrical signals that are fed into a computer. Small and more superficially located organs and structures lend themselves to this procedure. The images can be recorded like a moving picture and stored, or they can be viewed in real time on a TV monitor (Fig. 2-8).

Air and bone and other heavily calcified materials absorb almost all of the sound and are less echogenic than soft tissue. Fluid transmits sound so well that it is echo free, but it transmits echoes from underlying structures. Consequently, ultrasound can be used to determine whether a structure is solid or cystic. The walls of a cyst produce good echoes, but the cystic fluid does not. A cyst can also act as an acoustic enhancer, causing an amplification of the echoes from the tissues behind it. On the other hand, a stone causes a great reduction of echoes from the tissues behind it, producing a definitive acoustic shadow. Ultrasound has proved useful for examining salivary glands and cysts and for similar processes in the soft tissue of the cervicofacial region. Diagnostic sonography only images structure, so assessments of physiology or pathologic changes are possible only when architecture is affected. The reliability of an examination depends on the examiner’s experience. Piette et al found that results are more reliable when the maxillofacial surgeon performs the sonography.

To date, no harmful effects of this relatively inexpensive ultrasound examination have been documented. For a detailed description of the physical principles of sonography, as well as how to interpret the ultrasound image, see Sprawls and Yoshida et al.

Differential Diagnosis

This process is discussed in Chapter 4.

Working Diagnosis

This process is discussed in Chapter 4.

Medical Laboratory Studies

Certain pertinent laboratory tests may give helpful diagnostic information on clinical conditions whose identities remain obscure after the patient’s history and physical examination. Such tests are useful, however, only if the clinician is aware of what tests to order and how to interpret the results. For a description of the bewildering array of laboratory procedures available, their technical aspects, the circumstances in which they are appropriate, and the possibilities of both error and false reports, and for lists of substances that interfere with certain laboratory tests and the clinical application of test results, see Ravel.

Dental Laboratory Studies

The fabrication and analysis of articulated models of the dental arches and the attendant records are an integral
part of the examination of many patients. Metabolic diseases, neoplasms, odontogenic diseases, congenital deformities, developmental malformations, and acquired maladies affecting the configurations of the oral cavity are often well visualized in properly prepared models.

Biopsy

Biopsy is the term used to describe the process of surgically removing tissue from a patient for histopathologic examination. The procedure is undertaken as the most accurate means of establishing a definitive diagnosis (confirming the working diagnosis) usually before the initiation of therapy. Biopsy should be pursued in the case of oral ulcers that persist for 2 to 3 weeks beyond the elimination of their suspected cause, persistent red and white lesions on the oral mucosa, suspected neoplasms, or any unidentified tissue mass or any pathologic mass that has been removed. Artifacts can develop in the excised tissue if handled improperly. These can be caused by crushing the tissue with forceps, fulguration, injection, improper fixation, freezing, and curling of the specimen.36

There are at least three types of biopsy: excisional biopsy, incisional biopsy, and fine-needle aspiration. It is important that the tissue be sent to a specialist, such as a certified oral pathologist, trained in microscopic examination of disease from the oral cavity and maxillofacial region.37,38

The tissue specimen should be placed in a solution of 5% to 10% formalin and fixed immediately. If there are two or more samples, each should be placed in a separate container. Each container should then be identified with the patient's name, the clinician's name, and the specimen's measurements and location of the lesion from which the sample came. An adequate patient history should also be included with the specimen.

Excisional biopsy An excisional biopsy is a therapeutic and diagnostic procedure performed when the lesion is no larger than 1 cm or so in diameter and when its removal does not necessitate a major surgical procedure. Excisional biopsy has the advantage of only requiring one surgical encounter. In addition, it does not transect tumor tissue as in incisional biopsy.

Incisional biopsy An incisional biopsy is indicated if the lesion is too large for an excisional procedure. However, multiple tissue samples may be required (i.e., serial biopsy). The sample, taken from the most suspect area, should be relatively large and deep and should include the junction with surrounding normal tissue. Necrotic areas generally should be avoided because they will not be diagnostic. The sample should be handled gently, and electrosurgery should not be used to remove it.

Punch biopsies are a type of incisional biopsy that may be used on surface oral lesions.39 Wedge-shaped biopsies may be used for vesiculoerosive disease and to minimize postsurgical discomfort.40

For more detailed discussions of the indications for a biopsy and the mechanics of the techniques, see Bernstein41 and Sabes.42

Fine-needle aspiration In fine-needle aspiration (FNA, fine-needle biopsy, aspiration biopsy) a fine-needle (21-gauge to 23-gauge) is inserted into a tissue or suspected lesion. The needle may be guided with a fluoroscope or with ultrasound to ensure that an exact area of tissue is

Fig. 2-6. Sagittal magnetic resonance scan through tongue and surrounding structures showing the mandible, hyoid bone, geniohyoid and genioglossus muscles, epiglottis, oropharynx, hard and soft palate, nasal turbinate, sphenoid sinus, pons, and medulla oblongata. (Courtesy Dan Waite, Dallas.)

Fig. 2-7. Magnetic resonance image in coronal plane demonstrating a mass (desmoplastic fibroma) in the left ramus and angle of the mandible. (Courtesy Dan Waite, Dallas.)
sampled. A minute piece of tissue is sucked into the needle tip, expressed onto a glass slide, dried, and rapidly stained. The cytomorphology of the aspirated tissue is then studied. The main advantages of FNA are simplicity of technique (it can be easily performed on an outpatient basis using a local anesthetic), greater patient acceptance and less risk of delayed wound healing and infection than with incisional or excisional biopsy, rapid diagnosis, and economy (it eliminates the need for hospitalization and tissue processing and saves operating room time). Another advantage is that different areas within a mass can easily be sampled to ensure that representative material has been obtained. The risk of seeding the needle track with cancer cells that accompanies the use of a large needle is unlikely with FNA. A 90% to 100% accuracy range for the technique has been reported in lymph node aspiration (for metastatic carcinoma and melanoma, Hodgkin’s and non-Hodgkin’s lymphoma), salivary glands and the head and neck region (oral cavity, maxillary antrum, oropharynx, and nasopharynx), and other neck swellings. The positive predictive value of FNA for malignancy in the head and neck is considered to be 100% for patients with or without a prior history of malignancy. It is considered the definitive diagnostic technique and allows the clinician to begin treatment. A negative, unsatisfactory, or suspect FNA diagnosis should be considered an indication for open biopsy to confirm the nature of the lesion. FNA is a safe, reliable method of diagnosing suspect lesions in the head and neck area and greatly aids and speeds the implementation of appropriate treatment.

Exfoliative Cytology

The technique for the cytologic examination of exfoliated cells scraped from suspect oral lesions is similar to that used for the detection of uterine cervix cancer. However, it has not provided the same level of reliability in the diagnosis of oropharyngeal malignancy. The lesion is scraped with a moistened tongue blade or a cement spatula, and the cells obtained are smeared evenly over a glass slide, fixed, stained, and examined under the microscope for the presence of viral or fungal disease or malignant-appearing cells. The oral exfoliative technique has a tendency to produce a false-negative result an average of 37% of the time. Most of the false-negative results stem from unappreciated limitations of this modality. Exfoliative cytology is unsuitable for the following lesions: homogeneous leukoplakias, smooth-surfaced exophytic lesions, submucosal lesions, ulcerated pigmented lesions, verruca vulgaris, papilloma, condyloma acuminata, etc. On the other hand, exfoliative cytology can give useful information for erythroplakia, the “erythro” patch of erythroleukoplakia, ulcers, erosions, and fungal and viral infections such as oral herpes simplex. Bernstein and Miller discussed in detail the indications and contraindications of oral cytology. Oral exfoliative cytology is recommended as an adjunct to open biopsy, for prebiopsy assessment, for the examination of broad surface lesions, and for the evaluation of patients after definitive treatment.

Toluidine Blue Staining

Most epithelial surfaces stain blue after the application of a 1% toluidine blue solution, but the stain is lost after application of a 1% acetic acid solution to a normal epithelial surface or to benign erythematous lesions on oral mucosa. In contrast, premalignant and malignant erythematous lesions are not decolorized by the acetic acid. Toluidine blue is not a specific stain for cancer cells but is an acidophilic, metachromatic nuclear dye that selectively stains acid tissue components, particularly nucleic acids such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). It is believed to have greater affinity for nucleic DNA than for cytoplasmic RNA and dysplastic and anaplastic cells contain more DNA than normal cells.

Although toluidine blue staining has been shown to be ineffective when applied to hamster cheek pouch carcinomas in humans it has been shown effective in demonstrating dysplastic (premalignant) and early malignant lesions not otherwise clinically recognizable on most of the mucous membrane surfaces and linings of the body, including the oral cavity. The technique may be useful for differentiating the small dysplastic erythroplakia that requires biopsy from small erythematous lesions caused by infection, inflammation, or trauma. Also, benign ulcerations usually have a well-defined uptake of dye at the margins, whereas a diffuse marginal pattern is characteristic of the dysplastic or malignant lesion.
Nearly all false-positive staining (e.g., persistent blue color, no carcinoma) occurs (in 8% to 10% of cases) in keratotic lesions and at the regenerating edges of erosions and ulcerations. It follows that if all keratotic and erosive lesions are excluded, the test is highly sensitive and specific for dysplastic mucosal epithelium.\(^6^8\) False-negative results (no persistent blue staining, carcinoma present in 6% to 7% of cases) may occur in dysplasia with significant keratosis, which prevents penetration of the stain so the dye does not reach submucosal extensions of a tumor.\(^5^9\)

Although some contend that preoperative toluidine blue staining more reliably indicates the border of a lesion and serves as a guide for its surgical excision than does clinical examination alone,\(^6^0\) the technique cannot show tumor that is present under normal epithelium.\(^6^1\) A good general rule is that if positive staining occurs, biopsy is in order.\(^6^2\) In screening studies, sensitivity ranged from 93.5% to 97.8% and specificity from 73.3% to 92.9%.\(^6^3\)

The use of toluidine blue and Lugol's iodine in combination has produced better specificity than toluidine alone.\(^6^3\) These authors do not recommend the routine use of toluidine blue and Lugol's iodine for screening all patients, but they recommend this technique as an additional aid “in assessing high risk patients and suspicious oral lesions.”\(^6^3\)

It would seem that the routine use of toluidine blue oral rinse would make apparent some small or unnoticed red lesions that practitioners might miss clinically (NKW).

Toxic effects of toluidine blue have been described but are not associated with the minute doses incurred during vital staining of mucosal surfaces.\(^6^4\) Toluidine blue has been shown not to be carcinogenic in hamsters.\(^6^5\)

Consultation
Before considering a consultation, the clinician should be satisfied that he or she, by taking a reliable history and conducting a thorough physical examination, has made an effort to solve the problem. Reasonable consideration should also be given to the identity of an appropriate consultant. There should be a written form of the request for consultation, which includes a brief summary of the patient's history and physical examination, a description of the problem, and an indication of the nature of the request: advice, treatment of the patient, or transfer of the patient. Finally, when the report from the consultant is received, it should always be placed in the patient’s record along with the consultant’s name and address.

**FINAL DIAGNOSIS**

The final diagnosis is a statement that a precise diagnosis has been made on the basis of all required observations: the identification of definitive symptoms, the pathologist's report, and the patient's response to therapy.

**TREATMENT**

Treatment of specific lesions is discussed throughout this text.

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**REFERENCES**

1. Rose LF, Kaye D: Internal medicine for dentistry, ed 2, St Louis, 1990.
The diagnosis of oral lesions is fundamentally an exercise in clinical pathology, which, in turn, is a study of changes. Usually such changes are precipitated by pathogenic or disease-producing agents. If the clinician is going to recognize and describe these changes, he or she must have a reference to contrast with the suspected area of pathology.

For the clinical oral diagnostician, this reference state is the state of oral health. Therefore a thorough and basic knowledge of the normal oral cavity and surrounding regions is fundamental to the detection of oral disease.

In addition, it is quite difficult to appreciate the physical characteristics of a tissue without an awareness of the tissue’s microstructure because the microanatomy of the tissue establishes the clinical features on which diagnosticians base their judgments. Even the low-magnification photomicrograph of a tissue is very helpful.

**Oral and Perioral Systems**

The mucous membrane that lines the oral cavity consists of a layer of stratified squamous epithelium and a subepithelial layer, the lamina propria, which consists of a fibrous connective tissue and contains capillaries, nerves, and the minor salivary glands (Fig. 3-1).

The skin, like the mucous membrane, also possesses two layers—the epidermis and the underlying corium with its associated appendages, the sweat and sebaceous glands and the hair follicles (Fig. 3-2).

The remaining glandular systems of the perioral region of direct concern to the clinician are the major salivary glands and the thyroid and parathyroid glands. Either these glands are directly identified by the examiner or the effects of their pathologic involvement come to his or her attention when an adequate examination of the head and neck is completed.

When the examiner reviews radiographs of the region, knowledge of bone morphology and relationships of bones to each other is necessary to be able to anticipate and interpret the various forms their shadows may assume on the radiograph. The bones of the region include the maxilla, the mandible, the zygoma and vomer, the palatine, sphenoid, hyoid, and temporal bones, and the cervical vertebrae.

The oral examiner must be competent in appearances produced by the other systems, such as teeth, larynx, trachea, esophagus, and blood and lymphatic systems. Aberrations of these systems are also in the examiner’s area of responsibility and must be recognized.

The muscle systems with which the oral diagnostician must be familiar are those of facial expression, mastication, and swallowing, as well as those involved in movements of the head. These muscles, along with the bony and cartilaginous structures and vessels, provide landmarks that facilitate an effective examination. They also with the fascial planes tend to mechanically obstruct or guide invading and spreading disease processes such as infections and neoplasms. Consequently, the examiner must be aware of the exact location and plane of each muscle and the extent of its normal movements during function.
Oral and Perioral Tissues

The epithelial tissues of the oral and perioral region include the following:

1. Stratified squamous epithelial lining
2. Mucous, serous, and sebaceous glandular units
3. Enamel

The connective tissues, located beneath the surface epithelium, include the following:

1. Fibrous, adipose, and loose connective tissue
2. Muscle (skeletal and smooth) and nerves
3. Cartilage and bone
4. Dentin, cementum, and dental pulp

A well-defined layer of loose connective tissue is usually present beneath the skin or mucous membrane and permits these superficial layers to move over the deeper, firmer tissues such as muscle and bone. If this loose connective tissue layer is absent, the superficial layer is bound to the deep layer, and it cannot be moved separately from the underlying structures. Such a situation is normally found on the anterior hard palate and on the attached gingivae. Loose connective tissue contains blood and lymphatic vessels, nerves, adipose tissue, myxomatous tissue, sparse fibrous tissue, reticular fibers (that is, precollagen fibers), elastic fibers, undifferentiated mesenchymal cells, and blast cells of many varieties.

Only through a thorough understanding of these tissues, their specific natures, their physical relationships to each other, how they support or fail to support each other when subjected to the deforming pressures of the examiner's fingers, and even the characteristic sensations the examiner can feel when palpating them will a full appreciation of the precepts of a physical examination be obtained.

![Fig. 3-1. A, Diagram of the oral tissues, illustrating the component tissues and their relative positions: 1, stratified squamous epithelium; 2, lamina propria; 3, loose connective tissue; 4, mucous glands; 5, serous glands (occasionally); 6, sebaceous glands (Fordyce's granules); 7, nerve; 8, bone; 9, cartilage; 10, skeletal muscle. Fortunately, a firm platform of muscle, bone, or cartilage is present beneath the superficial tissues. This facilitates examination and palpation of oral lesions. Continued]
EXPLANATION OF CLINICAL FEATURES IN TERMS OF NORMAL AND ALTERED TISSUE STRUCTURE AND FUNCTION

Features Obtained by Inspection

The examiner can only visualize the surface tissue and its topography, including contours, color, and texture. For a more critical evaluation of irregularities, he or she must rely on other procedures.

Contours  The diagnostician must be familiar with the normal tissue contours in and around the oral cavity to be able to detect any disorder that might alter the usual configuration of the area. Changes in contour, however, are not in themselves specifically diagnostic, since so many vastly different types of pathoses can produce similar alterations in contour.

Color  The examiner must be familiar with the normal characteristic color of each region in the oral cavity and the normal variations in color and shadings these tissues can assume, and be able to recognize abnormal color changes in a specific region.

Pink.  The normal color of the oral mucosa in whites is pink because healthy stratified squamous epithelium is semitransparent. Therefore the red of the blood in the extensive capillary bed beneath shows through. However the oral mucosa is not uniformly pink throughout but has
Fig. 3-2. A, Diagram of the skin and deeper tissues, illustrating the component tissues and their relative positions: 1, keratinizing stratified squamous epithelium; 2, corium; 3, loose connective tissue; 4, hair follicle; 5, sebaceous glands; 6, sweat glands; 7, bone; 8, cartilage; 9, skeletal muscle. The firm platform below the oral tissues is also present beneath these dermal structures. Continued

For example, regions in the oral cavity that receive the greatest mechanical stimulation from mastication (the masticatory mucosa) react by developing a thicker layer of keratin for protection and a denser, less vascular lamina propria and so appear a light pink in color. These regions are the hard palate, the dorsal surface of the tongue, and the attached gingivae. On the other hand, regions such as the buccal mucosa, vestibule, floor of the mouth, and ventral surface of the tongue are not normally subjected to vigorous masticatory stimulation, so they require only a thin layer of stratified squamous epithelium, which retains little keratin and consequently permits the very vascular submucosa to show through and impart the redder color (Fig. 3-4). These areas are said to be covered with lining mucosa.

White. Because of the many white lesions that may occur in the oral cavity, not only must the clinician inspect the color of the soft tissues carefully, but he or she must also become intimately familiar with the normal color variations from region to region. These pathologic white lesions are discussed in detail in Chapter 8.
For example, although a chronic mild irritation may act as a stimulus and induce the changes necessary to cause the mucosa to take on a lighter pink color, a more acute intense irritation will produce a thinning of the stratified squamous epithelium and a consequent inflammation of the subepithelial tissues. Thus such an involved area of the mucosa changes from pink to red because of (1) a thinning of the epithelial covering combined with (2) an increased vascularity and (3) a dissolution of part of the collagen content of the subepithelial tissue.

**Yellow.** The soft palate in many persons appears quite yellow. A moderate distribution of adipose tissue just beneath the basement membrane produces this color. Fordyce’s granules, occurring in the buccal mucosa of most adults, are yellow, colored directly by the sebaceous material within the glandular units just beneath the epithelium.

**Brownish, bluish, or black.** Lesions of these colors are discussed in Chapter 12. The basis for the apparent clinical color of these lesions is frequently well demonstrated.
Correlation of Gross Structure and Microstructure with Clinical Features

CHAPTER 3

Fig. 3-3. Light pink region of oral mucosa. Photomicrograph of mucosa taken from the hard palate. The generous keratin layer (1) is combined with the dense fibrous and quite avascular lamina propria (2). This combination accounts for the lighter coloration seen clinically on the hard palate and attached gingivae.

histologic study whether the color is induced by melanin, hemosiderin, heavy metals, or pools of clear fluid.

Surfaces Normal mucosa is smooth and glistening except for the area of the rugae and the attached gingiva, which frequently demonstrates stippling and pebbling.

The surface of a pathologic mass may be smooth, papillomatous, ulcerated, eroded, keratinized, necrotic, or bosselated.

Masses that arise in tissues beneath the stratified squamous lining are, almost without exception, smooth surfaced. They may originate from mesenchyme, the salivary glands, an abscess, or an embryonic rest. As the nest of cells enlarges below and presses against the stratified squamous epithelium, the epithelium responds by a combination of stretching and minimal mitotic activity. Therefore, as the mass becomes larger and bulges into the oral cavity, it is covered with a smooth epithelial surface. Examples of such masses are fibromas, osteomas, chondromas, hemangiomas, intradermal and compound nevi, many of the minor salivary gland tumors, cysts, retention phenomena, lipomas, myomas, schwannomas, neurofibromas, space abscesses, subepithelial bullae of erythema multiforme, bullous lichen planus, and bullous pemphigoid (Fig. 3-5).

Even the malignant counterparts of such tumors often have smooth surfaces, especially in their early phases, but when these bulging lesions are situated in a region subjected to repeated trauma, their smooth surfaces become ulcerated and necrotic.

Some exceptions to this rule are the intraepithelial vesicles and blebs seen in herpetic lesions and pemphigus. They are smooth despite the fact that they originate in the surface epithelium.

As a rule, however, masses that originate in the stratified squamous epithelium almost invariably have corrugated or papillomatous surfaces. Examples of these are papillomas, verrucae vulgaris (warts), seborrheic keratoses, keratoacanthomas, verrucous carcinomas, and exophytic and ulcerative squamous cell carcinomas (Fig. 3-6). Exceptions would be the less than rough but pebbly surfaces

Fig. 3-4. This clinical picture illustrates the darker color of vestibular mucosa as contrasted with the lighter color of the attached gingivae. The histologic difference between the two regions explains these color differences.
sometimes seen overlying a granular cell myoblastoma and a lymphangioma. The granular cell myoblastoma often induces a pseudoepitheliomatous hyperplasia in the overlying epithelium, and this sometimes is severe enough to produce a pebbly surface (Fig. 3-7). The superficial lymphangioma frequently has dilated lymphatic spaces that extend right to the basement membrane, and these produce folds in the surface epithelium (Fig. 3-8).

The smooth-surfaced and rough-surfaced masses are categorized in Table 3-1.

**Flat and raised entities.** A macule is the result of a localized color change produced by the deposition of pigments or slight alterations in the local vasculature or other minimal local changes. This is a flat lesion, since there is usually no significant increase in the number (hyperplasia) or size (hypertrophy) of the cells. Significant hyperplasia and hypertrophy always result in an elevation, which may take the shape of a papule, a nodule, a polypoid mass, or a papillomatous mass (see Chapter 10).

For example, an ephelis or freckle is a brownish macule that on histologic examination represents only an increased production of melanin by the normal number of melanocytes. On the other hand, an intradermal or intramucosal nevus shows a significantly increased number of nevus cells producing melanin and an increased amount of collagen in the subepithelial area. Therefore both hypertrophy and hyperplasia are present, and the lesion appears clinically to be pigmented and elevated (Fig. 3-9).

**Aspiration** The primary value of aspiration is to investigate the fluid contents of soft, cheesy, or rubbery masses whose characteristics suggest that they may contain fluid. An awareness therefore of the nature of the material contained in a mass will contribute significantly to the formulation of the appropriate differential diagnosis.
Fig. 3-6. Rough-surfaced masses usually arise within the surface epithelium. A, Papilloma. B, Seborrheic keratosis.

Fig. 3-7. Pebbly surfaced mass (granular cell myoblastoma). Note the presence of the pseudoepitheliomatous hyperplasia, which is often severe enough in these lesions to produce a pebbled surface.
contrast to staphylococcal infections, the streptococcal variety is more often associated with painful regional lymphadenitis.

Actinomycosis in its early stage is indicated by firm red swellings. Later, pus pools under the surface and produce fluctuance. At this intermediate stage, aspiration often yields a yellowish-white pus with a few firm yellow granules in it. These are the “sulfur granules,” thought to be composed of mycelia and material produced as a by-product of the natural defenses of the host. Any aspirate from an infection should be sent to the laboratory for routine bacterial culture and sensitivity tests. If actinomycosis is suspected, special anaerobic cultures should be requested.

A sticky, clear, viscous fluid is obtained on aspiration or retention phenomena (mucoceles and cysts of the glands of Blandin and Nuhn and of the sublingual gland [ranulas] and sometimes from tumors of the minor salivary glands. This pooled liquid is a concentrated mucous secretion from which water is resorbed by the cells lining the cyst. Occasionally a low-grade mucoepidermoid tumor produces enough mucus to clinically resemble a mucocele and yields mucus on aspiration.

The papillary cystic adenoma and papillary cystadenoma lymphomatosum are often fluctuant and contain a thin, straw-colored liquid that can be aspirated.

Subcutaneous emphysemas and laryngoceles are soft masses that are filled with air, as are the rare pockets of carbon dioxide and hydrogen produced by Clostridium perfringens in gas gangrene. The former two entities can be completely deflated by aspiration.

Needle biopsy Needle biopsies can be performed with a special biopsy needle; this procedure can be advantageous in the biopsy of deeper structures such as the lymph nodes. The needle biopsy technique has the disadvantage of yielding a small-sized sample, and there is the added danger of lacerating some large blood vessels in the area (see Chapter 2, p. 10).

Features Obtained by Palpation

Knowledgeable examiners are able to distinguish the various tissues encountered in and around the oral cavity by palpation because, first, they are familiar with the normal gross anatomy of the structures and know where these tissues and organs are situated, their extent, in which plane they lie, and their anatomic relationship to each other. Second, examiners can visualize the microscopic structures of these tissues, which correlate so well with the tactile sensations elicited by the palpation of these structures and tissues.

Palpation is actually a “third eye”—the most informative method of clinically examining the tissues lying beneath the surface. Fortunately for the examiner, the soft tissues of the body lie over bones, cartilages, or skeletal muscles; therefore the superficial tissues can be palpated against a sturdy base.

Surface temperature Before attempting to make a judgment relative to the level of the surface temperature of a region or part, the examiner should first establish the patient’s systemic temperature as indicated on an oral thermometer. A rise in surface temperature of the skin is simple to detect. The examiner places the fingers of one hand on the skin in the area of concern and the fingers of the other hand on the skin on the contralateral spot of the body. Relatively subtle differences in temperature may be rapidly and comfortably detected and can frequently contribute significantly to arriving at the diagnosis.
The skin generally has an increased temperature when it is inflamed or when it overlies an inflamed or infected region. The increased metabolic rate of the inflamed tissue, together with the increased vascularity of the area, is responsible for the increased local temperature of the part. The surface temperature of the skin overlying superficial aneurysms, arteriovenous shunts, and relatively large recent hematomas may also be elevated, since the higher deep body temperature is carried by the blood to the skin overlying these areas. The estimation of normal surface temperature is a useful test on the skin, but trying to transfer such a reference to the oral cavity is of little value, since the oral mucosa has a higher normal temperature than the skin.

Anatomic regions and planes involved Since many of the structures in the head and neck region can be at least partly palpated through the skin or oral mucosa or both, it becomes imperative that normal structures be anticipated and recognized.

For example, if the diagnostician locates a firm mass high in the submandibular space, he or she must be aware that the submaxillary gland is peculiar to that area and must then establish whether the mass is discrete from the salivary gland. If the mass is separate from the gland, pathoses of this gland will be deemphasized in the differential diagnosis. If this cannot be determined, the diagnostician must consider salivary gland pathoses as a probable diagnosis.

It is also essential that the examiner be able to detect, identify, and evaluate the condition of the regional tissues by manual examination. The acquisition of such a capability requires not only the basic anatomic knowledge but also considerable experience examining the area.

Sometimes the information gained by palpation is limited, and the palpation itself may be difficult—especially if the area is swollen because the swelling will tend to obscure the definition of structures. Furthermore, the patient will seldom permit a thorough palpation of painful tissue. In such a case a complete palpation may not be possible until the patient is anesthetized.

Initially the examiner must determine whether a mass in question is located superficially or deep. Then it is very helpful to identify the actual tissue involved because this may give a valuable clue to tissue of origin and to the clinical diagnosis.

Mobility Once the examiner has defined a mass in terms of its location in an anatomic plane and the tissue and organ involved, he or she will determine whether the mass is mobile or fixed with regard to its neighboring tissues. By palpation the examiner can establish whether the mass is freely movable in all directions. If it is freely movable, it is most likely a benign, possibly encapsulated, process originating in the loose subcutaneous or submucosal tissue (such as epidermoid or dermoid cyst or lymph node) (Fig. 3-14).

The mobility can be illustrated by fixing the mass with the fingers of one hand while moving the skin or mucosa over the mass with the other hand. Next, an attempt is made to move the mass independent of its underlying tissue. This demonstrates whether it is freely movable in all directions. If the mass is fixed to the skin but not to the underlying tissue, this is an important clue and limits the differential diagnosis list. For instance, epidermoid and dermoid cysts would be regarded as unlikely alternatives because they are freely movable in all directions, unless fibrosis has resulted from a previous infection. On the other hand, sebaceous cysts would be high on the list of possibilities, since they are freely movable over underlying tissues but are bound to the skin. This diagnosis is logical considering that sebaceous cysts form when sebaceous units of the skin become blocked but retain their continuity with the cystic glandular elements and the skin (Fig. 3-15).
The mass that is independent of the skin but attached to the deeper structures presents different possibilities. It could be attached to muscle, bone, cartilage, fat, salivary gland, or thyroid gland. The tissue or organ to which the mass is most intimately attached will most often prove to be the tissue of origin (Fig. 3-16). For example, if the mass is located in or bound to the parotid gland, the most likely possibility is that it is of parotid origin.

If the mass is bound to the skin or mucosa and to the underlying structures, however, there are only four possibilities:

1. Fibrosis after a previous inflammatory episode
2. An infiltrating malignant tumor that originated in the skin or mucous membrane and has invaded the deep structures (Fig. 3-17)
3. A malignancy that originated in a deep structure and has invaded the subcutaneous or submucosal tissue and the skin or mucosa
4. A malignancy that originated in the loose connective tissue and has invaded both the superficial and the deep layers

When examining the oral cavity, the diagnostician should remember that under normal conditions the mucosa covering the hard palate and the gingivae is bound tightly to the underlying bone. In addition, the loose submucosal layer under the papillated, keratinized, stratified squamous epithelium of the dorsal surface of the tongue is very thin and frequently nonexistent. Therefore the mucosa of the dorsal surface cannot normally be moved independent of the deeper muscular part. The remainder is lining mucosa and has a substantial loose submucosal layer, which in the absence of disease permits the surface epithelial layer to be moved independent of the deeper tissues and structures.

The palpation of a mass during function frequently reveals whether the mass is fixed to deeper structures—and if so, which ones. For example, if a fluctuant mass in the anterior midline of the neck moves up and down as the patient swallows, it may be diagnosed as part of, or attached to, the hyoid bone, larynx, trachea, thyroid or parathyroid gland, or intervening muscles. If it elevates when the patient protrudes the tongue, the examiner may suspect that it is a thyroglossal cyst and that a persistent epithelial or fibrous cord or a fistula is leading to the tongue. (These are not always present in patients with thyroglossal cysts; however, if a mass does not elevate on protrusion of the tongue, a thyroglossal duct cyst is not necessarily ruled out.)

In some cases a mass may encroach on adjacent moving structures and impair or limit movement. For example, a chondroma or hyperplasia of the condyle may produce deviation and limitation of jaw movements.

Extent. The determination of the foregoing characteristics by palpation is important not only for masses located below the surface but also for visible superficial lesions.

Clinicians must always bear in mind that what is visible may represent just the tip of the iceberg. Consequently, it is important that the tissue surrounding and underlying the bases of these apparent surface lesions be carefully palpated to determine the maximum extent of the lesion into adjacent tissues. Positive identification of small cellular areas of penetration into the surrounding tissue can be made only by microscopic examination, but the surgeon must grossly estimate the extent of penetration in the surrounding tissue by palpation before surgery.

Whether a mass will have poorly defined, moderately defined, or well-defined borders, as determined by palpation, will depend on four factors:

1. Border characteristics of the mass
2. Relative consistency of the surrounding tissues
3. Thickness and nature of the overlying tissue
4. Sturdiness of the underlying tissue

Borders of the mass. Malignancies usually have ill-defined borders that are extremely difficult to delineate.
by palpation. This observation is readily evident if we consider two features characteristic of these disorders:

1. Malignant tumors often infiltrate adjacent tissue by extending many processes of tumor into the surrounding normal tissue.

2. Malignant tumors produce a scirrhous reaction in the infiltrated tissue.

The processes of the tumor are irregular in size, shape, and distribution. The result is an irregular and vague outline. These extensions anchor the neoplasm to neighboring tissue and preclude the possibility that the tumor may be moved manually independent of its surroundings.

The tumor, with its extensions, elicits an inflammatory reaction in the adjacent tissue that is somewhat similar to an allergic or foreign body reaction. This inflammatory reaction results in the sequel of fibrosis. The fibrosis develops in the irregular and diffuse areas that are inflamed and results in a more tenacious binding of the tumor to the adjacent tissues by an ill-defined fibrous attachment whose limits are impossible to perceive by manipulation of the mass.

One exception involves some of the slow-growing malignancies that develop definable fibrous borders. The borders are composed of (1) connective tissue from the stroma of the dislodged normal tissue and (2) fibrous tissue newly formed in response to the tumor. These masses have borders that may be detected and delineated by palpation.

Inflammation occurs much more frequently as a response to other insults than as a response to malignant tumors, and it usually has poorly defined borders regardless of etiology.

Inflammation in a nonencapsulated organ or tissue seldom develops a smooth, well-defined border; the subsequent scarring in the areas of resolved inflammation will duplicate the limits of the inflammatory process, which is vague and irregular. On the contrary, if the inflammation of an encapsulated organ or tissue is confined within the capsule, the margins of the affected tissue will possess the well-defined characteristics of the encapsulated organ.

Also, the resolution of the inflammation and reparative scarring within the capsule (e.g., a lymph node, the parotid gland) will result in a mass with a well-defined detectable border. This is of course is a consequence of the enclosing and restricting action of the capsule. If the inflammation breaks through the capsule and involves the surrounding tissue, however, the resultant extracapsular fibrosis will render the mass fixed to the surrounding tissue and the borders may then be ill defined. The postinflammatory fixed lymph node would be an example of such a process.

The limits of a pathologic process can be well defined by palpation depending on the shape of the lesion and the nature of its borders. The exact extent of a thin lesion or any lesion with a flattened, feather-edged border is difficult to determine. On the other hand, the limits of a plump lesion (e.g., spherical mixed tumor) are relatively easy to detect.

Consistency of surrounding tissue The consistency or the degree of firmness of a lesion, in contrast to that of its surrounding tissue, will affect the ease with which the lesion itself or its borders may be identified by palpation.

For example, the borders of a firm dermoid cyst occurring in loose subcutaneous tissue can be readily determined, whereas to ascertain the borders of a relatively soft lipoma when it occurs in the same type of loose connective tissue is difficult, if not impossible.

The same relative situation often pertains in the case of a firm mass occurring on or around the borders of a muscle. If the surrounding normal tissue is of the same consistency as the pathologic mass, the borders cannot be determined. Regardless of the physical circumstance attending the palpation of a lesion in or over bone, determining the extent of bony involvement without a radiograph is impossible.

When a radiograph indicates some degree of bone loss, identifying the site of origin as being soft tissue or bone itself without a biopsy may be difficult and often impossible. Even when the microscopic diagnosis is fibrosarcoma, the clinician still cannot be certain of the origin of the mass. If an adequate radiographic examination does not reveal a radiolucency in the bone, the clinician can proceed on the assumption that the lesion in question most likely has originated in the soft tissue.

Thickness of overlying tissue Clearly, the physical characteristics of a superficial mass are much easier to determine than in the case of a deep mass. Also, overlying dense fibrous tissue or tensed muscle tissue will obscure and may even obliterate the characteristic features of a lesion.

As an example, the borders of a branchial cleft cyst lying superficial to the sternocleidomastoid muscle may be readily delineated, and the mass is soft and fluctuant. In contrast, if the cyst lies beneath the sternocleidomastoid muscle, its borders may not be defined by palpation and the cystic mass feels firm and nonfluctuant. A covering of bone or cartilage precludes the palpation of an underlying mass, although if the mass has expanded the bone or cartilage, its presence may be suspected.

Sturdiness of underlying tissue Firm tissue situated beneath the mass promotes a more productive palpation of the mass. Soft issue platforms, on the other hand, frustrate the examiner. Fortunately, firm platforms for palpation are present in most regions of the body.

Size and shape The size and shape of a protuberant lesion may be determined by inspecting it and measuring it with a millimeter rule. In addition, a careful history frequently indicates the duration of the growth; on the basis of the present size, the growth rate can be approximated. Likewise, the history helps to establish whether a lesion is increasing in size at a steady rate, whether it is paroxysmal and predictable (like a retention phenomenon of the parotid gland, which enlarges just before eating), or whether it drains intermittently (like a rupturing abscess, which periodically decreases in size).
When masses are located within a tissue, however, palpation is necessary to determine their approximate size and shape. Round or ovoid masses are generally cysts, early benign tumors, or enlarged lymph nodes. Primary malignant tumors of lymph nodes and early metastatic tumors of lymph nodes are usually round or ovoid with a smooth border. As indicated, irregularly shaped masses are most likely to be inflammatory-fibrotic conditions or malignant tumors.

**Consistency** Consistency provides one of the most important clues to identification. Since the examiner must be as familiar with the texture and compressibility of normal tissue as with those of abnormal tissue, a description of the normal is given in Table 3-2.

The following terms are commonly used to define the consistency of tissue: soft, cheesy, rubbery, firm, and bony hard. The term soft is associated with easily compressible tissue such as a lipoma or a mucocele. Cysts filled with thin fluid are generally soft, but if they are under tension, they are rubbery. Cheesy indicates a somewhat firmer tissue that gives a more granular sensation but little or no rebound. Rubbery describes a tissue that is firm but can be compressed slightly and rebounds to its normal contour as soon as the pressure is withdrawn, such as skin. Firm identifies a tissue, such as fibrous tissue, that cannot be readily compressed. Bony hard is self-explanatory.

There are examples in each category that are borderline and appear to overlap adjacent categories, so it may not always be possible to explicitly describe a consistency with one of these terms. However, they are universally employed and connote a similar meaning to most individuals.

At least three different factors can modify the consistency of a tissue or mass as perceived by palpation:

1. The depth in the tissue will alter the consistency sensed by palpation; that is, a soft mass will seem firmer if it is deeper in the tissue than it would feel if it were situated more superficially.
2. A thick layer of overlying tissue, especially muscle or fibrous tissue, will appreciably modify or mask the true nature of a mass.
3. Soft glandular tissue surrounded by a dense connective capsule will be perceived as firmer than it is.

The examiner should be familiar with microstructure of tissue because it correlates so well with its consistency determined during palpation. The histologies of examples from each group of consistencies are shown together in Fig. 3-18 for comparison.

Once the examiner has become familiar with the location and consistency of normal tissues and organs, he or she will be quite capable of differentiating between normal and abnormal tissue when a consistency is detected that contrasts with the expected consistency of the tissue being palpated.

The consistency of abnormal tissue can be described with the same terms as those used for characterizing normal tissue: soft, cheesy, rubbery, firm, and bony hard. Representative segments of pathologic masses have been selected and categorized according to consistency in Table 3-3. Again, in an effort to underscore the correlation between microstructure and physical consistency, photomicrographs of pathologic tissues with similar consistencies have been grouped together in Fig. 3-19 on pp. 32-33.

**Fluctuance and emptiability** All soft, cheesy, or rubbery lesions or masses over 1 cm in diameter should be tested for fluctuance. This is done by placing the sensing finger of one hand on one side of the mass and gently pressing on the mass with the probing fingers of the other hand. If the sensing fingers can detect a wave or force passing through the lesion, the mass is said to be fluctuant (Fig. 3-20 on p. 34). The following four factors determine whether fluctuance can be perceived in a soft, cheesy, or rubbery lesion (Table 3-4 on p. 34):

1. The mass must contain liquid or gas in a relatively enclosed cavity (Fig. 3-20). Examples of such fluctuant masses are cysts, mucoceles, ranulas, pyogenic space abcesses, early hematomas, subcutaneous emphysemas, varicosities, Warthin's tumors, papillary cyst adenomas, lipomas, and plexiform neurofibromas (Fig. 3-21 on p. 35). Although a lipoma and a plexiform neurofibroma do not

---

**Table 3-2 Consistency of normal tissues and organs**

<table>
<thead>
<tr>
<th>Consistency</th>
<th>Tissues or organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft</td>
<td>Adipose tissue</td>
</tr>
<tr>
<td></td>
<td>Fasciae</td>
</tr>
<tr>
<td></td>
<td>Veins</td>
</tr>
<tr>
<td></td>
<td>Loose connective tissue</td>
</tr>
<tr>
<td></td>
<td>Glandular tissue, minor salivary glands, and sublingual salivary gland</td>
</tr>
<tr>
<td>Cheesy</td>
<td>Brain tissue</td>
</tr>
<tr>
<td>Rubbery</td>
<td>Skin</td>
</tr>
<tr>
<td></td>
<td>Relaxed muscle</td>
</tr>
<tr>
<td></td>
<td>Glandular tissue with capsule</td>
</tr>
<tr>
<td></td>
<td>Arteries and arterioles</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
</tr>
<tr>
<td>Firm</td>
<td>Fibrous tissue</td>
</tr>
<tr>
<td></td>
<td>Tensed muscle</td>
</tr>
<tr>
<td></td>
<td>Large nerves</td>
</tr>
<tr>
<td>Bony hard</td>
<td>Bone</td>
</tr>
<tr>
<td></td>
<td>Enamel</td>
</tr>
<tr>
<td></td>
<td>Dentin</td>
</tr>
<tr>
<td></td>
<td>Cementum</td>
</tr>
<tr>
<td></td>
<td>Cartilage†</td>
</tr>
</tbody>
</table>

*a Many normal tissues and organs (e.g., dental pulp, thyroid and parathyroid glands, lymph nodes, and lymphatic vessels) usually cannot be palpated under normal conditions, so they have not been categorized here.

†Cartilage is difficult to classify; it seems to fall into an intermediate category, being too firm to be included in the firm group and not firm enough to be placed in the bony hard group.
have a true lumen containing a fluid, the high liquid content of the cells and interstitial tissue is apparently sufficient to produce fluctuance in these tumors.

2. The mass must be located in a superficial plane. If the mass is covered by a thick layer of relatively inflexible tissue or a structure such as a muscle, it cannot be palpated in a manner that might demonstrate fluctuance (Fig. 3-22 on p. 35).

3. The mass must be in a fluctuant stage. Some clinical lesions represent a fluctuant stage in a multiphasic disease process. For example, an odontogenic infection that has broken through the cortical plates and commenced to involve the adjacent soft tissue is tender, red, and firm. As the process continues, pus produced by the typical odontogenic space infection results in a soft, fluctuant, painful, nonemptiable mass. As the abscess resolves, regardless of the treatment, the fluctuant stage gives way to a firm stage and the firm stage may either disappear completely or leave a small area of fibrosis. Actinomycosis often demonstrates the same cycle, as do infected cysts to some extent.

4. Developing fibrosis around the mass may obscure the fluctuance. Chronically infected cysts that flare up

---

Fig. 3-18. Normal tissues categorized according to consistency. The general appearance of the following normal tissues at low magnification reflects the consistency of the tissue to palpation. A, Tissues with soft consistency: 1, adipose tissue; 2, unencapsulated mucous glands; 3, loose connective tissue; note the presence of thin-walled vessels. B, Tissue with cheesy consistency: brain tissue. C, Tissues with firm consistency: 1, fibrous tissue; 2, skeletal muscle; tensed muscle feels firm, whereas relaxed muscle feels rubbery.

Continued
Fig. 3-18, cont’d. D, Tissues with bony hard consistency: 1, bone; 2, cementum; 3, dentin; 4, cartilage.

Table 3-3 Consistency of pathologic masses

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Soft</strong></td>
<td>Cysts under tension—rubbery</td>
</tr>
<tr>
<td>Cysts</td>
<td>Infected and fibrosed cysts—firm</td>
</tr>
<tr>
<td>Warthin’s tumors and papillary cystic adenomas</td>
<td>Sebaceous cysts, keratocysts, and dermoid cysts—cheesy</td>
</tr>
<tr>
<td>Vascular tumors and phenomena</td>
<td>Occasionally sclerosed types firm in some areas</td>
</tr>
<tr>
<td>Hemangiomas, lymphangiomas, varicosities, and cystic</td>
<td>Sclerosing types—firm</td>
</tr>
<tr>
<td>hygromas</td>
<td>Hemangioendotheliomas—firm</td>
</tr>
<tr>
<td>Fatty tumors</td>
<td>Hemangiosarcomas—firm</td>
</tr>
<tr>
<td>Lipomas, hibernomas, xanthomas, and liposarcomas</td>
<td>Sclerosing types of liposarcoma—firm</td>
</tr>
<tr>
<td>Myxomas</td>
<td>None</td>
</tr>
<tr>
<td>Plexiform neurofibromas</td>
<td>None</td>
</tr>
<tr>
<td>Inflammatory hyperplasias (granulomatous stage)</td>
<td>Fibrosed types—firm</td>
</tr>
<tr>
<td>Emphysemas</td>
<td>None</td>
</tr>
<tr>
<td>Laryngoceles</td>
<td>If high tension, rubbery</td>
</tr>
<tr>
<td>Retention phenomena</td>
<td>If fibrosed, firm</td>
</tr>
<tr>
<td>Mucoceles and ranulas</td>
<td></td>
</tr>
<tr>
<td><strong>Cheesy</strong></td>
<td>Infected and fibrosed types—firm or alternate areas of cheesiness and firmness</td>
</tr>
<tr>
<td>Cysts</td>
<td>Early or late tuberculosis nodes—firm</td>
</tr>
<tr>
<td>Sebaceous, dermoid, and epidermoid</td>
<td></td>
</tr>
<tr>
<td>Tuberculous nodes</td>
<td></td>
</tr>
</tbody>
</table>
### Table 3-3  Consistency of pathologic masses—cont’d

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rubbery</strong></td>
<td></td>
</tr>
<tr>
<td>Cysts with contents under tension</td>
<td>None</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>None</td>
</tr>
<tr>
<td>Myomas</td>
<td>None</td>
</tr>
<tr>
<td>Myoblastomas</td>
<td>None</td>
</tr>
<tr>
<td>Aneurysms</td>
<td>Those with severe pseudoepitheliomatous hyperplasia—firm</td>
</tr>
<tr>
<td>Pyogenic space infection</td>
<td>None</td>
</tr>
<tr>
<td>Edematous tissue</td>
<td>Early stages—firm</td>
</tr>
<tr>
<td>Early hematomas</td>
<td>None</td>
</tr>
<tr>
<td>Early hematomas</td>
<td>If not much tension, soft</td>
</tr>
<tr>
<td><strong>Firm</strong></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Streptococcus, early staphylococcus, early actinomycosis, and histoplasmosis</td>
<td></td>
</tr>
<tr>
<td>Benign tumors of soft tissue</td>
<td></td>
</tr>
<tr>
<td>Fibromas, neurofibromas, schwannomas, and amputation neuromas</td>
<td>Fatty tumors, plexiform neurofibromas, myxomas, and hemangiomas</td>
</tr>
<tr>
<td>Malignancies of soft tissues</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinomas, melanomas, fibrosarcomas, and sclerosing liposarcomas</td>
<td></td>
</tr>
<tr>
<td>Osteosarcomas</td>
<td>Occasionally bony hard</td>
</tr>
<tr>
<td>Chondrosarcomas</td>
<td>Occasionally bony hard</td>
</tr>
<tr>
<td>Metastatic carcinomas</td>
<td>Occasionally (osteoblastic, metastatic, and prostatic carcinomas) bony hard</td>
</tr>
<tr>
<td>Benign and malignant salivary gland tumors</td>
<td>Warthin’s tumors and papillary cyst adenomas—soft</td>
</tr>
<tr>
<td>Inflammation and infection of parotid and submaxillary salivary glands</td>
<td>Occasionally mucoepidermoid tumors with alternate soft and firm areas</td>
</tr>
<tr>
<td>Inflammation and infection of lymph nodes</td>
<td>None</td>
</tr>
<tr>
<td><strong>Bony hard</strong></td>
<td></td>
</tr>
<tr>
<td>Osteomas</td>
<td>None</td>
</tr>
<tr>
<td>Exostoses</td>
<td>None</td>
</tr>
<tr>
<td>Osteogenic sarcomas</td>
<td>Undifferentiated—firm</td>
</tr>
<tr>
<td>Pleomorphic adenomas occasionally</td>
<td>Usually firm</td>
</tr>
<tr>
<td>Chondromas</td>
<td>Occasionally firm</td>
</tr>
<tr>
<td>Chondrosarcomas</td>
<td>Occasionally firm</td>
</tr>
<tr>
<td>Osteoblastic, metastatic, and prostatic carcinomas, occasionally</td>
<td>Usually firm</td>
</tr>
</tbody>
</table>
Fig. 3-19. Pathologic tissues categorized according to consistency. The general appearance of each of the following pathologic tissues at low magnification reflects the consistency of the tissue to palpation. A, Soft consistency: 1, myxoma; 2, plexiform neurofibroma (low and high magnifications); 3, ranula. B, Cheesy consistency: 1, epidermoid cyst; note that the lumen is filled with keratin, which imparts the cheesy consistency; 2, tuberculous node; the large amorphous area is caseation necrosis, which imparts the cheesy consistency. C, Rubbery consistency: 1, rhabdomyoma; 2, lymphoma; the lymph node capsule helps to impart the rubbery consistency to this entity.
abscesses, are usually nonfluctuant and completely emptiable with ease. They rarely develop an architecture that results in fluctuance.

A number of factors influence the emptiability of a mass: course, number, diameter, and position of exit vessels or channels. Also, the width of the base of a lesion relates to the ease with which the lesion can be emptied.

Fig. 3-24 shows a diagram of an aneurysm. Note that the aneurysm could be readily emptied by digital pressure. The usual cavernous hemangioma is similar in this respect. The cavernous spaces are large but few, the exit channels large, and the base of the lesion sessile. Such a hemangioma would not demonstrate fluctuance, since it has all the features that permit rapid emptying.

Fig. 3-25, by contrast, is a diagram representing a capillary hemangioma with many blood sinuses connected by small vessels. Note that the exit vessels are few and small and the base is somewhat pedunculated. A hemangioma of this type would probably not be readily emptied by digital pressure, since the slight pressure that would empty the lesion would also tend to occlude the small exit vessels. Thus the lesion could consequently be partially fluctuant and partially emptiable.

Fig. 3-26 is an illustration of a capillary hemangioma that probably could not be emptied at all. The laryngocele, a developmental pouch projecting from the larynx, is inflated with air when the patient coughs. Frequently the connecting channel to the larynx is small and easily occluded, and although the laryngocele usually shows fluctuance, it can be slowly emptied by careful digital pressure. A cyst also would be fluctuant but not emptiable, since a channel for the egress of the fluid is not a usual feature of this lesion.

Position or location of the examiner's finger or fingers is important in determining whether a lesion can be emptied or not. In Fig. 3-27 the examiner's finger at point X would block the efferent channel and mask the fact that the lesion is really emptiable. This lesion would empty readily, however, with digital pressure if the finger were positioned at point Y.

The reason for the emptiability of a draining cyst or abscess is obvious and is illustrated in Fig. 3-28 on p. 38. Such a lesion generally is not fluctuant unless the opening is quite small.

Painless, tender, or painful During the digital examination it becomes apparent whether a mass is painless, tender, or painful. This information aids greatly in arranging a suitable list of diagnostic possibilities. In the development of a working diagnosis, it is helpful if the painful mass is evaluated on the basis of the following possible causes (Table 3-5):

1. Pain because of inflammation. The painful effect of an increase in the fluid content of a tissue by a pathologic agent is intensified when the tissue is confined within rigid or semirigid walls (dental pulp, lymph node, submaxillary or parotid salivary glands). The increased internal pressure that results from the interstitial accumulation of fluid is intensified by the external pressure of the examiner's fingers and is registered as pain or an increase in pain.

The most frequently encountered example is an inflammatory process resulting from mechanical trauma or

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Fluctuant</th>
<th>Emptiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cysts</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Abscesses</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Mucoceles</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ranulas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Early hematomas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Subcutaneous emphysemas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lipomas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Plexiform neuro-fibromas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Myxomas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Papillary cystic adenomas</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Warthin's tumors</td>
<td>Variable</td>
<td>No</td>
</tr>
<tr>
<td>Varicosities</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Cystic hygromas</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Laryngoceles</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Capillary hemangiomas*</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Lymphangiomas</td>
<td>Usually</td>
<td>Usually not</td>
</tr>
<tr>
<td>Cavernous hemangiomas</td>
<td>Usually not</td>
<td>Usually</td>
</tr>
<tr>
<td>Aneurysms</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Draining cysts</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Draining abscesses</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Inflammatory hyperplasias</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*Capillary hemangiomas are often less than 1 cm in diameter and are usually too small for fluctuance to be accurately detected.

Fig. 3-22. Diagram of muscle overlying a cyst and masking its characteristics.

Fig. 3-23. Diagram illustrating a nonemptiable cystlike lesion.
infection. Occasionally a tumor, especially of the malignant variety, indirectly causes pain by infiltrating a major duct of a major salivary gland—thereby inducing a retention phenomenon and an enlarged salivary gland that is tender or painful because of the markedly increased internal pressure. Also, a tumor located in adjacent normal tissue may become secondarily infected and thus change from a painless to an inflamed and painful lesion.

2. Painful tumors. Some neural tumors (e.g., the amputation neuroma, which actually is not a true neoplasm but represents an overexuberant misdirected repair process in a severed nerve) are commonly painful to palpation. As a rule, however, benign and malignant tumors are painless masses unless they are traumatized or secondarily infected.

3. Pain because of sensory nerve encroachment. Masses otherwise painless but located near relatively large sensory nerves may elicit pain when they rapidly enlarge and encroach on the nerve space. This most frequently happens when the nerve pathway is bone as opposed to soft tissue; in soft tissue, especially when the process is slow growing, the nerve is pushed ahead of the mass and pain is not elicited until an unyielding tissue is encountered. Occasionally a rapidly growing malignant tumor, such as an osteosarcoma growing within the bone, will cause pain because it expands more rapidly than the bone can be resorbed. Therefore the pressure on the surrounding bone and nerve tissue evokes pain.

Usually the pain produced by the encroachment of malignant tumor on a sensory nerve is of short duration since the rapidly growing tumor causes its early destruction. An exception is the adenoid cystic carcinoma, which frequently spreads through the perineural space.

Tenderness in a mass usually indicates the presence of a low-grade inflammation and internal pressure, which i
Fig. 3-24. Diagram illustrating complete emptiability in an aneurysm-like lesion.

Fig. 3-25. Diagram illustrating the difficulty encountered in attempting to completely empty a capillary hemangioma, which has many small channels and few exit vessels.

Fig. 3-26. Diagram illustrating a pedunculated capillary hemangioma, which would be nonemptiable by digital pressure.

Fig. 3-27. Diagram illustrating the importance of finger position when attempting to empty a lesion with this configuration. Careful pressure applied at point $Y$ would readily empty the lesion, whereas rapid pressure applied at point $X$ would tend to occlude the exit channel and render the lesion nonemptiable.
practice are frequently induced by the repeated manipulation of a painless mass by a series of examiners. Frequently, however, a tender mass indicates the presence of a chronic infection.

The degree of pain that a mass produces often varies, depending on the stage of development of the mass or the type of infection that may have caused the pain. For example, a retention phenomenon of major glands may be tender in the early stages but become excruciatingly painful as the situation worsens. Untreated bacterial infections are typically tender in the early stage, painful in the acute phase, and tender during resolution. Nevertheless, a low-grade bacterial infection occasionally may be tender throughout its course. Fungal, spirochetal, tuberculous, rickettsial, and viral infections, on the other hand, are more typically chronic in their nature and are tender throughout their development and resolution.

**Unilateral or bilateral** When a clinician encounters pathology, he or she should investigate the contralateral region of the body to determine whether the condition is bilateral. As a rule, if similar masses are present bilaterally and in the same locations, they are most likely normal anatomic structures. The carotid bulb in the bifurcation of the artery, the mastoid process, the lateral processes of the cervical vertebrae, and the wings of the hyoid bone are such bilaterally occurring anatomic structures that are frequently mistaken for pathologic masses. Bilateral palpation coupled with a knowledge of anatomy is obligatory if these normal structures are to be differentiated from pathologic masses.

**Solitary or multiple** A solitary lesion nearly always indicates a local benign condition or an early malignancy. Multiple lesions, on the other hand, must alert the examiner to the following possibilities:

- Systemic diseases
- Disseminated disease
- Syndromes

**Features Obtained by Percussion**

Percussion is the act of tapping a part of the body to evaluate the quality of the echo produced. The physician routinely percusses the chest to determine the outline of the heart and to evaluate the lung fields. The dentist frequently percusses teeth to determine whether they have adequate bone support and to determine whether they are sensitive. Percussion is not particularly useful, however for the examination of the lesions discussed in this text.

**Features Obtained by Auscultation**

Auscultation is the act of listening with or without the aid of a stethoscope to sounds produced inside the body. The physician routinely auscultates the chest to evaluate heart and lung sounds. The dentist may auscultate the temporomandibular joint to detect crepitus. Auscultation of pathologic masses is to be encouraged because this method detects the presence of bruits, which are a characteristic of aneurysms and arteriovenous shunts.
It is of paramount importance that the clinician follows a precisely formulated diagnostic sequence when a lesion is detected. Such an established approach will accomplish the following:

- Time will be used effectively and efficiently.
- All the pertinent features will be identified.
- A high success rate in diagnosis will be achieved.

Some authorities argue that the experienced diagnostician does not rely on such a cumbersome and formal procedure, since he or she is apparently able to diagnose a lesion after only a brief inspection. However, the expert diagnostician has seen many lesions on numerous occasions and is able to run through the diagnostic sequence very quickly in his or her mind and still maintain an excellent “batting average.”

We have found the following diagnostic sequence to be both effective and practical:

| DETECTION AND EXAMINATION OF THE PATIENT'S LESION | LISTING THE POSSIBLE DIAGNOSES | FORMULATING THE FINAL DIAGNOSIS |
| EXAMINATION OF THE PATIENT | DEVELOPING THE DIFFERENTIAL DIAGNOSIS | (PROVED BY BIOPSY, CULTURE, AND/OR RESPONSE TO TREATMENT) |
| Chief complaint(s) | DEVELOPING THE WORKING DIAGNOSIS (OPERATIONAL DIAGNOSIS, TENTATIVE DIAGNOSIS, CLINICAL IMPRESSION) |
| Onset and course | |
| REEXAMINATION OF THE LESION | |
| CLASSIFICATION OF THE LESION | |

DETECTION AND EXAMINATION OF THE PATIENT'S LESION

Most lesions are discovered during routine examination, but in some cases, the patients are aware of their lesions and have come for help. This is especially so when pain or discomfort are the symptoms.

Once the clinician has recognized or at least suspects that an abnormal change is at hand, he or she proceeds to examine it using the modalities described in Chapters 2 and 3. These include visual examination in combination with palpation, percussion, and auscultation. The findings are noted and mentally evaluated. As a matter of personal preference, the clinician may elect to perform either a cursory or a thorough examination of the lesion at this time, although the situation may dictate a thorough examination immediately. The importance of first examining the lesion is that the clinician can gain information that will alert him or her to look especially for possible related findings in the remainder of the patient examination.

EXAMINATION OF THE PATIENT

Patient examination has been discussed in depth in Chapters 2 and 3. In this chapter, we have chosen to enlarge on the sections of the interview dealing with the patient’s chief complaint(s) and the onset and course of
the present problem because information from these are so often pivotal.

**Chief Complaint(s)**

Common chief complaints related to oral diseases include sores, burning sensation, bleeding, loose teeth, recent occlusal problems, delayed tooth eruption, dry mouth, too much saliva, a swelling, bad taste, halitosis, paresthesia, and anesthesia. **Pain** The patient should be encouraged to describe the main characteristics of the pain; its nature (sharp or dull), severity, duration, and location; and the precipitating circumstances.

The following entities may produce oral and facial pain:

1. Teeth
   a. Pulpal disease
   b. Pulpoperiapical disease
   c. Gingival and periodontal disease
2. Mucous membrane disease
3. Tongue conditions
4. Salivary gland inflammations and/or infection
5. Lesions of the jaw bones
6. Lymph node inflammations and infections
7. Temporomandibular joint diseases
8. Tongue conditions
9. Maxillary sinus disease
10. Ear diseases
11. Psychoses
12. Angina pectoris
13. Tonsillar disease
14. Pretender (e.g., drug addict)
15. Central nervous system diseases
16. Neuralgias
17. Neuritis
18. Vasculitis
19. Berry aneurysms
20. Diaphragmatic hernia
21. Esophageal diverticulum
22. Eagle’s syndrome (calcification of stylohyoid ligament)
23. Trotter’s syndrome (pain caused by carcinoma of pharynx)
24. Self-mutilation
25. Iatrogenic

**Sores** When a patient uses the term “sore” or “a sore” to describe a complaint, this may indicate the presence of mucosal inflammations or ulcers from any cause except early ulcerative malignancies (which are usually painless).

**Burning sensation** A burning sensation is usually felt in the tongue and is often caused by a thinning or erosion of the surface epithelium. The following disease states may produce a burning sensation:

1. Burning mouth syndrome
2. Psychosis
3. Neurosis
4. Viral infection
5. Fungal infection
6. Chronic bacterial infection
7. Geographic tongue
8. Fissured tongue
9. Generalized oral mucositis diseases
10. Xerostomic conditions
11. Anemia
12. Achlorhydria
13. Multiple sclerosis
14. Vitamin deficiencies

A generalized burning sensation in the mouth is also frequently found to be associated with an increased interalveolar space.

**Bleeding** Intraoral bleeding may be caused by these disturbances:

1. Gingivitis and periodontal disease
2. Traumatic incidents, including surgery
3. Inflammatory hyperplasias
4. Allergies
5. Tumors (traumatized tumors and tumors that are very vascular, e.g., hemangiomas)
6. Diseases that cause or are associated with deficiencies in hemostasis

**Loose teeth** Loss of supporting bone or the resorption of roots may result in loose teeth and may indicate the presence of any of the following:

1. Periodontal disease
2. Trauma
3. Normal resorption of deciduous teeth
4. Pulpoperiapical lesions
5. Malignant tumors
6. Benign tumors that may induce root resorption (chondromas, myxomas, hemangiomas)
7. Histiocytosis X
8. Hypophosphatasia
9. Familial hypophosphatemia
10. Papillon-Lefèvre syndrome
11. Acquired immunodeficiency syndrome (AIDS)

**Recent occlusal problem** When a patient complains that “recently the teeth don’t bite right” or “recently some teeth are out of line,” the clinician must consider overcontoured restorations or the following:

1. Periodontal disease
2. Traumatic injury (fracture of bone or tooth root)
3. Pericementitis or periapical abscess
4. Cysts or tumors of tooth-bearing regions of the jaw
5. Fibrous dysplasia

**Delayed tooth eruption** Delayed eruption of a tooth may be related to any of the following:

1. Malposed or impacted teeth
2. Cysts
3. Odontomas
4. Sclerosed bone
5. Tumors
6. Maldevelopment

If there is a generalized delay, the clinician should consider the possibilities of anodontia, cleidocranial dysplasia, or hypothyroidism.
Dry mouth (xerostomia) A dry mouth may result from the following disorders:
1. Local inflammation
2. Infection and fibrosis of major salivary glands
3. Dehydration states
4. Drug therapy
   a. Tranquilizers
   b. Antihistamines
   c. Anticholinergics
5. Autoimmune diseases
   a. Mikulicz’s disease
   b. Sjögren’s syndrome
6. Chemotherapy
7. Postradiation changes
8. Psychosis
9. Alcoholism

Too much saliva The complaint of excessive saliva may be related to psychosomatic problems. It may be associated with the insertion of new dentures; if it continues, it may indicate a decreased or an increased vertical dimension.

Swelling When a patient’s chief complaint is a swelling, all the following entities must be considered as a probable cause:
1. Inflammations and infections
2. Cysts
3. Retention phenomena
4. Inflammatory hyperplasias
5. Benign and/or malignant tumors

Bad taste A complaint of bad taste may result from any of the following:
1. Aging changes
2. Heavy smoking
3. Poor oral hygiene
4. Dental caries
5. Periodontal disease
6. Acute necrotizing ulcerative gingivitis (ANUG)
7. Diabetes
8. Hypertension
9. Medication
10. Psychoses
11. Neurologic disorders
12. Decreased salivary flow
13. Uremia
14. Intraoral malignancies

Halitosis Although this is more frequently classified as an objective symptom, we have included it here because of its close relationship to bad taste.
1. Poor oral hygiene
2. Periodontal disease
3. Third molar opercula
4. Decayed teeth
5. ANUG
6. Oral cancer
7. Spicy food
8. Tobacco use
9. Nasal infection
10. Sinus infection
11. Tonsillitis
12. Pharyngeal infections or tumors
13. Gastric problems
14. Diabetes
15. Uremia

Paresthesia and anesthesia Such changes in sensation may be caused by any of the following:
1. Injury to regional nerves
   a. Anesthesia needles
   b. Jaw bone fractures
   c. Surgical procedures
2. Malignancies
3. Medications
   a. Sedatives
   b. Tranquilizers
   c. Hypnotics
4. Diabetes
5. Pernicious anemia
6. Multiple sclerosis
7. Acute infection of the jaw bone (unusual cause)
8. Psychoses

Onset and Course
The following classification of onsets and courses related to the growth rate of specific masses has proved helpful to us:
1. Masses that increase in size just before eating
   a. Salivary retention phenomena
2. Slow-growing masses (duration of months to years)
   a. Reactive hyperplasias
   b. Chronic infections
   c. Cysts
   d. Benign tumors
3. Moderately rapid-growing masses (weeks to about 2 months)
   a. Chronic infections
   b. Cysts
   c. Malignant tumors
4. Rapidly growing masses (hours to days)
   a. Abscesses (painful)
   b. Infected cysts (painful)
   c. Aneurysms (painless)
   d. Salivary retention phenomena (painless?)
   e. Hematomas (painless but sting on pressure)
5. Masses with accompanying fever
   a. Infections
   b. Lymphomas

REEXAMINATION OF THE LESION
At this point in the examination, unanswered questions frequently occur to the clinician, who may want to reexamine the lesion to reevaluate the original findings or to complete more detailed observations. For example, if the lesion is found to be soft, he or she may wish to determine whether it (1) is fluctuant, (2) can be emptied, (3) blanches on pressure, (4) pulsates, or (5) produces a gas or liquid on aspira-
tion and what the nature of the aspirate is. On the other hand, if the lesion is firm, the clinician may want to determine its extent, whether it is freely movable, whether it is fixed to the mucosa or the underlying tissue, and so on.

**CLASSIFICATION OF THE LESION**

By the time the clinician has reached this point in the diagnostic sequence, he or she should be able to classify the lesion according to whether it has originated in soft tissue or bone. Having arrived at a conclusion, he or she must next describe the lesion in terms of its clinical or radiographic appearance.

For example, the soft tissue lesions will be subclassified as white, exophytic, ulcerative, and so on, whereas the bony lesions may be categorized as periapical radiolucencies, cystlike radiolucencies, multiple radiopacities, and so on. If the examiner is unsure of the correct classification, it will be helpful to refer to the diagram for soft tissue classification on p. 47 and for bony lesions on p. 234.

**LIST OF THE POSSIBLE DIAGNOSES**

When the lesion has been correctly classified, a list of all the lesions that may produce a similar clinical or radiographic picture should be compiled. It will be helpful to refer directly to the corresponding chapter and the list of lesions at the beginning. Initially the order of the list is not important, since the primary objective of this step is merely to include every entity that is clinically and/or radiographically similar to the condition under study.

**DEVELOPMENT OF THE DIFFERENTIAL DIAGNOSIS**

The process of developing a differential diagnosis may be defined briefly as the rearranging of the list of possible diagnoses, with the most probable lesion ranked at the top and the least likely at the bottom.

The actual process of ranking the lesions may become complicated as the clinician attempts to match the features of the lesion being examined with the usual (or characteristic) features of the specific lesions in his or her list. To become competent in the art of differential diagnosis, therefore, not only must the clinician be familiar with the signs and symptoms produced by many diseases, but he or she must also possess some statistical knowledge relative to the incidence of each disease entity. It is particularly important that the clinician be aware of the relative incidences of individual lesions because in the completed differential diagnosis the most commonly occurring lesion will usually be ranked above the least commonly occurring unless other features prompt a modification of this ranking. Halstead and Weathers,1 Bouquot,2 Goltry and Ayer,3 and Weir et al,4 have reported extensively on the frequency of lesions.

Consequently, we strongly recommend that in developing the differential diagnosis, the clinician first ranks the lesions in order of their relative frequency of occurrence, as they are in the list at the beginning of each chapter. This order by frequency will then need to be modified by consideration of age, gender, race, country of origin, and anatomic location.

**Age**

The age of a patient may greatly modify the rankings. For example, an ulcer occurring in the floor of a 50-year-old man’s mouth indicates a reasonable probability of squamous cell carcinoma, but such a diagnosis would be unlikely if an ulcer occurred in a 10-year-old boy’s mouth. The boxes on p. 43 and p. 44 group the soft tissue and bony lesions that tend to occur in patients within particular age spans. Hand and Whitehill5 discussed the prevalence of oral mucosal lesions in elderly patients.

**Gender**

The fact that certain lesions occur more frequently in men or women also contributes to the ranking of the lesions in the differential diagnosis. For example, squamous cell carcinoma affects men two to four times more often than women. On the other hand, about 80% of periapical cemental dysplasia occurs in women over 30 years of age. The boxes on p. 45 group the soft tissue and bony lesions that show a predilection for occurring in female or male patients.

**Race**

The importance of racial (and hereditary) influences on the incidence of some diseases is illustrated by the well-known fact that a preponderance of patients with sickle cell anemia is black. Also, florid cemento-osseous dysplasia occurs predominantly in black women over 30 years of age.

**Country of Origin**

Information concerning the country of origin or residence may be an important clue for identification of the disease. Burkitt’s lymphoma seldom affects people of non-African origin. Also, the greater use of chewing tobacco and snuff in the southeastern section of the United States is related to the increased incidence of intraoral verrucous carcinoma observed in that region.

**Anatomic Location**

The extent to which the anatomic location of the lesion may affect the lesion’s ranking in the differential diagnosis is illustrated by the following examples:

1. Although the lower lip is a common site for the development of a mucocele but a rare location for a minor salivary gland tumor, both of these lesions may be in the same list of possible diagnoses.
2. The posterior region of the posterolateral hard palate is a characteristic location for a minor sali-
vary gland tumor but is an uncommon location for a mucocele.

3. Although the posterior hard palate is a characteristic site for a salivary gland tumor, this lesion is almost never found in the anterior hard palate and gingivae.

The box on p. 46 groups the various bony lesions that show a preference for either the maxilla or mandible and also for specific sites within these bones. Chapter 34 deals with intraoral lesions by anatomic region. Parapharyngeal masses are not discussed in this book. However, Pedlar and Ravindranathan discussed the differential diagnosis of these lesions. Frommer discussed differential diagnosis of lesions seen on panoramic radiographs.

The preceding pertinent facts are just a few examples from a large body of general information concerning the natural behavior of lesions that the clinician acquires from clinical experience in addition to the knowledge provided by formally structured sources.

After the ranking has been adjusted for incidence, the next step is to compare pertinent information, signs, symptoms, or other findings gained from examination of the patient with the usual features of the lesions in the list. The lesion showing the most correlation with the present findings should be ranked highest, and the lesion showing the least correlation should be ranked lowest. Halstead and Weathers did an extensive differential diagnosis of soft tissue lesions.

<table>
<thead>
<tr>
<th>Predilection of Soft Tissue Lesions for Special Age-Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants</strong></td>
</tr>
<tr>
<td>Candidiasis*</td>
</tr>
<tr>
<td>Eruption cyst</td>
</tr>
<tr>
<td>Hemangioma (85% by 1 year of age)</td>
</tr>
<tr>
<td>Lingual thyroid</td>
</tr>
<tr>
<td>Lymphangioma</td>
</tr>
<tr>
<td>Neuroectodermal tumor (before 6 months of age)</td>
</tr>
<tr>
<td>White sponge nevus</td>
</tr>
<tr>
<td><strong>Children</strong></td>
</tr>
<tr>
<td>Albright’s disease (ages 6-10)</td>
</tr>
<tr>
<td>Childhood infectious diseases</td>
</tr>
<tr>
<td>Eruption cyst</td>
</tr>
<tr>
<td>Herpes simplex</td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
</tr>
<tr>
<td>Juvenile melanoma</td>
</tr>
<tr>
<td>Pulp polyps</td>
</tr>
<tr>
<td>White sponge nevus</td>
</tr>
<tr>
<td><strong>Persons Under Age 40</strong></td>
</tr>
<tr>
<td>Albright’s disease (ages 6-10)</td>
</tr>
<tr>
<td>ANUG (ages 15-35; rare below age 12)</td>
</tr>
<tr>
<td>Benign salivary gland tumor (ages 30-39)</td>
</tr>
<tr>
<td>Branchial cyst</td>
</tr>
<tr>
<td>Candidiasis</td>
</tr>
<tr>
<td>Childhood infectious diseases</td>
</tr>
<tr>
<td>Cystic hygroma</td>
</tr>
<tr>
<td>Dermoid or epidermoid cyst</td>
</tr>
<tr>
<td>Eruption cyst</td>
</tr>
<tr>
<td>Erythema multiforme</td>
</tr>
<tr>
<td>Hemangioma (85% by 1 year of age)</td>
</tr>
<tr>
<td>Herpes simplex</td>
</tr>
<tr>
<td>Hodgkin’s disease (ages 20-40)</td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
</tr>
<tr>
<td>Juvenile melanoma</td>
</tr>
<tr>
<td>Lingual thyroid</td>
</tr>
<tr>
<td>Lymphangioma (88% before age 3)</td>
</tr>
<tr>
<td>Mucocele (65% before age 30)</td>
</tr>
<tr>
<td>Neuroectodermal tumor (before 6 months)</td>
</tr>
<tr>
<td>Palatal tori (peak before age 30)</td>
</tr>
<tr>
<td>Papilloma</td>
</tr>
<tr>
<td>Peripheral giant cell granuloma (over age 30)</td>
</tr>
<tr>
<td>Peripheral fibroma with calcification (peak at age 25)</td>
</tr>
<tr>
<td>Plasma cell gingivitis</td>
</tr>
<tr>
<td>Pulp polyps</td>
</tr>
<tr>
<td>Pyogenic granuloma (60%)</td>
</tr>
<tr>
<td>Recurrent aphthous ulcer</td>
</tr>
<tr>
<td>Thyroglossal cyst</td>
</tr>
<tr>
<td>White sponge nevus</td>
</tr>
<tr>
<td><strong>Persons Over Age 40</strong></td>
</tr>
<tr>
<td>Benign mucous membrane pemphigoid</td>
</tr>
<tr>
<td>Candidiasis†</td>
</tr>
<tr>
<td>Denture stomatitis</td>
</tr>
<tr>
<td>Desquamative gingivitis</td>
</tr>
<tr>
<td>Epulis fissuratum</td>
</tr>
<tr>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>Inflammatory papillary hyperplasia</td>
</tr>
<tr>
<td>Keratoacanthoma</td>
</tr>
<tr>
<td>Leukoedema</td>
</tr>
<tr>
<td>Leukoplakia (90%)</td>
</tr>
<tr>
<td>Lichen planus</td>
</tr>
<tr>
<td>Lipoma</td>
</tr>
<tr>
<td>Lymphoma</td>
</tr>
<tr>
<td>Malignant salivary gland tumors (ages 40-60)</td>
</tr>
<tr>
<td>Melanoma</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
</tr>
<tr>
<td>Metastatic carcinoma to cervical nodes</td>
</tr>
<tr>
<td>Pemphigus (seldom under age 30)</td>
</tr>
<tr>
<td>Radiation mucositis</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Verrucous carcinoma (ages 60-80)</td>
</tr>
</tbody>
</table>

*Also common in persons over age 40.
†Also common in infants.
### PREDISPOSITION OF BONY OR CALCIFIED LESIONS FOR SPECIAL AGE-GROUPS

#### Infants
- Caffey’s disease (birth to 2 years of age)
- Letterer-Siwe disease (ages 1-3)
- Lingual mandibular bone defect?
- Osteopetrosis (malignant)
- Rickets
- Thalassemia major

#### Children
- Acute leukemia
- Basal cell nevus syndrome (ages 5-30)
- Burkitt’s tumor (ages 2-14)
- Central hemangioma (ages 10-20)
- Cherubism
- Dentigerous cyst (ages 10-20)
- Fibrous dysplasia (ages 10-20)
- Hand-Schüller-Christian disease (ages 1-10)
- Lingual mandibular bone defect
- Multilocular cyst (over age 15)
- Osteoid osteoma
- Osteopetrosis (malignant)
- Proliferative periostitis (ages 5-12)
- Rickets
- Thalassemia major

#### Persons Under Age 30
- Acute leukemia
- Adenomatoid odontogenic tumor (peak at age 16)
- Ameloblastic fibroma (peak at age 16)
- Aneurysmal bone cyst (under age 20)
- Basal cell nevus syndrome (ages 5-30)
- Burkitt’s tumor (ages 2-14)
- Caffey’s disease (birth to 2 years of age)
- Cancer
  - Ewing’s sarcoma (peak at ages 14-18)
  - Osteogenic sarcoma of jaws (ages 10-40, peak at age 27)
  - Reticulum cell sarcoma of bone (70% under age 40)
- Cementifying and ossifying fibroma (young adults)
- Cementoblastoma (under age 25)
- Central giant cell granuloma (60% under age 20)
- Central hemangioma (ages 10-20)
- Cherubism
- Dentigerous cyst (ages 10-20)
- Developing tooth crypt (under age 20)
- Eosinophilic granuloma
- Fibrous dysplasia (ages 10-20)
- Hand-Schüller-Christian disease (ages 1-10)
- Letterer-Siwe disease (ages 1-3)
- Lingual mandibular bone defect
- Multilocular cyst (over age 15)
- Mural ameloblastoma (ages 18-30)
- Odontogenic fibroma (under age 25)
- Odontogenic keratocyst (ages 10-20)
- Osteoblastoma in developing stages (under age 20)
- Osteoid osteoma
- Osteopetrosis (malignant)
- Parulis
- Primordial cyst (ages 10-30)
- Proliferative periostitis (under age 25)
- Rickets
- Sickle cell anemia
- Thalassemia major
- Thalassemia minor
- Traumatic bone cyst (under age 25)

#### Persons Over Age 30
- Ameloblastoma (ages 20-50, peak at age 40)
- Chondrosarcoma (ages 20-60, peak in 50s)
- Osteopetrosis (benign)
- Pindborg tumor (ages 28-48)
- Primary hyperparathyroidism (ages 30-60)
- Residual cyst (peak at age 52)
- Florid cementoosseous dysplasia

#### Persons Over Age 40
- Artery calcification
- Calcified node
- Cancer
  - Chondrosarcoma (ages 20-60; peak in 50s)
  - Metastatic carcinoma
  - Minor salivary tumor
  - Multiple myeloma (ages 40-70)
  - Squamous cell carcinoma (peripheral)
- Osteomalacia
- Osteomyelitis
- Paget’s disease
- Periapical cemental dysplasia
- Postextraction sockets
- Secondary hyperparathyroidism (ages 50-80)
- Sialolith

### TWO OR MORE LESIONS PRESENT

From time to time, clinicians examine patients with various combinations of lesions. Perhaps one patient will present with two lesions in the oral cavity. Another patient may have a lesion in the oral cavity and another in the neck. In still another patient, the examination may reveal a lesion in the oral cavity and another in a more distant site, for example, the lung. After some thought, it becomes obvious that it is necessary to develop the differential diagnosis along distinctly contrasting lines in each of these cases. Basically, when two or more lesions are present, several possibilities or propositions must be considered (modified from Mitton et al8):

1. Lesions are related
   a. Lesion A and lesion B are identical (two aphthous ulcers)
DEVELOPING THE WORKING DIAGNOSIS
(OPERATIONAL DIAGNOSIS, TENTATIVE DIAGNOSIS, CLINICAL IMPRESSION)

Although the clinician has completed a differential diagnosis, he or she is not yet completely prepared to treat the lesion. He or she must now recheck the credibility of these top choices. This is done by further examination of the lesion, by asking the patient more definitive questions to expand the history, by perhaps ordering additional tests, and finally by reevaluating all the assembled pertinent data. Once their validity has been supported, the top choices will be referred to as the working diagnosis or clinical impression. The clinician may in some cases be so confident of the first-ranked entity that he or she excludes all the others from the working diagnosis.

The working diagnosis will dictate the proper management, especially if the management is to include surgery.

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**GENDER PREDILECTION OF SOFT TISSUE LESIONS (RATIOS OR PERCENTS ARE GIVEN IN PARENTHESES)**

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer (except minor salivary gland tumors and metastatic carcinoma from distant sites)</td>
<td>Benign mucous membrane pemphigoid (2:1)</td>
</tr>
<tr>
<td>Lymphoma (2:1)</td>
<td>Desquamative gingivitis</td>
</tr>
<tr>
<td>Melanoma (2:1)</td>
<td>Geographic tongue (2:1)</td>
</tr>
<tr>
<td>Metastatic carcinoma to cervical nodes</td>
<td>Hemangioma</td>
</tr>
<tr>
<td>Squamous cell carcinoma (3:1 to 2:1)</td>
<td>Lichen planus (2:1)</td>
</tr>
<tr>
<td>Buccal (10:1)</td>
<td>Lipoma (7:1 or equal)</td>
</tr>
<tr>
<td>Floor (93%)</td>
<td>Palatal tori (2:1)</td>
</tr>
<tr>
<td>Lip (98%)</td>
<td>Peripheral giant cell granuloma (2:1)</td>
</tr>
<tr>
<td>Tongue (75%)</td>
<td>Peripheral fibroma with calcification</td>
</tr>
<tr>
<td>Verrucous carcinoma (3:1)</td>
<td>Plasma cell gingivitis</td>
</tr>
<tr>
<td>Erythema multiforme</td>
<td>Pyogenic granuloma (3:1)</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>Ranula</td>
</tr>
<tr>
<td>Keratoacanthoma (2:1)</td>
<td>Recurrent aphthous ulcers</td>
</tr>
<tr>
<td>Leukoplakia</td>
<td>Salivary gland tumors (2:1)</td>
</tr>
<tr>
<td>Lymphoepithelial cyst (3:1)</td>
<td></td>
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<tr>
<td>Median rhomboid glossitis</td>
<td></td>
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<tr>
<td>Mucocele</td>
<td></td>
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<tr>
<td>Radiation mucositis</td>
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</tbody>
</table>

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**GENDER PREDISPONITION OF BONY LESIONS**

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Metastatic carcinoma</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>Minor salivary gland tumors</td>
</tr>
<tr>
<td>Ewing’s sarcoma (2:1)</td>
<td>Central giant cell granuloma (2:1)</td>
</tr>
<tr>
<td>Lymphoma (2:1)</td>
<td>Central hemangioma (2:1)</td>
</tr>
<tr>
<td>Melanoma (2:1)</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Multiple myeloma (2:1)</td>
<td>Periapical cemental dysplasia</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>Primary hyperparathyroidism (7:1)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>Florid cementoosseous dysplasia</td>
</tr>
<tr>
<td>Central (2:1)</td>
<td>Secondary hyperparathyroidism (2:1)</td>
</tr>
<tr>
<td>Peripheral (3:1 to 2:1)</td>
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b. Lesion B is secondary to lesion A (metastatic tumor and primary tumor)
c. Lesion A is secondary to lesion B (metastatic tumor and primary tumor)
d. Lesion A and lesion B are both secondary to a third lesion, which may be occult (metastatic tumors and primary tumor)
e. Lesion A and lesion B are manifestations of systemic disease (infections, histiocytosis X, disseminated malignancy)
f. Lesion A and lesion B form part of a syndrome (café-au-lait spots and multiple neurofibromas in von Recklinghausen’s disease)

2. Lesions are completely unrelated to each other and occur together only as a matter of chance
JAWBONE AND REGIONAL PREDILECTION OF BONY LESIONS

Mandible and Predominant Region

Ameloblastic fibroma (molar, premolar)
Ameloblastoma (80%; posterior, 70%)
Aneurysmal bone cyst (much more common in molar)
Benign nonodontogenic tumors (molar, ramus)
Caffey’s disease
Calcifying odontogenic cyst (70%)
Cancer
Acute leukemia (molar)
Ewing’s sarcoma
Metastatic carcinoma (95%; molar, premolar)
Osteogenic sarcoma (body)
Reticulum cell sarcoma (molar, angle, ramus)
Squamous cell carcinoma
Peripheral (3:1, molar)
Central (2:1)
Cementifying and/or ossifying fibroma (molar, premolar)
Cementoablastoma (first molar, premolar)
Cementoma (90%; incisor)
Central giant cell granuloma (65%; two thirds are anterior to molar)
Central hemangioma (65%; ramus, premolar)
Cherubism (ramus, third molar)
Complex odontoma
Condensing osteitis
Eosinophilic granuloma
Follicular cyst

Garré’s osteomyelitis
Odontogenic fibroma
Odontogenic keratocyst (65%)
Odontogenic myxoma (molar, premolar)
Osteomyelitis (7:1; body)
Pindborg tumor (2:1; molar, premolar)
Postextraction sockets
Primordial cyst (third molar)
Proliferative periostitis
Sclerosing cemental masses

Maxilla and Predominant Region

Adenomatoid odontogenic tumor (canine)
Chondrosarcoma (2:1)
Compound odontoma
Fibrous dysplasia (4:3)
Paget’s disease (20:3)
Residual cyst (65%)

Rare in Maxilla

Caffey’s disease
Cementifying and/or ossifying fibroma
Ewing’s sarcoma
Osteomyelitis
Proliferative periostitis
Reticulum cell sarcoma
Traumatic bone cyst

because it will aid the surgeon in planning any operation—
how long to reserve the operating room, what instrument
setups to have prepared, whether to do an incisional or an
excisional biopsy or a frozen section, whether to have
blood available, and, if so, how much and what type.

Before the surgery commences, the surgeon may
choose to do one last test, such as aspiration of the lesion.
This is an excellent precaution in certain instances and
will rule out or identify vascular tumors, thereby avoid­
ing the dangerous surprise that awaits the unsuspecting
surgeon who encounters an unrecognized vascular tumor
at surgery.

FORMULATING THE FINAL DIAGNOSIS

The final diagnosis in most cases of oral pathoses is pro­
vided by the oral pathologist who evaluates a biopsy in
light of all the available clinical data. In some instances
the microscopic picture is quite diagnostic. In other
cases, however, the microscopic picture may be so equiv­
ocal that the pathologist must depend heavily on the ac­
companying clinical symptoms in establishing the final
diagnosis. In still other cases (e.g., an empty traumatic
bone cyst) the clinician must establish the final diagnosis
at the time of the surgery, since there may not be a speci­
men available for microscopic examination.

REFERENCES

1. Halstead CL, Weathers DR: Differential diag­
osis of oral soft tissue pathoses: site unit(s)
3379: instructional materials for health pro­
fessional education, National Library of
Medicine/National Medical Audiovisual Cen­
ter, Washington, DC, 1977, US Department

2. Bouquot JE: Common oral lesions found dur­
ing a mass screening examination, J Am Dent

3. Goltry RR, Ayer WA: Head, neck, and oral
abnormalities in dentists participating in the
health assessment program, J Am Dent

4. Weir JC, Davenport WD, Skinner RL: A diag­
nostic and epidemiologic survey of 15,783 oral

5. Hand JA, Whitehall JM: The prevalence of
oral mucosal lesions in an elderly population,

agnosis and surgical management of parapha­
ryngeal masses: review and an unusual illus­

7. Frommer HH: Differential diagnosis from pan­
tomograms, Dent Radiogr Photogr 55:25-36,
1982.

8. Mitton VA, Eversole LR, Kramer HS, Stern
M: Clinical- Pathological Conference: case
16, part 1 and part 2. Stafne’s bone cyst of the
mandible and concurrent pulmonary coc­
cidioomycosis, J Oral Surg 34:616-617,
SOFT TISSUE LESIONS

- Red
  - Keratotic
  - Necrotic
  - Red and white
    - Solitary
    - Generalized
    - Red tongue lesions

- White
  - Ulcers
  - Exophytic

- Yellow
  - Draining and pits
  - Brownish, bluish, or black
## CHAPTER 5

**Solitary Red Lesions**

**NORMAN K. WOOD**  
**EDWARD PETERS**  
**GEORGE G. BLOZIS**

This chapter deals primarily with pathologic conditions appearing as single red lesions or else diffuse lesions that affect only one mucosal surface. These are listed as follows:

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<td>NONPYOGENIC SOFT TISSUE ODONTOGENIC INFECTION CELLULITIS</td>
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<td>ERYTHROPLAKIA, CARCINOMA IN SITU, AND RED MACULAR SQUAMOUS CELL CARCINOMA</td>
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<td>ERYTHROPLAKIA, CARCINOMA IN SITU, AND RED MACULAR SQUAMOUS CELL CARCINOMA</td>
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<td>Subacute necrotizing sialadenitis</td>
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<td>Tumoral calcinosis</td>
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### NORMAL VARIATION IN ORAL MUCOSA

#### Masticatory and Lining Mucosa

The normal oral mucosa demonstrates a wide spectrum of pink colors, varying from a dark pink (reddish) to a very pale pink (almost white).

The healthy masticatory mucosa (over the hard palate, the gingiva, and dorsal surface of the tongue) is light pink (Fig. 5-1). These surfaces are exposed to forces and pressure of mastication and have adapted by producing (1) a protective layer of keratin and (2) a subepithelial connective tissue that is densely fibrous, relatively avascular, and firmly attached to bone or muscle.

In contrast, the lining mucosa (the oral mucosa over the vestibule, cheeks, lips, floor of the mouth, and ventral surface of the tongue) is protected from such intense mechanical and chemical stimulations, so similar tissue...
PART II  Soft Tissue Lesions

Fig. 5-1. Clinical view showing the paler pink of the attached gingiva (masticatory mucosa) in contrast to the deeper pink of the vestibular mucosa (lining mucosa).

Modification does not occur in these areas. Therefore the color from the underlying vasculature is transmitted through the more transparent overlying tissue and imparts a more reddish color to the surface in comparison with the light pinkish hue of the masticatory mucosa.

Individual variations in the color of the oral mucosa will be apparent and are probably an expression of one or more genetically controlled factors; that is, some people readily form keratin as a result of minor stimuli, whereas others require a strong stimulus to produce minimal keratinization. Also, a patient’s hemoglobin concentration will affect the shade of pink. For example, the patient with polycythemia will have a redder mucosa than will the patient with anemia.

Palatoglossal Arch Region

In a significant number of individuals, areas of apparently normal mucosa covering the palatoglossal arch region are a deep dusky red in contrast to the light red color of the surrounding tissues (Fig. 5-2 and Plate A, 1).

These entirely painless red macular bands are usually present bilaterally and, although the size and shape of the areas in the same individual may not be uniform, persist unchanged. In some cases, bands are also found on the mucosa lining the tonsillar fossa, particularly in individuals who have had tonsillectomies some years before. These regions have a richer blood supply than the surrounding tissues and may be associated with Waldeyer’s ring. Although this entity must be considered an individual normal variation, it is important that the clinician be familiar with the condition because it is often misdiagnosed as “sore throat.”

PATHOLOGIC RED LESIONS

The basic tissue changes or causes that produce abnormal red conditions are as follows:

I. Vascular dilatation from:
   A. Inflammation (erythema)
      1. Mechanical trauma (e.g., cheek biting, ill-fitting denture)
      2. Thermal trauma (e.g., hot food)
      3. Chemical trauma (strong mouthwashes, iatrogenic spills)
      4. Infection (cellulitis, Ludwig’s angina)
      5. Allergy or autoimmune disease (e.g., Sjögren’s syndrome)
      6. Ulcer with inflamed rim (e.g., recurrent herpetic lesion)
   B. Congenital defects (e.g., hemangioma)
   II. Extravasation of blood (e.g., trauma or hemostatic disease or both)
   III. Atrophy or erosion of mucosa (e.g., atrophic candidiasis [inflammatory component usually present also])
   IV. Marked increase in hemoglobin concentration of circulating blood (polycythemia)

White keratin areas and sloughing white patches, representing necrotic tissue and fibrinous exudate, may appear in areas where the mucosa is erythematous (see Chapter 9).

TRAUMATIC ERYTHEMATOUS MACULES AND EROSIONS

Mechanical trauma to the oral mucosa can produce a variety of clinical lesions depending on the nature and circumstances of the insult, as well as factors that govern reactions in the host. Some of the clinical lesions are listed in the box on p. 51.

The erythematous macule and erosion, the purpuric macule, and the granulomatous stage of the inflammatory hyperplastic lesion are essentially red and are discussed in this chapter.

Fig. 5-2. Note the red appearance of the palatoglossal arch (arrows) in this healthy asymptomatic patient.
Fig. 5-3. Traumatic erythematous macules. These red patches all blanched on digital pressure. A, Palatal lesion caused by ill-fitting palatal connector of a partial denture. B, Red lesion at anterolateral border of tongue caused by a carious tooth with a sharp edge. C, Red and white traumatic lesion of the tongue caused by the patient chewing his tongue while it was anesthetized. The darker areas (red) are erythematous, and the white areas are necrotic. D, Small red macule on lip of middle-aged woman who repeatedly touched this spot with the incisal edge of her maxillary incisor.

**Features**

The usual sites for erythematous macules are on the anterior and lateral borders of the tongue, the floor of the mouth, the posterior palate, buccal mucosa, and mucosal surfaces of the lips. The macule may show considerable variation in the intensity of its red color. The size of the red zone corresponds closely to the size of the traumatic agent. Consequently, size and shape may vary considerably. The margins of macular lesions are not usually sharply defined but may be in some instances (Fig. 5-3 and Plate A, 2). Symptoms may vary from mild tenderness to considerable pain. The causative agent is usually easily identified through either the history or the clinical examination. The lesion generally regresses quickly after the cause is removed; however, if the lesion is located on the tongue, it may persist for several weeks and heal as a bald pink area devoid of papillae.

Microscopic changes include an inflamed lamina propria covered perhaps with a slightly thinned or eroded stratified squamous epithelium that is nonkeratinized. It may blanch when digital pressure is applied because this lesion is basically inflammatory.

**RESPONSE TO TRAUMA**

- Keratotic lesion (increased retention of keratin)
- Necrotic white lesion (necrosis of the epithelium and possibly the subepithelial tissue to some extent)
- Reddish erythematous macule (an area of inflammation)
- Purpuric macule (subepithelial hemorrhage within the tissue spaces)
- Bleb (a pooling of tissue fluid in the tissue)
- Erosion
- Ulcer
- Exophytic lesion (inflammatory hyperplasia)

Traumatic erythematous macules are produced by a low-grade, usually chronic physical insult. A more intense degree of brief trauma would be expected to produce a purpuric macule, an erosion, or a frank ulcer, in order of increasing severity. Common causes include sharp margins of teeth or restorations and ill-fitting prostheses. Self-inflicted trauma such as cheek biting or other habits also may produce traumatic erythematous macules.
Differential Diagnosis
For a discussion of the differential diagnosis of traumatic erythematous macules and erosions, refer to the differential diagnosis section under Purpuric Macules.

Management
The mechanical irritant should be identified and eliminated and the lesion kept under surveillance until it disappears. Healing noticeably occurs in 3 or 4 days. If the lesion does not disappear soon, additional workup should be done. If the suspicion index is high, a biopsy should be performed to rule out more serious conditions such as erythroplakia, squamous cell carcinoma, and fungal diseases such as candidiasis and histoplasmosis.

PURPURIC MACULES (EARLY STAGE)
The purpuric macule is produced by a blunt traumatic insult to the mucosa or skin of sufficient force to cause the extravasation of blood into the superficial tissues. If the patient is examined soon after the traumatic incident has occurred, petechial (small pinpoint) or ecchymotic (larger) areas that are quite red are observed. If sufficient time has lapsed for the reduction of oxyhemoglobin, the bruise will appear blue and later green and yellow as the hemoglobin pigment breaks down.

Features
The size of the purpuric macule varies according to the size and force of the physical agent inflicting the damage. Usually, the borders are poorly demarcated, blending almost imperceptibly with the surrounding normal tissue (Fig. 5-4). Blanching on pressure does not usually occur because the red blood cells are within the tissues rather than in vessels. Nevertheless, purpuric macules may also have an accompanying inflammatory component, and in such cases the clinician may observe some blanching on palpation. Virtually any of the oral surfaces may be involved, but the palate, buccal mucosa, and floor of the mouth are the most common sites.

Frequently, reddish elliptic purpuric macules occurring on the palatal mucosa near the junction of the hard and soft palate may result from oral sexual practices and are caused by the repeated bumping of the male organ on the soft tissue in this region (Fig. 5-4). In such a case the lesion disappears within 2 or 3 days only to return again when the act is repeated. A judicious history taken in a confidential setting frequently reveals the true identity of such a lesion.

Differential Diagnosis
When transient reddish macules are observed near the junction of the hard and soft palates, the following entities should be considered: traumatic erythematous macule, purpuric macule of oral sex, palatal bruising because of severe coughing or severe vomiting, macular hemat-
gioma, atrophic candidiasis, mononucleosis, and herpangina. The first four lesions are usually painless, and a careful history establishes the occurrence of a traumatic incident. Hemangiomas seldom occur on the posterior palate, and both the erythematous macule and the hemangioma blanch somewhat on pressure. In contrast to the purpuric macule and the erythematous macule, the hemangioma is not transient.

**Management**

Once the diagnosis of purpuric macule has been established, the patient should be advised of its nature. Follow-up examinations are necessary to ensure that the lesion has disappeared.

If several purpuric areas are present, the patient should be asked if he or she has always bruised excessively and how extensive the trauma was. If the correlation is unsatisfactory, the patient should be tested for the presence of a bleeding disorder.

**INFLAMMATORY HYPERPLASIA LESIONS**

Inflammatory hyperplasia (IH) lesions are discussed in considerable detail in Chapter 10. Etiology is similar to the traumatic erythematous macule and the purpuric macule except that the precipitating insults are invariably chronic irritants such as calculus, ragged margins of cavities, overhanging restorations, overextended denture flanges, sharp spicules of bone, or chronic biting of the cheek or lip. Such prolonged chronic insults stimulate the production of granulation tissue. A list of IH lesions includes pyogenic granuloma, hormonal tumor, traumatic hemangioma, epulis fissuratum, epulis granulomatous, papillary hyperplasia, peripheral giant cell granuloma, parulis, and the peripheral fibroma with calcification.

In the life cycle of one of these lesions the entity initially develops as a mass of inflamed granulation tissue and clinically appears soft and very red. Later, when fibrous tissue is laid down, the lesion becomes firmer and less red. If the irritant is eliminated at this stage, the remainder of the inflammation disappears and the lesion shrinks noticeably, becomes firm, and takes on a pale hue. This endpoint lesion is an inflammatory fibrous hyperplasia.

**Features**

Features of IH lesions are discussed in detail in Chapter 10. In the stage being considered here, the lesions are quite red, moderately soft, polypoid or nodular masses (Fig. 5-5 and Plates A, 4 to A, 6).

Microscopy of the early IH lesions reveals granulomatous tissue covered with an intact layer of stratified squamous epithelium that is nonkeratinized. If the surface becomes traumatized, a white necrotic area usually develops in the region of the injury and the lesion becomes a pyogenic granuloma.

Fig. 5-5. Reddish IH lesions. All of these lesions contained a large inflammatory component. A, Red pyogenic granuloma of the lingual gingiva caused by the sharp edges of a large carious lesion on the lateral incisor. B, Large red epulis fissuratum. C, Red papillary hyperplasia in its earliest stages, caused by an ill-fitting upper denture. D, Red parulis on the labial mucosa in an early stage of development. Parulis at the opening of a sinus that was draining the infected periapical region of the maxillary right central incisor. (A courtesy E. Seklecki, Tucson, Ariz.)
PART II Soft Tissue Lesions

LESIONS
- Hemangioma
- Metastatic tumor
- Primary malignant tumor
- Kaposi's sarcoma (Chapters 12, 36)
- Papilloma/condyloma/verruca

Differential Diagnosis
The early IH lesion must be differentiated from other raised lesions listed in the box above. In the case of most IH lesions in their early stages of development, a precipitating irritant is usually identifiable. This strengthens the impression and supports a working diagnosis of IH.

However, if an irritant is not apparent, the possibility the lesion is either a primary (probably not squamous cell carcinoma [SCC]) or secondary malignant tumor beginning beneath a normal surface epithelium is given more consideration in the differential diagnosis. In turn, a history of treatment or symptoms of a primary tumor elsewhere prompts the ordering of these possibilities in favor of a metastatic tumor (see Fig. 5-21). Excluding SCC and salivary gland tumors, primary malignant tumors of the oral soft tissue are quite uncommon. It is rare for a squamous cell carcinoma to appear as a small exophytic red lesion with a smooth nonulcerated surface.

In the case of gingival IH lesions adjacent to alveolar bony changes, malignant tumors must be given a high ranking except in the case of obvious chronic infection of the bone.

A congenital hemangioma is present from birth, whereas a traumatic (acquired) hemangioma is really a type of IH lesion.

Papillomas, condylomas, verrucae, and verrucous and squamous cell carcinomas are included for the sake of completeness. However, since the IH lesions have a basically smooth, evenly contoured surface, they should be readily differentiated from these epithelial growths that have rough pebbly to a cauliflower-like surface. The pyogenic granuloma may have an area on its otherwise smooth surface that is white, but this is necrotic material and can be easily removed, leaving a raw bleeding surface.

Management
Excisional biopsy in combination with elimination of the irritant is the treatment of choice for lesions of substantial size when the suspicion index is moderate to high. When the suspicion index is low, elimination of the irritant will result in significant reduction of the inflammatory component, making surgery easier. Small red lesions may shrink to a size that precludes treatment when the irritant is eliminated.

REDDISH ULCERS OR ULCERS WITH RED HALOS
Ulcers are discussed at length in Chapter 11. They are included here for completeness because ulcerative conditions frequently are first manifested as erythematous macules, for example, the recurrent herpetic lesion and the recurrent aphthous ulcer. Furthermore, in these conditions, when the reddish area ultimately ulcerates, the defect frequently has a reddish border (Fig. 5-6 and Plate B.4). Such an observation might prompt the clinician to classify the entity as a red lesion; however, experience has demonstrated that for the purpose of a differential diagnosis it is more beneficial to classify these lesions as ulcers.

Differential Diagnosis
The differential diagnosis of the various oral ulcers is covered in Chapter 11.

NONPYOGENIC SOFT TISSUE ODONTOGENIC INFECTION (CELLULITIS)
This section includes a discussion of soft tissue odontogenic infections that either are caused by nonpyogenic bacteria or represent prepyogenic or postpyogenic stages of infections; that is, the causative bacteria may be nonpyogenic, or the infection has not reached the pus-forming or pus-pooling stage. Odontogenic infection may originate in three sites: the canals and periapex of pulpless teeth, the gingiva or bony pockets in periodontal disease, and the gingival operculum over an erupting tooth.

Features
In most of these cases a suitable history and clinical and radiographic examinations coupled with pulp testing usually clearly indicate the diagnosis of dental infection (Fig. 5-7).

The alveolar mucosa and gingiva are the most frequent sites of dental infection, but if the infection is permitted to spread, a number of the oral mucosal surfaces and the overlying skin may become involved. Various degrees of swelling show a hot, red, tender to painful surface. However, pus that has formed and pooled near the surface of the swollen tissue imparts a yellowish-white color to the central region of the swelling and renders the swelling rubbery and fluctuant to the touch (see Chapter 3).

Ludwig's angina is an unusual example of a reddish soft tissue infection that is produced by a mixed infection of nonspecific microorganisms, but a nonpyogenic strain of streptococcus is almost invariably present. This condition causes a sudden swelling of the floor of the mouth and also of the submental and submaxillary spaces, often of such a magnitude that obstruction of the airway is threatened. In most cases a very red, moderately firm, painful swelling of the floor of the mouth produces an elevation of the tongue. The skin of the neck overlying the
swollen submental and submaxillary spaces is usually red and feels hot on palpation (Fig. 5-8 and Plate B, 3).

Cervical or intraoral actinomycosis is a specific infection that frequently occurs as a tender, reddish swelling (Fig. 5-8).

**Differential Diagnosis**

When a patient has a reddish painful swelling of the oral soft tissues with an accompanying tender cervical lymphadenitis, the diagnosis of infection is reasonably certain. An extremely high percentage of these infections are odontogenic in origin and therefore bacterial. However, the clinician should at least consider the less likely possibilities of actinomycosis, tuberculosis, and various fungal infections such as histoplasmosis, coccidioidomycosis, and blastomycosis.

**Management**

When a diagnosis of odontogenic infection has been established, the associated dental problem should be eliminated by root canal therapy, extraction, curettage, excision, or incision and drainage. In addition, in acute cases, concomitant oral administration of amoxicillin is recommended.

Patients with infections that are or may become a threat to their airway should be hospitalized so that any respiratory complication can be managed promptly and properly.

**CHEMICAL OR THERMAL ERYTHEMATOUS MACULE**

The cause of a chemical or thermal erythematous macule is usually a caustic drug or hot foods or beverages. Obviously, the severity of the tissue damage varies with the intensity and duration of the insult, so several different clinical appearances may be produced. Caustic or hot agents may produce a coagulation necrosis of the superficial tissue that appears whitish and can be scraped off. Fig. 8-43 illustrates such a change precipitated by aspirin/acetaminophen. More intense or prolonged insults may still result in ulceration and possibly stripping of the mucosa. Milder agents or briefer applications of strong agents produce the mildest clinically detectable reaction, an erythema of the superficial tissues, which explains why this condition is included in this chapter (Fig. 5-9). Sometimes a mixed reaction is produced, so the clinical lesion may appear as necrotic white dots or patches on an erythematous base (Fig. 5-9).

**Features**

The red area is tender to painful, may blanch somewhat on pressure, and may bleed on the slightest manipulation. The size and shape corresponds to the area of contact with the caustic agent. The buccal and palatal mucosa are the sites most commonly affected. Mild aspirin burns are good examples, as are mild palatal burns from hot food. A careful history identifies the causative agent in almost all cases.

**Differential Diagnosis**

Many of the lesions discussed in this chapter should be considered in the differential diagnosis: erythema from mechanical trauma, purpuric macule, cellulitis (nonpyogenic odontogenic infection), allergic manifestations, erythroplakia, atrophic candidiasis (formerly known as atrophic candidosis), herald spot of disseminated red conditions, and fungal infections. A recent history of chemical or thermal injury along with uncomplicated resolution of the lesion in question eliminates these possibilities and establishes the correct diagnosis.
Fig. 5-8. Red infectious lesions. A, Ludwig's angina. Note the swelling of the submental and submandibular spaces. Unfortunately, the redness of the overlying skin does not show in this black-and-white photo. The patient also had a red painful sublingual swelling. B and C, A case of actinomycosis in the submandibular space of a 56-year-old man. C shows the redness of the lesion. (B and C courtesy E. Seklecki, Tucson, Ariz.)
Solitary Red Lesions

CHAPTER 5

**Fig. 5-9.** Reddish lesions caused by chemical burns. A, Red and white acetaminophen burn. B, Reddish area on mucosa of lower lip represents a stage in healing of lesion caused by the overzealous use of Listerine mouthwash. (B from Bernstein ML: Oral mucosal white lesions associated with excessive use of Listerine mouthwash. Report of two cases, Oral Surg 46:781-785, 1978.)

**Management**

The majority of these cases are mild and relatively painless. Systemic analgesics and topical applications of corticosteroid in an emollient base can be used when pain is a problem. When diagnosis is uncertain or the injury appears to be superimposed on a serious lesion, surveillance is required. A biopsy should be performed if the lesion in question does not resolve promptly.

**NICOTINE STOMATITIS**

Nicotine stomatitis is discussed at length as a white lesion of the palate in Chapter 8. This lesion is included in the present chapter because it may be a red lesion in its earliest stage, before keratosis has been produced. Also, in the later keratotic stage the inflamed minor salivary duct openings appear as small red dots in the center of low flat nodules of hyperplastic tissue. This mixed red-and-white appearance accounts for the inclusion of the lesion in Chapter 9. Nicotine stomatitis is seen primarily on the palate of pipe smokers.

**Differential Diagnosis**

The following conditions particularly have to be considered as somewhat similar clinical pictures when early-stage nicotine stomatitis is suspected: multiple papillomatosis, denture stomatitis, atrophic candidiasis, or atrophic/erythematous candidiasis alone. Multiple papillomatosis and denture stomatitis can be quickly excluded if the condition is on the hard palate because nicotine stomatitis does not occur under a denture as do the former two entities. A smear quickly identifies atrophic candidiasis. A history of pipe smoking and the relatively greater prevalence of nicotine stomatitis gives it a higher rank in the differential diagnosis than atrophic candidiasis barring the presence of decreased immunocompetence.

**ERYTHROPLAKIA, CARCINOMA IN SITU, AND RED MACULAR SQUAMOUS CELL CARCINOMA**

The term *erythroplakia* (EP) is used in this book as a clinical term for a specific red lesion much as *leukoplakia* is used for white lesions of a specific spectrum. Therefore EP can be defined as a persistent velvety red patch that cannot be identified as any other specific red lesion such as inflammatory erythemas or those produced by blood vessel anomalies or infection. Etiology is that described for oral cancer in Chapter 35. EP is often regarded as the earliest sign of asymptomatic oral cancer. It is reported that invasion may occur in small lesions of less than 1 cm in diameter. Indeed, the term erythroplakia carries a more serious implication than its white counterpart because almost all EPs show malignant changes. In a study of 58 cases by Shafer and Waldron, 51% were invasive carcinoma and 41% were carcinoma in situ or severe epithelial dysplasia.

EP’s reddish color results from the absence of a surface keratin layer and occurs because the connective tissue papillae, containing enlarged capillaries, project close to the surface. There is a general failure of the epithelial cells to achieve significant maturation (keratinization). Cellular maturation may commence when actual invasion occurs.

**Features**

EP usually appears as a velvety red or granular red macule (patch) that may be slightly raised (Fig. 5-10 and Plates H, 1 and H, 2). This painless lesion varies greatly in size, and the borders may be well circumscribed or may blend imperceptibly with the surrounding normal mucosa. Small lesions are easily overlooked, but the chances for their detection are greatly enhanced by first drying the mucosa with a gauze, since this intensifies the red color. The use of toluidine blue rinse is discussed in Chapter 2. This method may be helpful in rendering small red lesions or those that have minimal red color more noticeable during the soft tissue examination.
Three different clinical appearances were described by Shear\textsuperscript{12}: (1) the \textit{homogeneous form}, which is completely red in appearance (Fig. 5-10 and Plate G, 1); (2) \textit{patches} of EP and leukoplakia occurring together (Fig. 5-11 and Plate G, 12); and (3) \textit{speckled EP}, in which small leukoplakic specks are scattered over an area of EP (Fig. 5-12 and Plate G, 7 to G, 9). The term \textit{speckled leukoplakia} used in Chapter 8 is synonymous with the term \textit{speckled EP} used here. Homogeneous EP is generally much more aggressive than leukoplakia or speckled EP.\textsuperscript{13} There is no gender predilection and the peak age of occurrence falls between 50 and 70 years.\textsuperscript{11} The floor of the mouth is the most common site in men, whereas the mandibular gingival–alveolar mucosa–mandibular sulcus is the most common site in women. The retromolar region is the second most common site in both genders.\textsuperscript{11}

\textbf{Differential Diagnosis}

The lesions to be considered in the differential diagnosis of erythroplakia are listed in the box on the next page.
DIFFERENTIAL DIAGNOSIS OF EP

- Traumatic erythema
- Atrophic candidiasis
- Purpuric macule (early stage)
- Macular hemangioma
- Contact allergy
- Other infection
- Localized gingivitis
- Kaposi's sarcoma (early stage)

Although all the red macular lesions listed in this chapter should be considered in a differential diagnosis of an EP lesion, the lesions that are obviously macular hemangiomas and telangiectasias can be readily eliminated on the basis of their characteristic features. In a similar way the traumatic lesions, odontogenic infections, and allergies can be given a low ranking on the basis of their transient nature, pain, and often obvious events in the history. The traumatic erythematous macules of the tongue are often more difficult to differentiate because these may persist for weeks after the irritants have been eliminated. Red lesions of atrophic candidiasis may also be indistinguishable clinically. In cases of candidiasis, features in the history suggest susceptibility and a smear is diagnostic. Tuberculosis and fungal lesions such as histoplasmosis should be considered, but their probability is low on the basis of incidence alone.

EP areas on the gingiva may be overlooked or misinterpreted as local areas of gingivitis. Cases of EP squamous cell carcinoma of the gingiva have been initially considered as periodontal disease. If a red area of the gingiva has no apparent cause or does not respond to the usual periodontal therapeutic measures, it should be considered to be an EP lesion until proved otherwise.

**Management**

If a red lesion persists for more than 14 days after all local trauma and infectious foci have been eliminated, a biopsy is mandatory. Obviously, if the suspicion index is moderate to high, arrangements should be made for immediate referral to a practitioner competent to manage malignant lesions of the oral cavity. Horch et al discussed the use of laser surgery with oral premalignant lesions.

**EXOPHYTIC, RED SQUAMOUS CELL CARCINOMA**

Exophytic squamous cell carcinoma (ESCC) is discussed in Chapter 10 without emphasis on color. Macular red SCC is discussed under EP earlier in this chapter. To further develop the differential picture, it is necessary to include and describe an additional clinical lesion: the exophytic, red squamous cell carcinoma. Fig. 5-13 illustrates two examples of this entity. Oral cancer is discussed at length in Chapter 35.

**Features**

The lesions of ESCC illustrate the rule of thumb (Chapter 10) that a mass arising in the covering epithelial surface has a rough contour and surface. These ESCCs usually have a broad base and are irregular in shape. The
Three different clinical appearances were described by Shear\textsuperscript{12}: (1) the \textit{homogeneous form}, which is completely red in appearance (Fig. 5-10 and Plate G, 1); (2) \textit{patches} of EP and leukoplakia occurring together (Fig. 5-11 and Plate G, 12); and (3) \textit{speckled} EP, in which small leukoplakic specks are scattered over an area of EP (Fig. 5-12 and Plate G, 7 to G, 9). The term \textit{speckled leukoplakia} used in Chapter 8 is synonymous with the term \textit{speckled EP} used here. Homogeneous EP is generally much more aggressive than leukoplakia or speckled EP.\textsuperscript{13} There is no gender predilection and the peak age of occurrence falls between 50 and 70 years.\textsuperscript{11} The floor of the mouth is the most common site in men, whereas the mandibular gingival–alveolar mucosa–mandibular sulcus is the most common site in women. The retromolar region is the second most common site in both genders.\textsuperscript{11}

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Exophytic, Red Squamous Cell Carcinoma

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Features

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Also, it is interesting that genetically dissimilar commensal strains occur in different anatomic regions of the same healthy women, and it is possible that infection in one region could be caused by the strain from the other region. Another possibility would be that replacement exogenous strains are the causative agent of infection rather than the commensal strain. An exogenous strain would have to be the causative agent when candidal infections occur in noncarriers. These same authors raise the academic possibility that all cases of infection could be caused by exogenous replacement strains. Exogenous replacement strains appear to have been the infectious agent in a cohort of AIDS patients in Leicester, England. Another consideration involves the allergenic characteristics of Candida. How much of the reaction in clinical infection is the result of allergic response?

Features

The various types of clinical lesions are listed in the box below.

Various sets of circumstances will promote a certain type of clinical lesion. These factors relate to the numbers, virulence, and strains of C. albicans; intensity of the tissue reactions; acuteness, chronicity, and duration of the infection; resistance of the patient; presence or absence of treatment; anatomic location; and patient habits. The pseudomembranous type is the most acute, followed by the erythematous, whereas the atrophic type would be more chronic or else a resolving phase of the first two. The hyperplastic type is chronic also, but the infection may be more deep seated.

At least 50% of patients complain of oral burning and infections. This disease is more common in patients over 40 years of age, and there is a higher incidence in women excluding the younger cohort of AIDS patients. The burning may range in degree from tenderness to pain. The more acute types will more often be painful, whereas the hyperplastic types will be painless.

Diagnostic Procedure

Smears of the pseudomembranous and erythematous types will usually show significant members of pseudohyphae and possibly some yeast forms. Culturing C. albicans from

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**Fig. 5-14.** Pseudohyphae of C. albicans in tissue. (Courtesy P. Fotos, Iowa City.)

**PREDISPOSING CONDITIONS TO ORAL CANDIDIASIS**

<table>
<thead>
<tr>
<th>Drugs/Medications</th>
<th>Hyperimmunoglobulinemia E syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte Disorders</td>
<td>Chronic mucocutaneous candidiasis</td>
</tr>
<tr>
<td>Leukocyte Disorders</td>
<td>Myeloperoxidase deficiency</td>
</tr>
<tr>
<td>Leukocyte Disorders</td>
<td>Agranulocytosis/leukopenia/neutropenia</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Leukemia</td>
</tr>
<tr>
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<td>Lymphoma</td>
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<td>Thymoma</td>
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<tr>
<td>Malignancy</td>
<td>Advanced cancer</td>
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<tr>
<td>Nutritional Deficiencies</td>
<td>Iron deficiency</td>
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<tr>
<td>Nutritional Deficiencies</td>
<td>Folic acid deficiency</td>
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<td>Nutritional Deficiencies</td>
<td>Biotin deficiency</td>
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<td>Nutritional Deficiencies</td>
<td>Vitamin B deficiency</td>
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<td>Nutritional Deficiencies</td>
<td>Vitamin C deficiency</td>
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<td>Nutritional Deficiencies</td>
<td>Malnutrition</td>
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<td>Malabsorption</td>
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<tr>
<td>Other</td>
<td>Radiation therapy</td>
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<td>Other</td>
<td>Sjögren’s syndrome</td>
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<tr>
<td>Other</td>
<td>Pregnancy</td>
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<tr>
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<td>Xerostomia</td>
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<td>Other</td>
<td>Old age</td>
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<tr>
<td>Other</td>
<td>Infancy</td>
</tr>
<tr>
<td>Other</td>
<td>Denture use</td>
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</tbody>
</table>


**CLINICAL LESIONS OF CANDIDIASIS**

- Pseudomembranous—white necrotic (Chapter 8)
- Erythematous—red (Chapters 5, 6)
- Atrophic—red (Chapters 5, 7)
- Hyperplastic—white, red raised (Chapter 8)
- Mixed—red/white keratotic/white necrotic
- Mucocutaneous—lip, angle (Chapter 33)
- Esophagitis and other systemic

saliva samples or swabs of lesions does not provide a definitive diagnosis because a large percentage of healthy patients are carriers, although such information may be helpful when integrated with all the other findings.

It is important to consider that any oral lesion with surface debris may harbor candidal organisms to the extent of a secondary candidiasis. Nystatin treatment in such cases would produce some improvement, but full remission must await successful treatment of the primary lesion.

**Management**

Several appropriate medications are available for the treatment or management of oropharyngeal candidiasis. Both topical and systemic agents are available (Table 5-1), and choices are dictated by specific findings of each case. Drug therapy should be continued at least 1 week after signs and symptoms have disappeared because of the tendency to recur. In one study, 50% of patients that showed initial resolution experienced a recurrence. Postinfection drug therapy should continue for a longer period in patients with serious predisposing conditions.

**Topical therapy** Generally, topical agents are indicated for milder superficial cases where the patient’s resistance is relatively good and there is immunocompetency. Another topical agent can be tried in cases where the disease is refractory to the first topical drug used. Otherwise, therapy can be switched to a systemic agent. Topical and systemic medications can be used jointly.

Topical medications are available in the following forms: capsules, oral troches, pastilles, vaginal tablets, creams, and rinses. To be successful, these agents must remain in contact with the infected mucosal surface for a significant period. Therefore solid agents that must dissolve will have more prolonged contact than rinses. Sufficient saliva must be present to aid the dissolution of the solid types. Sipping water may be used in cases of xerostomia as a salivary substitute, or oral rinses or creams may be used instead of the solid agents. Sucrose is the sweetening agent used in some preparations, and caries-prone individuals should use fluoride gels with prolonged administration of the antifungal. Vaginal troches are unsweetened and so are not cariogenic, but the unpleasant taste may affect patient compliance. Topical agents should be continued for at least 14 days and in some cases 2 to 3 weeks after resolution of symptoms.

**Nystatin.** Nystatin pastilles are probably the most widely used form. Each pastille carries 200,000 units, and 1 to 2 should be dissolved slowly in the mouth 4 to 5 times per day. Side effects with nystatin products are unusual, and the agent is not absorbed through the gastrointestinal tract. MOTS-Nystatin contains 200,000 units of nystatin in a controlled-release system and is found to be more effective in AIDS patients than regular nystatin. This polyene drug destroys the cell membrane by binding to ergosterol in the cell membrane. It is also available in oral suspension, ointment/creams, vaginal troches, powder, and tablets.

**Table 5-1 Drugs used in treatment of fungal disease**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Form</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>IV</td>
<td>Aspergillosis, cryptococcus, systemic candidiasis</td>
</tr>
<tr>
<td></td>
<td>Topical cream</td>
<td></td>
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<tr>
<td></td>
<td>Topical lotion</td>
<td></td>
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<tr>
<td></td>
<td>Topical ointment</td>
<td></td>
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<tr>
<td>Nystatin</td>
<td>Oral troche</td>
<td>Oral candidiasis</td>
</tr>
<tr>
<td></td>
<td>Oral rinse</td>
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<tr>
<td></td>
<td>Vaginal tablet</td>
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<tr>
<td></td>
<td>Topical cream</td>
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<tr>
<td></td>
<td>Topical lotion</td>
<td></td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>Oral troche</td>
<td>Oral candidiasis</td>
</tr>
<tr>
<td></td>
<td>Oral suspension</td>
<td></td>
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<tr>
<td></td>
<td>Topical cream</td>
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<tr>
<td></td>
<td>Vaginal cream</td>
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<tr>
<td></td>
<td>Vaginal tablet</td>
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</tr>
<tr>
<td>Miconazole</td>
<td>IV</td>
<td>Histoplasmosis, blastomycosis</td>
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<tr>
<td></td>
<td>Topical cream</td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>Oral tablet</td>
<td>Histoplasmosis, Blastomycosis</td>
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<tr>
<td></td>
<td></td>
<td>Oropharyngeal candidiasis</td>
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<td></td>
<td></td>
<td>Chronic mucocutaneous candidiasis</td>
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<tr>
<td></td>
<td>Topical cream</td>
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<tr>
<td>Fluconazole</td>
<td>Oral tablet</td>
<td>Cryptococcus</td>
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<tr>
<td></td>
<td>IV</td>
<td>Mucosal candidiasis</td>
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<tr>
<td>Itraconazole</td>
<td>Oral capsule</td>
<td>Blastomycosis</td>
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<tr>
<td></td>
<td></td>
<td>Aspergillosis*</td>
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<tr>
<td></td>
<td></td>
<td>Candidiasis*</td>
</tr>
</tbody>
</table>

*Use is not currently included in the labeling approved by the U.S. Food and Drug Administration.


**Clotrimazole.** Clotrimazole is produced in a 10 mg oral troche (Mycelax) that is dissolved slowly in the mouth 5 times a day. Administration should be continued for 2 to 4 weeks and at least 1 week after manifestations have disappeared. This drug is an azole that changes Candida’s membrane permeability by blocking the production of ergosterol.

**Chlorhexidine.** Chlorhexidine 0.1%-0.2% mouth rinse has become well established as an agent that reduces the microbial load in the oral cavity. It is active against Candida and some bacteria by increasing cell membrane permeability. In addition, chlorhexidine interferes with candidal adhesion to oral mucosal cells. It appears that clotrimazole is of prophylactic use and may
Solitary Red Lesions

also be helpful as an adjunct to other antifungals. Liver profiles must be done in prolonged use.

**Gentian violet.** This deep-violet alcohol solution is painted directly on the lesions. It has been used with some success over the years. Its main disadvantages are the dehydrating effect of the alcohol and the deep color, which is unsightly and hinders visualization of tissue change. Years ago, it was overutilized for the treatment of white oral lesions of various diagnoses and so fell out of vogue. Perhaps it is now enjoying a resurgence especially in third world countries. In a Zaire AIDS study, it was found to be as effective as ketoconazole and much more effective than nystatin rinse. This agent is economical, can be quickly applied by a clinician, and so does not depend on patient compliance.

**Systemic therapy** Systemically administered drugs are chosen for chronic deep-seated infections and for superficial cases that are refractory to topical agents. Considerable candidal resistance has developed to individual antifungal agents, and this may occur through phenotype switching, particularly in the azoles. Topical and systemic agents may be used conjointly in difficult cases.

**Ketoconazole.** Nizoral is available as an orally administered 200 mg systemic tablet and as an intravenous (IV) preparation. One or two tablets are taken daily with food for at least 2 weeks and continued for 1 or 2 weeks after symptoms disappear. This is a very effective drug and is still used. As anazole, it affects the permeability of the fungal cell membrane. Although ketoconazole is not as toxic to the liver as other azoles, liver profile tests should be obtained if chronic administration is considered. During the last few years, usage has shifted from long-term to shorter-term treatment to minimize side effects. IV administration is used with refractory infections in AIDS patients.

**Flucconazole.** Diflucan is produced as a 50 mg systemically administered tablet. It is an effective triazole antifungal agent with less toxicity than the azoles. Recommended dosage is 50 mg per day as a single dose. This can be raised to 400 mg per day in difficult cases. This is a very useful drug especially in AIDS patients both for prophylaxis and treatment, but significant candidal resistance is occurring.

**Amphotericin B.** This antifungal agent’s major role is as an intravenously administered agent in serious cases of systemic distribution that are resistant to other antifungals. It is significantly toxic to several systems, including the kidney.

**Atrophic/Erythematous Candidiasis**

This condition is red and may present as a single lesion or else as a generalized mucositis, which is discussed in Chapter 6. This red lesion may be either atrophic (Plate E, 5) or erythematous or a mix. Tenderness, burning, and in some instances significant pain are usual symptoms. Minor bleeding might be observed, and the lesion may blanch somewhat to digital pressure. Some of these cases will represent resolving stages in pseudomembranous infections, whereas others will represent cases that are less acute and did not progress to the more intense necrotic type (Fig. 5-15).

![Fig. 5-15. Erythematous candidiasis. A, Palatal lesion showing some traces (white) of pseudomembranous type as well. B, Lesion on dorsal surface of tongue in HIV-positive man. (A courtesy S. Fischman, Buffalo, NY; B courtesy M. Glick, Philadelphia.)](image_url)
**Features** Denture stomatitis occurs under either complete or partial dentures and is found more frequently in women. The lesions are usually confined to the palate and seldom if ever involve the mandibular ridge. In approximately 50% of the patients, there is an associated angular cheilitis with or without an inflammatory papillary hyperplasia of the palate. A high correlation has also been established between the occurrence of this condition and wearing dentures at night.

The lesions may be totally asymptomatic, or the patient may complain of a soreness and dryness of the mouth. This soreness may also be described as a burning sensation. The palatal tissue is bright red, somewhat edematous, and granular. Only the tissue covered by the denture is involved. The redness usually involves the entire area covered by the denture but may be focal in its distribution (Fig. 5-16 and Plate A, 12).

When seen microscopically, the lesion is rather nonspecific. The epithelium is atrophic and may be ulcerated in areas. An intense chronic inflammatory infiltrate is present in the lamina propria and also involves the epithelium. Usually the *C. albicans* organism is not found in tissue specimens. The most accurate diagnostic test is a smear from the area of the lesion stained with periodic acid—Schiff's reagent. This will show the yeast and hyphal forms of *Candida*.

**Differential diagnosis** The clinical picture of denture stomatitis is rather specific; few if any other diseases appear the same. Infections by other organisms, however, could be responsible for a similar diffuse redness either alone or in combination with *Candida*. Contact allergy to the denture base acrylic happens occasionally. In such cases, redness will not be restricted to tissue under the denture, but all mucosal surfaces in contact with the acrylic will be red. Epicutaneous tests of the material will usually be diagnostic. From time to time, generalized mucositis conditions will affect the tissue under dentures, but the general distribution of these will differentiate from denture stomatitis. Some of these could be secondarily infected with *Candida*.

**Management** Treatment of candidiasis is discussed on pp. 62-63. Management of denture stomatitis includes correcting denture faults, improving denture and oral hygiene, and antifungal therapy. Ill-fitting dentures must be adjusted or replaced. The patient must remove the dentures at bedtime and place them in chlorhexidine or nystatin solution at night after proper cleaning, although some clinicians recommend dry storage. One study indicated that a hydrogen peroxide denture cleaner was as effective as using antifungal agents on the denture. (On occasion, fungi will have so thoroughly impregnated the denture that it will have to be discarded and a new denture made.) Antifungal ointments and pastes may be worn with the denture during the day, and oral antifungal rinses or lozenges may be used possibly in combination with a systemic agent. A recent report indicates considerable success utilizing a miconazole lacquer applied to the tissue surface of the denture. Recurrences are common, and it is important to ensure that levels of denture plaque are reduced.

**Angular Cheilitis**

Angular cheilitis is usually a reddish ulcerative or proliferative condition marked by one or a number of deep fissures spreading from the corners of the mouth. The lesions are most often bilateral, usually do not bleed, and are usually restricted to the vermilion and skin surface.

---

**Fig. 5-16.** Denture stomatitis. **A,** Only the palatal tissue contacted by an acrylic transitional partial denture is inflamed. Smears containing *Candida* were obtained from both the palatal tissue and the denture. **B,** Patchy redness covers the entire patient who wore a full denture. An exfoliative cytologic smear was positive for *Candida*. **C,** Same patient after therapy with nystatin for 1 week.
Although such factors as decreased vertical dimension of dentures, iron deficiency anemia, and vitamin B deficiencies may be predisposing factors or at least associated with the development of this lesion, infection with *C. albicans* and in some cases with a mixture of other microorganisms such as *Staphylococcus aureus* seems to represent a major cause. Therefore the lesions usually persist even though the predisposing factors have been eliminated, unless they are treated with an antifungal ointment such as nystatin in conjunction with an *S. aureus* agent or metronidazole. Resolution is relatively easily obtained if angular cheilitis is an isolated finding. However, if it is part of a generalized oral/systemic candidal infection, it may be very deep seated and resistant to eradication. That is, major priority of treatment must be directed to the main reservoir of infection in the body.

**MACULAR HEMANGIOMAS**

**AND TELANGIECTASIAS**

The majority of the oral hemangiomas of soft tissue are exophytic and bluish and are discussed in Chapter 12. However, red macular hemangiomas (Plate A, 3) and exophytic red hemangiomas occur as both nonsyndrome and syndrome manifestations (Figs. 5-18 and 5-19). Red hemangiomas are usually of the capillary rather than the cavernous variety, which are usually more bluish. These reddish macular hemangiomas also occur as port-wine stains or nevus flammeus on the skin. People who have Sturge-Weber syndrome usually have both facial and intraoral macular hemangiomas (Fig. 5-19), although the intraoral hemangiomas may also be of the exophytic variety. An additional characteristic is the “tramline” calcifications seen in lateral skull radiographs.

The macular hemangiomas are readily differentiated from erythemas by the history of long duration, the non-tenderness, and the fact that an inflammatory component is not present. They can be differentiated from red pur-
Fig. 5-19. Red macular hemangiomas associated with Sturge-Weber syndrome. A and B, Macular hemangiomas on the lip and alveolar mucosa in a 17-year-old patient who also had a port-wine stain on the left side of the face. The intraoral lesions blanched readily on digital pressure. C and D, Another patient with Sturge-Weber syndrome. C, Full-face view showing large superficial hemangioma (port-wine stain) on the left side of the face and upper lip terminating at the midline. D, Intraoral view of same patient showing the large red macular hemangioma that has involved the maxillary alveolar and gingival mucosa on the left side of the midline. The lip involvement on the left side can also be seen. (Courtesy S. Raibley, River Forest, Ill.)

Fig. 5-20. Red allergic manifestations. A, Petechiae in red patch (arrows), which was allergic reaction to topical anesthetic (unfortunately, the red patch is not clearly visible in this black-and-white picture). B, Allergic reaction to agents in periodontal dressing. Note the deep mostly uniform color of all the mucosa in this picture. (A courtesy E. Rainieri, Maywood, Ill.)
HERALD LESION OF GENERALIZED STOMATITIS OR VESICULOBULLOUS DISEASE

Vesiculobullous disease and other conditions that may cause a generalized stomatitis are discussed in Chapter 6. Occasionally, such conditions occur first as a solitary lesion (erythema, bleb, or ulcer) perhaps one or several months before a full-blown attack occurs. Fig. 5-21 illustrates two cases of herald lesions.

METASTATIC TUMORS TO SOFT TISSUE

Metastatic tumors to the oral cavity and jaws are uncommon lesions and represent about 1% of all metastases in humans.63 These oral metastases represent about 1% of all oral malignancies as well.64,65 The majority of these are metastatic lesions to bone. Various studies showed soft tissue metastasis in a range of 8% to 16%,65,66 although one study63 reported 44% of all metastases to the oral region were to soft tissue. Some metastatic bony lesions involved the oral soft tissues by extension.67

Features

Hirshberg et al received 157 cases of soft tissue metastasis to the oral cavity from the English-language literature.68 These authors reported that 64% occurred in the fifth and seventh decade, and that these lesions were more common in men (61.6%) than in women. The primary site differed between genders, but overall the most common primaries in descending order of frequency were from the lung, breast, kidney, genital organs, and skin. The gingiva and alveolar mucosa accounted for 54.8%, followed by the tongue and then much less commonly the tonsil, palate, lip, buccal mucosa, and floor of mouth. The vast majority of these lesions resembled hyperplastic or reactive lesions.68 This would indicate many of these would be red (NKW).

Exophytic metastatic tumors are usually asymptomatic rapidly growing nodular or polypoid masses. The surfaces may be smooth and covered with intact mucosa, which varies from light pink to normal mucosal pink to red, depending on the integrity of the covering epithelium, the vascularity, the fibrosis, and the amount of inflammation present (Fig. 5-22 and Plates J. 1 to J. 3). Larger tumors frequently develop an ulcerated surface from chronic

Fig. 5-21. Herald lesion of generalized stomatitis. A, Two ruptured vesicles with red rims on the buccal mucosa of a patient. These soon disappeared, but a full-blown case of pemphigus developed in the patient several months later. B, Solitary reddish lesion with a keratotic white component that was observed in a 45-year-old woman. Several months later a severe disseminated attack of erosive lichen planus was observed in the patient.

Fig. 5-22. Red metastatic tumors. A, Mass of 3 cm on the right maxillary gingiva of a 58-year-old man, which proved to be a metastatic adenocarcinoma from the lung. B, Reddish granuloma-like mass on the anterior gingiva of a 27-year-old man, which proved to be metastatic synovial sarcoma. (A and B from Ellis GL, Jensen J, Reingold IM, et al: Malignant neoplasms metastatic to gingivae, Oral Surg 44:238-245, 1977.)
trauma. The resultant appearance will be red or red and white and will ulcerate and bleed easily.

These peripheral lesions may invade adjacent bone and produce a radiographic appearance of a solitary, ragged, poorly marginated radiolucency.

**Differential Diagnosis**
The most common lesions that have similar clinical appearance to red metastatic tumors are listed in the box below.

*Amelanotic melanoma* of the oral cavity is a very rare tumor but may occur as a pink or reddish exophytic lesion (see Fig. 10-31, A), so it cannot be completely dismissed.

*Proliferative chronic infections*, for example, hyperplastic/hypertrophic candidiasis and other fungal and chronic bacterial infections, will resemble metastatic tumors and SCC on occasion.

*Primary malignant mesenchymal tumors* represent less than 1% of all oral malignancies; they are less common than the metastatic variety. Nevertheless, some of these primary tumors are red, especially the vascular variety, and must be considered, although they are assigned a lower ranking in differential diagnosis.

*Minor salivary tumors* are almost never red, but if the red exophytic tumor in question is located in the postero-lateral hard palate, the possibility of a tumor of the minor salivary glands would have to be considered.

*Kaposi’s sarcoma*: This lesion is discussed in detail in Chapter 36.

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**DIFFERENTIAL DIAGNOSIS OF RED METASTATIC TUMORS**

- Inflammatory hyperplasia
- Squamous cell carcinoma
- Kaposi’s sarcoma
- Minor salivary tumors
- Primary mesenchymal malignancies
- Proliferative chronic infections
- Amelanotic melanoma

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*Squamous cell carcinoma*: Metastatic tumors and SCC look quite different in the early stages; SCC will have a rough surface, whereas metastatic lesions have smooth surfaces. When the secondary tumor ulcerates, it may be quite similar to SCC.

*Inflammatory hyperplastic lesions* are the most common by far. They can usually be tentatively identified by finding a chronic irritant associated with the lesion. However, the gingiva is the most common site for soft tissue metastatic lesions and for IH, so the metastatic lesions must always be included in the list. If the underlying bone shows bone resorption, malignancy must be seriously considered.

The suspicion of *metastatic tumor* is enhanced by symptoms of a primary tumor elsewhere or a history of previous treatment of such a tumor. However, the metastatic oral lesion may be the first indication of the presence of a primary tumor in as high as 33% of cases.²⁹

**Management**

Treatment of individual cases of metastatic carcinoma in the oral cavity depends on the general prognosis of the patient. If the patient is terminal as a result of disseminated tumor, observation or palliative measures are the management of choice. On the other hand, if the oral lesion appears to be the only existing metastatic lesion, a serious attempt should be made to eradicate it.

**KAPOSI’S SARCOMA (AIDS)**

AIDS and associated Kaposi’s sarcoma are discussed in Chapter 36. A red color is one of the frequent characteristics of Kaposi’s sarcoma. Fig. 5-23 illustrates several nodular red Kaposi’s sarcomas on the soft palate of an HIV-positive patient.

**RARITIES**

The rare oral red lesions are listed on the first page of this chapter.

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*Fig. 5-23.* Kaposi’s sarcomas. Note the four red nodular lesions on the soft palate of a man with AIDS. One of the more anterior lesions has a white necrotic surface. (Courtesy S. Silverman, San Francisco.)
REFERENCES


CHAPTER 6

Generalized Red Conditions and Multiple Ulcerations

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This chapter deals primarily with the diffuse red conditions, multiple vesicles or blebs, and multiple ulcerations that occur in the oral cavity and affect several oral surfaces simultaneously. The majority of these occur as multiple ulcerations distributed over erythematous mucosal surfaces. They include:

RECURRENT APHTHOUS STOMATITIS AND BEHÇET’S SYNDROME
PRIMARY HERPETIC GINGIVOSTOMATITIS
EROSIVE LICHEN PLANUS
LICHENOID DRUG REACTION
ERYTHEMA MULTIFORME
ACUTE ATROPHIC CANDIDIASIS
BENIGN MUCOUS MEMBRANE PEMPHIGOID
PEMPHIGUS
CHRONIC ULCERATIVE STOMATITIS
DEQUAMATIVE GINGIVITIS
RADIATION AND CHEMOTHERAPY MUCOSITIDES
XEROSTOMIA
PLASMA CELL GINGIVITIS
STOMATITIS AREATA MIGRANS
ALLERGIES
POLYCYTHEMIA
LUPUS ERYTHEMATOSUS
RARITIES
Actinomycosis
Acute gangrenous stomatitis
Agranulocytosis
Amyloidosis
Bullous pemphigoid
Cheilitis granulomatosa (Melkersson-Rosenthal syndrome)
Crohn’s disease
Darier’s disease
Diabetic ulcerations
Epidermolysis bullosa
Giardia lamblia infection
Gonococcal stomatitis
Graft-versus-host disease
Granulomatous disease of the newborn
Hand-foot-and-mouth disease
Heavy metal poisoning
Hereditary mucoepithelial dysplasia
Hereditary telangiectasia
Herpangina
Herpes zoster (primary and secondary)
Histoplasmosis
Impetigo
Job’s syndrome
Kaposi’s sarcoma (multiple)
Leukemia
Major aphthous ulcerations (Sutton’s disease)
Maple syrup urine disease
Measles
Metastatic hemangiosarcomas
Monoclonal plasmacytic ulcerative stomatitis
Mycosis fungoides
Paraneoplastic pemphigus
Pernicious anemia
Polyarteritis nodosa
Psoriasis
Psoriasis variants
Pustular psoriasis
Acrodermatitis continua
Impetigo herpetiformis
Pyostomatitis vegetans
Reiter’s syndrome
Scurvy
Streptococcal stomatitis
Thermal and chemical burns (mild, recent)
Ulcerative colitis
Uremic stomatitis
Varicella
Vincent’s angina
Vitamin B deficiencies (severe)
Wegener’s granulomatosis

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Chapter 5 is devoted to solitary red lesions. In contrast, this chapter discusses those diseases that simultaneously produce multiple red lesions and multiple ulcerations on several oral mucous membranes. The lesions may also appear on other mucous membranes and on the skin. Also included are those vesicular lesions that appear red both before the eruption of the vesicles and after their rupture.

For a variety of reasons, these conditions represent the most difficult challenge to clinical diagnosis. There is a wide variation in the degree of severity of individual cases. In many instances the specific cause is unknown, and frequently laboratory and biopsy results are nonspecific. Many of these conditions are relatively uncommon; even the specialist may not have the opportunity to study a sufficient quantity of cases to gain expertise.

Although the initial clinical appearance of the diseases varies, they all appear similar in their later stages. For example, the vesiculobullous group is quite distinctive in the early stages, but after the “blisters” rupture and disappear, the resultant ulcerative stomatitis is quite nonspecific in appearance.

The vesicular diseases are a particular enigma because the “blisters” may form and rupture within 24 hours; consequently the clinician and patient may be unaware that vesicles were even present in a given case. Presentation, remission, and recurrence make up the frequent course of many of these diseases. Treatment is palliative for the vast majority of them.

An overview of the various conditions reveals a considerable divergence; for instance, polycythemia is present as a painless, deep, dusty red color of the mucosa usually without inflammation, blisters, or ulcerations. The stomatitis accompanying xerostomia does not produce bullae and is otherwise nonspecific except for the decrease in salivary pooling. The bullous diseases are similar in that vesicles or blebs are the first lesions to appear. However, these soon rupture to form ulcers on inflamed mucosal surfaces. Diseases such as lichen planus, lichenoid drug reaction, lupus erythematosus, stomatitis areata migrans, and psoriasis form a fifth group frequently demonstrating both white (keratotic) and red lesions.

These conditions have in common the generalized reddened appearance of the oral mucosa. Pain is usually a symptom.

ETIOLOGY

The spectrum of causes of generalized red conditions is especially broad and varied. It includes the following (unfortunately, the specific cause is unknown in many conditions):

- Hereditary conditions
- Allergic conditions
- Autoimmune conditions
- Infections (bacterial, fungal, viral)
- Altered host state (e.g., diabetes, uremia)
- Altered local resistance (e.g., xerostomia)
- Trauma
- Iatrogenic conditions
- Neoplasia
- Gastrointestinal conditions
- Deficiency states (e.g., vitamin deficiencies)
- Idiopathic conditions

RECURRENT APHTHOUS STOMATITIS AND BEHÇET’S SYNDROME

Solitary recurrent aphthous ulcers (RAUs) are discussed in detail in Chapter II. Their characteristic history and clinical picture permit ready recognition. A patient occasionally is seen with multiple aphthous ulcers distributed over several inflamed mucosal surfaces (Fig. 6-1 and Plate B. 4). The differential diagnosis of this condition, known as recurrent aphthous stomatitis, should therefore include those diseases that appear as generalized red ulcers.

Features

The ulcers of recurrent aphthous stomatitis are basically round or ovoid, have yellowish necrotic bases, and are surrounded by a region of inflamed mucosa. When the lesions are less than 1 cm, they are referred to as “minor” ulcers; if larger than 1 cm, they are referred to as “major” ulcers. The lesions are multiple and invariably painful, and they occur most frequently on the labial or buccal mucosa, floor of the mouth, and soft palate (Fig. 6-1). The recurrent attacks each last for about 10 days. If major aphthous ulcers are present, they may persist for months. The patient may then enjoy a disease-free period varying from a few weeks to several months before having a recurrence of aphthous stomatitis. As with all the other stomatides, a painful lymphadenitis may accompany each ulcerative episode.

Fig. 6-1. Recurrent aphthous stomatitis. This middle-aged woman had many ulcers scattered throughout the oral mucosa. Note the characteristic reddened (darker) mucosa surrounding these ulcers in the sublingual region.
If extraoral signs and symptoms accompany recurrent aphthous stomatitis, the diagnosis of Behçet’s syndrome may be made. Behçet’s syndrome is characterized by oral and genital ulcers and ocular inflammation. At least two of these symptoms are required to establish the diagnosis. Behçet’s syndrome is further classified as mucocutaneous (oral, genital, or skin lesions, or all three), arthritic (arthritis in addition to mucocutaneous lesions), and neuroocular (neurologic or ocular symptoms or both in addition to the mucocutaneous and arthritic signs).

**Differential Diagnosis**

All the ulcerative mucosities listed at the beginning of this chapter should be considered. The absence of vesicles and blebs plus the usual healing in 7 to 14 days and well-defined circumscribed appearance of the lesions rules out benign mucous membrane pemphigoid and pemphigus and partially eliminates erythema multiforme. The ulcers in recurrent aphthous stomatitis are quite uniform in appearance and somewhat similar in size. This uniformity differentiates this condition from the lesions of erythema multiforme, which vary greatly from one another in appearance: erythematous macules, blebs, ulcers, and crusted lesions on the lip. The presence of crusted lesions on the vermilion border is not compatible with a diagnosis of recurrent aphthous ulceration. The absence of a white (keratotic) component tends to rule out lichen planus, lichenoid drug reaction, lupus erythematosus, and psoriasis.

Atrophic candidiasis may also appear red, but predisposing conditions are found in the patient evaluation. Most cases of candidiasis, even the atrophic type, pass through a white necrotic phase or have a minor keratotic component. Negative results on a cytologic test for Candida albicans rules out this diagnosis.

**Primary herpetic gingivostomatitis** must be differentiated from recurrent aphthous stomatitis. Herpetic gingivostomatitis is a systemic herpesvirus infection. The patient usually has a fever and complains of malaise and often nausea. Small vesicles precede herpetic ulceration. The vesicles and subsequent ulcers are pinpoint size, and the attached gingivae are almost invariably involved, whereas in recurrent aphthous stomatitis the gingivae are seldom involved. A history of contact with an active lesion on another person can often be established in patients with primary herpetic gingivostomatitis or in patients who have a habit of biting the cuticle.

Recurrent herpetic infections develop in about one third of those patients who have had a primary infection. These are discussed in detail in Chapter 11.

Patients with immunodeficiency states such as AIDS or patients undergoing chemotherapy may suffer recurrent herpetic attacks as severe as those of primary herpetic stomatitis.

**Differential Diagnosis**

The aspects of this condition have been reviewed in the Differential Diagnosis section of recurrent aphthous stomatitis. In addition, hand-foot-and-mouth disease (Coxsackie A virus etiology) needs to be considered as it presents with multiple pinpoint oral vesicles and ulcers, as well as fever. The absence of lesions on the palms and soles eliminates hand-foot-mouth disease from consideration. Herpangina (also Coxsackie A virus) can generally
PART II  Soft Tissue Lesions

Fig. 6-2. Primary herpetic gingivostomatitis. A and B, Example in a woman. Note the inflamed gingivae and the ragged appearance with a faint whitish pattern. Close inspection revealed that the ragged white appearance was produced by the rupture and ulceration of the many pinpoint vesicles. C, Example in a 9-year-old boy; the primary infection was mostly confined to the gingivae. D, Case in which the prominent manifestations involved the mucosa of the lip and the anterior portion of the tongue in a 13-year-old girl. E, Gingival inflammation and swelling in leukemia. The ragged appearance with the multiple pinpoint ulcerations is not present in this disease. (A and B courtesy E. Ranieri, Maywood, Ill; E courtesy P. Akers Evanston, Ill.)

be identified by the distribution of the small vesicles and ulcers limited to the soft palate and oropharynx.

Occasionally a very severe intraoral manifestation of recurrent herpes occurs (e.g., small pinpoint vesicles and ulcers covering the whole palate). It is important to note that only one surface is involved in the recurrence, whereas multiple surfaces are involved in primary herpetic gingivostomatitis.

Establishment of diagnosis The diagnosis of primary herpetic gingivostomatitis is usually made on a clinical basis. The patient has a number of vesicles or small painful ulcers throughout the oral cavity. A history of systemic signs and symptoms of a viral illness helps to establish the diagnosis.

Confirmation of the viral infection by laboratory methods is available but not routinely used. The virus
may be isolated in tissue culture if fluid can be obtained from an intact vesicle. Primary infections are associated with an increase in antibody titer, and paired acute and convalescent sera may be studied. Histologic and cyto-
logic examination of tissue may be done, but identification of the specific virus requires expensive and time-
consuming procedures and is generally not indicated.

There are two types of herpes simplex virus that cause disease in humans. The type 1 virus is primarily associated with infections of the skin and oral mucous membrane, and type 2 is associated with infections of the genitalia (although the converse can and does occur).

Management
There is no specific treatment for primary herpetic ginvostomatitis. Acyclovir (Zovirax) is effective in the management of initial herpes genitalis. It is also useful in treating non-life-threatening mucocutaneous herpes simplex virus infections in immunocompromised patients. In these patients a decrease in the duration of viral shedding has been reported. There is no reported clinical evidence of benefit in treating herpes labialis in nonim-
munocompromised patients.

The usual supportive measures for an acute viral infec-
tion should be instituted, including maintenance of proper oral hygiene, adequate fluid intake to prevent dehydration, and the use of systemic analgesics for control of pain. An-
tipyretic agents are also prescribed when fever is a symp-
tom. In severe cases, it may be necessary to use a topical anesthetic mouth rinse such as viscous lidocaine, dyclono-
ine, or elixir of diphenhydramine. The patient is often able to tolerate cold liquids, which may aid in preventing dehy-
dration. Secondary bacterial infection of the many small punctate ulcers invariably is a major contributor to the pain.

EROSIVE LICHEN PLANUS
The lesions of lichen planus may take several different forms and have been classified into the following types: keratotic, vesiculobullous, atrophic, and erosive. The les-
ions of the atrophic and erosive forms are somewhat dis-
tinct, but they are discussed under the common heading of erosive lichen planus.

Features
The keratotic form of lichen planus is discussed in Chap-
ter 8 along with a review of the epidemiology and etiol-
ology. The white lesion of lichen planus has been consid-
ered the most common. One report suggests that the erosive form may be seen more often, but this may rep-
resent a population skewed towards referral for manage-
ment of the painful erosive lesions.

Although the keratotic form of lichen planus is usually asymptomatic, the patient with the atrophic or erosive va-
riety usually complains of a burning sensation or pain. The atrophic lesions appear smooth and erythematous and
may have a feathery, white, keratotic border. In the erosive form the surface is usually granular and bright red and tends to bleed when traumatized. A pseudomembrane composed of necrotic cells and fibrin covers the more se-
vere areas of erosion. The patterns of involvement change from week to week. However, almost invariably a white keratotic component is clinically apparent in a reticular, feathery, or plaque pattern (Fig. 6-3 and Plate C).

Cases have been reported in which lichen planus was associated with squamous cell carcinoma, and conse-
quently it has been speculated that lichen planus might be a premalignant lesion. It is difficult to determine whether there is an increased rate of malignancy in cases of oral lichen planus. The results of most studies are inconclusive, showing a slightly increased risk of malignancy, some of which may be related to tobacco use. In recent follow-up studies the number of patients with lichen planus in whom squamous cell carcinoma developed ranged from less than 1% to 2.5%. These results do not confirm the previous reports and leave the question unresolved. As a matter of precaution, such patients should be observed carefully so that any changes can be detected early and biopsies obtained.

On histopathologic study, the atrophic form of lichen planus shows a thinned epithelium with hydropic degen-
eration in the basal cell layer. A dense bandlike infiltrate of lymphocytes is confined to the area immediately be-
neath the epithelium. In the erosive form, either the ep-
ithelium is completely missing or only remnants of ep-
thelium tissue are seen. The underlying lymphocytic inflammatory infiltrate becomes mixed with polymor-
phonuclear leukocytes and loses its distinctive bandlike pattern. The diagnosis of lichen planus can be confirmed only by a biopsy.

The changes are usually characteristic in the atrophic les-
sions, in which the epithelium is still intact. Unfortunately, an intact epithelium does not exist in erosive lesions and the diagnosis may be difficult if not impossible. A biopsy specimen from the edge of an erosive lesion is usually more helpful than one from the erosive central area in es-
ablishing a diagnosis. When more typical lesions are pre-
sent on other areas of the mucosa or skin, it may be as-
sumed that the red lesions represent lichen planus (Fig. 6-3). However, if the lesions are clinically suggestive of squamous cell carcinoma, biopsy is imperative.

Lichenoid dysplasia Lichenoid dysplasia is the term ap-
plied to lichenoid lesions that show dysplastic areas. Specific histologic criteria are used to differentiate ep-
thelial dysplasia, oral lichen planus, and other inflamma-
tory conditions. Lichenoid dysplasia and lichen planus are thought to be biologically distinct lesions. Lovas et al. contended that “some, if not most, cases of apparent malignant transformation of lichen planus likely repre-
sent red and white lesions that were dysplastic from their inception, but mimic oral lichen planus both clinically and histologically.”
PART II  Soft Tissue Lesions

Fig. 6-3. Erosive lichen planus. A-D, Four cases of erosive lichen planus. Note the various proportions of keratotic and erythematous involvement in each.

**Differential Diagnosis**

Other diseases that contain a clinically apparent keratotic component in combination with a mucositis and therefore present lesions similar to those of lichen planus are speckled leukoplakia, squamous cell carcinoma, lichenoid drug reaction, electrogalvanic mucosal lesions, psoriasis, stomatitis areata migrans, atrophic candidiasis with a keratotic border, and discoid lupus erythematosus. Each of these diseases is discussed in detail elsewhere in this chapter.

When red lesions are confined to the gingivae, it is virtually impossible to distinguish atrophic or erosive lichen planus from benign mucous membrane pemphigoid and desquamative gingivitis on the basis of clinical and histologic examination. Immunofluorescence findings in gingival biopsies are diagnostic of benign mucous membrane pemphigoid and some forms of desquamative gingivitis. Kilpi et al. summarized the use of this technique.

**Special diagnostic procedures** In lichen planus, immunofluorescence studies of biopsies reveal characteristic but not diagnostic findings (Table 6-1). Globular deposits, sometimes called cytoid bodies or Civatte’s bodies, contain immunoglobulins and fibrin, or they may contain complement and are observed in the papillary dermis along the dermoepidermal junction (Fig. 6-4). Cytoid bodies are more often seen in active stages of the disease and are more common in lesions than in normal tissue. Although cytoid bodies are neither disease specific nor diagnostic, their identification can be helpful when routine histopathologic studies are inconclusive. Cytoid bodies are seen in biopsy specimens in 97% of lichen planus, 41% of systemic lupus erythematosus, 70% of discoid lupus erythematosus, 75% of dermatomyositis, 50% of erythema multiforme, 50% of pemphigoid, 40% of pemphigus, and 40% of normal specimens. The findings in lichen planus can be partially differentiated from the other diseases and the normal specimens on the basis of size and number of cytoid bodies and other immunologic findings. In addition to revealing cytoid bodies, immunofluorescence studies also reveal fibrin deposits along the basement membrane. These fibrin deposits, found in later stages of lesions, are not disease specific and occur in other diseases, particularly in the healing phase. Diagnostic immunofluorescence findings can also be seen in biopsy specimens of lupus erythematosus, pemphigus, and pemphigoid (Table 6-1). In normal biopsy specimens, smaller and fewer cytoid bodies are observed.

**Management**

Because of the increased incidence of lichen planus in diabetic patients, it is important to obtain medical consultation for the possibility of this disease. If the patient has diabetes, prompt stabilization of the condition is beneficial to management of the oral condition.

A specific and uniformly successful treatment for erosive lichen planus is not available. Nevertheless, the pa-
Table 6-1 Immunofluorescence findings important in the diagnosis of red conditions

<table>
<thead>
<tr>
<th>Disease</th>
<th>Types of antibodies</th>
<th>Pattern of staining</th>
<th>Findings</th>
<th>Findings</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign mucous membrane pemphigoid or cicatricial pemphigoid</td>
<td>Basement membrane antibodies</td>
<td>Basement membrane zone</td>
<td>+</td>
<td>+ (100%)</td>
<td>Diagnostic</td>
</tr>
<tr>
<td>Bullous pemphigoid</td>
<td>Basement membrane antibodies</td>
<td>+ (80%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lichen planus</td>
<td>Negative</td>
<td></td>
<td></td>
<td>+ (97%)</td>
<td>Characteristic</td>
</tr>
<tr>
<td>Pemphigus, all forms</td>
<td>Intercellular antibodies of epithelium</td>
<td>Intercellular epithelial deposits</td>
<td>+ (100%)</td>
<td></td>
<td>Diagnostic</td>
</tr>
<tr>
<td>Discoid lupus erythematosus</td>
<td>Negative or low titer of antinuclear antibodies</td>
<td>Dermoepidermal deposits of immunoglobulins and complement; lesion only</td>
<td>+ (80%)</td>
<td></td>
<td>Highly characteristic</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>High titer of antinuclear antibodies</td>
<td>Dermoepidermal deposits of immunoglobulins and complement; lesion and normal tissue</td>
<td>+ (&gt;95%)</td>
<td></td>
<td>Diagnostic</td>
</tr>
</tbody>
</table>

Patient can usually be greatly helped to reduce the degree of pain and produce regression of the lesions with extended drug therapy. A spontaneous remission has been reported in many cases, and the oral lesions are especially prone to recurrence and remission.

Milder cases may be managed successfully with the application of steroid creams such as fluocinonide or Kenalog in Orabase after meals and at bedtime.

For more severe cases the standard treatment has been the oral administration of adequate doses of prednisone for 2 weeks. If the lesions are well into remission by this time, the dosage of systemic corticosteroids may be tapered off and discontinued. If small isolated lesions are still present, these can be managed with the topical application of corticosteroid pastes such as fluocinonide or Kenalog in Orabase. When the systemic administration of corticosteroids must be continued for several weeks, the complications of extended corticosteroid therapy must be considered.

When a remission has been induced and drug therapy discontinued for a variable period of weeks or months, the painful lesions may recur and drug therapy has to be reinstituted.

The following are among the drugs that may cause a lichenoid drug reaction:

- Bismuth
- Captopril
- Carbamazepine
- Chloroquine
- Chlorpropamide
- Dapsone
- Demeclocycline
- Furosemide
- Gold
- Labetalol
- Methyldopa
- Nonsteroidal antiinflammatory agents
- Para-aminosalicylic acid
- Penicillamine
- Penicillin
- Phenothiazines
- Propranolol
- Quinacrine
- Spironolactone
- Streptomycin
- Tetracycline
- Thiazides
- Tolbutamide

Lichenoid Drug Reaction

Lichenoid drug reactions resemble lichen planus. Numerous medications have been implicated, and virtually any drug has the potential to provoke this reaction. Various degrees of severity occur, ranging from painless keratotic lesions to painful severely erosive cases. Diagnosis is by clinical appearance and history. Under the physician’s supervision, the putative drug is discontinued and alternate therapy prescribed. Healing is usually prompt but may be prolonged in some cases. Severe cases of lichenoid drug reaction may clinically resemble erythema multiforme. The allergic state usually responds to the administration of prednisone or similar steroid agents.
ERYTHEMA MULTIFORME

Erythema multiforme is a disease of unknown etiology that has many different manifestations. When seen in its classic form, it is easily recognized. Although it is a vesiculobullous disease, vesicles and bullae usually are present for only a limited time.

Although an attack of erythema multiforme usually occurs without apparent reason, certain agents have been identified as precipitating the disease. Among the most common is a herpes simplex infection, but other infections and many drugs have also been implicated.

Features

The disease occurs primarily in young adults, usually men. It has a sudden onset and runs a course of 2 to 6 weeks. Recurrences are common. Lesions may be limited to the oral mucosa and involve, in descending order of frequency, the buccal mucosa, lips, palate, tongue, and
fauces (Fig. 6-5 and Plates C, 4 and D). The gingivae are rarely involved. In one large study,12 70% of cutaneous cases showed oral lesions.

Sloughing of the mucosa and diffuse redness are the most frequent clinical features. The initial lesions are small red macules that may enlarge and show a whitish center. The macules progress to form bullae that soon rupture, leaving a sloughing mucosal surface that appears bright red and raw. In time, the denuded surface becomes covered with a pseudomembrane of fibrin and cells and assumes a grayish appearance. Involvement of the oral tissues may be limited to merely a diffuse redness.

Skin lesions of erythema multiforme are pathognomonic. They may accompany the oral condition, or there may be cutaneous manifestation without oral involvement. Skin lesions have a characteristic “bull’s eye” or “target” appearance (Fig. 6-5). Although the palms of the hands are a classic location, these lesions may occur anywhere on the skin. Patients may complain of pruritus.

A microscopic examination of vesicles and bullae reveals a subepithelial cleft. The underlying connective tissue contains a mixed inflammatory infiltrate with numerous eosinophils. The light microscopic changes and immunologic findings seen in immunofluorescence examination of biopsy specimens are not diagnostic but can be used to rule out other diseases. Buchner et al13 reported on the histologic spectrum of oral erythema multiforme. There are no useful laboratory studies.

The diagnosis is made on the basis of clinical information. Obviously, this can pose a problem if the lesions are limited to the oral cavity. A history of previous attacks that involved other mucous membranes or the skin is most useful in making the diagnosis. Stevens-Johnson syndrome is a severe episode of erythema multiforme that involves the mucosa, conjunctiva, and skin.

Differential Diagnosis

Similar oral lesions may be seen in pemphigus vulgaris, benign mucous membrane pemphigoid, allergic reactions, erosive lichen planus, primary herpetic gingivostomatitis,
and xerostomia. Oral lesions resulting from drug reactions may appear similar to those of erythema multiforme and may vary from focal or diffuse areas of erythema to areas of erosion and ulceration. At times, it may be difficult to decide whether the drug precipitated an attack of erythema multiforme or the lesions resulted from drug allergy.

**Management**

Since erythema multiforme is a self-limiting disease, usually only supportive care is necessary. When areas other than the oral cavity are involved, the patient is best managed through a cooperative effort of physician and dentist. If the oral cavity is severely involved, systemic corticosteroids usually bring prompt and dramatic relief. Lozada reported that if 50 to 100 mg of azathioprine were combined with prednisone, a lower dosage of prednisone could be used. A corticosteroid such as dexamethasone elixir used as an oral rinse may provide symptomatic relief in mild cases.

**ACUTE ATROPHIC CANDIDIASIS**

The lesions of acute atrophic candidiasis (formerly known as acute atrophic candidosis) represent a less common form of *Candida* infection. They may be the sequelae to the typical lesions of acute pseudomembranous candidiasis. When the white plaque of pseudomembranous candidiasis is shed or removed, often a red, atrophic, and painful mucosa remains (Fig. 6-6 and Plate E, 5). At times the lesion may be asymptomatic.

**Features**

The lesions are seen in the same types of patients as other clinical types of candidiasis (see box on p. 61). Tissue sections show an atrophic epithelium that may contain a few hyphae in the superficial layers. The lamina propria usually has a mild acute inflammatory infiltrate and increased vascularity. An exfoliative cytologic smear of the lesions may be useful in establishing a diagnosis.

**Differential Diagnosis**

The red lesions of acute atrophic candidiasis are often seen in association with those of the pseudomembranous type and so do not pose a diagnostic problem. When present as multiple red lesions, they are rather nonspecific in appearance. Lesions produced by chemical burns, drug reactions, and other organisms have a similar clinical appearance, as may the predominantly red lesions of erosive lichen planus, mild cases of erythema multiforme, and discoid lupus erythematosus.

**Management**

This is discussed in Chapter 5, p. 62.

**BENIGN MUCOUS MEMBRANE PEMPHIGOID**

The specific cause of benign mucous membrane pemphigoid, or cicatricial pemphigoid, is unknown. However, it is known to have an autoimmune component.

**Features**

Benign mucous membrane pemphigoid is seen twice as frequently in women as in men. The disease affects older individuals, with the highest incidence occurring in those in their late 50s. It is usually reported in the white population. Lesions are found primarily on the mucous membranes, infrequently involving the skin. The mucous membranes of the oral cavity and eyes are most often involved. Lesions occur on the gingiva, buccal mucosa, and palate.

The gingivae, the most common site, become edematous and bright red—a striking feature of the disease. This involvement may be patchy or diffuse. Subsequent to bulla formation or trauma, the surface epithelium may be lost, leaving a raw, red, bleeding surface. The vesiculobullous lesions in other areas of the oral cavity do not appear as red, nor do they bleed as readily. The ulcers that result from the collapse of bullae are surrounded by a zone of erythema (Fig. 6-7 and Plate C, 1) and are relatively asymptomatic. Unless treated, the dis-
ease follows a chronic course of partial remission and exacerbation.

A clinical feature common to these three diseases is the production of a gingival bleb by a strong jet of air. This occurs because of the defect in the basement membrane region. Manton and Scully emphasized the necessity of using a combination of clinical, histologic, and immunostaining examinations to establish a diagnosis of mucous membrane pemphigoid.

The histologic changes are only characteristic if the epithelium is intact. Frequently the roof of the subepithelial bulla is lost and the histologic changes become non-specific, characterized by a chronic inflammatory infiltrate of the connective tissue.

Immunofluorescence is an important and useful diagnostic technique because it can help to differentiate the gingival lesions of benign mucous membrane pemphigoid from those of erosive lichen planus and desquamative gingivitis. If the surface is intact, direct immunofluorescence study of the biopsy is particularly important, since the immunofluorescence findings are diagnostic. The basement membrane zone contains a deposition of immunoglobulins and complement (Fig. 6-8). The immunofluorescence findings can also be observed in the adjacent clinically normal mucosa. The biopsy site of choice for immunofluorescence is the perilesional and the clinically normal mucosa, since these areas have the dermoepidermal relationships necessary for evaluation (see Table 6-1). In approximately 25% of the cases, low titers of serum antibodies to the basement membrane are also observed. When these occur, they are also diagnostic of pemphigoid.

**Differential Diagnosis**

Other diseases that should be considered in a differential diagnosis of benign mucous membrane pemphigoid are pemphigus vulgaris, bullous pemphigoid, bullous lichen planus, chronic ulcerative stomatitis, and early cases of erythema multiforme.

Benign mucous membrane pemphigoid and bullous pemphigoid are clinically, histologically, and immunologically similar but differ in sites of involvement. Benign mucous membrane pemphigoid characteristically involves the mucous membranes, most commonly the oral cavity and next the conjunctiva. Skin lesions are infrequently observed. In bullous pemphigoid, the usual site of involvement is the skin. In approximately 30% of cases the oral mucosa is involved. The immunofluorescence pathologic findings in both diseases are identical, showing immune deposits along the basement membrane. However, the two diseases differ in the incidence and titer of basement membrane zone antibodies in sera. In bullous pemphigoid, basement membrane zone antibodies, generally of high titer (greater than 1:80), occur in approximately 97% of patients. In benign mucous membrane pemphigoid, antibody titers (usually less than 1:40) occur in only approximately 20% to 25% of patients.

**Management**

The patient with benign mucous membrane pemphigoid may be extremely difficult to treat. Corticosteroids are the only useful form of therapy, but their side effects must be considered. The use of corticosteroids on alternate days has been somewhat successful as a way to prevent these complications. Because the mucous membranes of the eyes are often involved, patients with benign mucous membrane pemphigoid are at risk for blindness and should be referred to an ophthalmologist for examination.

Rogers et al recommended topical corticosteroids for mild cases and dapsone (a bacteriostatic sulfone derivative) for more symptomatic cases. Dapsone therapy must be carefully monitored, since it can cause hemolysis and methemoglobinemia, particularly in patients with glucose-6-phosphate dehydrogenase deficiency.

**PEMPHIGUS**

Pemphigus is a vesiculobullous disease of unknown cause with an autoimmune etiology that may affect mucous membranes and skin. The four major forms of pemphigus...
are pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, and pemphigus erythematous. They have similar immunologic findings, which are diagnostic (see Table 6-1).

**Features**

Pemphigus affects men and women approximately equally, and the vast majority of patients are white. In one report,\(^1^7\) 74% of the patients with the vulgaris or vegetans type were Jewish, approximately 98% of the patients were over 31 years of age at the time of onset, and 80% of cases of the vulgaris variety (by far the most common type) first occurred intraorally. Laskaris and Stoufi\(^1^8\) reviewed the rare cases of pemphigus vulgaris in children.

The lesions of pemphigus vulgaris may appear as areas of erosion, but more often they are seen as ulcers, bullae, or areas of sloughing mucosa or skin (Fig. 6-9 and Plate C, 5). Diffuse erythematous involvement of the gingiva has been reported but is not the typical manifestation of the disease. In the typical case, initial lesions occur orally, followed by skin lesions.

The histologic study of intact vesicles or bullae reveals an intraepithelial defect. The individual cells separate from one another, and a pooling of fluid occurs. The basal layer of epithelial cells remains in position on the basement membrane.

**Differential Diagnosis**

All the vesiculobullous conditions listed at the beginning of this chapter should be considered in the differential diagnosis. As a general rule, the pemphigus bulla is smaller than the bulla in benign mucous membrane pemphigoid and considerably larger than those seen in the viral diseases such as herpes and hand-foot-and-mouth disease.

**Special diagnostic procedures** Immunofluorescence studies of sera and biopsy specimens reveal antibodies confined to the intercellular substance of epithelium and intercellular deposits of IgG (Fig. 6-9). The sera from more than 95% of pemphigus patients with active disease contain intercellular epithelial antibodies. During early stages of the disease or during remission, the

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Fig. 6-9. Pemphigus. A and B. Clinical views of the same case. The mucosa of the lower lip is much more severely involved than the buccal mucosa. C. Direct immunofluorescence test on oral biopsy specimen from patient with pemphigus revealing IgG deposits intercellularly in the epithelium. Epithelial intercellular antibodies are also seen in the serum. Both are diagnostic. (A and B courtesy M. Lehnert, Minneapolis.)
Plate A. 1, Normal red palatoglossal arch. 2, Traumatic erythematous macule. 3, Capillary hemangioma. 4, Inflammatory hyperplasia. 5, Inflammatory hyperplasia. 6, Epulis fissuratum. 7, Red parulis. 8, Early papillary hyperplasia. 9, Papillary hyperplasia. 10, Pseudomembranous candidiasis. 11, Healed candidiasis. 12, Erythematous candidiasis. (3 courtesy G. Blozis, Columbus, Ohio; 7 courtesy J. Guggenheimer, Pittsburgh.)
Plate B. 1, Red macule from oral sex. 2, Red macule from coughing. 3, Ludwig’s angina. 4, Recurrent aphthous stomatitis. 5, Major aphthous ulcer. 6, Two chancre. 7, Erythroplakia (squamous cell carcinoma). 8, Erythroplakia (squamous cell carcinoma). 9, Pregnancy gingivitis. 10, Cocaine lesion. 11, Pyogenic granuloma. 12, Jaundice. (7 courtesy P. O’Flaherty, Chicago; 10 courtesy A. Gargiolo, Chicago; 11 courtesy G. MacDonald, San Jose, Calif; 12 courtesy R. Gier, Kansas City, Mo.)
Plate C. 1, Benign mucous membrane pemphigoid. 2, Same patient as 1. 3, Benign mucous membrane pemphigoid. 4, Primary herpetic gingivostomatitis. 5, Pemphigus. 6, Erythema multiforme. 7, Stevens-Johnson syndrome. 8, Bullous lichen planus. 9, Reticular and erosive lichen planus. 10, Erosive and reticular lichen planus. 11, Atrophic lichen planus. 12, Atrophic and erythematous lichen planus. (5 and 6 courtesy S. Fischman, Buffalo, NY; 12 courtesy P. Toto, Waukegan, Ill.)
Plate D. 1, Plasma cell gingivitis. 2, Primary herpetic gingivostomatitis. 3, Reaction to periodontal surgical dressing. 4, Cinnamon reaction. 5, Drug reaction. 6, Radiation mucositis. 7, Candidiasis. 8, Tylenol burn. 9, Cheek biting. 10, Nicotine stomatitis. 11, Lupus erythematosis. 12, Ectopic geographic tongue. (1, 5, and 6 courtesy G. Blozis, Columbus, Ohio; 4 courtesy M. Bernstein, Louisville, Ky; 12 courtesy S. Fischman, Buffalo, NY.)
antibody titers may be low or negative. The significance of the antibody titer must be considered together with the clinical and histologic findings. Low titers (10 to 20) are significant when there are typical clinical and histologic findings. Low titers of intercellular antibodies with atypical clinical and histologic findings may be termed “pemphigus-like” antibodies rather than true pemphigus antibodies. Pemphigus-like antibodies may occur as a result of extensive burns and after some drug eruptions but do not bind in vivo as do those in true pemphigus.

The intercellular antibody titer frequently relates to disease activity by rising with exacerbations and falling with remissions. In many cases, titer changes of two or more doubling dilutions precede clinical changes and provide a prognostic test for control of drug therapy. Sera should be tested every 2 to 4 weeks until the patient is in remission and then every 1 to 6 months.

Almost all patients with active pemphigus have intercellular deposits of IgG and sometimes IgA, IgM, and complement in biopsy specimens. These findings are diagnostic. Biopsies of oral lesions should be taken from the periphery of the lesion, where the epithelium is still intact. Immunoperoxidase techniques may be an alternative method to immunofluorescence as a diagnostic aid in cases of pemphigus.

**Management**

Corticosteroid therapy is the preferred treatment for severe pemphigus. Other modes of treatment include alternate-day steroid and gold therapy and immunosuppressive treatment with methotrexate or azathioprine. Favorable results with a combination of levamisole and prednisone, in which lower dosages of prednisone were effectively used, have been reported.

**DESQUAMATIVE GINGIVITIS**

There is some question whether desquamative gingivitis is a specific disease entity or a clinical manifestation of several different diseases. In a study of 40 patients with clinical desquamative gingivitis, McCarthy and Shklar histologically identified 17 cases of benign mucous membrane pemphigoid, 2 cases of pemphigus, and 4 cases of lichen planus. The remainder were considered hormonal, idiopathic, or abnormal responses to local factors. In an immunofluorescence study of 100 patients with clinical desquamative gingivitis, 35 had benign mucous membrane pemphigoid, 3 had pemphigus, and 1 patient had psoriasis. Of the remaining 61, 28 had findings consistent with lichen planus. Although the cause of desquamative lesions of the gingivae is not always known, it is generally considered to represent a degenerative pathosis of the gingivae. Because it occurs more frequently in postmenopausal women, there may also be an underlying hormonal factor.

**Features**

Desquamative gingivitis is seen in both genders but is far more prevalent in women. Usually it occurs after the age of 40, but it may occur at any age after puberty. The labial gingivae become bright red and edematous. The palatal and lingual surfaces are not often involved. Changes may be limited to a few small areas (Fig. 6-10), or they may be diffuse and extend throughout the gingivae (Plate C,3). The epithelium is quite friable and can be easily removed from the underlying connective tissue, leaving a red surface that bleeds readily after minimal trauma. Patients may complain of a burning sensation but often are asymptomatic.

On histologic examination, the epithelium is thin and atrophic. The rete ridges are blunted, and there may be clefting below the basement membrane. Edema and a mild chronic inflammatory infiltrate are seen in the underlying connective tissue. The microscopic findings are not diagnostic and serve only to exclude other diseases. Immunofluorescence studies of gingival biopsy specimens are especially valuable in determining if the underlying cause is benign mucous membrane pemphigoid, pemphigus, or lichen planus. The diagnosis is made on the basis of a careful history, physical examination, and laboratory tests.

**Differential Diagnosis**

Other diseases that produce similar lesions are erosive lichen planus, benign mucous membrane pemphigoid, bullous pemphigoid, chronic ulcerative stomatitis, and, rarely, pemphigus vulgaris.

**Management**

Treatment of desquamative gingivitis is directed at providing symptomatic relief. It is important that all possible local irritating factors be removed. Different drugs such as estrogens and steroids have been applied topically and do provide variable degrees of improvement. Systemic steroids are also indicated.
CHRONIC ULCERATIVE STOMATITIS

Chronic ulcerative stomatitis (CUS), a recently identified entity,\textsuperscript{26-28} is a subset of desquamative gingivitis. Clinically, it appears similar to lichen planus but with a distinct immunopathology and different response to therapy.

Features

Patients with CUS generally exhibit chronic, painful, burning mouths characterized by erythematous and ulcerative lesions.

Differential Diagnosis

The lesions of CUS most resemble lichen planus, and similar ulcerative and erosive lesions may occur in benign mucous membrane pemphigoid and pemphigus.

Management

On the basis of fewer than 20 patients reported in the literature, it appears that topical and systemic steroid therapy is frequently ineffective. Several patients have reported improvement with the antimalarial hydroxychloroquine (Plaquenil).

Special diagnostic procedures

Immunofluorescent findings in perilesional and normal mucosal biopsies reveal a characteristic diagnostic immunopathology of particulate antinuclear antibodies in the basal stratified epithelium. Serum antinuclear antibodies that react primarily on the lower third of stratified epithelial substrates also occur.

RADIATION AND CHEMOTHERAPY MUCOSITIDES

The diagnosis of mucositis occurring as a result of radiation or chemotherapy should be readily established from the patient history. Kolbinson et al\textsuperscript{29} discussed the early oral changes after chemotherapy and radiation therapy. The dental management of the patient with cancer has been reviewed by Little and Falace.\textsuperscript{30} Since radiation therapy and chemotherapy will adversely affect preexisting periodontal disease, prior periodontal therapy is strongly advised.

Radiation Mucositis

Features

Radiation therapy produces characteristic and dramatic changes. During the course of therapy, which may continue for 6 weeks, a diffuse inflammatory change develops in the mucosa. The amount of tissue involved is determined by the portal used for the radiation therapy.

Tissue changes do not become apparent until the last part of the first week or the beginning of the second week of radiation therapy. Distinct blebs may be produced, or a whitish area resulting from decreased cellular division and retention of squamous cells may be seen. In subsequent weeks the surface layers are lost and a thin erythematous mucosa is present. Focal areas may ulcerate and then become covered with a tan-yellow, fibrous exudate considerably among patients. Profound changes resolve a few weeks after therapy is completed, but there may be some residual redness for variable periods of time.

Management

Symptomatic relief is necessary because the pain can be severe, especially when eating. Topical anesthetics such as elixir of diphenhydramine or lidocaine can be combined with milk of magnesia, Maalox, or Kaopectate and used as oral rinse. Analgesics may be necessary.

Chemotherapy Mucositis

Features

Oral lesions resulting from chemotherapy may occur during and after the course of therapy. Initially, patients may complain of a burning sensation; lesions may or may not be associated with this sensation. The lesions begin as focal areas of redness that may persist and ultimately ulcerate. Infrequently the ulcerations become numerous and large.

Management

Treatment is directed toward providing symptomatic relief. Topical anesthetics such as lidocaine, dyclonine, or diphenhydramine may be prescribed. If the lesions become debilitating, it may be necessary to briefly interrupt chemotherapy. When secondarily infected, the lesions respond well to an oral suspension of tetracycline used as a mouthwash and then swallowed. Chlorhexidine mouth rinses are indicated for prophylaxis.
XEROSTOMIA

Dryness of the mouth is not a disease but a sign of reversible or irreversible impaired function of the salivary glands. Infectious lesions of the salivary glands such as mumps produce a transient xerostomia. When the primary disease resolves, the flow of saliva returns to normal. Diseases such as Mikulicz’s disease or Sjögren’s syndrome produce irreversible changes that result in a progressive decrease in the production of saliva. Radiation to the head and neck area causes atrophy of the glands and a decrease in the amount of saliva secreted. Dehydration and senile atrophy of the glands reduce the amount of saliva produced by the glands. Many widely used medications decrease salivary gland activity. Ganglionic blocking agents used to control hypertension, many psychotherapeutic agents (tranquilizers and antidepressants), and antihistamines have this side effect.

Features
In mild short-term cases of xerostomia, the patient may be asymptomatic and the mucosa appears normal. In moderately severe cases the patient may complain of a dry mouth or burning sensation. When these symptoms are intense, patients experience difficulty with speech, mastication, and the retention of artificial appliances. Patches of mucosa appear very atrophic and take on a dark, dusty red appearance. In severe xerostomia, erosion and ulceration of the inflamed mucosa occur.

The combined features of decreased salivary and lacrimal production suggest a diagnosis of Mikulicz’s disease. In Sjögren’s syndrome, xerostomia, conjunctivitis sicca, rhinitis sicca, and arthritis are seen.

Differential Diagnosis
A lack of saliva is the symptom that enables the clinician to differentiate the mucositis of xerostomia from the other types listed in this chapter.

Historical evidence is useful in establishing the type of xerostomia. A history of radiation treatment, antisyaliagogues, and combinations of features suggesting one of the syndromes associated with xerostomia are clues that direct the clinician to the correct diagnosis.

Management
Artificial saliva preparations may be helpful.

PLASMA CELL GINGIVITIS

Plasma cell gingivitis, also called atypical gingivostomatitis, is a disease that was recognized as a distinct entity in 1968. Studies indicate that the lesions may be caused by some ingredient in chewing gum, and a type of allergic response is the proposed etiology. Although this condition was frequently seen in the 1960s and early 1970s, it has been seen much less frequently in recent years.

Features
Plasma cell gingivitis occurs much more frequently in women than in men and is seen predominantly in young adults. The patient complains of a sore or burning mouth. The most striking and characteristic feature of the disease is the gingival involvement. The entire free and attached gingivae are edematous and bright red (Fig. 6-12). Frequently, there are associated lesions of the lips, tongue, and buccal mucosa; a scaling of the lips; and an angular cheilitis. The tongue is erythematous and devoid of filiform papillae. The patient may state that the problem has been present for as long as 3 years.

The most spectacular microscopic changes are seen in the lamina propria, which is densely infiltrated by plasma cells. The other changes are nonspecific. A diagnosis is made primarily on the basis of the clinical appearance of the lesions and is supported by a biopsy.

Differential Diagnosis
The clinical features of plasma cell gingivitis are distinctive and are not simulated by other diseases. However, early leukemic infiltrate of the gingiva may appear somewhat similar, as may allergies to toothpaste ingredients.

Management
The patient usually shows a marked improvement shortly after he or she stops chewing gum or changes brands of toothpaste. Complete remission of the disease takes approximately 4 weeks.

STOMATITIS AREATA MIGRANS

Stomatitis areata migrans is also known as migratory mucositis or ectopic geographic tongue.

Features
Most frequently, the lesions of geographic tongue are confined to the dorsal surface and lateral borders of the tongue (see Fig. 7-1, A). Occasionally, similar lesions have been reported on other mucosal surfaces of the oral cavity and are considered a more extensive involvement of the same disease process.
process. The basic appearance is that of red patches of various sizes and shapes surrounded by white (keratotic), raised rims (Fig. 6-13 and Plate D, 12). The white rims may show a radiating, feathery appearance as they fade into the surrounding normal mucosa. The patterns change continuously and finally fade completely as the condition enters a remission. Stomatitis areata migrans is usually asymptomatic and found on routine oral examination.

The histopathologic study of stomatitis areata migrans shows a thinning of the surface epithelium in some areas and an epithelial hyperplasia in others. The epithelium may show spongiosis and infiltration by acute and chronic inflammatory cells, often in focal arrangement (Munro’s abscesses).

**Differential Diagnosis**

Lesions that should be differentiated from stomatitis areata migrans are lichen planus, psoriasis, lupus erythematosus, Reiter’s syndrome, and electrogalvanically induced lesions.35

**Management**

Most cases of stomatitis areata migrans are asymptomatic. Patients who complain of burning tenderness or pain may be placed on a bland diet and use diphenhydramine mouth rinses until the condition becomes asymptomatic.

**ALLERGIES**

Diffuse erythematous lesions may be seen on the oral mucosa as a result of allergies or as a toxic effect from drugs. These lesions take a variety of forms and have been classified as “erythema multiforme caused by medication” (stomatitis medicamentosa) or as “lichenoid drug reaction” (lichen planus caused by medication). The clinical presentation is identical to that of erythema multiforme and lichen planus, and the diagnosis is made from a careful history. Cessation of drug therapy with the concurrent administration of antihistaminic agents usually results in prompt resolution.

Reactions to topical agents used in the oral cavity are relatively unusual. Individual idiosyncrasies to agents used in preparations such as surgical dressings, mouth rinses, toothpaste, and chewing gums have been reported36 (Fig. 6-14 and Plate D). A careful history is usually of assistance in making the diagnosis. The patient frequently reports changing from one brand of oral product to another immediately before development of the symptoms. Prompt withdrawal of the etiologic agent is usually both therapeutic and diagnostic.

Patients and clinicians frequently confuse the irritating effects of poorly fitting prosthetic appliances with allergy to a denture base material. Denture base materials are rarely allergenic, but poorly fitting appliances may produce such pathologic changes as papillary hyperplasia. Appliances that are not kept clean may be associated with an increased incidence of intraoral candidiasis. Improperly cured acrylic materials and improperly used denture relining materials can also cause injury to the oral mucosa, but this injury is a “burn” rather than a true allergy.

**POLYCYTHEMIA**

Polycythemia, also called erythremia, is a chronic and sustained elevation in the number of erythrocytes and level of hemoglobin. One form, primary polycythemia (polycythemia vera), is a neoplastic condition of the erythropoietic system analogous to leukemia. Transition between polycythemia and myelogenous leukemia has been reported.

The other form, secondary polycythemia, is a sustained elevation of erythrocytes and hemoglobin, usually resulting from bone marrow stimulation caused by living at high altitudes or by chronic pulmonary diseases such as emphysema. It is also seen in untreated congenital heart disease.
The entire oral mucosa of patients with polycythemia has a deep red or purple color. This discoloration is particularly noticeable in the gingivae and soft palate. The gingivae usually are prone to easy bleeding, and petechial hemorrhages may be seen on the palate and labial mucosa. These changes are seen much more frequently in polycythemia vera. Infarcts may occur in the smaller vessels because of increased viscosity of the blood and may result in multiple ulcers in the red mucosa. Laboratory tests indicating a marked increase in erythrocytes, hemoglobin concentration, and hematocrit values quickly establish the general diagnosis of polycythemia and thus separate this condition from the other mucosities.

**LUPUS ERYTHEMATOSUS**

Lupus erythematosus (LE) is a connective tissue disease of unknown cause in which the host produces antibodies to nuclear constituents. Because nearly every organ in the body runs the risk of involvement, the disease produces a vast array of signs and symptoms. Depending on the involvement, two forms of the disease occur—discoid lupus erythematosus (DLE) and systemic lupus erythematosus (SLE). The term DLE has been applied to cases in which there is only skin involvement; this is usually a benign disease with a good prognosis. Changes of conversion of DLE to SLE are small.

**Features**

Lupus erythematosus occurs predominantly in adult women; most are affected before the age of 40. Oral manifestations of DLE occur in about 20% of patients. The oral lesions may occur with or without skin involvement, before skin lesions develop, after skin lesions develop, or simultaneously with the skin lesions. Oral lesions may also be seen in patients with SLE (Plate D, 11).

Schiodt et al\(^{37}\) studied 32 patients (26 women, 6 men) with LE lesions of the oral mucosa. The age of the patient at onset of the oral lesions ranged from 6 to 75 years with a mean age of 41 years. The mean duration of the oral lesions was 4.2 years. Symptoms such as discomfort, burning, and pain associated with hot spicy food were present in 75% of the patients. The lesions were most often located on the buccal mucosa, gingiva, labial mucosa, and vermilion border. The oral lesions were infected by yeast in more than half the patients.

In Schiodt’s study, early lesions were characterized by erythema without striae. The classic well-developed discoid lesions appeared as an area of central erythema with white spots and a 2 to 5 mm border of white striae radiating from the center. Some lesions were white plaques, as in leukoplakia; still others had areas of Wickham’s striae, as in lichen planus, usually on a reddish base.

On microscopic examination the epithelium shows hyperkeratosis or parakeratosis or both, acanthosis, and pseudopitheliomatous hyperplasia interspersed with inflammatory cells. The epithelial membranes show undermining ulceration, acantholytic degeneration, and atrophy. The basal layer shows liquefaction degeneration, and keratin plugs can be found. A lymphocytic infiltrate, present beneath the epithelial layer, may concentrate around vessels and extend deeply into the subepithelial tissue. In some cases the microscopic study of lesions may be inconclusive. Schiodt and Pindborg\(^{38}\) completed a blind study of oral lesions from 21 patients with LE and 21 patients with oral lichen planus and leukoplakia. The correct histologic diagnosis was made in less than half the cases. In one third of the cases, differentiation could not be made between DLE and lichen planus.

**Differential Diagnosis**

Multiple lesions on several surfaces are the rule in LE. When the lesions are mostly of the red variety, conditions that should be considered are lichen planus, lichenoid drug reaction, ectopic geographic tongue, psoriasis, diffuse leukoplakia with erythroplakic components, and electrogalvanic lesions. Oral lesions of LE may be differentiated from lichen planus on the basis of immunofluorescence studies of sera and biopsy specimens (Table 6-1).

**Special Diagnostic Procedures**

**Serum findings** Antinuclear antibodies (ANA) and antibodies to specific nuclear antigens occur in patients with LE, mixed connective tissue disease (MCTD), scleroderma, and other collagen disorders. These antibodies have various specificities for nuclear antigens leading to a variety of nuclear staining patterns in immunofluorescence tests. Antibody tests include ANA, native deoxyribonucleic acid (DNA) antibodies, deoxyribonucleoprotein (DNP) antibodies, antibodies to extractable nuclear antigens (ENAs): Sm, ribonucleoprotein (RNP), SS-A (Ro), SS-B (La), SCL-70, JO-1, PCNA, KU\(^{39,40}\).

In suspected SLE, ANA tests are useful as a screen and are usually followed by tests for antibodies to native DNA and Sm, which are specific for SLE. Antibodies to RNP, Sm, SS-A (Ro), SS-B (La), and PCNA are less specific for SLE but are often useful tests because these antibodies occur in a limited number of diseases. Antibodies to SS-A (Ro) also occur in 60% of patients with subacute, cutaneous LE, in almost all patients with neonatal LE, and in two thirds of SLE patients with C\(_3\) deficiency. In addition, a majority (>60%) of SLE patients who are ANA negative are positive for SS-A (Ro) antibodies. The presence of antibodies to native DNA, Sm, and SS-A (Ro) has been associated with an increased incidence of nephritis as compared with patients who have RNP and SS-B (La) antibodies.

**Biopsy findings** The “lupus” or “IF” band immunofluorescent test is important in the diagnosis of LE. Immunoreactants detected in LE occur at the dermoepidermal junction of the skin. This test also differentiates DLE from SLE in that positive lupus band tests occur only in the lesional but not in the normal skin biopsies of patients with DLE, whereas they appear in both lesional and normal skin biopsies of SLE patients. The incidence of a
positive band test is influenced by the site's exposure to sun, its age and location, and treatment.

Management
Treatment of LE consists of the administration of systemic corticosteroids or antimalarials. Topical steroids may be used on symptomatic intraoral lesions.

RARITIES
The rare generalized red conditions are listed at the beginning of the chapter and must be considered in the differential diagnosis. Some rare conditions are illustrated in Figs. 6-15 to 6-17.

Fig. 6-15. Psoriasis (red macular areas) on palate. (From White DK, Leis HJ, Miller AS: Intraoral psoriasis associated with widespread dermal psoriasis, Oral Surg 41(2):174-181, 1976.)

Fig. 6-16. Reiter's syndrome. A, Erythema involving the sclera. B, Anterior intraoral view. Note small erythematous patches (arrows). C, View showing reddish macules on tongue. D, View of palate showing reddish patches. (Courtesy M. Lehnert, Minneapolis.)
REFERENCES


Fig. 6-17. Uremic stomatitis. Note erythematous and eroded areas on the lateral border of the tongue. (Courtesy M. Lehner, Minneapolis.)