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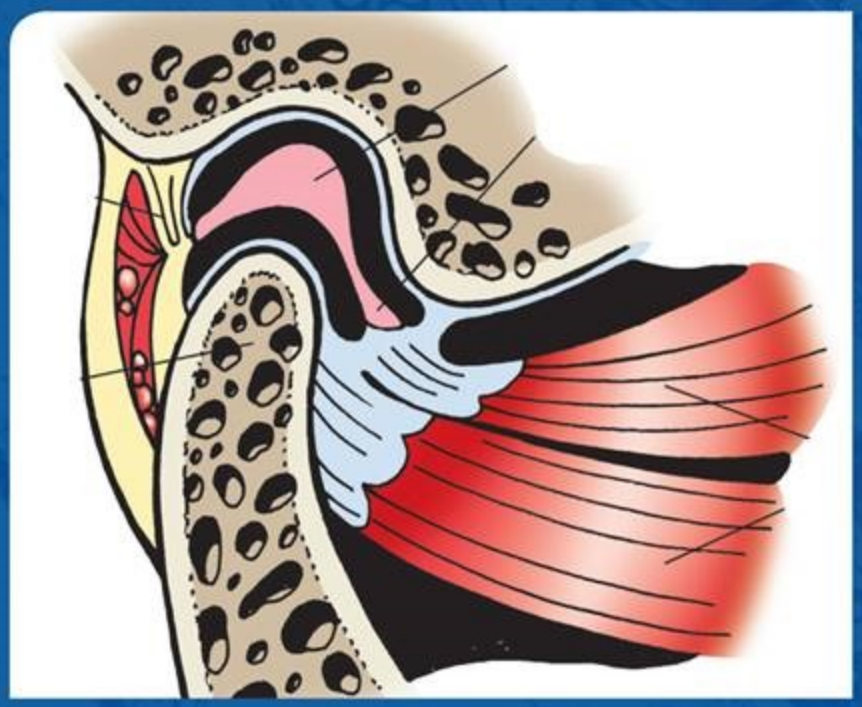
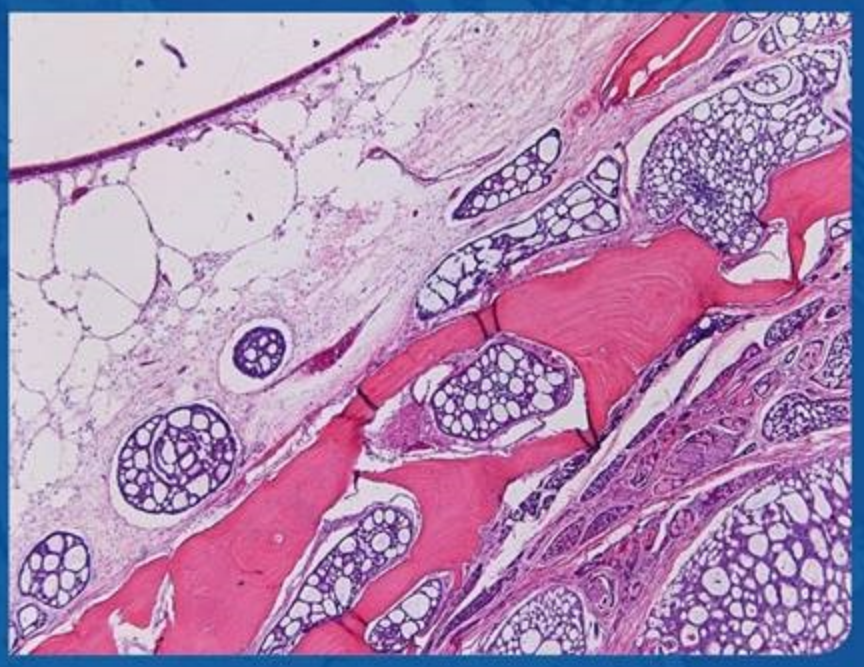
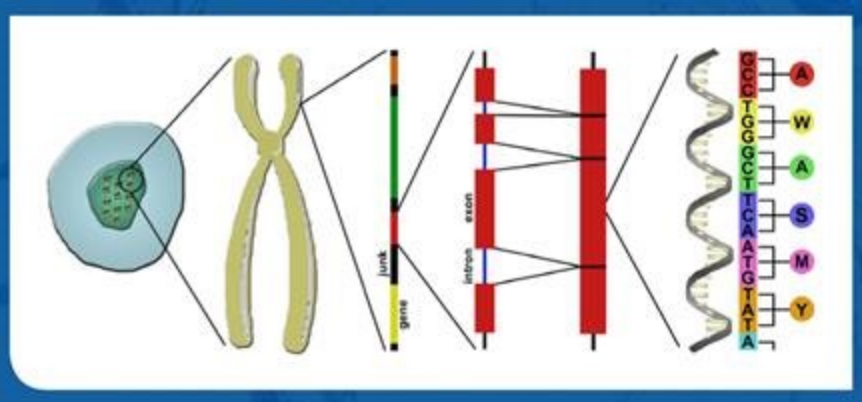
Burket's ORAL MEDICINE







Michael Glick

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12th edition

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DEDICATION

In memory of my mother, Siv Glück, who encouraged me to be the best person I could be; and my friend and colleague Jonathan Ship, whose life sadly ended much too early.
For my father, Dan Glück, with love and appreciation.

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Preface

In the introduction to the first edition of *Burket's Oral Medicine* published in 1946, Dr. Appleton, Dean of the School of Dentistry at the University of Pennsylvania, wrote "The practitioner of medicine, physician and internist, would do well to read at least the Table of Contents. If he does that, I believe he'll delve deeper. It should convince him that the mouth contains much more than the doubly unruly tongue. There are many situations and ways in which he can help the neighboring dentist, and the dentist can in turn help him. Both physician and dentist will benefit, but the patient would benefit most." Although our knowledge of oral medicine has dramatically increased in the past 70 years, this new 12th edition could have been introduced in a similar fashion. Oral medicine is at the forefront of interprofessional education and practice, and the 12th edition of *Burket's Oral Medicine* will be a resource to all health professionals.

In order to reflect changes in the reach of the discipline of oral medicine, the 12th edition of this seminal text includes five new chapters: Research Design and Evaluation, Oral Complications of Cancer Therapy, Geriatric Oral Medicine, Pediatric Oral Medicine, and Radiologic Interpretations, and 28 new contributors. Together, the more than 70 contributors of the chapters included in the 12th edition represent seven countries and present a text truly international in scope.

Due to the complexity of the "art and science" of the field of oral medicine, there will be inconsistencies among the chapters in cases in which lack of evidence for specific protocols results in reliance on clinical judgment. Such discrepancies add rather than detract from our knowledge base and, when found, were left as is.

The 12th edition of this definitive text on oral medicine delivers indispensable content to students, residents, and clinicians from many different health disciplines seeking to advance their knowledge in this exciting field of healthcare delivery. The text offers support with necessary diagnostic skills, basic research, and clinical advice needed to treat medically complex dental patients, as well as a myriad of oral complications.

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Chapter 1

Introduction to Oral Medicine and Oral Diagnosis: Evaluation of the Dental Patient

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Oral medicine is a specialized discipline within dentistry that focuses on provision of dental care for medically complex patients, and the diagnosis and management of medical disorders involving the mouth, jaws, and salivary glands. Offering care to a patient seeking diagnosis and treatment is a responsibility that entails both broad and detailed knowledge and should only be provided by a health-care professional with appropriate training and experience.

Clinicians are presently caring for an aging population who are living longer with complications of chronic illnesses and multiple comorbidities, and having endured complex surgical procedures while taking multiple medications. This population of patients requires oral health professionals with an increased knowledge of medical diseases and their effect on oral diseases and provision of oral health care. What previously was considered the purview of hospital-based dentists has become a common occurrence in general and specialty dental practice. Oral health is an integral part of total health, and oral health professionals must adapt to

[*] Deceased

these demographic changes by increasing their knowledge of medicine related to oral and dental health care.[1]

Technological advances are influencing all aspects of patient interactions, from our initial contact with a patient, through medical history taking, diagnosis, and treatment options. Electronic health records (EHRs) afford a means for sharing health information among multiple clinicians caring for the same patient and can provide point-of-care algorithms for eliciting and using health information.[2] Modern imaging techniques such as computed tomography and magnetic resonance imaging provide more detailed information but require increased interpretation skills. Technology is a means to acquire more sophisticated data but requires increased training for accurate interpretation; and yet, the most important skills for accurate diagnosis remain an experienced clinician who has developed the skills to listen and examine.

The initial encounter with a patient will influence all subsequent care. The skilled, experienced practitioner has learned to elicit the clinical, laboratory, and other necessary information required for an accurate diagnosis. Performing a diagnostic evaluation, including a patient interview and a physical examination, is an art as well as a skill. Although mastering a patient evaluation can be assisted by specific clinical protocols, the experienced practitioner will add his or her own skills to the diagnostic methodology.

A variety of accessible sources of health-care information are now readily available to patients, and many will use this information to self-diagnose, as well as demand specific treatments.[3] Although, a patient-centered approach is encouraged, in which a patient's preferences and values will influence care, the practitioner has the responsibility for treatment decisions and needs to educate the patient to make informed, scientific- and evidence-based choices.

Obtaining, evaluating, and assessing a patient's oral and overall health status is the obligation of the treating oral health-care professional. This process can arbitrarily be divided into four major overlapping parts:

1. Information gathering
2. Establishing a differential and final diagnosis
3. Formulating a plan of action
4. Initiating treatment and follow-up

INFORMATION GATHERING

An appropriate interpretation of the information collected through a medical history and patient examination achieves several important objectives; it affords an opportunity for

1. gathering the information necessary for establishing the diagnosis of the patient's chief complaint (CC)
2. assessing the influence of the patient's systemic health on patient's oral health
3. detecting underlying systemic conditions that the patient may or may not be aware of
4. providing a basis for determining whether dental treatment might affect the systemic health of the patient
5. providing a basis for determining necessary modifications to routine dental care
6. monitoring known medical conditions

Medical History

Obtaining an appropriate and accurate medical history is the *sine qua non* of all patient care. A patient's medical history is elicited through a systematic review of the patient's chief or primary complaint, a detailed history related to this complaint, information about past and present medical conditions, pertinent social and family histories, and a review of symptoms by organ system. A medical history also includes biographic and demographic data used to identify the patient.

There is no universally agreed upon method for obtaining a medical history, but a systematic approach will help the practitioner to gather all necessary information without overlooking important facts. The nature of the patient's oral health visit (i.e., initial dental visit, complex diagnostic problem, emergency, elective continuous care, or recall) often dictates how the history is obtained. The two most common means of obtaining initial patient information are a patient-self- administered preprinted health questionnaire or by recording information during a systematic health interview without the benefit of having the patient fill out a questionnaire. The use of self-administered screening questionnaires is the most commonly used method in dental settings (Figure 1-1). This technique can be useful in gathering background medical information, but the accurate diagnosis of a specific oral complaint requires a history of the present illness and other information that is necessary to obtain verbally. The challenge in any health-care setting is to use a questionnaire that has enough items to obtain the essential medical information but is not too long to deter a patient's willingness and ability to fill it out. These questionnaires should be constructed in a manner that allows the clinician to query the patient about the most essential and relevant required information yet provides a starting point for a dialogue with the patient about other pertinent information not included on the health form. Preprinted self-administered health questionnaires are readily available, standardized, and easy to administer and do not require significant "chair time." They give the clinician a starting point for a dialogue to conduct more in-depth medical queries but are restricted to the questions chosen on the form and are therefore limited in scope. The questions on the form can be misunderstood by the patient, resulting in inaccurate information, and they require a specific level of reading comprehension. Preprinted forms cover broad areas without necessarily focusing on particular problems pertinent to an individual patient's specific medical condition. Therefore, the use of these forms requires that the provider has sufficient background knowledge to understand reason for the questions on the forms. Furthermore, the

provider needs to realize that a given standard history form necessitates timely and appropriate follow-up questions, especially when positive responses have been elicited. An established routine for performing and recording the history and examination should be followed conscientiously.

The oral health-care professional has a responsibility to obtain relevant medical and dental health information, yet the patient cannot always be relied upon to know this information or provide an accurate and comprehensive assessment of his or her medical or dental status.

All medical information obtained and recorded in an oral health-care setting is considered confidential and constitutes a legal document. Although it is appropriate for the patient to fill out a history form in the waiting room, any discussion of the patient's responses must take place in a private setting. Furthermore, access to the written or electronic (if applicable) record must be limited to office personnel who are directly responsible for the patient's care. Any other release of private information should be approved, in writing, by the patient and retained by the dentist as part of the patient's medical record.

Changes in a patient's health status or medication regimen should be reviewed at each office visit prior to initiating dental care. This is important as medical status and medication regimens often change. The monitoring of patients' compliance with suggested medical treatment guidelines and prescribed medications is part of the oral health-care professional's responsibilities.[4] The following strategies are common to all methods of history taking

- review available patient information prior to meeting the patient;
- make the patient feel comfortable and pay attention to the patient's concerns; do not rush the interview process;
- pay attention to the patient; greet the patient; use the patient's name; ensure privacy; sit rather than stand; maintain eye contact as often as possible; do not concentrate chiefly on entering the information into an EHR as this may distract the clinician from listening to pertinent information;
- use the patient's own words to describe her primary reason(s) ("CC") to seek care/consultation;
- use open-ended questions that allow the patient to express herself;
- although all information should be collected in a systematic fashion, the order is not as important as is initiating a dialogue with the patient about her health;
- create a timeline of the reported patient-related events; an accurate chronology is an extremely important element to establish a causative relationship.

The medical history traditionally consists of the following subcategories:

1. *Identification*: Name, date and time of the visit, date of birth, gender, ethnicity, occupation, contact information of a primary care physician, and referral source.
2. *CC*: The main reason for the patient seeking care or consultation—recorded in the patient's own words.
3. *History of present illness*: A chronologic account of events; state of health before the presentation of the present problem; description of the first signs and symptoms and how they may have changed; description of occurrences of amelioration or exacerbation; previous clinicians consulted and prior treatment. For those who favor mnemonics, nine dimensions of a medical problem can be easily recalled using OLD CHARTS (Onset, Location/radiation, Duration, Character, Habits, Aggravating factors, Reliving factors, Timing, and Severity). (Modification of Reference 5).
4. *Medical history*: General health; childhood illnesses; major adult illnesses; immunizations; surgeries (date, reason, and outcome); pregnancies (gravid); births (para); medications (prescribed medications, over-the-counter medications, supplements, and home remedies); and allergies.
5. *Family history*: Blood relatives with illnesses similar to the patient's concern; specific genetic disorders, cardiovascular diseases, diabetes mellitus, different types of cancers.
6. *Personal and social history*: Birthplace; marital status; children; habits (tobacco use, alcohol use, recreational drug use); sexual history; occupation; religious preferences that may have an impact on types of care.
7. *Review of systems (ROS)*: Identifies symptoms in different body systems (Table 1-1).

The ROS is a comprehensive and systematic review of subjective symptoms affecting different bodily systems. It is an essential component for identifying patients with an undiagnosed disease that will affect dental treatment or associated symptoms that will help determine the primary diagnosis; for example, identifying a patient with skin, genital, or conjunctival lesions who also has oral mucosal disease or a patient with anesthesia, parasthesia, or weakness who also complaints of orofacial pain. The clinician records both negative and positive responses. Direct questioning of the patient should be aimed at collecting additional data to assess the severity of a patient's medical conditions, monitor changes in medical conditions, and assist in confirming or ruling out those disease processes that may be associated with a patient's symptoms.

Patient Examination

The examination of the patient represents the second stage of the evaluation and assessment process. An established routine for examination decreases the possibility of overlooking undiscovered pathologic conditions. The examination is most conveniently carried out with the patient seated in a dental chair, with the head supported. When dental charting is involved,

FIGURE 1-1 Health history questionnaire.

Health History Form

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Email: Today's Date:

As required by law, our office adheres to written policies and procedures to protect the privacy of information about you that we create, receive or maintain. Your answers are for our records only and will be kept confidential subject to applicable laws. Please note that you will be asked some questions about your responses to this questionnaire and there may be additional questions concerning your health. This information is vital to allow us to provide appropriate care for you. This office does not use this information to discriminate.

Name: *Last* *First* *Middle* | Home Phone: *Include area code* ( ) | Business/Cell Phone: *Include area code* ( )

Address: *Mailing address* | City: | State: | Zip:

Occupation: | Height: | Weight: | Date of Birth: | Sex: M F

SS# or Patient ID: | Emergency Contact: | Relationship: | Home Phone: *Include area code* ( ) | Cell Phone: *Include area code* ( )

If you are completing this form for another person, what is your relationship to that person?

Your Name *Relationship*

Do you have any of the following diseases or problems: *(Check DK if you Don't Know the answer to the the question)*

	Yes	No	DK
Active Tuberculosis	☐	☐	☐
Persistent cough greater than a 3 week duration	☐	☐	☐
Cough that produces blood	☐	☐	☐
Been exposed to anyone with tuberculosis	☐	☐	☐

If you answer yes to any of the 4 items above, please stop and return this form to the receptionist.

Dental Information *For the following questions, please mark (X) your responses to the following questions.*

	Yes	No	DK
Do your gums bleed when you brush or floss?	☐	☐	☐
Are your teeth sensitive to cold, hot, sweets or pressure?	☐	☐	☐
Is your mouth dry?	☐	☐	☐
Have you had any periodontal (gum) treatments?	☐	☐	☐
Have you ever had orthodontic (braces) treatment?	☐	☐	☐
Have you had any problems associated with previous dental treatment?	☐	☐	☐
Is your home water supply fluoridated?	☐	☐	☐
Do you drink bottled or filtered water?	☐	☐	☐

If yes, how often? *Circle one:* DAILY / WEEKLY / OCCASIONALLY

Are you currently experiencing dental pain or discomfort?	☐	☐	☐

	Yes	No	DK
Do you have earaches or neck pains?	☐	☐	☐
Do you have any clicking, popping or discomfort in the jaw?	☐	☐	☐
Do you brux or grind your teeth?	☐	☐	☐
Do you have sores or ulcers in your mouth?	☐	☐	☐
Do you wear dentures or partials?	☐	☐	☐
Do you participate in active recreational activities?	☐	☐	☐
Have you ever had a serious injury to your head or mouth?	☐	☐	☐

Date of your last dental exam:
What was done at that time?

Date of last dental x-rays:

What is the reason for your dental visit today?

How do you feel about your smile?

Medical Information *Please mark (X) your response to indicate if you have or have not had any of the following diseases or problems.*

	Yes	No	DK
Are you now under the care of a physician?	☐	☐	☐

Physician Name: Phone: *Include area code* ( )

Address/City/State/Zip:

Are you in good health?	☐	☐	☐
Has there been any change in your general health within the past year?	☐	☐	☐

If yes, what condition is being treated?

Date of last physical exam:

	Yes	No	DK
Have you had a serious illness, operation or been hospitalized in the past 5 years?	☐	☐	☐

If yes, what was the illness or problem?

Are you taking or have you recently taken any prescription or over the counter medicine(s)?	☐	☐	☐

If so, please list all, including vitamins, natural or herbal preparations and/or dietary supplements:

Medical Information

Please mark (X) your response to indicate if you have or have not had any of the following diseases or problems.

(Check DK if you Don't Know the answer to the question)

	Yes	No	DK
Do you wear contact lenses?	☐	☐	☐
Joint Replacement. Have you had an orthopedic total joint (hip, knee, elbow, finger) replacement?	☐	☐	☐
Date: _____ If yes, have you had any complications? _____			
Are you taking or scheduled to begin taking an antiresorptive agent (like Fosamax®, Actonel®, Atelvia, Boniva®, Reclast, Prolia) for osteoporosis or Paget's disease?	☐	☐	☐
Since 2001, were you treated or are you presently scheduled to begin treatment with an antiresorptive agent (like Aredia®, Zometa®, XGEVA) for bone pain, hypercalcemia or skeletal complications resulting from Paget's disease, multiple myeloma or metastatic cancer?	☐	☐	☐
Date Treatment began: _____			

	Yes	No	DK
Do you use controlled substances (drugs)?	☐	☐	☐
Do you use tobacco (smoking, snuff, chew, bidis)?	☐	☐	☐
If so, how interested are you in stopping? *Circle one:* VERY / SOMEWHAT / NOT INTERESTED			
Do you drink alcoholic beverages?	☐	☐	☐
If yes, how much alcohol did you drink in the last 24 hours? _____			
If yes, how much do you typically drink i n a week? _____			
WOMEN ONLY Are you:			
Pregnant?	☐	☐	☐
Number of weeks: _____			
Taking birth control pills or hormonal replacement?	☐	☐	☐
Nursing?	☐	☐	☐

Allergies. Are you allergic to or have you had a reaction to:
To all **yes** responses, specify type of reaction.

	Yes	No	DK
Local anesthetics _____	☐	☐	☐
Aspirin _____	☐	☐	☐
Penicillin or other antibiotics _____	☐	☐	☐
Barbiturates, sedatives, or sleeping pills _____	☐	☐	☐
Sulfa drugs _____	☐	☐	☐
Codeine or other narcotics _____	☐	☐	☐
Metals _____	☐	☐	☐
Latex (rubber) _____	☐	☐	☐
Iodine _____	☐	☐	☐
Hay fever/seasonal _____	☐	☐	☐
Animals _____	☐	☐	☐
Food _____	☐	☐	☐
Other _____	☐	☐	☐

Please mark (X) your response to indicate if you have or have not had any of the following diseases or problems.

	Yes	No	DK
Artificial (prosthetic) heart valve	☐	☐	☐
Previous infective endocarditis	☐	☐	☐
Damaged valves in transplanted heart	☐	☐	☐
Congenital heart disease (CHD)			
Unrepaired, cyanotic CHD	☐	☐	☐
Repaired (completely) in last 6 months	☐	☐	☐
Repaired CHD with residual defects	☐	☐	☐

Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD.

	Yes	No	DK
Cardiovascular disease	☐	☐	☐
Angina	☐	☐	☐
Arteriosclerosis	☐	☐	☐
Congestive heart failure	☐	☐	☐
Damaged heart valves	☐	☐	☐
Heart attack	☐	☐	☐
Heart murmur	☐	☐	☐
Low blood pressure	☐	☐	☐
High blood pressure	☐	☐	☐
Other congenital heart defects	☐	☐	☐
Mitral valve prolapse	☐	☐	☐
Pacemaker	☐	☐	☐
Rheumatic fever	☐	☐	☐
Rheumatic heart disease	☐	☐	☐
Abnormal bleeding	☐	☐	☐
Anemia	☐	☐	☐
Blood transfusion If yes, date: _____	☐	☐	☐
Hemophilia	☐	☐	☐
AIDS or HIV infection	☐	☐	☐
Arthritis	☐	☐	☐

	Yes	No	DK
Autoimmune disease	☐	☐	☐
Rheumatoid arthritis	☐	☐	☐
Systemic lupus erythematosus	☐	☐	☐
Asthma	☐	☐	☐
Bronchitis	☐	☐	☐
Emphysema	☐	☐	☐
Sinus trouble	☐	☐	☐
Tuberculosis	☐	☐	☐
Cancer/Chemotherapy/ Radiation Treatment	☐	☐	☐
Chest pain upon exertion	☐	☐	☐
Chronic pain	☐	☐	☐
Diabetes Type I or II	☐	☐	☐
Eating disorder	☐	☐	☐
Malnutrition	☐	☐	☐
Gastrointestinal disease	☐	☐	☐
G.E. Reflux/persistent heartburn	☐	☐	☐
Ulcers	☐	☐	☐
Thyroid problems	☐	☐	☐
Stroke	☐	☐	☐

	Yes	No	DK
Glaucoma	☐	☐	☐
Hepatitis, jaundice or liver disease	☐	☐	☐
Epilepsy	☐	☐	☐
Fainting spells or seizures	☐	☐	☐
Neurological disorders If yes, specify: _____	☐	☐	☐
Sleep disorder	☐	☐	☐
Do you snore?	☐	☐	☐
Mental health disorders Specify: _____	☐	☐	☐
Recurrent Infections Type of infection: _____	☐	☐	☐
Kidney problems	☐	☐	☐
Night sweats	☐	☐	☐
Osteoporosis	☐	☐	☐
Persistent swollen glands in neck	☐	☐	☐
Severe headaches/ migraines	☐	☐	☐
Severe or rapid weight loss	☐	☐	☐
Sexually transmitted disease	☐	☐	☐
Excessive urination	☐	☐	☐

	Yes	No	DK
Has a physician or previous dentist recommended that you take antibiotics prior to your dental treatment?	☐	☐	☐

Name of physician or dentist making recommendation: _____ Phone: *Include area code* ( )

	Yes	No	DK
Do you have any disease, condition, or problem not listed above that you think I should know about?	☐	☐	☐

Please explain: _____

NOTE: Both doctor and patient are encouraged to discuss any and all relevant patient health issues prior to treatment.
I certify that I have read and understand the above and that the information given on this form is accurate. I understand the importance of a truthful health history and that my dentist and his/her staff will rely on this information for treating me. I acknowledge that my questions, if any, about inquiries set forth above have been answered to my satisfaction. I will not hold my dentist, or any other member of his/her staff, responsible for any action they take or do not take because of errors or omissions that I may have made in the completion of this form.

Signature of Patient/Legal Guardian: _____ Date: _____

Signature of Dentist: _____ Date: _____

FOR COMPLETION BY DENTIST

Comments: _____

Table 1-1 Review of Systems Is a Systematic Approach to Ascertain Mostly Subjective Symptoms Associated With the Different Body Systems

General: Weight changes, malaise fatigue, night sweats
Head: Headaches, tenderness, sinus problems
Eyes: Changes in vision, photophobia, blurring, diplopia, spots, discharge
Ears: Hearing changes, tinnitus, pain, discharge, vertigo
Nose: Epistaxis, obstructions
Throat: Hoarseness, soreness
Respiratory: Chest pain, wheezing, dyspnea, cough, hemoptysis
Cardiovascular: Chest pain, dyspnea, orthopnea (number of pillows needed to sleep comfortably), edema, claudication
Dermatologic: Rashes, pruritus, lesions, skin cancer (epidermoid carcinoma, melanoma)
Gastrointestinal: Changes in appetite, dysphagia, nausea, vomiting, hematemesis, indigestion, pain, diarrhea, constipation, melena, hematochezia, bloating, hemorrhoids, jaundice
Genitourinary: Changes in urinary frequency or urgency, dysuria, hematuria, nocturia, incontinence, discharge, impotence
Gynecologic: Menstrual changes (frequency, duration, flow, last menstrual period), dysmenorrhea, menopause
Endocrine: Polyuria, polydipsia, polyphagia, temperature intolerance, pigmentations
Musculoskeletal: Muscle and joint pain, deformities, joint swellings, spasms, changes in range of motion
Hematologic: Easy bruising, epistaxis, spontaneous gingival bleeding, increased bleeding after trauma
Lymphatic: Swollen or enlarged lymph nodes
Neuropsychiatric: Syncope, seizures, weakness (unilateral and bilateral), changes in coordination, sensations, memory, mood, or sleep pattern, emotional disturbances, history of psychiatric therapy

having an assistant record the findings saves time and limits cross-contamination. Before seating the patient, the clinician should observe the patient's general appearance and gait and should note any physical deformities or impediments.

The routine oral examination should be carried out at least once annually or at each recall visit. This includes a thorough inspection and, when appropriate, palpation, auscultation, and percussion of the exposed surface structures of the head, neck, and face and a detailed examination of the oral cavity, dentition, oropharynx, and adnexal structures. Laboratory studies and additional special examination of other organ systems may be required for the evaluation of patients with orofacial pain, oral mucosal disease, or signs and symptoms suggestive of otorhinologic or salivary gland disorders or pathologies suggestive of a systemic etiology. A less comprehensive but equally thorough inspection of the face and oral and oropharyngeal mucosae should be carried out at each dental visit. The tendency for the oral health professional to focus on only the tooth or jaw quadrant in question should be strongly resisted.

Each visit should be initiated by a deliberate inspection of the entire face and oral cavity prior to the scheduled or emergency procedure. The importance of this approach in the early detection of head and neck cancer and in promoting the image of the dentist as the responsible clinician of the oral cavity cannot be overstated (see Chapter 8, "Oral and Oropharyngeal Cancer").

Examination carried out in the dental office is traditionally restricted to that of the superficial tissues of the oral cavity, head, and neck and the exposed parts of the extremities. On occasion, evaluation of an oral lesion logically leads to an inquiry about similar lesions on other skin or mucosal surfaces or about the enlargement of other regional groups of lymph nodes. Although these inquiries can usually be satisfied directly by questioning the patient, the oral health professional may also quite appropriately request permission from the patient to examine axillary nodes or other skin surfaces provided that the examination is carried out competently and there is adequate privacy for the patient. A male oral health professional should have a female assistant present in the case of a female patient; a female oral health professional should have a male assistant present in the case of a male patient. Similar precautions should be followed when it is necessary for a patient to remove tight clothing for accurate measurement of blood pressure. A complete physical examination should not be attempted when facilities are lacking or when religious or other customs prohibit it.

The degree of responsibility accorded to the oral health professional in carrying out a complete physical examination varies from institution to institution, hospital to hospital, state to state, and country to country.

The examination procedure in a dental office setting includes five areas:

1. Registration of vital signs (respiratory rate, temperature, pain level, pulse, and blood pressure)
2. Examination of the head, neck, and oral cavity, including salivary glands, temporomandibular joints, and head and neck lymph nodes
3. Examination of cranial nerve function
4. Special examination of other organ systems
5. Requisition of appropriate laboratory studies

Consultations

Consultations with other health-care professionals are initiated when additional information is necessary to assess a patient's health status. Consent from the patient is needed before a consultation is initiated.[6] All verbal and written consultation should be documented in the patient's record. A consultation letter should identify the patient and contain a brief overview of the patient's pertinent medical history and a request for specific medical information (Figure 1-2). A physician cannot "clear" a patient for treatment.[7]

A physician's advice and recommendation may be helpful in managing a dental patient, but the responsibility to provide safe and appropriate care lies ultimately with the oral health-care provider.

Patients for whom a dentist may need to obtain medical consultation include (1) the patient with known medical problems who is scheduled for either inpatient or outpatient dental treatment and cannot adequately describe all of his or her medical problems; (2) the patient in whom abnormalities are detected during history taking, on physical examination, or through a laboratory study of which the patient is not aware; (3) the patient who has a high risk for the development of particular medical problems; and (4) the patient for whom additional medical information is required that may impact the provision of dental care or assist in the diagnosis of an orofacial problem.

When there is a need for a specific consultation, the consultant should be selected for appropriateness to the particular problem, and the problem and the specific questions to be answered should be clearly transmitted to the consultant in writing. Adequate details of the planned dental procedure, including, when appropriate, expected amount of bleeding; an assessment of time and stress to the patient; expected period of posttreatment disability; and details of the particular symptom, sign, or laboratory abnormality that gave rise to the consultation should be provided to the consultant. The written request should be brief and should specify the particular concern and items of information needed from the consultant. Importantly, requests for "medical clearance" should be avoided.[7]

ESTABLISHING A DIFFERENTIAL AND FINAL DIAGNOSIS

Before establishing a final diagnosis in the orofacial region, the oral health-care professional often needs to formulate a differential diagnosis based on the history and physical examination findings. The disorders included in the differential diagnosis will determine which laboratory tests, such as biopsies, blood tests, or imaging studies, are required to reach a final diagnosis.

The rapidity and accuracy with which a diagnosis or set of diagnoses can be achieved depends on the history and examination data that have been collected and on the clinician's knowledge and ability to match these clinical data with

Consultation

Date: February 26, 2007

To: John Doc, MD

From: Martin Dent, DMD

Patient name and DOB: Oscar Jones; DOB – February 1, 1945

Summary and request:

A 62-year-old African American man presents to our dental office for multiple extractions. This is a very stressful procedure with anticipated bleeding from multiple intraoral sites. Local anesthesia will be used and will include 3.6–7.2 mL of 2% lidocaine with 1:100,000 concentration of epinephrine.

Examination revealed a slightly overweight male in no apparent distress. His BP was 172/100 mm Hg, with a pulse of 65 beats/min with regular rate and rhythm.

His medical history is remarkable for multiple medical problems, including hypertension ×20 years; multiple angina attacks, the last one in 1998; reported history of renal disease; and multiple medications.

Review of systems is remarkable for polyurea, polydipsia, and occasional shortness of breath at rest.

Please advise as to the patient's hypertensive control, stable versus unstable angina, any other type of cardiovascular diseases or target organ damage, type and severity of renal disease, possible diabetes mellitus, and types and regimen of medications.

Patient signature and date:

_____

Oral health-care professional signature and date:

_____

Please return this consultation to:

_____

FIGURE 1-2 Consultation.

suspected disease processes. Experienced clinicians who have an extensive knowledge of human physiology, disease etiology, and a broad knowledge of the relevant literature can usually rapidly establish a correct diagnosis. Such "mental models" of disease syndromes also increase the efficiency with which experienced clinicians gather and evaluate clinical data and focus supplemental questioning and testing at all stages of the diagnostic process.

For effective treatment, as well as for health insurance and medicolegal reasons, it is important that a diagnosis (or diagnostic summary) is entered into the patient's record after the detailed history and physical, radiographic, and laboratory examination data. When more than one health problem is identified, the diagnosis for the primary complaint (i.e., the stated problem for which the patient sought medical or dental advice) is usually listed first, followed by subsidiary diagnoses of concurrent problems. Previously diagnosed conditions that remain as actual or potential problems are also included, with the qualification "by history," "previously diagnosed," or "treated" to indicate their status. Problems that were identified but not clearly diagnosed during the current evaluation can also be listed with the comment "to be ruled out." Because oral medicine is concerned with regional problems that may or may not be modified by concurrent systemic disease, it is common for the list of diagnoses to include both oral lesions and systemic problems of actual or potential significance in the etiology or management of oral lesions. Items in the medical history that do not relate to the current problem and that are not of major health significance usually are not included in the diagnostic summary. For example, a diagnosis might read as follows:

1. Alveolar abscess, mandibular left first molar
2. Rampant generalized dental caries secondary to radiation-induced salivary hypofunction
3. Carcinoma of the tonsillar fossa, by history, excised and treated with 65 Gy two years ago
4. Cirrhosis and prolonged prothrombin time, by history
5. Hyperglycemia; R/O (rule out) diabetes

A definite diagnosis cannot always be made, despite a careful review of all history, clinical, and laboratory data. In such cases, a descriptive term (rather than a formal diagnosis) may be used for the patient's symptoms or lesion, with the added word "idiopathic," "unexplained," or (in the case of symptoms without apparent physical abnormality) "functional" or "symptomatic." The clinician must decide what terminology to use in conversing with the patient and whether to clearly identify this diagnosis as "undetermined." Irrespective of that decision, it is important to recognize the equivocal nature of the patient's problem and to schedule additional evaluation, by referral to another consultant, additional testing, or placement of the patient on recall for follow-up studies.

Unfortunately, there is no generally accepted system for identifying and classifying diseases, and diagnoses are often written with concerns related to third-party reimbursement and medicolegal and local peer review, as well as for the purpose of accurately describing and communicating the patient's disease status. Within different specialties, attempts have been made to achieve conformity of professional expressions and language.

Some standardization of diagnoses has been achieved in the United States as a result of the introduction in 1983 of the diagnosis-related group (DRG) system as an obligatory cost-containment measure for the reimbursement of hospitals for inpatient care. In August 2006, the Centers for Medicare and Medicaid Services (CMS) issued a final ruling that initiated a transition plan for replacing, at the time, existing CMS DRGs with a classification methodology that more accurately reflects a patient's severity of disease. Beyond cost containment, patient grouping classifications also are used for epidemiologic monitoring, clinical management, and comparison of hospital activity and as a prospective payment system. Yet, groupings are mostly based on medical diagnoses, such as the *International Classification of Diseases, Tenth Revision* (ICD-10).[8] ICD-11 is expected to be available in 2017.

Although scientifically derived, the DRG system is designed for fiscal use rather than as a system for the accurate classification of disease. It also emphasizes procedures rather than diseases and has a number of serious flaws in its classification and coding system. The ICD system, by contrast, was developed from attempts at establishing an internationally accepted list of causes of death and has undergone numerous revisions in the past 160 years, related to the various emphases placed on clinical, anatomic, biochemical, and perceived etiologic classification of disease at different times and different locations. There is still no official set of operational criteria for assigning the various diagnoses included in the ICD. In addition, the categories for symptoms, lesions, and procedures applicable to oral cavity conditions are limited and often outdated. Medicare and other third-party reimbursers are usually concerned only with diagnoses of those conditions that were actively diagnosed or treated at a given visit; concurrent problems not specifically addressed at that visit are omitted from the reimbursement diagnosis, even if they are of major health significance. The clinician, therefore, must address a number of concerns in formulating a diagnosis, selecting appropriate language for recording diagnoses on the chart, and documenting requests for third-party reimbursement.

The patient (or, when appropriate, a responsible family member or guardian) should also be informed of the diagnosis, as well as the results of the examinations and tests carried out. Because patients' anxieties frequently emphasize the possibility of a potentially serious diagnosis, it is important to point out (when the facts allow) that the biopsy specimen revealed no evidence of a malignant growth, the blood test revealed no abnormality, and no evidence of diseases, such as diabetes, anemia, leukemia, or other cancer, was found. Equally important is the necessity to explain to the patient the nature, significance, and treatment of any lesion or disease that has been diagnosed.

Medical risk assessment of patients before dental treatment offers the opportunity for greatly improving dental services for patients with compromised health. It does require considerably more clinical training and understanding of the natural history and clinical features of systemic disease processes than have been customarily taught in predoctoral dental education programs[9]; however, a partial solution to this problem has been achieved through undergraduate assignments in hospital dentistry and (most important) through hospital-based dental general practice dentistry, oral medicine, and oral and maxillofacial surgery residency programs. It is hoped that revisions in dental predoctoral curricula will recognize this need and provide greater emphasis on both the pathophysiology of systemic disease and the practical clinical evaluation and management of medically complex patients in the dental student's program.

FORMULATING A PLAN OF ACTION

Medical Risk Assessment

The information gathering described above is also designed to help the oral health professional (1) recognize a general health status that may affect dental treatment; (2) make informed judgments on the risk of dental procedures; and (3) identify the need for medical consultation to provide assistance in diagnosing or treating systemic disease that may be an etiologic factor in oral disease or that is likely to be worsened by the proposed dental treatment. The end point of the diagnostic process and the formulation of a plan of action is usually not a simple process. To minimize any adverse events, an assessment of any special risks associated with a patient's compromised medical status that could be triggered by the planned anesthetic, diagnostic, or medical or surgical treatment procedure must be entered in the patient record—usually as an addendum to the plan of treatment. This process of medical risk assessment is the responsibility of all clinicians prior to initiating any treatment or intervention and applies to outpatient and inpatient situations.

A routine of initial history taking and physical examination is essential for all dental patients as even the apparently healthy patient may on evaluation be found to have a history or examination findings of sufficient significance to cause the oral health professional to modify the plan of treatment, change a medication, or even defer a particular intervention until additional diagnostic data are available. To respect the familiar medical axiom *primum non nocere* (first, do no harm), all procedures carried out and all prescriptions given to a patient should be preceded by the oral health professional's conscious consideration of the risk of the particular procedure. Establishing a formal medical risk assessment ensures a continuous evaluation process by the clinician. A summary of the medical risk assessment, delineating potential risks to the patient due to the proposed plan of action, should be entered in the patient record.

The oral health professional traditionally arrives at a decision for or against dental treatment for a medically complex patient by requesting the patient's physician to "clear the patient for dental care." Unfortunately, in many cases, the physician is provided with little information about the nature of the proposed dental treatment (type of treatment, amount of local anesthetics, anticipated bleeding, etc.) and may have insufficient data (other than personal experience with dental care) on which to judge the stress (physical or psychological) likely to be associated with the proposed dental treatment. The response of a given patient to specific dental interventions may also be unpredictable, particularly when the patient has a number of comorbidities and is taking multiple medications. In addition, the practitioner identified by the patient as her physician may not have adequate or complete data from all previous medical evaluations—a requisite to make an informed judgment on the patient's likely response to dental care. All too frequently, the oral health professional receives the brief comment "OK for dental care," which suggests that a recommendation for safe dental care is often given casually and subjectively rather than being based on objective physiologic data. As mentioned earlier, another health professional cannot from a legal standpoint "clear" a patient for any dental procedure.[7]

More importantly, the practice of having the patient "cleared" for dental care confuses the issue of responsibility for untoward events occurring during dental treatment. Although the dentist often must rely on the physician or a consultant for expert diagnostic information and for an opinion about the advisability of dental treatment or the need for special precautions, the oral health professional retains the primary responsibility for the procedures actually carried out and for the immediate management of any unexpected or unfavorable complication, that is, the safety of the patient. The oral health professional is most familiar with the procedures she is carrying out, as well as with their likely complications, but the oral health professional must also be able to assess a patient for medical or other problems that are likely to set the stage for the development of complications. Therefore, physicians can only advise on what types of modifications are necessary to treat a patient; it is ultimately the responsibility of the treating oral health-care professional to ensure a patient's safety.

Numerous protocols have been proposed to facilitate efficient and accurate preoperative assessment of medical risk.[10–12] Many of the earlier guides were developed for the assessment of risks associated with general anesthesia or major surgery and focus on mortality as the dependent variable; guides for the assessment of hazards associated with dental or oral surgical procedures performed under local or regional anesthesia usually take the same approach. Of these, the most commonly used is the American Society of Anesthesiologists (ASA) Physical Scoring System (Table 1-2).[13] Although scores such as the ASA classification are commonly included in the preoperative evaluation of patients admitted to hospitals for

Table 1-2	American Society of Anesthesiologists' Physical Status Classification
P1	A normal healthy person
P2	A patient with a mild disease
P3	A patient with a severe systemic disease that limits activity but is not incapacitating
P4	A patient with an incapacitating systemic disease that is a constant threat to life
P5	A moribund patient who is not expected to survive without the operation
P6	A declared brain-dead patient whose organs are being removed for donor purposes

In the event of an emergency, precede the number with an "e."
Adapted from American Society of Anesthesiologists.[22]

dental surgery, they use relatively broad risk categories, and their applicability to both inpatient and outpatient dental procedures is limited. Furthermore, in medicine, the ASA score is used to assess a patient's ability to tolerate general anesthesia and should not be used to predict complications associated with the actual surgery. Thus, using an ASA score for medical risk assessment in a dental setting is not appropriate. The validity of preanesthetic risk assessment has also been questioned by several authors in light of data, suggesting that the "demonstrable competence" of the anesthetist can also be a significant factor in anesthetic outcome.[14]

A more appropriate medical assessment for dental care, the Medical Complexity Status (MCS), was specifically developed for dental patients and has been used successfully for patients with medical problems ranging from nonsignificant to very complex diseases and conditions.[11] The MCS protocol is based on the premise that very few complications will arise during provision of routine dental care in an outpatient setting to patients with stable or controlled medical conditions. However, modification of dental care may be still necessary and should be based on the level of the anticipated complication. The MCS classification and protocol, with examples, are described in more detail in Table 1-3.

Modification of Dental Care for Medically Complex Patients

In this book, many different medical conditions are discussed, and protocols for the modification of dental care are suggested. Yet the assessment of risk to any medically complex patient follows similar guidelines. It is helpful to focus on the following three questions, which will change according to the severity of the underlying disease or condition:

1. What is the likelihood that the patient will experience an adverse event due to dental treatment?
2. What is the nature and severity of the potential adverse event?
3. What is the most appropriate setting in which to treat the patient?

Each of these questions can be subdivided into smaller entities, which will facilitate the assessment of the patient.

The four major concerns that must be addressed when assessing the likelihood of the patient experiencing an adverse event are as follows:

1. Possible impaired hemostasis
2. Possible susceptibility to infections
3. Drug actions and drug interactions
4. The patient's ability to withstand the stress and trauma of the dental procedure

Patients are designated to a MCS category at their initial dental visit, which may be modified during subsequent visits according to patients' changing medical status. Based on several critical items—MCS category, experience of the oral health-care professional, the patient's ability to tolerate dental care, adequacy of the dental facility—a determination of where the patient is best treated should be made: (1) a non-hospital-based outpatient setting; (2) a hospital-based outpatient setting; (3) an inpatient short-procedure unit setting; or (4) an inpatient operating room setting. Most medically complex patients can be safely treated when the aforementioned factors have been addressed.

The diagnostic procedures (obtaining and recording the patient's medical history, examining the patient, establishing a differential diagnosis, acquiring the additional information required to make a final diagnosis, such as relevant laboratory and imaging studies and consultations from other clinicians) outlined in the preceding pages are designed to assist the oral health-care professional in establishing a plan of treatment directed at those disease processes that have been identified as responsible for the patient's symptoms. A plan of treatment of this type, which is directed at the causes of the patient's symptoms rather than at the symptoms themselves, is often referred to as rational, scientific, or definitive (in contrast to symptomatic, which denotes a treatment plan directed at the relief of symptoms, irrespective of their causes).

The plan of treatment (similar to the diagnostic summary) should be entered in the patient's record and explained to the patient in detail. This encompasses the procedure, chances for cure (prognosis), complications and side effects, and required time and expense. As initially formulated, the plan of treatment usually lists recommended procedures for the control of current disease as well as preventive measures designed to limit the recurrence or progression of the disease process over time. For medicolegal reasons, the treatment that is most likely to eradicate the disease and preserve as much function as possible (i.e., the ideal treatment) is usually entered in the chart, even if the clinician realizes that compromises may be necessary to obtain the patient's consent to treatment. It is also unreasonable for the clinician to prejudge a patient's decision as to how much time, energy, and expense should be expended on treating the patient's disease or how much discomfort and pain the patient is willing to tolerate in achieving a cure. Patient involvement in deciding the final treatment plan is highly suggested to achieve a satisfactory outcome. Such an approach has been promulgated by the Institute of Medicine as "patient-centered care" and is defined as

Table 1-3 Medical Complexity Status Classification and Protocol

Major categories
MCS 0 Patients with no medical problems
MCS 1 Patients with controlled or stable medical conditions
MCS 2 Patients with uncontrolled or unstable medical conditions
MCS 3 Patients with medical conditions associated with acute exacerbation, resulting in high risk of mortality
Subcategories
A. No anticipated complications
B. Minor complications are anticipated. "Minor complications" are defined as complications that can be successfully addressed in the dental chair.
C. Major complications are anticipated. "Major complications" are defined as complications that should be addressed by a medical provider and may sometimes require a hospital setting.
Examples of different MCS categories
MCS–0
A healthy patient
MCS–1A
A patient with controlled hypertension (No modifications to routine dental care are necessary.)
MCS–1B
A patient with epilepsy (petite mal) that is controlled with medications (The patient's epilepsy status is controlled, but if the patient has a seizure, it will pass without any interventions from the oral health-care practitioner. It would be pertinent to avoid any dental treatment that may bring about a seizure.)
MCS–1C
A patient with a penicillin allergy (The allergy will not change a stable condition, but if penicillin is given, a major complication may ensue.)
MCS–2A
A patient with hypertension and a blood pressure of 150/95 mm Hg but without any target organ disease (see Chapter 15, "Diseases of the Cardiovascular System") (The patient's hypertension is by definition not controlled, i.e., above 140/90 mm Hg. Yet this level of blood pressure, in an otherwise healthy patient, does not justify instituting any dental treatment modifications.)
MCS–2B (see Chapter 23, "Diabetes Mellitus and Endocrine Diseases")
A patient with diabetes mellitus and a glycosylated hemoglobin of 11% (Because of the patient's poor long-term glycemic control, the patient may be more susceptible to infections and poor wound healing. Dental modifications, such as possible antibiotics before a surgical procedure, may be indicated.)
MCS–2C
A patient with uncompensated congestive heart failure (Because of the patient's compromised medical condition, it is important to avoid placing the patient in a supine position in the dental chair as this may induce severe respiratory problems for the patient.)
MCS–3
A patient with unstable angina

"Providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions."[15]

The plan of treatment may be itemized according to the components of the diagnostic summary and is usually written prominently in the patient record to serve as a guide for the scheduling of further treatment visits. If the plan is complex or if there are reasonable treatment alternatives, a copy should also be given to the patient to allow consideration of the various implications of the plan of treatment he or she has been asked to agree to. Modifications of the ideal plan of treatment, agreed on by patient and clinician, should also be entered in the chart, together with a signed disclaimer from the patient if the modified plan of treatment is likely to be significantly less effective or unlikely to eradicate a major health problem.

Monitoring and Evaluating Underlying Medical Conditions

Several major medical conditions can be monitored by oral health-care personnel.[16,17] Signs and symptoms of systemic conditions, the types of medications taken, and the patient's compliance with medications can reveal how well a patient's underlying medical condition is being controlled. Signs of medical conditions are elicited by physical examination, which includes measurements of blood pressure and pulse

and laboratory or other diagnostic evaluations. Symptoms are elicited through a ROS, whereby subjective symptoms that may indicate changes in a patient's medical status are ascertained. A list of the patient's present medications, changes in medications and daily doses, and a record of the patient's compliance with medications usually provide a good indicator of how a medical condition is being managed. The combined information on signs, symptoms, and medications is ultimately used to determine the level of control and status of the patient's medical condition.

ORAL MEDICINE CONSULTATIONS

Both custom and health insurance reimbursement systems recognize the need of individual practitioners to request the assistance of a colleague who may have more experience with the treatment of a particular clinical problem or who has received advanced training in a medical or dental specialty pertinent to the patient's problem. However, this practice of specialist consultation is usually limited to defined problems, with the expectation that the patient will return to the referring primary care clinician once the nature of the problem has been identified (diagnostic consultation) and appropriate treatment has been prescribed or performed (consultation for diagnosis and treatment).

There are three categories of oral medicine consultations:

1. Diagnosis and nonsurgical treatment of orofacial problems. This includes oral mucosal disease, temporomandibular and myofascial dysfunction, chronic jaw and facial pain, dental anomalies and jaw bone lesions, salivary hypofunction and other salivary gland disorders, and disorders of oral sensation, such as dysgeusia, dysesthesia, and glossodynia.
2. Dental treatment of patients with medical problems that affect the oral cavity or for whom modification of standard dental treatment is required to avoid adverse events.
3. Seeking an opinion on the management of dental disease that does not respond to standard treatment, such as rampant dental caries or periodontal disease in which there is a likelihood that systemic disease is an etiologic cofactor.

In response to a consultation request, the diagnostic procedures outlined in this chapter are followed, with the referral problem listed as the CC and with supplementary questioning (i.e., history of the present illness) directed to the exact nature, mode of development, prior diagnostic evaluation/treatment, and associated symptoms of the primary complaint. A thorough examination of the head, neck, and oral cavity is essential and should be fully documented, and the ROS should include a thorough exploration of any associated symptoms. When pertinent, existing laboratory, radiographic, and medical records should be reviewed and documented in the consultation record, and any additional testing or specialized examinations should be ordered.

A comprehensive consultation always includes a written report of the consultant's examination, usually preceded by a history of the problem under investigation and any items from the medical or dental history that may be pertinent to the problem. A formal diagnostic summary follows, together with the consultant's opinion on appropriate treatment and management of the issue. Any other previously unrecognized abnormalities or significant health disorder should also be xcommunicated to the referring clinician. When a biopsy or initial treatment is required before a definitive diagnosis is possible, and when the terms of the consultation request are not clear, a discussion of the initial findings with the referring clinician is often appropriate before proceeding. Likewise, the consultant usually discusses the details of his or her report with the patient unless the referring dentist specifies otherwise. In community practice, patients are sometimes referred for consultation by telephone or are simply directed to arrange an appointment with a consultant and acquaint him or her with the details of the problem at that time; a written report is still necessary to clearly identify the consultant's recommendations, which otherwise may not be transmitted accurately by the patient.

In hospital practice, the consultant is always advisory to the patient's attending oral health professional or physician, and the recommendations listed at the end of the consultation report are not implemented unless specifically authorized by the attending physician, even though the consultation report becomes a part of the patient's official hospital record. For some oral lesions and mucosal abnormalities, a brief history and examination of the lesion will readily identify the problem, and only a short written report is required; this accelerated procedure is referred to as a limited consultation.

THE DENTAL AND MEDICAL RECORD: ORGANIZATION, CONFIDENTIALITY, AND INFORMED CONSENT

The patient's record is customarily organized according to the components of the history, physical examination, diagnostic summary, plan of treatment, and medical risk assessment described in the preceding pages. Test results (diagnostic laboratory tests, radiographic examinations, and consultation and biopsy reports) are filed after this, followed by dated progress notes recorded in sequence. Separate sheets are incorporated into the record for the following: (1) a summary of medications prescribed for or dispensed to the patient, (2) a description of surgical procedures, (3) the anesthetic record, (4) a list of types of radiographic exposures, and (5) a list of the patient's problems and the proposed and actual treatment. This pattern of organization of the patient's record may be modified according to local custom and varying approaches to patient evaluation and diagnostic methodology taught in different institutions.

Organization

In recent years, educators have explored a number of methods for organizing and categorizing clinical data, with the aim of maximizing the matching of the clinical data with the "mental models" of disease syndromes referred to earlier in this chapter. The problem-oriented record (POR) and the condition diagram are two such approaches; both use unique methods for establishing a diagnosis and also involve a reorganization of the clinical record.

Problem-Oriented Record

The POR focuses on problems requiring treatment rather than on traditional diagnoses. It stresses the importance of complete and accurate collecting of clinical data, with the emphasis on recording abnormal findings rather than on compiling the extensive lists of normal and abnormal data that are characteristic of more traditional methods (consisting of narration, checklists, questionnaires, and analysis summaries). Problems can be subjective (symptoms), objective (abnormal clinical signs), or otherwise clinically significant (e.g., psychosocial) and need not be described in prescribed diagnostic categories. Once the patient's problems have been identified, priorities are established for further diagnostic evaluation or treatment of each problem. These decisions (or assessments) are based on likely causes for each problem, risk analysis of the problem's severity, cost and benefit to the patient as a result of correcting the problem, and the patient's stated desires. The plan of treatment is formulated as a list of possible solutions for each problem. As more information is obtained, the problem list can be updated, and problems can be combined and even reformulated into recognized disease categories. The POR is helpful in organizing a set of complex clinical data about an individual patient, maintaining an up-to-date record of both acute and chronic problems, ensuring that all of the patient's problems are addressed, and ensuring that preventive and active therapy is provided. It is also adaptable to computerized patient-tracking programs. However, without any scientifically based or accepted nomenclature and operational criteria for the formulation of the problem list, data cannot be compared across patients or clinicians. An additional concern that has been put forth is the reliance of a POR to "automatically" generate a diagnosis.[18] Although the POR will allow for a systematic approach to delineate specific problems, clinicians need to be able to synthesize findings into an appropriate diagnosis.[19]

Despite these shortcomings, two features of the POR have received wide acceptance and are often incorporated into more traditionally organized records: the collection of data and the generation of a problem list. The value of a problem list for individual patient care is generally acknowledged and is considered a necessary component of the hospital record in institutions accredited by the Joint Commission on Accreditation of Healthcare Organizations.

Condition Diagram

The condition diagram uses a standardized approach to categorizing and diagramming the clinical data, formulating a differential diagnosis, prevention factors, and interventions (treatment or further diagnostic procedures). It relies heavily on graphic or nonnarrative categorization of clinical data and provides students with a concise strategy for summarizing the "universe of the patient's problems" at a given time. Although currently used in only a limited number of institutions, the graphic method of conceptualizing a patient's problems is supported by both educational theory and its proven success with medical students.

The SOAP Note

The four components of a problem—subjective, objective, assessment, and plan (SOAP)—are referred to as the SOAP mnemonic for organizing progress notes or summarizing an outpatient encounter (see Figure 1-3). The components of the SOAP mnemonic are as follows:

- S or subjective: The patient's complaint, symptoms, and medical history (a brief review)
- O or objective: The clinical examination, including a brief generalized examination, and then a focused evaluation of the CC or the area of the procedure to be undertaken
- A or assessment: The diagnosis (or differential diagnosis) for the specific problem being addressed
- P or plan: The treatment either recommended or performed

The SOAP note is a useful tool for organizing progress notes in the patient record for routine office procedures and follow-up appointments. It is also quite useful in a hospital record when a limited oral medicine consultation must be documented.

S—"I have had severe pain in a lower right tooth since last night."
O—Examination reveals tooth #30 with large caries lesion; #30 not responding to cold or heat stimulation; #30 sensitive to percussion (9, on a 1–10 scale). Afebrile, pulse 68, respiration 18, blood pressure 125/85. No enlarged lymph nodes. Radiograph shows large radiolucent area surrounding the apex of the mesial root of tooth #30.
A—Irreversible pulpitis in tooth #30.
P—Root canal therapy, with subsequent post/core build-up and a fixed prosthesis.
Confidentiality of patient records

Figure 1-3 Example of a SOAP note.

Confidentiality

Patients provide dentists and physicians with confidential dental, medical, and psychosocial information with the understanding that the information (1) may be necessary for effective diagnosis and treatment, (2) will remain confidential, and (3) will not be released to other individuals without the patient's specific permission. This information may also be entered into the patient's record and shared with other clinical personnel involved in the patient's treatment unless the patient specifically requests otherwise. Patients are willing to share such information with their dentists and physicians only to the extent that they believe that this contract is being honored.

There are also specific circumstances in which the confidentiality of clinical information is protected by law and may be released to authorized individuals only after compliance with legally defined requirements for informed consent (e.g., psychiatric records and confidential HIV-related information). Conversely, some medical information that is considered to be of public health significance is a matter of public record when reported to the local health authorities (e.g., clinical or laboratory confirmation of reportable infectious diseases such as syphilis, hepatitis, or AIDS). Courts may also have the power to subpoena medical and dental records under defined circumstances, and records of patients participating in clinical research trials may be subject to inspection by a pharmaceutical sponsor or an appropriate drug regulatory authority. Dentists are generally authorized to obtain and record information about a patient to the extent that the information may be pertinent to the diagnosis of oral disease and its effective treatment. The copying of a patient's record for use in clinical seminars, case presentations, and scientific presentations is a common and acceptable practice provided that the patient is not identified in any way.

Conversations about patients, discussion with a colleague about a patient's personal problems, and correspondence about a patient should be limited to those occasions when information essential to the patient's treatment has to be transmitted. Lecturers and writers who use clinical cases to illustrate a topic should avoid mention of any item by which a patient might be identified and should omit confidential information. Conversations about patients, however casual, should never be held where they could possibly be overheard by unauthorized individuals, and discussion of patients with nonclinical colleagues, friends, family, and others should always be kept to a minimum and should never include confidential patient information.

Informed Consent

Prior consent of the patient is needed for all diagnostic and treatment procedures, with the exception of those considered necessary for treatment of a life-threatening emergency in a comatose patient.[20] In dentistry, such consent is more often implied than formally obtained, although written consent is generally considered necessary for all surgical procedures (however minor), the administration of general anesthetics, and clinical research.

Consent of the patient is often required before clinical records are transmitted to another dental office or institution. In the United States, security control over electronic transmission of patient records has since 1996 been governed by the Health Insurance Portability and Accountability Act. The creation and transmission of electronic records are an evolving process that is mainly dependent on technological advances and fast movement of the integration of electronic patient information.[21]

There may also be specific laws that discourage discrimination against individuals infected with HIV by requiring specific written consent from the patient before any HIV-related testing can be carried out and before any HIV-related information can be released to insurance companies, other practitioners, family members, and fellow workers.[22,23]

Oral health-care professionals treating patients whom they believe may be infected with HIV must therefore be cognizant of local law and custom when they request HIV-related information from a patient's physician, and they must establish procedures in their own offices to protect this information from unauthorized release. In response to requests for the release of psychiatric records or HIV-related information, hospital medical record departments commonly supply the practitioner with the necessary additional forms for the patient to sign before the records are released. Psychiatric information that is released is usually restricted to the patient's diagnoses and medications.

ELECTRONIC HEALTH RECORDS

The oral health-care sector has in recent decades undergone extensive computerization with focus on the EHR. However, EHR specifically developed for oral medicine are virtually nonexistent, due to low commercial incentives, and instead, oral medicine clinicians often have to rely on the use of electronic records that are developed for general dentistry or medicine. It is desirable that these records have the capability to incorporate modules created to allow structured recording of information related to oral medicine. This is of great importance for the discipline of oral medicine to take advantage of benefits provided by EHR. EHR systems can incorporate many capabilities, but the following specific functionalities hold great promise in improving oral medicine healthcare.

1. To facilitate registration of structured recording of patient data:

   Registration of clinical data using a digital form ensures consistent information collection from patient to patient, and at the same time minimizes loss of important information. It is essential that the clinical information recorded have high reliability and validity. *Reliability* is the extent to which, for example, a repeated question yields the same answer. If independent practitioners are not able to replicate questions to yield consistent answers, it is not possible to draw conclusions or make claims about the

generalizability of their clinical data. *Validity* refers to how collected data reflect precise answers, that is, the degree of closeness of a measurement to its true value. Unfortunately, most data in EHR are not tested for reliability and validity, which weakens the potential for evaluation and research. Any EHR designed for oral medicine should have the capability to allow for continuous modification and needs and should be evaluated for reliability and validity before introduction in a clinical setting. Assessment of validity and reliability should be a continuous process.

Many EHRs allow registration of free text, which makes extraction of information more difficult and therefore becomes less useful for clinical evaluation and research. However, free text may have its place in EHRs as it allows the record to become more readable and understandable. Some clinical information is too specific to be captured by predetermined items. Thus, when developing an oral medicine EHR, a distinction need to be made between information necessary for health analysis and information essential to understand the clinical findings of a particular patient.

2. To facilitate the visualization of the data as needed:

   Oral medicine is a discipline that is image oriented with clinical images, radiologic images, and histopathologic images. EHRs developed for general dental care may not offer access to these types of images.

   A limitation of the conventional paper record is the lack of an easy method of compiling clinical information. Poor penmanship may further lessen the ability to compile and evaluate data. Unfortunately, most EHR has an interface that is not always designed to fully utilize the benefits that an electronic tool can provide. This is usually not due to lack of technical solutions but due to the difficulty of defining a successful treatment outcome.

3. To facilitate clinical follow-up of both individual patients and larger patient groups to provide the basis for clinical development and research

   The capability to convert collected clinical datasets into new evidence-based knowledge is the prime rational to justify the substantial financial investments made to implement EHR. However, most available EHRs do not prioritize this feature and therefore do not effectively support the compilation and analysis of the recorded information. This deficiency is probably due to attempts to reproduce traditional paper records as the framework and conventional analogous interfaces. The information recorded in most current EHRs cannot, even with considerable effort, facilitate clinical decisions. Furthermore, integrated clinical decision support, for instance in the form of drug interactions, is not available in all systems.

   For most clinicians the current daily workflow does not contain any moments for reflection and analysis of recorded information, which lessens the utilization of the full potential of an EHR. It is therefore necessary to create time to take advantage of these electronic tools. In the development and selection of an appropriate EHR, it is important to consider the ability of the systems to provide chairside decision support.

4. To enable data mining for research and improved patient care:

   A well-designed EHR provides an opportunity for easy retrieval of data for the purposes of research and, consequently, better patient care. Furthermore, EHRs can facilitate communication between different EHR systems and offer plenty opportunities for multicenter trials, as well as co-care of patients by different health professionals in different settings.

   A useful EHR system is designed to support clinical care; it should have a clean and simple visual design where each element clearly shows what should be done and the next steps in an intuitive manner; it should provide integrated decision support and store data in a form that makes for easy retrieval and analysis. Ultimately, EHR records, with appropriate security, should enable sharing of information among all care providers of the patient.

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CHAPTER 2

Overview of Clinical Research

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Medicine, including oral medicine and traditional dentistry, is now taught and practiced to a greater or lesser extent using evidence-based practice.[1] This evidence base comes from clinical research. The purpose of this chapter is to provide a very brief overview of types of research involving human subjects and the features of good clinical research, including ethical and regulatory considerations. Those seeking additional information should read recent textbooks written about the topic.

DEFINITION OF CLINICAL RESEARCH

"Clinical research" can be defined broadly as patient-oriented research. This includes all studies in which investigators interact directly with subjects to collect research data and studies utilizing existing specimens from human subjects if the identity of the subject is known to at least one investigator.[2] If the codes identifying previously collected specimens or clinical data cannot be traced back to the subjects' identity, research using the specimens or data is usually not considered human subjects research.

Many types of studies are included under this definition of clinical research. Human subjects research includes studies of human disease mechanisms, natural history studies of disease, epidemiological studies, behavioral studies, studies of technologies used to diagnose human diseases, outcomes research, and health services research. If the study is testing an intervention as a treatment for disease, the study is a clinical trial. "Intervention" includes anything that can alter the course of a disease, such as a pharmaceutical agent, a medical device, a surgical technique, a behavioral intervention, or a public health program. Therefore, clinical trials are a subset of clinical research. Clinical research studies, whether

interventional or observational, require approval by an institutional review board (IRB) and provision of informed consent by the research subjects if supported by US federal funds.

STUDY DESIGNS

Several types of designs are available to collect research information about individuals with diseases and conditions. The designs described below are commonly employed in clinical research.

Case Report and Case Series

A case report (singular) or case series (plural) is a description of one or several individuals with a disease or syndrome of interest. Examples include descriptions of the clinical course of a patient during a hospital stay, unusually shaped teeth in a child or children with a genetic syndrome, or an adult presenting with orofacial pain from an unusual source such as a metastatic tumor. The description should be complete enough for use by another clinician who may evaluate a similar case. If the study is a case series, the same diagnostic criteria should be used to group the cases together for a report.

Case series can be very valuable in the description of new diseases or conditions. A good example is the case series describing 63 cases of osteonecrosis of the jaw (ONJ) associated with the use of bisphosphonates.[3] An obvious limitation of this study design is the lack of a population of individuals without the disease or condition, or a "control" group. Other limits of a case series include the fact that most are performed retrospectively with data taken from existing clinical records. This introduces the potential for recall bias as the researchers are "looking back" at events and extracting record information, which is often a mixture of complete and incomplete facts. Also, the information is recorded for clinical care and not research purposes. Therefore, clinicians will use varying methods to evaluate patient outcomes, such as a nonhealing extraction site. If the patients were evaluated as part of a research study, the study team would use a predefined set of criteria to judge clinical outcomes and would collect a predefined set of information from the patients such as current and past medications.

Cross-Sectional Studies

Cross-sectional studies are employed frequently in clinical research. Research participants (also known as subjects) are evaluated at one time point and are not followed up over time, creating a dataset that is a "snapshot" of the condition under study. Prevalence studies use cross-sectional designs that involve describing the population under study, deriving a representative sample of that population, and defining the characteristics under study to establish the prevalence of a disease or condition in a population.[4] For example, the prevalence of oral human papillomavirus infection has been estimated through the National Health and Nutrition Examination Survey (NHANES) 2009–2010. The NHANES study uses a statistically representative sample of the civilian non institutionalized US population.[5] Many factors must be considered when designing a cross-sectional prevalence study. First, it is not usually feasible to examine an entire population of individuals with a disease or condition. Therefore, the sample being examined should represent the entire population at risk and not only those most severely affected. In the example of ONJ, patients with small nonhealing affected sites that healed in two to three months without any intervention should be included as well as those with large lesions that persisted for months to represent the entire spectrum of the disease. Second, all research participants should be evaluated using the same, standardized methods (see the section "Outcome Assessment"). Prevalence studies for rare diseases usually require very large sample sizes and, therefore, may not be suitable for studies conducted at only one institution or when there are limited numbers of individuals with the disease of interest.[4]

Cross-sectional studies may also be utilized to draw associations between an exposure or risk factor and the presence of disease. Because research participants are evaluated at one time point, causal inferences cannot be drawn between the risk factor and disease, representing a major limitation of this study design. Using the example of periodontal disease and cardiovascular disease, the two conditions can occur together in a person because of a common underlying etiology, such as smoking, unhealthy personal habits, and/or limited access to the health care system.[6] Nevertheless, such cross-sectional designs have value in research, particularly to develop hypotheses for future studies. An initial association between a risk factor and presence of disease may be established in a cross-sectional study before consideration of a more resource-intensive study design in which risk factors for disease can be evaluated over time. When establishing initial associations using a cross-sectional design, the biologic plausibility between the risk factor(s) and disease and the strength of this association should be described.

Case-Control Studies

A case-control study is a type of observational retrospective study. The objective is to evaluate persons with the disease of interest (cases) and compare them with another group of persons with similar traits (controls) to determine whether certain exposures(such as being a current smoker) or characteristics are associated with the disease or lack of the disease. If the exposure is found more frequently in the cases, it is termed a "risk factor" for having the disease. Sometimes the exposure is found more frequently in the control group, suggesting that it might be a "protective factor" that helps protect against a disease. There are critical design issues that must be considered in a case-control study.[4] The exposure and disease in both cases and controls should be assessed in the same manner. Patients who have a severe disease may experience recall bias in that they remember more or over-report past exposures or symptoms than generally

healthy controls because they are seeking an explanation for why they have a disease. The cases need to represent the entire population of those with the disease, and the controls must be selected from the same population as the cases. Finally, most experts recommend evaluating at least an equal number of controls as cases. Selection of controls for a case-control study can be difficult and can introduce bias into the study if not chosen carefully, as discussed at length in the literature.[7–9] A case-control study example performed across three dental practice-based research networks assessed risk factors for ONJ. ONJ cases were defined as having maxillary or mandibular exposed bone that clinically appeared necrotic, without regard to duration or size. For each case, three controls with no current or previous history of bone necrosis were selected from the same primary care practice where a case was diagnosed. Risk factors were ascertained in cases and controls, and the association between bisphosphonate use and ONJ was determined.[10]

Case-control studies are particularly beneficial when studying rare diseases. If the disease of interest is sufficiently rare, such as salivary gland cancers, it may be safe to assume that a sample of cases is representative of the entire population of those with the disease. Findings in case-control studies are typically reported in odds ratios, whereas cohort study findings are expressed in terms of relative risk. When interpreting the results of case-control studies, the strength of the association between the exposure and disease and the confidence interval of the association should be considered before making conclusions about the validity of the results. A finding of a "dose-response" (in which increasing levels of the exposure such as pack-years of smoking are associated with increasing rates of the disease or condition) increases the strength of the evidence.

Because of criticisms related to control selection in case-control studies, researchers may choose to utilize more than one control population when designing studies. In a classic example from the medical literature, the relation between estrogen use and endometrial cancer was established using a well-designed case-control study design and two control populations.[11]

Longitudinal Cohort Studies

Longitudinal cohort studies allow the opportunity to collect data over time. The purpose of this study design is to assess associations between an exposure or risk factor and subsequent development of disease or to determine outcomes of standard of care treatment. When performed prospectively to assess associations, a representative sample of the population of interest is assessed for an exposure at the beginning of the study, and then new cases of disease accrue during a period of follow-up evaluation. At the end of the study, the differences between those with and without the disease are evaluated. In some cases, a single population is observed over a period of time to observe the natural incidence of a condition or the natural history of a disease. For example, a study of Swedish adolescents estimated the incidence of temporomandibular muscle and joint disorder (TMJD) pain. All individuals aged 12–19 years in all Public Dental Service clinics in a Swedish county from 2000 to 2003 were followed over 3 years for development of TMJD pain.[12] Subjects with TMJD were evaluated for differences that distinguished them from subjects without TMJD. In this study, TMJD incidence was found to be greater in older children and girls. More frequently, research subjects may be selected for a particular exposure, along with a comparable group of controls, and both groups are followed up over time for development of disease.[13] An example of a longitudinal cohort study examining outcomes of treatment was a study of 264 implants placed in 51 individuals with ectodermal dysplasia who were followed to determine the incidence of implant failure.[14]

Cohort studies may also be retrospective, in which the exposure was captured in a standardized manner in the past, and disease status is determined at the time the study is initiated and subjects are followed. This study design assumes that the subject population (exposed and unexposed subjects) is representative of the general population, and exposure history is collected accurately. Definitions of disease outcome should be reliable and reproducible and held constant during the study duration. Standard criteria for determining the disease outcome should be applied to exposed and unexposed subjects to avoid bias. An important factor in longitudinal cohort studies is the ability to retain the cohort over time. Subjects who drop out of research studies may differ from those who remain and may introduce attrition biases into the population sample.

One significant advantage of well-conducted prospective cohort studies over other study designs is that the exposure is collected in a standardized fashion, and cases are incident (new cases). This design provides more information about the natural history of the disease, as well as direct estimates of incidence and relative risk.[4] Longitudinal cohort studies have the potential to initially or further establish the temporal relationship between exposure and disease and a dose response relationship, both of which increase the strength of the study conclusions.

Longitudinal studies by their nature are resource intensive, and large populations are often required to study rare diseases. Large sample sizes for rare diseases and long durations for chronic diseases may be required. Maintaining the use of consistent study methods, such as standardized collection of the exposure, and keeping subjects from dropping out of the study are continual challenges.

Randomized Controlled Trials

The purpose of randomized controlled trials (RCTs) is to determine whether a particular intervention is associated with a change in disease incidence or severity as determined by an outcome measure. An example of an outcome measure in an RCT testing an intervention for periodontal disease is reduction in pocket depth. RCTs provide the strongest

evidence for the causal nature of a modifiable factor (such as inflammation in a periodontal pocket) and the effect that modifying the factor has on disease outcomes. Potential research subjects from a well-defined study population are assigned at random to receive or not receive the intervention(s) under study and then are observed for a specified time period for the occurrence of well-defined endpoints. One intervention may be compared to another intervention, "usual care", or placebo treatment. Large RCTs should not be undertaken until there is a substantial body of evidence suggesting that the intervention may be effective, but not so much evidence such that conducting the study would be considered unethical. In other words, there should be clinical equipoise before a study is launched.[15]

Clinical trials can be classified into four phases (phase I, II, III, or IV) or stages.[16] This stepwise approach reduces risks to people enrolled in the trial and allows investigators to determine potential effectiveness of a new treatment while minimizing time and costs. A phase I trial often is the "first-time in human" study, meaning trial participants are the first humans to receive the new drug. These studies are not randomized or blinded (masked). The primary goal is to evaluate the safety of the agent and determine a safe dose range for subsequent studies. A phase II trial tests the new drug in individuals who are randomized to different treatments, with goals of determining potential effectiveness and establishing a more complete safety profile. Feasibility of using the treatment also can be determined. The phase III trial enrolls hundreds or thousands of subjects and is sometimes called a "pivotal study." These trials are designed to enroll a much larger segment of the population with the disease, and results are used to gain drug approval from government agencies. Phase III trials should generate generalizable results and determine the *efficacy* of a treatment. Phase IV trials are post marketing studies to determine how well a treatment found to be efficacious in a phase III trial works in the community, and to assess any side effects associated with its long-term use. Studies designed to determine how well a treatment works in practice determine the *effectiveness* of a therapy.

A key component of RCTs is that subjects are assigned to one of the study arms at random to eliminate the potential for bias in treatment assignment. Certain forms of randomization that do not allow for random sequence generation, such as rolling dice, using hospital chart numbers, or using a birth date, are not acceptable randomization practices. Another important consideration is the random, concealed or "blinded" or "masked" allocation of treatment to ensure that any baseline differences in the treatment groups arise by chance alone. The random allocation process involves generating an unpredictable random sequence and then implementing the sequence in a way that conceals the interventions until subjects have been formally assigned to their groups.

Both randomization and concealment are necessary to avoid bias and maximize validity in RCTs, and reproducibility of the allocation order and the concealment process are necessary to maintain integrity of the research study. Other important features of high-quality RCTs include independent or "blind" assessment of research endpoints and data analysis based on the treatment assignment, also known as analysis by "intention to treat." Intention-to-treat analysis removes artifacts from the study that are caused by unequal attrition in the two study arms, or by treatment crossover.

There are three levels of concealing treatment (blinding or masking) in an RCT: (1) subjects are unaware of their study treatment group, (2) the investigators are unaware of the subject's study treatment group, and (3) the statistical analyses are conducted without knowledge of the groups' study treatment. Recent oral health RCTs that followed the strict principles of clinical trials were two phase III studies testing periodontal therapy as a treatment to prevent preterm birth[17] and to improve glycemic control.[18]

A limitation of the RCT study design is the concern about external validity, or the extent to which RCT results are applicable beyond the research study. In addition, RCTs are expensive because of the logistics involved in sampling, blinding, treating, and following hundreds of participants; in addition, extremely large sample sizes are required to study rare outcomes. Consequently, some research questions may be more appropriately addressed using other study designs.

Systematic Reviews

A systematic review is a structured process of comprehensively reviewing the literature focused on a research question in which inclusion and exclusion criteria for study selection are established *a priori*. The purpose of the systematic review is to determine the "state of the science" by objectively identifying, appraising, selecting, and synthesizing high-quality research evidence. Such reviews may also elucidate a paucity of high-quality evidence and, therefore, identify research questions to be addressed in future studies. Key principles of systematic reviews include the following[19]:

- Literature search: Develop a search strategy using multiple sources, checking of reference lists, handsearching of key journals.
- Study selection: Develop criteria for inclusion and exclusion, eligibility checks by more than one reviewer, develop a strategy to resolve disagreements, keep a log of excluded studies with reasons for exclusion.
- Study quality assessment: Quality assessment by more than one observer, using established and standardized criteria for study quality assessment.
- Systematic extraction of data.
- Analysis, presentation, and interpretation of results: Address risk of bias (including the fact that negative studies are less likely to be published), consider strength of evidence, address limitations, consider implications for future research.

A meta-analysis pools data from different studies and treats them as one large study using statistical tools. Only

high-quality evidence of a similar design, usually limited to RCTs, should be included in a meta-analysis. Observational studies are often limited by the effects of confounding and bias, therefore precluding their inclusion in pooled analyses.

EVIDENCE HIERARCHY

Clinical evidence is generated from a variety of study types. In general, evidence from literature that is classified as expert opinion, bench research with human samples that demonstrate biological plausibility, case reports, and case series is considered low-level evidence.[20] Higher level evidence (from lower to highest) is evidence from case-control studies, cohort studies, randomized controlled clinical trials, and systematic reviews/meta-analyses of clinical trials. However, consumers of medical literature should be cognizant of critical components of any research study when judging its value, and not accept that evidence is superior just because it ranks higher in traditional evidence pyramids. If a clinical trial is conducted poorly, its value is diminished and its conclusions may be meaningless. Critical elements of high-quality clinical research are discussed below.

Clinical research, regardless of its type, is a scientific study. Therefore, investigators must take care to conduct studies that minimize bias and maximize reproducibility. Many factors should be considered when evaluating clinical studies, including study design, sample size, subject selection, methods to ascertain disease and outcomes, ethical and human subjects concerns, and analytical approaches. Organizations such as the Cochrane Collaboration have developed sophisticated methods including systematic reviews to evaluate and synthesize the best literature to help develop practice guidelines that are based in evidence.[21] Other systems have been published to guide the evaluation of evidence by organizations developing guidelines.[22–25]

ISSUES IN THE DESIGN, IMPLEMENTATION, AND INTERPRETATION OF CLINICAL RESEARCH

Below are short descriptions of some of the features of clinical research to consider when reading the scientific literature. More complete descriptions of factors used to evaluate the quality of research are available in the *Cochrane Handbook for Systematic Reviews of Interventions*[21] or can be found as components of the GRADE system.[24,25]

Study Design

Investigators should employ a study design that is suitable for answering the clinical research question at hand. In general, an intervention should be tested in a clinical trial to assess whether it is an effective treatment for a disease. If an expert publishes a paper detailing the use of a new surgical approach to treat maxillary fractures of six patients and declares the technique effective, a practitioner using evidence-based decision making should recognize that the paper does not provide sufficient evidence to declare the approach a success. This type of publication is a case series, and the expert's assertion of the effectiveness of the approach is termed "Expert Opinion." Assessing the efficacy of the new treatment approach requires that it be compared to either no treatment or the standard of care treatment in a controlled clinical trial, such as the clinical trials testing periodontal therapy as a means to prevent preterm birth[17] or to improve glycemic control in type 2 diabetes.[18]

Sample Size

Sample size is a critical issue in clinical trials. If the sample is too small, the findings on the efficacy of an intervention cannot be generalized to the population having the disease. This is particularly critical for phase III clinical trials that are designed to change clinical practice or impact public policy.

Many clinical studies suffer from small sample sizes, making it difficult to generalize study findings. Observational studies of select patient groups often make conclusions about the condition from small numbers of patients who are in active treatment in one medical center and who have the most severe disease. However, the patients evaluated in the study may not represent all patients in the general population. A single-center study does have value in generating new hypotheses for more research, but the studies need to be replicated in larger, more representative samples.[26] Studies of rare diseases can be difficult because few patients with the condition of interest are available for study. To overcome this problem, multicenter registries can be established that enroll and follow up subjects with a particular condition. Examples include the chromosome 22q11.2 deletion syndrome registry that has characterized the highly variable spectrum of the clinical consequences associated with this deletion in 906 affected individuals[27] and the international registry to assess safety of denosumab, an agent associated with ONJ.[13]

Case-control studies of dental disease (either caries or periodontal disease) must be large enough to make meaningful comparisons, especially given the complex, multifactorial etiologies of the diseases. Small sample size is often a reason why studies are excluded from evidence-based reviews.[28]

Selection of Controls

Another critical factor to consider when evaluating a case-control study is the selection of the control group. Are the controls drawn from the same population? Do they differ from patients with the disease of interest in many ways, or are they very similar?[7] Are equal numbers of cases and controls evaluated?[7]

Study Bias

Great care must be taken to avoid study bias. Methods to avoid bias in cohort studies include enrolling consecutive individuals reporting to a clinic with a disease of interest,

or enrolling individuals randomly selected from an existing large population. Clinical trials should use randomization to assign subjects to the different treatment arms to avoid bias. Ideally, a clinical examiner collecting a study outcome should not know the group assignment of the subject being evaluated. This is best practice for both case-control studies and randomized clinical trials.

Another more complicated issue in clinical trials is the use of restrictive inclusion/exclusion criteria. To determine whether a new drug or a technique is effective for treating a disease, potential subjects with coexisting conditions may be excluded, or study participation may be limited to a particular age group. This creates a potential for study results to be only valid for a population similar to that enrolled in the trial, which may be a smaller subset of individuals with disease. An example of this problem is clinical trials testing therapies for non-Hodgkin's lymphoma (NHL). Although the majority of patients with NHL are older than 65 years, older adults were poorly represented in NHL RCTs.[29] Most RCTs testing caries preventive treatments studied children, although therapies are recommended for adults.[30]

Outcome Assessment

One challenge when conducting a clinical study is assessment of outcomes. Study outcomes or endpoints used in a clinical trial or study must provide reliable (consistent and repeatable) and valid signals to determine the efficacy of the intervention being tested or to reliably document disease prevalence and/or progression. The outcome must be reproducible, and there should be published evidence of its validity. For example, if the goal of a study is quantifying oral cancer pain, the investigator should use a validated instrument to collect pain measures appropriate for the population being studied. In this example, an appropriate instrument would be a pain scale that had been tested previously in a group that was similar culturally and had pain from the same origin, cancer. The methods for ascertainment of study outcomes also need to be standardized. In addition, examiners should be calibrated by having them each examine the same group of patients to measure their agreement with each other (interrater reliability) and to examine a set of patients repeatedly to measure their agreement with themselves (intrarater reliability).[31] Studies that include caries and periodontal disease changes as outcomes usually conduct yearly calibration sessions during which examiners are calibrated to a gold-standard examiner and compared numerically using percentage agreement or kappa scores.[17,32]

Loss to Follow-Up and Retention

Minimizing loss to follow-up is critical to study validity. There is no way to assure that a study is valid if loss to follow-up is not minimal, and when participant loss approaches the number included in study outcomes, any study conclusions are specious. Every effort should be made to avoid loss to follow-up. Both simple and sophisticated analytic methods are available to model missing data, but these cannot protect against bias created by subject loss. One can look at how participants lost to follow-up differ from those retained and undertake bootstrapping or other methods to impute missing data, but the truth lies somewhere between rigorous sensitivity analysis done by calculating results assuming that all those lost to follow-up were treatment failures and comparing them to results that assume all those lost to follow-up were treatment successes. Although neither is likely to be the complete truth, a range will be established though one will never know what happened to those lost from the study. From an ethical perspective, clinical research should always adhere to quality standards including minimizing loss to follow-up; to do otherwise is to disrespect the human subjects participating in the study and to squander resources.[33–35]

Thus, retention is a key issue in any well-designed and conducted study that involves subject follow-up. Pilot studies to test retention can be invaluable. Retention plans should be designed well in advance of study implementation. Many strategies can be used; however, it is not acceptable to take a wait-and-see attitude because the study could be undermined at the outset. Retention should be tracked carefully throughout the study and retention strategies improved during the study if they are found to be lacking.

Examples of retention strategies that can be considered when designing a study:

- Having a run-in period at the beginning of a study to eliminate those who will be lost or cannot comply.
- Obtaining reliable, complete subject contact information that may include alternate phone numbers, e-mail, and physical addresses.
- Obtaining names and contact information for designated family or friends who could be contacted for information on missing participants.
- Sending out communications such as newsletters and educational pieces that inform study participants of new findings in the field or progress of the study, as allowable.
- Sending out reminders such as birthday cards, text messages, phone messages, postcards, or letters.
- Having dedicated and professional study staff with low turnover to establish rapport with study participants.
- Employing outreach workers to find those who may be lost to follow-up.
- Having the data center follow-up individuals via phone or e-mail should they fail to respond to contacts made by the clinic or site. It is possible the participant has a personal reason for not continuing in the study.
- Reviewing death records and registries to account for those missing by demise.
- Reviewing public media to search for obituaries and accidents.
- Offering study visits during hours that accommodate clinical subjects; this may include evenings or weekends.
- Scheduling study visits with other necessary patient care to minimize the number of trips to the study site.

- Creating satellite clinics or sites near where patients are situated so that they are not required to travel as much. Venues for data collection may include visits to participants' homes, churches, schools, or worksites to allow study visits to be less disruptive to subjects' lives.
- Providing incentives that make it easier to participate in the study such as:
  - Child care
  - Paid transportation to the site
  - Remuneration for expenses as deemed appropriate by the IRBo

All these strategies should be presented to the IRB for their approval. They all must be agreed to by the participants as part of consent for participation, and to the extent possible, must protect participants' privacy. It is also important to obtain buy-in from all those who must cooperate for the strategy to be successful. Examples of those who must be engaged might include the board of education, ministry of health, other health care providers, or employers. With the exception of review of public information such as death registries or public media, subjects must provide consent for any strategy that involves contacting them to prevent privacy impingement. An engaged, informed, and interested study population is far more likely to be retained than one that is not.[34]

Analytical Issues

It is impossible in this limited space to discuss analytical issues fully. However, unless a study is fully hypothesis-generating and exploratory, the principal study hypothesis, sample size, power, and statistical analyses should be pre specified to protect against ad hoc analyses that attempt to milk provocative conclusions from the data. It is all too tempting to conduct analyses for which the study was not specifically designed; it is most unusual that convincing, robust conclusions can be drawn from such *a posteriori* analysis. Another grave threat to the validity of analysis is multiple comparisons or making too many comparisons for the study sample size. This will quickly undermine study power. Although many statistical corrections are available for multiple comparisons, there is no perfect method, and as such, this approach should be avoided unless necessary. Inappropriate use of statistical methods threatens the reproducibility of science.[36]

One should also predefine endpoints that will represent clinical significance in the study findings, independent of statistical significance. A common mistake is to conflate statistical significance with clinical significance. For example, an epidemiological study may result in a caries prevalence difference of 0.1 surfaces between sample groups. Because of a large sample size the difference may be statistically significant, but the clinical significance of the finding is open to question. The articulation of study analysis can be included in the protocol or in a separate statistical analysis plan depending on how complex and detailed the analysis will be.[37]

To improve the quality of randomized clinical trial reports, many journals require that investigators follow the principles articulated in the Consolidated Standards of Reporting Trials statement.[38] This statement includes a 25-item checklist and flow diagram that provides guidance for reporting results. Items that should be reported include the number of individuals screened for trial eligibility, the number of participants randomized overall and per treatment group, the number of study participants lost to follow-up, the number of those randomized whose results were analyzed, and the reasons for excluding participants' results from the final analysis.[38]

ETHICAL CONSIDERATIONS AND REGULATORY REQUIREMENTS

Regulatory requirements for research with human subjects vary according to the type of study conducted and the region or country in which the research is conducted. In the United States, starting an interventional clinical trial to test the safety and efficacy of an investigational new drug (IND) for disease treatment will require an IND application filed with the United States Food and Drug Administration (FDA) and approval from a local IRB. In the European Union (EU), the trial of an investigational drug may be started after a clinical trial authorization (CTA) dossier is authorized by a National Competent Authority and an Ethics Committee issues a positive opinion. The IND application or CTA dossier provides information about the properties of the drug and details of its manufacturing process, evidence of safety from preclinical (animal) studies, and plans for its clinical testing. For a simple observational study intended, for example, to identify the risk factors for a disease or condition, regulations for the protection of human subjects must be followed. These may vary with the region or country in which the research is conducted.

For any research study that involves human subjects, sponsors and investigators have an obligation to protect the participants, by weighing the foreseeable risks and anticipated benefits before initiating a study and by conducting the study with adequate rigor to produce scientifically valid results. The regulations and guidelines followed by clinical researchers today have their foundations in a variety of codes, resolutions, and guidelines adopted by national and international bodies, including the Nuremberg Code (1947),[39] the Declaration of Helsinki[40] (adopted in 1964 and amended several times through 2013), the Belmont Report prepared by the United States National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979),[41] the International Ethical Guidelines for Biomedical Research Involving Human Subjects published by the Council for International Organizations of Medical Sciences (released 1993, revised 2002),[42] and the E6 Good Clinical Practice guidelines developed by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).[43]