University of Florida – College of Dentistry

Management of Medically Complex Patients
and
Medical Consultation Guidelines

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Revised: March 11, 2019.

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Medical Consultations: Indications and Format Guidelines

A medical consultation with the patient's physician(s) and subsequent review and approval by faculty (preferably from oral medicine) before initiating physiologically stressful or invasive dental treatment is usually required for any patient who meets any of the following criteria listed below.

Please note this is not meant to be a comprehensive list. There are many additional medical problems that would necessitate a medical consultation that are not specifically listed here.

1. The patient has a potential allergy to a local anesthetic (or any preparation component, e.g. sulfites), dental material (e.g., mercury, nickel, methylmethacrylate), other materials used in dental treatment or likely to be environmentally encountered in the dental school clinic.

2. The patient has any medical problem(s) that could result in potential medical complications secondary to physiologically stressful or invasive dental treatment. Examples include (but are not limited to):
   - Angina pectoris
   - History of myocardial infarction
   - History of cerebrovascular accident / transient ischemia attack
   - Cardiac insufficiency / congestive heart failure
   - Hypertension (defined as BP > 140 mm Hg systolic and/or 90 mm Hg diastolic)
   - Cardiac arrhythmia
   - Diabetes mellitus
   - Chronic obstructive pulmonary disease
   - Poorly controlled and/or exercise-induced and/or stress-induced asthma
   - Symptomatic hypo- or hyperthyroidism
   - Poorly controlled seizure disorder (defined as > 1 seizure per month)
   - Hepatitis, hepatic failure, or cirrhosis
   - Chronic kidney disease, renal failure and/or dialysis
   - Adrenal insufficiency

3. The patient has any medical problem(s) that could result in an adverse reaction or potential medical complication due to drugs we may administer as part of dental treatment, such as antibiotics, local anesthetics, vasoconstrictors, N_2O, or analgesics such as narcotics or NSAID's. (See examples in #2 above)

4. The patient has any medical problem(s) or takes any medication(s) that places them at an increased risk for post-treatment infection due to immunosuppression and/or delayed wound healing.
   Examples include (but are not limited to):
   - HIV/AIDS
   - Blood dyscrasias, aplastic anemia
   - Myeloproliferative disease (e.g., leukemia, myelofibrosis), lymphoma
   - Use of systemic corticosteroids and/or other immunosuppressive drug use (e.g., tumor necrosis factor blockers [e.g., etanercept, infliximab, adalimumab, etc.], azathioprine, methotrexate)
   - Undergoing antineoplastic cytotoxic chemotherapy
   - History of radiation therapy involving the maxillofacial region
   - Status-post organ, bone marrow or stem cell transplant

5. The patient has any medical problem(s) or takes any medication(s) that could result in clinically significant impaired hemostasis.
   Examples include (but are not limited to):
   - Hemophilia, von Willebrand's disease
   - Thrombocytopenia, thrombocytopathia
   - Warfarin (Coumadin)
   - Direct thrombin inhibitors (e.g., Pradaxa)
   - Factor Xa inhibitors (e.g., Xarelto, Eliquis)
   - Low-molecular-weight heparin (LMWH) such as enoxaparin (Lovenox)
   - Valproic acid (valproate sodium)

6. The patient has any medical, psychiatric or cognitive problem(s) that could:
   - effect (complicate) our ability to provide dental care to the patient, or;
   - impair the patient's ability to follow or understand instructions, or;
   - make the patient unable to provide legal informed consent to dental treatment or make informed consent decisions.

7. The patient has a history of a possibly unresolved (still active) infectious disease that could pose a transmission risk to others during dental treatment, despite the use of "universal precautions" (e.g., tuberculosis, pulmonary MRSA).

A General Outline for Medical Consults

Suggested opening:

- Mr./Ms. X, is a dental patient of the UFCD and has been diagnosed with (specify diagnoses, [e.g., dental caries, periodontal disease, partial edentulism, etc.]). Treatment will include (summarize anticipated treatment with emphasis on the most invasive treatment the patient is anticipated to receive such as extraction[s], osseointegrated implants, periodontal surgery, osseous reduction surgery, etc.) using (specify anesthesia: local anesthesia [2% lidocaine with 1:100,000 epinephrine], I.V. sedation, general anesthesia). This treatment will be performed over approximately (x) appointments, each being of 2 to 3 hours in duration.

Body of consult:

- The patient's current medical problems and pertinent past medical history includes: (list)*
- The patient's current medications are reported as: (list drug names and doses)*
  * Note: This means you should list <u>all</u> of the patient's current medical problems and medications, (<u>not</u> just those relating to why the consult is being sent [e.g., status of diabetes]).
- Give reason(s) for consult: (<u>be specific</u> and <u>number each question / item separately</u>)

Suggested closing phrases:

- Please indicate any additional significant medical history or changes in medication.
- Please specify any contraindications or precautions regarding the proposed dental treatment for this patient.
- Thank you for your assistance in my care of our mutual patient.

Please note that for any patient, you should write only ONE medical consultation PER physician (even if that physician is treating the patient for multiple medical problems that you need addressed in your consultation).

ALLERGIES / HYPERSENSITIVITY

Background:
Many dental patients will report a sensitivity or allergy to medications or dental materials such as latex, "novocaine," or metal (probably nickel). Careful questioning about the history of the allergy is helpful, including the specific type of reaction, the timing related to exposure, any previous testing and/or treatment for the allergy. Allergic reactions are highly variable from person to person and from time to time for an individual; some people will 'outgrow' an allergy, although for most, the response increases with time and exposures.

- Local anesthetics: True hypersensitivity reactions to amide local anesthetics are extremely rare and usually consist of delayed contact dermatitis; anaphylaxis from amide local anesthetics occurs rarely if ever. Large-scale studies have found that, following full evaluation, virtually all patients with a history of purported "allergy" to amide local anesthetics are able to tolerate these drugs. Unfortunately, patients who experience any adverse reaction to local anesthetics are frequently labeled "allergic" and told to avoid all ''-caines'' in the future
  Pseudoallergic responses to local anesthetics, however, particularly in dentistry, occur relatively frequently and often lead to allergy consultations. It is more likely that the patient had a physiologic reaction to the vasoconstrictor in the local anesthetic solution, or a reaction to endogenous adrenaline due to stress, or possibly a true allergic reaction to some other substance found in the local anesthetic solution.
  There are some patients who are allergic to the antioxidant preservative agent used when vasoconstrictors are included in the anesthetic cartridge. After 1984, the PABA preservatives (e.g., methylparaben) were replaced by sulfites (e.g., sodium sulfite or sodium metabisulfite), and this has greatly reduced the number of patients with allergic reactions, but it is still possible, and using a local anesthetic without vasoconstrictor is indicated for patient with sulfite sensitivity. Some patients reporting an allergic reaction to a local anesthetic may have experienced such a reaction due to latex sensitivity since latex was previously used in the stopper and diaphragm of the local anesthetic cartridge.

- Latex: The true prevalence of latex sensitivity is unknown with estimates for the general population at 5-10%, and healthcare workers ranging from 0.5-17%. Persons who have undergone multiple surgical procedures are at also increased risk for latex sensitivity, especially if these procedures involved extensive or chronic mucosal contact with latex products. Thus, high-risk groups include patients with neural tube defects (e.g., spina bifida, myelomeningocele), spinal cord trauma, urogenital malformations, and neurogenic bladder.
  Adverse reactions following exposure to latex products may be categorized as irritant contact dermatitis, allergic contact dermatitis (type IV hypersensitivity), or immediate (type I) hypersensitivity reactions (urticaria, angioedema, allergic rhinitis, asthma, or anaphylaxis).
  There is a possible cross-allergy to some fruits including avocados, bananas, chestnuts, figs, and kiwis, (it is estimated a patient with a history of fruit allergy has 11% risk of concurrent latex allergy). Additionally, many people will have a sensitivity reaction to wearing rubber gloves that manifests as redness and itching, but this may be a reaction to the natural rubber proteins that have not been completely cured during the manufacture of the gloves.

The dental clinics at the UFCDUFCD are essentially "latex-free" as far as dental materials, disposables, instruments, and other clinical materials are concerned. Consequently, it appears that our dental clinic patients' risk for latex exposure is no more (and probably much less) than in any other environmental setting (i.e., at home, or at work from rubber bands, pencil erasers, etc.) while receiving dental treatment at the UFCDUFCD.

- Metals: Nickel is typically the allergen for these patients. Many are exposed to nickel in costume jewelry at a young age. In the past, dental prostheses (RPD framework, metal crowns) may have contained nickel, and these patients could show an area of erythema where their tissue came in contact with the metal. At present, nickel is no longer used in dental materials in the USA.

Dental Management of a Patient with a Suspected Allergy to Dental Materials or Drugs Used in Dental Treatment

- If there is concern about the potential for an allergic (especially anaphylactic) reaction due to a drug (e.g., local anesthetic, etc.) or dental material (e.g., mercury, silver, methacrylate, etc.) that is planned for use in a dental patient, the patient should be referred to an allergist or immunologist for appropriate allergy sensitivity testing.
- For the investigation of a local anesthetic allergy, it is usually helpful to provide the allergist/immunologist with a few cartridges of the specific local anesthetic(s) that is/are planned for use it the patient so that they may be used for provocation testing.
- For other dental materials, it is usually helpful to provide the allergist/immunologist with documentation of the specific chemical composition of the dental material in question, or the material or product safety data sheet (MSDS or PSDS). This information is usually available through the website of the manufacturer of the dental material.
- Copies of all test results and a summary of the allergist's/immunologist's findings should be requested so they may be included in the patient's dental record.

ANTICOAGULANT and ANTIPLATELET THERAPY

Background:

- Normal hemostasis is altered using anticoagulant or antiplatelet drugs to help prevent stroke, heart attack, deep venous thrombosis and embolus formation.
- Patients with many different diseases or conditions are prescribed these medications. The underlying disease must be considered *in addition to* the bleeding tendencies when managing these patients.
- The patient's dental condition and the proposed dental treatment must be considered as well.
- For many patients, the thrombotic risks of discontinuing these medications outweigh the potential bleeding complications with continuing therapy.

Dental Implications for Patients Taking Warfarin (Coumadin):

- These patients are likely to have frequent, possibly monthly, evaluations of the INR (international normalized ratio) to measure the therapeutic level of warfarin. The range of INR is based on the condition being treated, (e.g., a patient with a prosthetic mechanical heart valve may have an INR of 2.5 – 3.0).
- According to the current literature, patients (*outside of the UFCDUFCD-student dental clinics*) who require oral surgery or dental treatment likely to cause bleeding (including uncomplicated tooth extractions without flap elevation) usually do not require alteration of their warfarin therapy regimen unless their INR is greater than an upper limit range of 3.5 - 4.0, provided that adjunctive local hemostatic measures* are used when indicated.

  * Adjunctive local hemostatic measures include: absorbable gelatin or oxidized cellulose sponges, sutures, local pressure (with sterile gauze pads moistened with water, normal saline, 5% ε-aminocaproic acid (Amicar) solution, or 5% tranexamic acid solution).

- **For patients taking warfarin being treated by <u>DH- or DMD-students in the DMD clinics</u>, routine (invasive) non-surgical dental treatment may proceed if the <u>INR is 3.0 or below</u>**.
  - INR results must be <u>from a test preformed within the previous</u> **<u>48 hours</u>** (*preferably from within the previous 12 hours*) <u>prior to routine invasive or surgical dental procedures</u>. However, in a patient with a history of long-term stability of the INR (as evidenced by their INR flow sheet) and no signs of easy bruising or bleeding, <u>diagnostic</u> or <u>non-invasive procedures</u> may be accomplished without a recent INR.
- **For patients taking warfarin who require <u>surgical dental procedures</u> (e.g., <u>extractions</u>), treatment should be performed the Graduate Clinics (e.g., Grad Oral Surgery).**
  - <u>Oral and Maxillofacial Surgery faculty</u> have the prerogative to allow a patient taking warfarin (especially one with a dental emergency and with an acceptable, recent INR value) to have simple extractions performed by a DMD-student <u>in the OMFS Clinic</u>. Local hemostatic measures should be employed as necessary (pressure, with gauze or stent, sutures, Gelfoam, Surgicel, etc.).

What to Include in a Medical Consultation:

- **A medical consultation is indicated for a patient taking warfarin (Coumadin) and who will require any invasive dental treatment.**
- Be sure to include the words '*oral surgery*' or '*extractions*' when requesting information about the patient's status, as well as:

  "*In our DMD-student dental clinics, routine, invasive dental treatment and simple oral surgery procedures may proceed if the patient's INR is 3.0 or less. We will require an INR test to be performed on this patient no more than 48 hours prior to any invasive dental procedures in order to verify their INR is within acceptable limits.*
  ***For our records, please send us a copy of this patient's INR flow sheet (that includes an indication of their desired [goal] INR range).*"**

IMPORTANT:

1. No patient should be advised to discontinue an anticoagulant (or antiplatelet) medication prescribed by a physician unless the physician has been consulted and given their approval.
2. **For patient's taking warfarin**, it is the **DH- or DMD-student's responsibility to coordinate the patient's invasive dental treatment appointment(s)** (where their INR must be ≤ 3.0) **with the patient's physician's office or lab in order to make certain the patient has an INR test performed within 48 hours of their dental appointment.** *If the DH- or DMD-student does not do this, then it probably won't get done and the patient is likely to arrive for their invasive dental treatment appointment without a current INR, which will usually necessitate cancelling/rescheduling the appointment.*
   Alternatively, the patient may be able to have their INR checked prior to their dental treatment at the Medical Exam room in clinic 2-B.
3. It would also be very beneficial if you informed the patient that throughout the course of their dental treatment, to please make certain that each time they have blood drawn for an INR, they ask the lab or physician's office to be sure to fax a copy of the INR results to the Clinical Administration Office in room D3-9 at: (352) 392-5606. This will help ensure that you always have the patient's most recent INR results in their axiUm record.

Dental implications for patients using direct oral anticoagulants (DOAs), (e.g., dabigatran [Pradaxa], rivaroxaban [Xarelto], apixaban [Eliquis], edoxaban [Savaysa], betrixaban [Bevyxxa]) and undergoing dental treatment or oral/maxillofacial surgical procedures include the following:

- Consult with the patient's physician concerning the planned dental or oral/maxillofacial surgical procedures (and the possible need to discontinue DOAs prior to surgery).
- For dental procedures that involve bleeding (including most uncomplicated tooth extractions), it does not appear that it would be necessary to discontinue the use of DOAs in patients with normal renal function, and without other risks for impaired hemostasis, especially if adjunctive local hemostatic measures are used appropriately when indicated.

- In situations where oral/maxillofacial surgical procedures may require the temporary discontinuation of DOAs due to concerns for possible complications resulting from excessive bleeding and/or impaired hemostasis, DOAs should be discontinued at least 24 hours prior to elective surgery or longer, depending on the risk of bleeding based on the type and complexity of the surgical procedure, the presence and degree of any renal impairment, and the presence of other risks for impaired hemostasis.
- Conventional (more readily available) coagulation tests (PT, aPTT, TT) have significant limitations when used to quantify these DOAs' effect on hemostasis and bleeding. However, despite their limitations, more readily available coagulation tests may provide qualitative information regarding the hemostatic effect of these DOAs prior to oral surgery, and normal results suggest very low drug levels and intact hemostatic function:
    - **Dabigatran**: aPTT or TT (*acceptable in acute situations*)
    - **Rivaroxaban**: PT / INR (?) (*no reliable routine test available*)
    - **Apixaban:** PT / INR or aPTT (?) (*no reliable routine test available*)
    - **Edoxaban:** (?) (*no reliable routine test available*)
    - **Betrixaban:** (?) *(no reliable routine test available)*
- Primary closure and the use of adjunctive local hemostatic measure is recommended for surgical procedures when possible.
- Administration of DOAs should not be restarted after oral/maxillofacial surgical procedures until the risk of post-operative bleeding is minimal (usually in 24-48 hours following surgery).
- If post-surgical bleeding occurs, contact the patient's physician,
    - Minor bleeding should be managed using local hemostatic measures. A short period of anticoagulant withdrawal may be considered, but should be balanced against individual thromboembolic risk and followed by re-initiation of drug.
    - Severe/life-threatening bleeding requires transfer to an intensive care setting with provision of life-supporting therapies (e.g., volume replacement, vasopressors, mechanical ventilation) as required.

Dental Implications for Patients Using Aspirin and/or Platelet Inhibitor Drugs (e.g., clopidogrel [Plavix], prasugrel [Effient], ticagrelor [Brilinta]):

- Patients may be taking aspirin at a low-dose (81 - 325 mg/day) and/or platelet inhibitor drugs to reduce the rate of atherothrombotic events (e.g., myocardial infarction, stroke).
- The clinical effect on hemostasis of platelet inhibitor drugs such as clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta) is dose-dependent and similar to that seen with low dose (≤ 325 mg) daily aspirin therapy.
- The clinical effect on hemostasis of low-dose daily (81 - 325 mg) aspirin and/or platelet inhibitor drugs is unlikely to result in significant bleeding problems associated with routine dental procedures (including minor oral surgery) that cannot be readily controlled with local hemostatic measures. **Therefore, in most circumstances, no discontinuation or alteration in aspirin and/or platelet inhibitor drug dose is necessary before routine dental procedures.**
    - It is usually **not** necessary for a medical consultation to address the use of low dose (≤ 325 mg) daily aspirin therapy and/or antiplatelet drugs in consideration of dental treatment.

- If clinical necessity requires discontinuation of daily aspirin or platelet inhibitor drugs prescribed for the prevention of atherothrombotic events prior to surgical or invasive dental treatment, then **no patient should be advised to discontinue this regimen unless their physician has been consulted and given their approval.**

- **EXCEPTIONS:**
  1. Patients taking more than 1,000 mg of aspirin per day (e.g., for arthritis or other inflammatory diseases) should discontinue taking aspirin for 3 to 5 days prior to the surgical procedure, and then aspirin may be re-started the day after.
  2. Concurrent use of aspirin and clopidogrel is the primary prevention strategy against stent thrombosis after placement of coronary artery drug-eluting metal stents in patients with CAD. Premature discontinuation of this combination antiplatelet therapy strongly increases the risk of a catastrophic event of stent thrombosis leading to myocardial infarction and/or death, according to a science advisory issued in Jan. 2007 from the AHA in collaboration with the ADA. The advisory stresses a 12-month therapy of aspirin and clopidogrel combination after placement of a drug-eluting stent in order to prevent thrombosis at the stent site.
     - Any elective surgery that would necessitate discontinuing aspirin and clopidogrel should be postponed for 1 year after stent implantation, and if surgery must be performed, consideration should be given to continuing the antiplatelet therapy during the perioperative period in high-risk patients with drug-eluting stents.
     - **Therefore, a medical consultation is necessary prior to surgical procedures that would necessitate discontinuing aspirin/antiplatelet drug therapy in patients who are less than 1 year post-op for drug-eluting coronary artery stent placement.**
- **NOTE:**
  - PT/INR will **not** disclose alterations in hemostasis caused by aspirin or antiplatelet drugs. If is it absolutely necessary to assess aspirin and/or antiplatelet drugs' effect on hemostasis, **closure time (CT, or CLT) (as measured by PFA-100)** is the preferred laboratory testing method, **however CT is a poor (unreliable) predictor of intraoperative or postoperative bleeding due to ASA or NSAIDs**.

ASTHMA and CHRONIC OBSTRUCTIVE PULMONARY DISEASE

ASTHMA

Definition:

- Asthma is a disease process characterized by airway obstruction due to bronchospasm resulting from an increased responsiveness or hyperirritability of the trachea and bronchi to various stimuli. The airflow obstruction is usually reversible, either spontaneously, or through pharmacologic therapy. Symptoms of asthma are typically paroxysmal or episodic and include coughing, wheezing, and dyspnea.
- Asthma can be classified by etiology into two general categories: extrinsic (allergic, atopic) asthma and intrinsic asthma.
  - Extrinsic (allergic, atopic) asthma is believed to be a manifestation of type I hypersensitivity localized to the airways, and is mediated by the interaction of various external allergens, sensitized IgE antibodies, and proinflammatory mast cells which line the tracheobronchial tree. Common asthma allergens include grasses, pollens, molds, animal danders (e.g., cats and dogs), feather pillows, and house dust mites.
  - Intrinsic asthma: may be the result of a hyper-irritable state of the tracheobronchial tree due to a defective functioning or blockade of beta-adrenergic receptors and/or excessive cholinergic activity. Subtypes of intrinsic asthma include:
    - Exercise induced asthma, in which bronchospasm occurs 5-10 minutes after the start of physical activity. This is believed to be due to heat loss and/or water loss from the bronchial surface. Hyperventilation of cold, dry air can also precipitate an asthma attack. Emotional stress has been known to trigger an asthmatic attack in some individuals as well.
    - Occupational or environmental asthma can be triggered by exposure to any number of agents occurring in the workplace or environment.
    - Triad asthma is a combination of asthma, aspirin (and possibly other nonsteroidal anti-inflammatory drug) sensitivity, and nasal polyposis which occurs in about 10% of asthma patients.

Clinical Presentation:

- Signs and symptoms of an asthmatic attack vary with its severity but are generally characterized by wheezing, dyspnea, coughing, and a feeling of tightness in the chest. Prolonged respiratory expiration, tachypnea, hyperresonance, intercostal retraction, use of accessory muscles of respiration, tachycardia, arterial hypoxemia, and respiratory acidosis may also be present in more severe episodes.

Clinical Classification of Asthma Severity:

- The Expert Panel of the National Asthma Education and Prevention Program of the National Heart, Lung and Blood Institute has developed asthma classification schemes which are useful in directing asthma therapy and identifying patients at high risk of developing life-threatening asthma attacks.
  - Figure 1 is to be used to classify the severity of asthma, and make initial treatment recommendations for patients <u>not currently receiving long-term asthma control medications.</u>

Figure 1

Classifying Asthma Severity and Initiating Treatment in Adults and Children 12 Years of Age and Older

Components of Severity		Classification of Asthma Severity (≥ 12 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8 - 19 yr: 85% 20 - 39 yr: 80% 40 - 59 yr: 75% 60 - 80 yr: 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime Awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung Function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Recommended Step for Initiating Treatment (See Stepwise Approach for Managing Asthma for treatment steps)		Step 1	Step 2	Step 3 And consider short course of oral systemic corticosteroids.	Step 4 or 5 And consider short course of oral systemic corticosteroids.
		In 2-6 weeks evaluate level of asthma control that is achieved and adjust therapy accordingly.			

Dental Implications of a Patient with Asthma:

- Specific oral conditions have been related to the use of asthma medications, including xerostomia, (from inhaled beta-2 agonists), increased caries and oral pharyngeal candidiasis (presumably from inhaled corticosteroids as well as xerostomia).
- Direct affect of asthma medications may also be manifested by soreness of the oral mucosa. The use of aerosol holding chambers ("spacers") in conjunction with metered dose inhalers, as well as mouth rinsing after medication usage, have been very helpful in preventing oral mucosal disorders.
- Complications of asthma include exhaustion, dehydration, airway infection, cor pulmonale, tussive syncope and status asthmaticus (small airway obstruction that is refractory to sympathomimetic and anti-inflammatory agents and that may progress to respiratory failure without prompt and aggressive intervention).
- Acute hypercapnic and hypoxic respiratory failure can occur in severe asthma.

Dental Evaluation of a Patient with a History of Asthma:

- Medical History - determine the following (a medical consultation with the patient's

physician will usually be required to obtain some of this information):

a.. Age of asthma onset

b. Type asthma and (intrinsic versus extrinsic) precipitating factors (e.g., pollens, dusts, odors, exercise, stress, drugs [especially aspirin and NSAID's])

c. Medications currently taken to control asthma

d. Classification of asthma severity and adequacy of medical control:
   - Table 1 outlines some general questions used when gathering information for assessing the severity and adequacy of medical control of asthma for a patient that is currently receiving long-term control medications.

e. Current adequacy of medical control of asthma:
   - Figure 2 is used to assess the degree and adequacy of medical control of a patient with asthma that is currently receiving long-term control medications.

- Physical and Dental Exam:
  1. Check blood pressure and pulse:
     - Elevated blood pressure, tachycardia or irregular pulse rhythm may indicate toxic reactions or overdose of a sympathomimetic or anticholinergic bronchodilator, or methylxanthines. Additional symptoms of toxicity or overdose of these drugs includes anxiety, tremors, palpitations, dizziness, nausea, and vomiting.
  2. Check intraorally for signs of candidiasis or xerostomia:
     - Both systemic and inhaled corticosteroids may predispose a patient for oral candidiasis, while anticholinergics, methylxanthines, and sympathomimetic bronchodilators may cause xerostomia.

Table 1: Questions to Ask When Assessing the Severity and Adequacy of Medical Control of Asthma for a Patient that is Currently Receiving Long-term Control Medications.

Assessing and Monitoring Severity of Asthma Symptoms

In the past week, how many days:

____ have you had chest tightness, cough, shortness of breath, or wheezing (whistling in your chest)?

____ have you awakened at night from sleep because of chest tightness, cough, shortness of breath, or wheezing (whistling in your chest)?

____ have you awakened in the morning with asthma symptoms?

____ did you have asthma symptoms that did not improve within 15 minutes of inhaling your bronchodilator (short-acting beta-2-agonist) inhaler?

____ has asthma restricted your physical activity?

____ have you missed from work/school due to asthma?

____ have you had asthma symptoms while exercising or playing?

- Have you had any unscheduled visits to a doctor, including to the emergency department due to asthma? (Yes / No)

Assessing and Monitoring Lung Function

- What is your highest and lowest peak expiratory flow (PEF) since your last visit? Highest: _____, Lowest: _____
- Has your PEF dropped below ___x___L/min since your last visit? (where x = 80% of the patient's personal best PEF)

Figure 2:

Assessing Asthma Control and Adjusting Therapy in Adults and Children 12 Years of Age and Older

Components of Control		Classification of Asthma Control (≥ 12 years of age)		
	Level of Control	Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime Awakenings	≤2x/month	1-3x/week	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $beta_2$-agonist use for symptom control	≤2 days/week	>2 days/week	Several times per day
	FEV_1 or peak flow	>80% predicted/personal best	60-80% predicted/personal best	<60% predicted/personal best

Functional Classification of Asthma:

- The Asthma Control Test (ACT) is a short, simple, patient-based tool (i.e, a 5-item questionnaire) that has been developed for identifying patients with poorly controlled asthma. The ACT is reliable, valid, and responsive to changes in asthma control over time (Schatz M, et al. J Allergy Clin Immunol. 2006 Mar;117(3):549-56).
- In a clinical setting the ACT is a useful tool to help healthcare providers identify patients with poorly/inadequately controlled asthma and facilitates their ability to follow patients' progress with treatment.
- Possible scores on the ACT range from 5 points (uncontrolled asthma) to 25 points (well-controlled asthma). A cutoff score of 19 or less points on the ACT identifies patients with inadequately controlled asthma, and that are likely to benefit from reassessment and modification (improvement) of their asthma control treatment regimen.

Table 2: ASA Risk Classification for Asthma

Presentation *	ASA Risk Category
• "Well controlled asthma"	II
• "Not well controlled asthma" • Stress-induced asthma attacks	III
• "Very poorly controlled asthma"	IV ‡

* This refers to asthma status (signs, symptoms, exacerbations) with current medications and treatment as described in Figure 2 (above).
‡ Refer to physician for evaluation.

What to Include in a Medical Consultation:

- A medical consult is indicated for a patient with "not well controlled" or "very poorly controlled" asthma (as defined in Figure 2) OR scoring 19 points or less on the Asthma Control Test (ACT) (A printable copy of the 5-item ACT questionnaire is included at the end of this section).
- Inform the physician of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient's disease. Also, inform the physician that we plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.
- It is important to advise the physician of the signs and symptoms being experienced by the patient that are indicative of poorly controlled (or uncontrolled) asthma.

- Example:

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine) (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

1. Mr. X has scored (n) points on the Asthma Control Test today (copy attached) and is currently experiencing significant asthma symptoms including, (specify: e.g., has persistent daily asthma symptoms, asthma is interfering or limiting normal daily activity [e.g., missed work/school], asthma symptoms awaken him at night, has asthma symptoms that do not improve within 15 minutes of using an inhaled short-acting bronchodilator [e.g,, albuterol], and so forth).
2. Please provide your assessment of the current severity and adequacy of medical control of this patient's asthma, as well as any changes in your treatment plan (if indicated) for Mr. X
3. Please provide your assessment of Mr. X's medical risk in relation to their ability to safely tolerate the proposed dental procedures.
4. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

Dental Management of a Patient with a History of Asthma:

Patents with "Very Poorly Controlled" Asthma (ASA IV):

- Elective dental care should be deferred pending attainment of better medical control of asthma. Dental treatment should be limited to urgent care only such as treatment of acute infection, bleeding, or pain; preferably in a hospital dental clinic. If treatment is necessary, it should be provided in consultation with the physician.

Other Patients with Asthma:

- If patient uses a short-acting bronchodilator (beta $_2$ selective agonist [or

sympathomimetic]) inhaler (e.g., albuterol), have the patient bring their inhaler to each appointment and place it so it is readily available to them during treatment. Having the patient use the inhaler prophylactically just prior to the start of dental treatment may also prove to be beneficial especially for patients with stress-induced asthma.

- Avoid patient contact with any known precipitating factor(s) which could trigger an asthmatic reaction (e.g., the vapors from methyl methacrylate monomer can precipitate asthma attacks in some patients).
- If anxiety or stress is a known to induce an asthmatic attack in a patient, then premedication with a benzodiazepine and/or nitrous oxide-oxygen inhalation sedation may be indicated. Use of nitrous oxide-oxygen inhalation sedation can usually be used safely and effectively in patients with mild to moderate asthma. Use of nitrous oxide-oxygen inhalation sedation is usually only contraindicated in patients with severe (usually intrinsic) asthma where there a risk of precipitating an asthma attack due to nitrous oxides' effect as a local irritant on the bronchial airways. A consultation with the patient's physician may be indicated before using nitrous oxide in these circumstances.
- Avoid the use of aspirin or NSAIDs in patients with a history of asthma induced by these drugs, or a history of asthma with nasal polyps or angioedema (approximately 20% of asthmatics are sensitive to aspirin).
- Local anesthetics containing vasoconstrictors are contraindicated in patients with a known sulfite sensitivity, and also in severe asthmatics such as those dependent on systemic steroids to control their disease due to an increased risk of sulfite allergy in these patients. Sulfites, such as sodium metabisulfite, are used in the formulation of dental local anesthetic agents as preservative for the vasoconstrictor. In addition, patients demonstrating cardiovascular side effects (i.e., elevated blood pressure and/or tachycardia) secondary to their asthma medication may represent a contraindication or require a dose limitation in the use of local anesthetics containing vasoconstrictors.
- Patients taking systemic corticosteroids to control their asthma may be at risk for adrenal suppression and immunosuppression (see the section on Corticosteroid Use and Adrenal Insufficiency). These patients should be carefully evaluated prior to invasive dental treatment in order to determine the need for supplemental corticosteroids to prevent a hypoadrenal crisis and prophylactic antibiotics to prevent postoperative infection. Patients who have discontinued the use of systemic corticosteroids within the past 2 weeks may still be at risk for adrenal suppression and may require corticosteroid supplementation. Patients using inhaled corticosteroids only are usually not considered to be at risk for these complications.
- The use of a pulse oximeter during dental treatment is useful in determining the oxygen saturation (SaO_2) of the patient. Normally, patients should remain between 97% and 100% when breathing room air. A drop in SaO_2 to 90% or lower with room air indicates impaired oxygen exchange and the need for intervention.
- There are no specific contraindications to the use of a rubber dam in patients with a history of asthma.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Definition:

- Chronic obstructive pulmonary disease (COPD) encompasses several diffuse pulmonary diseases including chronic bronchitis, cystic fibrosis, bronchiectasis, and emphysema. The term usually refers to a mixture of chronic bronchitis and emphysema.
  - Chronic bronchitis is characterized by excessive secretion of bronchial mucus and is manifested by productive cough for 3 months or more in at least 2 consecutive years in the absence of any other disease that might account for this symptom.
  - Emphysema denotes abnormal, permanent enlargement of air spaces distal to the terminal bronchiole, with destruction of their walls (interalveolar septa) and without obvious fibrosis.

Dental Implications of a Patient with COPD:

- Patients with COPD already have compromised respiratory function, therefore, efforts must be directed toward the avoidance of anything that could further depress respiration.
- Since patients with COPD often have coexisting heart disease such as congestive heart failure and/or hypertension, these conditions must also be addressed (if present) when considering the dental management of the patient.

Clinical Classification of COPD:

- According to the Global Initiative Chronic Obstructive Lung Disease (GOLD), COPD is now classified (staged) as follows:
  - # Stage 0 - At risk:
    - Spirometry still normal
    - Typically, chronic cough and sputum production
  - # Stage I - Mild COPD:
    - $FEV_1/FVC < 70\%$, but $FEV_1 > 80\%$ of predicted value*
    - Usually, but not always, chronic cough and sputum production
    - Patient may not be aware that lung function is abnormal
  - # Stage II - Moderate COPD:
    - $FEV_1/FVC < 70\%$ with FEV_1 between 50 - 80% of predicted value*
    - Typically, the stage at which patients first seek medical attention because of dyspnea developing on exertion or an exacerbation of their disease
  - # Stage III - Severe COPD:
    - $FEV_1/FVC < 70\%$ with FEV_1 between 30 - 50% of predicted value*
    - Increased shortness of breath and repeated exacerbations, impacting on the quality of life
  - # Stage IV - Very severe COPD:
    - $FEV_1/FVC < 70\%$ with $FEV_1 < 30\%$ of predicted value, or presence of chronic respiratory failure*, or

      Clinical signs of right-sided heart failure due to cor pulmonale; or

      Respiratory failure: $PaO_2 < 60$ mmHg with or without $PaCO_2 > 50$ mmHg while breathing room air (21% oxygen) at sea level.

      Note: Patients may have severe COPD even if FEV_1 is > 30% of predicted value when complications of right-sided heart failure or respiratory failure are present.
  - * Indicates primary determining criteria.

Functional Classification of COPD:

- The COPD Assessment Test (CAT) is a patient-completed instrument (i.e., an 8-item questionnaire) that complements existing approaches to assessing COPD, such as FEV_1 measurement. It has been designed to provide a simple and reliable measure of health status in COPD and assists patients and their physicians in quantifying the impact of COPD on the patient's health.
- The CAT Development Steering Group and the GOLD strategic document recommend that patients routinely complete the CAT questionnaire every 2 to 3 months to detect changes and trends in CAT score.
- Possible scores on the CAT range from 0 points (asymptomatic, well-controlled COPD) to 40 points (uncontrolled COPD with severe symptoms). A cutoff score of 10 or more points on the CAT identifies patients with inadequately controlled COPD, and that are likely to benefit from reassessment and modification (improvement) of their COPD control treatment regimen.

Dental Evaluation of the Patient with COPD:

1. Review patient's medical history pertaining to COPD:
   a. Determine time of original diagnosis / duration of disease
   b. Review history for evidence of concurrent heart disease such as hypertension or congestive heart failure (take appropriate precautions if heart disease is present)
   c. Determine / record present medication(s) and/or history of surgical treatment for COPD
   d. Determine the current clinical status / severity of the patient's COPD (i.e., GOLD classification):
      - assess the functional severity of the patient's COPD: Have the patient complete the COPD Assessment Test (CAT) (A printable copy of the 8-item CAT questionnaire is included at the end of this section).
        - Patients with a CAT score of 10 or higher should have a medical consultation regarding the status and degree of medical control of their COPD.
      - obtain the most recent pulmonary function tests(PFTs)/spirometry results ; arterial blood gas test results are also useful, but are usually not performed routinely due to their invasiveness (a medical consultation with the patient's physician may be needed to obtain this information).
   e. Determine the presence of factors that may exacerbate COPD such as the presence of an acute respiratory infection or continued tobacco smoking
2. Check blood pressure and pulse:
   - Elevated blood pressure, tachycardia or irregular pulse rhythm may indicate toxic reactions or overdose of a sympathomimetic or anticholinergic bronchodilator, or methylxanthines. Additional symptoms of toxicity or overdose of these drugs includes anxiety, tremors, palpitations, dizziness, nausea, and vomiting.

CONTINUED ON THE NEXT PAGE

Table 3: Dental Evaluation of the Patient with COPD

Risk Category	Clinical Presentation:
Patients at Low Risk (ASA II)	• dyspnea only on significant exertion • FEV_1 > 65% of predicted • SaO_2 (on room air) > 95% • normal blood gases: - $PaCO_2$: 40 mm Hg; PaO_2: 100 mm Hg; pH: 7.40
Patients at Moderate Risk (ASA III)	• dyspnea on exertion • chronic bronchodilator therapy • recent use of systemic corticosteroids • SaO_2 (on room air): 90 - 95% • FEV_1 40% to 65% of predicted • hypoxemia (PaO_2 < 85 mm Hg) but not carbon dioxide retention
Patients at High Risk (ASA IV)	• previously undiagnosed symptoms of COPD • acute exacerbation of COPD (e.g., acute respiratory infection) • significant dyspnea at rest or cor pulmonale who require chronic (long-term) oxygen therapy • SaO_2 (on room air) < 90% • FEV_1 < 40% of predicted • CO_2 retention ($PaCO_2$ greater than 45 mm Hg)

What to Include in a Medical Consultation:

- A medical consult is indicated for any patient with a COPD Assessment Test (CAT) score of 10 or higher.
- Inform the physician of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient's disease. Also, inform the physician that we plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.

- Example:

  "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine). (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here).
  Mr. X presents today with a COPD Assessment Test (CAT) score of x/40 (copy attached).

  1. Please provide your assessment of the current severity (e.g., GOLD classification) and adequacy of medical control of this patient's COPD. Please include copies of their most recent PFTs/spirometry results, and any other pertinent lab tests.

2. Please provide your assessment of Mr. X's medical risk in relation to their ability to safely tolerate the proposed dental procedures.
3. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

Dental Management of the Patient with COPD:

Patents with GOLD class III or IV COPD, or ASA IV COPD:

- These patients will generally need to have all invasive dental treatment performed in hospital dental clinic (i.e., ACB), and/or by dental specialty residents. Under most circumstances they should be able to receive non-invasive dental treatment (e.g., denture fabrication) by DMD-student in the General Dental Clinic.

Other Patients with COPD:

Because patients with COPD already have compromised respiratory function, efforts must be directed toward the avoidance of anything that could further depress respiration. Since patients with COPD often have coexisting cardiovascular disease such as congestive heart failure and/or hypertension, these conditions must also be addressed (if present) when considering the dental management of the patient.

- Patients should be placed in a semisupine or upright chair position for treatment (as indicated by the presence of orthopnea) in order to avoid orthopnea and the feeling of respiratory discomfort.
- There is no contraindication to the use of local anesthetic; however, bilateral mandibular blocks or bilateral palatal blocks are not recommended because of a possible unpleasant choking sensation or difficulty swallowing.
- Patients demonstrating cardiovascular side effects (i.e., elevated blood pressure and/or tachycardia) secondary to their COPD medication may represent a contraindication or require a dose limitation in the use of local anesthetics containing vasoconstrictors.
- If sedative medication is required, low-dose oral benzodiazepines (e.g., alprazolam, triazolam) may be used.
- Narcotic analgesics and barbiturates also are to be used with caution (or avoided in patients with more severe COPD) because of their respiratory depressant properties.
- The use of a pulse oximeter during dental treatment is useful in determining the oxygen saturation (SaO_2) of the patient. Normally, patients should remain between 97% and 100% when breathing room air. A drop in SaO_2 to 90% or lower with room air indicates impaired oxygen exchange and the need for intervention.
  - Supplemental humidified low-flow oxygen (2 to 3 L/min via nasal cannula) should be considered for use in patients with COPD presenting for dental treatment with an SaO_2 less than 95% on room air.
- Most patients with COPD can safely tolerate N_2O-O_2 inhalation sedation. Use of N_2O-O_2 inhalation sedation may be challenging for patients with <u>severe COPD</u> (as indicated by the presence of <u>CO_2 retention</u>).
  - This is due to the fact these patients with very severe COPD are hypoxic drive breathers. They respond to low oxygen levels rather than to the elevated CO_2 levels which drives

breathing in normal (disease free) individuals, and may respond with decreased respirations (hypoventilation) due to the high oxygen levels administered with nitrous oxide.

- To avoid potential complications when using N_2O-O_2 inhalation sedation in a patient with severe COPD, overall flow rates should be reduced to no more than 3L/min, and the dentist should anticipate induction and recovery times twice as long a normal than as seen with healthy patients.

• With severe COPD, the use of a rubber dam may be problematic, unless low flow of oxygen is provided during the dental procedure, because the rubber dam may result in a feeling of compromised air supply. When needed, low-flow humidified oxygen is generally provided between 2 and 3 L/min via nasal cannula.

University of Florida College of Dentistry

1395 Center Drive

Gainesville, FL 32610

Today's Date: ___ __21_____

Patient's Name: — — — — — — — —

FOR PATIENTS:

Take the Asthma Control Test™ (ACT) for people 12 yrs and older. Know your score. Share your results with your doctor.

Step 1 Write the number of each answer in the score box provided.

Step 2 Add the score boxes for your total.

Step 3 Take the test to the doctor to talk about your score.

---

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?

All of the time CD | Most of the time O | Some of the time | 4 | None of the time | SCORE D

2. During the past 4 weeks, how often have you had shortness of breath?

once a day | Once a day | a week | 4 | Not at all | e

More than | CD | O | 3 to & times | D

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week | 2 or 3 nights a week | O | Once a week | O | 4 | Not at all | e | D

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albutero

3 or more times per day | 1 or 2 times per day | 2 or 3 times per week. | O | 4 | Not at all | e | D

TOTAL

5. How would you rate your asthma control during the past 4 weeks?

Not at all controlled | CD | Poorly controlled | O | Somewhat controlled | 3 | Well controlled | 4 | Completely controlled | 5 | D

If your score is 19 or less, your asthma may not be controlled as well as it could be. Talk to your doctor.

FOR PHYSICIANS:

The ACT is:

- A simple, 5-question tool that is self-administered by the patient
- Recognized by the National Institutes of Health
- Clinically validated by specialist assessment and spirometry1

Reference: 1. Nathan RA et al. *j Allergy Clin lmmunol.* 2004;113:5965.

05081-025 (Revised 9-08) RegionalHealth Education

Your name:

Today's date:

How is your COPD? Take the COPD Assessment Test™ (CAT)

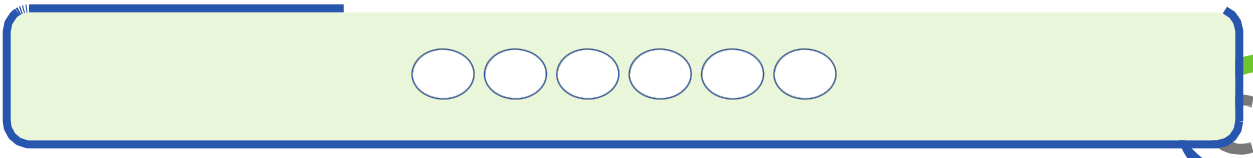
This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 X 2 3 4 5 I am very sad

SCORE

I never cough	0 1 2 3 4 5	**I cough all the time**
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	**My chest is completely full of phlegm (mucus)**
My chest does not feel tight at all	0 1 2 3 4 5	**My chest feels very tight**
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	**When I walk up a hill or one flight of stairs I am very breathless**
I am not limited doing any activities at home	0 1 2 3 4 5	**I am very limited doing activities at home**
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	**I am not at all confident leaving my home because of my lung condition**
I sleep soundly	0 1 2 3 4 5	**I don't sleep soundly because of my lung condition**
I have lots of energy	0 1 2 3 4 5	**I have no energy at all**



TOTAL SCORE

Last Updated: February 24, 2012

AUTOIMMUNE DISEASE

Definition:

- Autoimmune diseases are caused by immune reactions against self. Generally three characteristics are needed to classify a disease as being of autoimmune etiology: the presence of an autoimmune reaction; evidence that such a reaction is not secondary to tissue damage (e.g., resulting from infection, but is of primary pathogenetic significance); and the absence of another well-defined cause of the disease.
- Autoimmune diseases form a spectrum, on one end of which are conditions in which the immune response is directed against a single organ or tissue, resulting in organ-specific (localized) disease, and on the other end are diseases in which the autoimmune reaction is against widespread antigens, resulting in generalized or systemic disease.

Table 1: Examples of More Frequently Occurring Autoimmune Diseases

Organ-Specific (Localized) Disease	Systemic (Generalized) Disease
Celiac sprue disease	Systemic lupus erythematosus
Pernicious anemia / atrophic gastritis	Rheumatoid arthritis
Vitiligo	Sjögren's syndrome
Psoriasis	Inflammatory bowel disease (Crohn's disease, Ulcerative colitis)
Hashimoto's thyroiditis	Scleroderma (progressive systemic sclerosis)
Addison's disease	Wegner's granulomatous
Graves' disease	Sarcoidosis
Type 1 diabetes mellitus	Goodpasture's syndrome
Multiple sclerosis	Reiter syndrome (reactive arthritis)
Myasthenia gravis	Behçet's disease

Overview:

- The two most important implications that an autoimmune disease has on a patient's dental treatment are:
  1. The deleterious effect the autoimmune disease has on the function of major organ systems, especially:
     - cardiovascular, hepatic, renal and hematopoietic (i.e., resulting in increased risk for infection and/or impaired hemostasis / increased risk for bleeding).
  2. The effects of that the drug(s) used to treat an autoimmune disease have on the function of major organ systems, especially:
     - - hepatic, renal and hematopoietic (i.e., resulting in increased risk for infection and/or impaired hemostasis / increased risk for bleeding).

- As a general rule, a patient with an active, generalized/systemic, autoimmune disease and/or receiving immunosuppressive or immunomodulatory drug therapy for an autoimmune disease should have a medical consultation prior to invasive dental treatment in order to:
    1. Ascertain the current status and severity of their autoimmune disease (including the presence of significant organ involvement that might have implications for dental treatment).
    2. Assess the patient for dentally-significant adverse reactions / side-effects resulting from drugs being used to treat their autoimmune disease.
- * It is beyond the scope of this Guide to provide examples of medical consults for the all the autoimmune disease that a dental patients may present with. Please consult with one of the Oral Medicine Faculty for assistance in writing a medical consultation for a patient with an autoimmune disease when necessary.

- Two of the most commonly encountered systemic autoimmune diseases are systemic lupus erythematous, and rheumatoid arthritis. Sjögren's syndrome is also a systemic autoimmune diseases that has the most specific orally-related presentation and sequela.

Systemic lupus erythematosus (SLE):

- SLE is the prototypical multisystem autoimmune disease characterized by the production of numerous autoantibodies. SLE is a disease with multiorgan involvement. Immunocomplex deposition causes small-vessel vasculitis, which then leads to renal, cardiac, hematologic, mucocutaneous, and central nervous system destruction. In addition, inflammation of the serous membranes results in joint, peritoneal, and pleuropericardial symptoms.

- Physical Findings & Clinical Presentation:
    - Constitutional: Fatigue, anorexia, weight loss, unexplained fever, lymphadenopathy.
    - Skin: malar rash sparing nasolabial folds (acute cutaneous lupus); annular or papulosquamous rash (subacute cutaneous lupus); raised erythematous patches with subsequent edematous plaques and adherent scales (discoid cutaneous lupus); alopecia, nasal, or oropharyngeal ulcerations; Raynaud's phenomenon; petechiae, palpable purpura, skin ulceration, or digital ischemia (vasculitis); livedo reticularis or livedo racemosa (secondary antiphospholipid antibody syndrome).
    - Musculoskeletal: arthritis (tenderness, swelling, effusion) typically affecting peripheral joints; myositis.
    - Cardiac: pericardial rub (pericarditis), heart murmur (Libman-Sacks endocarditis and other valvular heart disease), congestive heart failure (myocarditis), premature atherosclerotic heart disease.
    - Pulmonary: pleuritis, pneumonitis, diffuse alveolar hemorrhage.
    - Gastrointestinal: abdominal pain, intestinal vasculitis, ascites.
    - Neurologic: headache, psychosis, seizure, acute confusional states, peripheral or cranial neuropathy, transverse myelitis, cerebral vascular accident, chronic cognitive impairment.
    - Hematologic: anemia (hemolytic, anemia chronic disease, aplastic anemia), thrombocytopenia, leukopenia, lymphadenopathy, secondary antiphospholipid antibody syndrome.

- Renal: acute renal failure, proteinuria, nephritic syndrome, nephrotic syndrome.
- Oral: Predominant types of oral lesions seen in patients with SLE include:
  - Ulcerations: seen in lupus cannot be easily distinguished from other common oral mucosal conditions, such as aphthous ulcers, although they occur with increased frequency on the palate and in the oropharynx and are characteristically painless.
  - Discoid lesions: are similar to those occurring on the skin and appear as whitish striae frequently radiating from the central erythematous area, giving a so-called brush border.
    - Atrophy and telangiectases are also frequently present.
    - Buccal mucosa, gingiva, and labial mucosa are the most commonly affected intraoral sites.
  - Erythematous lesions: isolated erythematous areas are also common, especially on the palate. It may be difficult to differentiate these lesions from other common mucosal disorders such as oral candidiasis or lichen planus, especially if there are few lesions and there is no systemic or cutaneous involvement.

  Patients with SLE also exhibit a high incidence of signs and symptoms of oral conditions, including glossodynia, dysgeusia, dysphagia, and xerostomia. Approximately 33% of patients with SLE also have Sjögren's syndrome.

- Treatment:
  - No single drug of choice is available to treat SLE. Treatment is symptomatic with certain exceptions.
  - Antimalarials (hydroxychloroquine, 200 or 400 mg/day) may be helpful in treating lupus rashes or joint symptoms and appear to reduce the incidence of severe disease flare-ups..
  - Corticosteroids (e.g., prednisone 40 – 60 mg/day) is often needed initially) for the control of certain complications such as glomerulonephritis, hemolytic anemia, pericarditis or myocarditis, alveolar hemorrhage, central nervous system involvement, and thrombotic thrombocytopenic purpura (TTP).
  - Methotrexate (5 – 25 mg oral or subcutaneous, weekly in one single dose) has been effective as a "steroid sparer" management of arthritis, rash, serositis or fever.
  - Immunosuppressive agents such as cyclophosphamide, mycophenolate mofetil (MMF), and azathioprine are used in cases resistant to corticosteroids.
  - Warfarin: is used to prevent thrombotic complications in patients that are positive for antiphospholipid antibodies (lupus anticoagulant and/or anticardiolipin antibody). Moderately intensive anticoagulation with warfarin to achieve an INR of 2.0 – 3.0 is as effective as more intensive regimens.
  - Belimumab (Benlysta) is a human monoclonal antibody drug, and is the first in a new class of drugs called BLyS-specific inhibitors that recognize and inhibit the biological activity of B-lymphocyte stimulator [BLyS]. Belimumab (IV, 10 mg/kg every 2 – 4 weeks) has been found to reduce disease activity and possibly decrease the number of severe flare-ups and corticosteroid use in patients with SLE when used in combination with standard therapy.

Dental Implications of a Patient with Systemic Lupus Erythematosus:

1. The following lab tests are recommended prior to invasive dental treatment in a patient with SLE:
   - Complete blood count (with differential and platelets):

- Patients with SLE can frequently develop normochromic normocytic anemia, and/or hemolytic anemia, (hemoglobin [Hgb] should be > 11 g/dL).
- Comprehensive metabolic panel with estimated GFR:
  - Additional precautions would be required for patients with severe renal function impairment / chronic renal disease, and/or are receiving hemodialysis (see section on "Renal Disease").
- If taking warfarin: PT/INR (see section on "Anticoagulants and Antiplatelet Drugs").

2. Proceed with caution in performing invasive dental treatment (especially oral surgery) in patients who have a history of post-surgery lupus flare-ups.
3. Patients with:
   - high SLE disease activity (impaired immune function that is part of SLE is believed to contribute to their increased susceptibility to infection), or
   - being treated with immunosuppressive drugs (particularly cyclophosphamide, belimumab, or higher doses of prednisone [> 10 mg/day] or other corticosteroids), or
   - have an absolute neutrophil count (ANC) < 500/mm^3 or a total WBC count < 2,000/mm^3

   are at increased risk from infections that may result from invasive dental treatment (e.g., post-surgical infections).
4. Drugs that are used to treat SLE cause numerous, potentially serious, side-effects that may impact on dental treatment (see: Table 2).
5. Drugs that have been related to acute lupus flare-ups and should be used with caution and include sulfonamides and antibiotics with photosensitizing potential (e.g., tetracyclines)
6. Secondary Sjögren's syndrome (when present) results in xerostomia that increases the risk of caries and other oral complications, and should be managed accordingly.

What to Include in a Medical Consultation:

- A medical consult with the patient's physician is usually required for a patient with active systemic lupus erythematosus that requires medical management in order to ascertain the current status and severity of their SLE and assess the patient for dentally-significant adverse reactions / side-effects resulting from drugs being used to treat their SLE.

Example of a Medical Consultation for a Patient with Systemic Lupus Erythematosus:

"Mrs. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

1. Please provide us with copies of this patient's most recent lab test results including CBC (with platelets), and CMP with estimated GFR.
2. Please provide a summary of the severity and current status of this patient's systemic lupus erythematosus including the presence of any significant systemic involvement (e.g., renal, cardiovascular, hematologic, neurologic, etc.) and/or secondary Sjögren's syndrome.

3. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.
4. For patients taking Coumadin (warfarin): See the section on,"Anticoagulant and Antiplatelet Therapy" for more information about what you need to add to this medical consultation).

Thank you for your assistance in my care of our mutual patient."

Rheumatoid Arthritis (RA)

- Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory polyarthritis, which affects peripheral joints, especially the small joints of the hands and feet. Chronic untreated inflammation may lead to joint erosions and joint destruction.

Physical Findings & Clinical Presentation:

- Initial presentation:
  - Greater than six weeks of pain, swelling, warmth in one or more peripheral joints, frequently with symmetric joint involvement involving wrists, hands, and/or feet, and often associated with greater than one hour of morning stiffness.
  - Most common joints involved include metacarpophalangeal (MCP), proximal interphalangeal (PIP), wrists, metatarsophalangeal (MTP), and ankles. Also elbows, shoulders, hips, and knees. Distal interphalangeal (DIP) joints are spared. Sacroiliac and vertebral joints are spared except for C1 to C2.
- Chronic longstanding disease:
  - Joint damage of wrists, elbows, shoulders, hips, and knees can lead to severe osteoarthritis, necessitating joint surgery and/or replacement.
  - "Swan-neck" (DIP flexion and PIP hyperextension) and "boutonniere" PIP flexion and DIP hyperextension) deformities as well as MCP subluxation resulting in ulnar drift.
  - C1-C2 (atlantoaxial) inflammation can lead to odontoid erosion and transverse ligament laxity, resulting in atlantoaxial subluxation and cord compression.
  - Radiographic changes of the TMJ may be detected commonly in up to 75% of patients with RA, but may be asymptomatic. RA patients with symptomatic TMJ involvement may complain of increased TMJ pain and difficulty/limitation in opening their mouth.
- Extraarticular manifestations:
  - Secondary Sjögren's syndrome (~ 35% of patients): immune-mediated inflammation of lacrimal and salivary glands resulting in dry mouth and eyes (keratoconjunctivitis sicca).
  - Rheumatoid nodules (~ 25% of patients) on extensor surfaces and pressure points, in rheumatoid factor positive (RF+) disease.
  - Normocytic normochromic anemia.
  - Felty's syndrome: RA with splenomegaly and leukopenia.
  - Pulmonary disease: pleural disease (effusions, pleuritis); interstitial lung disease (up to 10% clinically significant).
  - Skin vasculitis
  - Cardiovascular disease: pericarditis, intracardiac rheumatoid nodules causing valvular or conduction abnormalities (arrhythmias)
  - Amyloidosis can occur in patients with longstanding RA. Can affect heart, kidney, liver, spleen, intestines, and skin.

Functional Status Classification of Rheumatoid Arthritis:

- Grading of functional ability as measured by restriction of normal activities (i.e., activities of daily living [ADL]) due to RA as defined by (Pincus, et al): To dress self; To get in and out of bed; To eat and drink with utensils; To walk outside on flat ground; To wash and dry entire body; To bend down and pick up clothing from floor; To turn regular faucets on and off; To get in and out of a car.
    + Class I: Complete function; able to perform usual duties without handicap.
    + Class II: Moderate restriction; adequate function for normal activities, despite presence of pain or limited range of motion in 1 or more joints.
    + Class III: Marked restriction; inability to perform most of the patient's usual occupation or self-care, some assistance required.
    + Class IV: Incapacitation or confinement to a bed or wheelchair; largely or wholly incapacitated and dependent on assistance.

Treatment:

- NSAIDs (e.g., meloxicam, piroxicam, celecoxib [Celebrex]): Sometimes used initially to relieve pain and mild inflammation, or used later in the disease course for additional control of mild pain. NSAIDs are NOT disease modifying drugs for RA.
- Corticosteroids (e.g., prednisone): oral or intraarticular, frequently used initially to reduce inflammation rapidly until oral disease-modifying antirheumatic drug (DMARD) treatments take effect. They may also be used during acute flares or in low doses for additional control of inflammation. They have many, potentially serious side-effects, including but not limited to weight gain, increased risk of diabetes, increased risk for infections, osteoporosis, and avascular necrosis of bones.
- Early identification and treatment of RA with disease-modifying antirheumatic drugs (DMARDs) are crucial. More than half of patients have radiographic joint damage within 2 years of disease onset, but early aggressive treatment (with DMARDs) is associated with less damage.
- DMARDs: Can be classified into "nonbiologic" and "biologic" treatments.
    - Nonbiologic DMARDs: commonly used agents are methotrexate (MTX), Plaquenil (hydroxychloroquine [HCQ]), sulfasalazine (SSZ), and leflunomide. Less commonly used nonbiologic DMARDs include D-penicillamine, cyclosporin, and gold salts.) Most of these are associated with potential toxicity and require close monitoring. They are also slow-acting drugs that require more than 8 weeks to become fully effective. MTX is the most commonly used DMARD worldwide for the treatment of RA. "Triple therapy" using MTX, HCQ, and SSZ are superior to MTX alone.
    - Biologic DMARDs: newer biologically engineered therapies, which target cytokines and cells involved in the RA inflammatory response. Major side effects include an increased risk of severe infection, most notably reactivation of tuberculosis with TNF-á inhibitors. Biologic DMARDs are most effective when used in combination with a nonbiologic DMARD, usually MTX.
        - Tumor necrosis factor alpha (TNF-á) inhibitors (e.g., infliximab, etanercept, adalimumab, certolizumab pegol, and golimumab).
        - Abatacept (Orencia) (selective T-Cell costimulation blocker): A recombinant protein that prevents costimulatory binding of antigen presenting cell to T cell, preventing T cell activation.

- Tocilizumab (Actemra) (interleukin-6 [IL-6] receptor-inhibiting monoclonal antibody): A monoclonal antibody against the IL-6 receptor. Inhibition of IL-6 receptors by leads to a reduction in cytokine and acute phase reactant production.
- Tofacitinib (Xeljanz) (Janus kinase 3 [JAK3] inhibitors): Inhibits the JAK-STAT intracellular signaling pathway, thus preventing the production of inflammatory mediators. (This is the first orally-administered biologic DMARD).
- Rituximab (anti-CD20): A monoclonal antibody against CD20 antigen on B-lymphocytes. Signs and symptoms of RA are reduced by targeting B-cells and the progression of structural damage is delayed.

Dental Evaluation of the Patient with Rheumatoid Arthritis:

- Determine the functional ability of the patient especially in regards to any impairment of their ability to perform oral hygiene tasks.
- Determine the presence of symptomatic TMJ disease secondary to RA
- Determine the presence of systemic manifestations and/or complications of RA (e.g, Sjögren's syndrome)
- Determine patients current medications and dosage used to treat RA
  - Evaluate the patient for any adverse or toxic reactions associated with these drugs. (see: Table 2).
- Determine any history of surgical treatment for RA, especially prosthetic joint replacement(s).

Dental Management of the Patient with Rheumatoid Arthritis:

1. Because patients may have multiple joint involvement with varying degrees of pain and immobility, dental appointments should be kept as short as possible, and the patient should be allowed to make frequent position changes as needed.
2. The patient also may be more comfortable in a sitting or semisupine position as opposed to supine. Physical supports, such as a pillow or rolled towel, may be needed to provide support for deformed limbs, joints, or neck.
3. Drug considerations:
   a. Aspirin and NSAIDs:
      - Impaired hemostasis may become clinically significant with higher doses of aspirin (typically > 2 grams per day).
      - Patients with RA taking NSAIDs may demonstrate mild impaired hemostasis, but it in the absence of additional risks for impaired hemostasis, it should not be of sufficient magnitude to be clinically significant in regards to dental treatment including routine oral surgical procedures.
   b. Corticosteroids, DMARDs:
      These drugs have numerous, potentially serious, side effects (see: Table 2) that may impact on dental treatment including immunosuppression/increased risk of infection, marrow suppression (resulting in possible anemia, leukopenia, or thrombocytopenia), nephrotoxicity, hepatotoxicity, and stomatitis. Depending of the specific DMARDs the patient is taking, one of more of the following may need to be evaluated prior to dental treatment:
      - a complete blood cell count with differential (including platelet count)
      - liver function tests (e.g., AST, ALT, serum bilirubin, serum albumin)

- renal function tests (e.g., BUN, serum creatinine, estimated GFR)

- Consider the use of peri-operative antibiotic prophylaxis to prevent post-operative wound infection if significant immunosuppression and/or neutropenia is present.
- Defer surgical dental treatment if platelet count is < 50,000 mm^3.
- Treat stomatitis symptomatically if present.

What to Include in a Medical Consultation:

- A medical consult with the patient's physician is usually (only) required for a patient with active rheumatoid arthritis who is receiving immunosuppressive drug therapy (e.g., high-dose corticosteroids, methotrexate, cyclosporin, TNF-á inhibitors, Janus kinase (JAK) inhibitors, etc.) in order to ascertain the current status and severity of their RA and assess the patient for dentally-significant adverse reactions / side-effects resulting from drugs being used to treat their RA.

Example of a Medical Consultation for a Patient with Rheumatoid Arthritis:

"Mrs. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

1. Please provide us with copies of this patient's most recent lab test results including CBC with platelets and CMP.
2. Please provide a summary of the severity and current status of this patient's rheumatoid arthritis including the presence of any significant extraarticular involvement and/or secondary Sjögren's syndrome.
3. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in my care of our mutual patient."

(TABLE 2 is on the Next Page)

Table 2: Dental-Treatment-Significant Potential Adverse Effects of Drugs Used to Treat Autoimmune Disease

Drug	Dental-Treatment-Significant Potential Adverse Effects
Azathioprine	Bone marrow suppression (leading to thrombocytopenia and leukopenia), hepatitis, or pancreatitis; stomatitis and opportunistic infections.
Belimumab (Benlysta)	Leukopenia (4%), increased risk of serious and sometimes fatal infections.
Corticosteroids (e.g., prednisone)	Immunosuppression, increased risk of infection, adrenocortical and pituitary unresponsiveness (in times of stress).
Cyclosporin	Hypertension (8% to 53%), renal insufficiency (10% to 38%), increased susceptibility to infection (3% to 25%), leukopenia (<1% to 6%), anemia, thrombocytopenia, mouth sores, swallowing difficulty, gingivitis, gingival bleeding, gingival hyperplasia (2% to 16%), xerostomia (normal salivary flow resumes upon discontinuation), abnormal taste.
Cyclophosphamide	Bone marrow suppression (leading to leukopenia, neutropenia, and thrombocytopenia), mucositis, stomatitis, cardiotoxicity, congestive heart failure.
D-penicillamine	Bone marrow suppression (leading to thrombocytopenia, leukopenia, and aplastic anemia), renal toxicity, hepatotoxicity, drug-induced pemphigus; stomatitis, oral ulcers, loss of taste.
Gold salts (Myochrysine [gold sodium thiomalate])	Neutropenia, nephropathy with proteinuria; stomatitis, alterations in taste.
Hydroxychloroquine	Bluish-black discoloration limited to the hard palate. (Hematologic adverse effects such as anemia, aplastic anemia, and thrombocytopenia are rare).
Interleukin-1 (IL-1) receptor antagonist (anakinra)	Increased risk of serious and sometimes fatal infections and neutropenia.
Janus kinase 3 (JAK3) inhibitors (e.g., tofacitinib)	Immunosuppression, increased risk of serious and sometimes fatal infections , and bone marrow suppression (leading lymphopenia, neutropenia and/or anemia).
Methotrexate	Suppression of hematopoiesis may cause myelosuppression including thrombocytopenia, hepatotoxicity, ulcerative stomatitis, gingivitis, glossitis, and mucositis.
Mycophenolate mofetil	Leukopenia (23% to 46%), anemia (26% to 43%); thrombocytopenia (24% to 38%), increased risk of opportunistic infections, hypertension, tachycardia, hyperglycemia, elevated serum creatinine and BUN, abnormal liver function test results, dyspnea, anxiety oral ulceration and stomatitis, gingival hyperplasia, gingivitis, xerostomia, dysphagia, oral candidiasis.
Sirolimus	Anemia (23% to 33%), thrombocytopenia (14% to 30%), hypertension (49%), leukopenia, oral ulcerations / stomatitis, oral candidiasis, stomatitis, gingival hyperplasia, gingivitis, and dysphagia.

Tacrolimus	Anemia (5% to 50%; hemoglobin <10 g/dL 65%), leukopenia (11% to 48%), leukocytosis (8% to 32%), thrombocytopenia (14% to 24%), serious infection (19% to 24%), hypertension (13% to 89%), hyperglycemia / diabetes mellitus (16% to 70%), renal function abnormality (36% to 56%), abnormal hepatic function tests (6% to 36%), oral ulcerations / stomatitis, oral candidiasis, dysphagia, gingival hyperplasia.
TNF-a inhibitors: (e.g., etanercept, infliximab adalimumab)	Immunosuppression, increased risk of serious and sometimes fatal infections, anemia, thrombocytopenia and hemolytic anemia.

MEDICATION-RELATED OSTEONECROSIS of the JAWS (MRONJ)

Overview:

Medication-related (drug-induced) osteonecrosis of the jaws (MRONJ) is a debilitating bone disorder. MRONJ development has been associated with the use of bisphosphonates, anti–receptor activated nuclear factor KB ligand (anti-RANKL) monoclonal antibody (denosumab), as well as some other drugs with antiangiogenic properties (see Table 1).

It has been postulated that MRONJ results from reduced bone turnover caused by the antiresorptive drugs, by which denosumab seems to have an equal or greater extent of bone turnover suppression than bisphosphonates.

- Intravenous (IV) Bisphosphonates (BPs) Use in Patients with Cancer: BPs are antiresorptive drugs used to manage cancer-related conditions including hypercalcemia of malignancy, skeletal-related events associated with bone metastases in the context of solid tumors such as breast cancer, prostate cancer and lung cancers, and for management of lytic lesions in the setting of multiple myeloma. While the potential for BPs to improve cancer-specific survival remains controversial, these medications have had a significant positive effect on the quality of life for patients with advanced cancer involving the skeleton. It is important to note that BPs are incorporated into the skeleton without being degraded, thus they are remarkably persistent drugs with a half-life of approximately 10 to 12 years and have the ability to remain in bone for over 40 years. Because of the long half-life of BPs, recovery of normal osteoclast function and bone turnover after discontinuance is very gradual and the risk for ONJ in patients treated with (high-dose) BPs for cancer therapy is prolonged for many years.

  More than 90% of cases of MRONJ occur in patients with cancer receiving high doses of IV bisphosphonates (or SC denosumab). In patients with cancer, the incidence of ONJ appears to be related to dose and duration of the BP.

  - In a study of patients with advanced breast cancer receiving 4 mg of zoledronate every four weeks, the incidence of ONJ at years 1, 2, and 3, were 0.5%, 1.2%, and 1.4%, respectively (Stopeck AT, et al. J Clin Oncol. 2010 Dec;28:5132-5139).

- Bisphosphonates for the Treatment of Osteoporosis: BPs are most frequently used for the treatment of osteoporosis and are often used to treat osteopenia as well. They are also used for a variety of less common conditions such as Paget's disease of bone, and osteogenesis imperfecta.
  - When compared to cancer patients (who receive 6- to 12-fold higher doses of BPs than those used to treat osteoporosis), the risk of ONJ for patients with osteoporosis exposed to bisphosphonate medications is about 100 times smaller. In patients prescribed BPs for the treatment of osteoporosis:
    - the prevalence of ONJ ranges from 0% to 0.04%, with the majority being below 0.001% and,
    - the incidence of ONJ is estimated to be between 0.01 and 0.001% and may be only slightly higher than the incidence of ONJ seen in the general population of less than 0.001%; more specifically, the incidence of ONJ in patients receiving oral BPs for

the treatment of osteoporosis as been reported to be 1.04 – 69 per 100,000 patient-years.
- The highest risk for ONJ in patients with osteoporosis is seen in those with a cumulative exposure to oral BPs for greater than 3 years (the median duration of oral BP exposure for patients with ONJ and ONJ-like features was 4.4 years).

- RANK Ligand Inhibitors (Denosumab): is an antiresorptive drug that exists as a fully humanized antibody against RANK ligand (RANK-L) and inhibits osteoclast function and associated bone resorption. When denosumab (Prolia) is administered subcutaneously every 6 months there is a reduction in the risk of vertebral, non-vertebral, and hip fractures in osteoporotic patients. Denosumab (Xgeva) is also effective in reducing skeletal-related events secondary to metastatic bone disease from solid tumors when administered subcutaneously monthly. Denosumab therapy is not indicated for the treatment of multiple myeloma. Interestingly, in contrast to bisphosphonates, RANK ligand inhibitors do not bind to bone. Denosumab has half-life of 25.4 days with complete clearance of its effects on bone remodeling 4 to 5 months after cessation.
  - In a study of patients with advanced breast cancer receiving 120 mg of denosumab every four weeks, the incidence of ONJ at years 1, 2, and 3, were 0.8%, 1.9%, and 2.0% respectively. (Stopeck AT, et al. J Clin Oncol. 2010 Dec;28:5132-5139)
  - The risk for ONJ among patients treated with denosumab for the treatment of osteoporosis is reported to increase with the duration of exposure to denosumab:
    - 0.04% at 3 years, 0.06% at 5 years, and 0.44% at 10 years.

- Antiangiogenic medications: Angiogenesis inhibitors (e.g., bevacizumab, sunitinib) interfere with the formation of new blood vessels by binding to various signaling molecules disrupting the angiogenesis-signaling cascade. These novel medications have demonstrated efficacy in the treatment of gastrointestinal tumors, renal cell carcinomas, neuroendocrine tumors and others.
  - The risk for ONJ among cancer patients treated with to bevacizumab is 0.2% (20 cases per 10,000). The risk may be higher among patients treated with both bevacizumab and zoledronate (0.9% [90 cases per 10,000 patients]).

  While the FDA has issued an ONJ advisory only for bevacizumab and sunitinib, concerns remain about a similar potential risk associated with several other medications within the same drug class and/or which have a similar mechanism of action (i.e., sorafenib and sirolimus).

Inciting Factors for MRONJ:
- MRONJ usually develops following a local infection of, or trauma to, bone or overlying mucosal (mucoperiosteal) tissue. Most (~ 60%) reported cases of MRONJ have been associated with an oral surgical or dental procedure as the inciting factor. This includes, but is not limited to: extractions (45%), dental implant placement, periodontal surgery involving osseous injury, and periapical surgery.
- MRONJ also may occur spontaneously (or at least without any identifiable precipitating factor) in ~ 10 – 15% of cases. Many of these 'spontaneous' cases may be related to minor, unrecognized oral mucoperiosteal trauma due to eating, oral hygiene procedures, and so forth.

Table 1: Drugs Associated with Medication-Related Osteonecrosis of the Jaws (MRONJ)

Drug	Class	Primary Indication(s)	Route	Typical Dose
Alendronate (Fosamax)	Bisphosphonate	Osteoporosis	Oral	10 mg/day or 70 mg/week
Risedronate (Actonel)	Bisphosphonate	Osteoporosis	Oral	5 mg/day or 35 mg/week
Ibandronate (Boniva)	Bisphosphonate	Osteoporosis Bone Metastases	Oral IV Oral IV	2.5 mg/day, or 150 mg/month 3 mg/3 months 50 mg/day 6 mg/3-4 weeks
Pamidronate (Aredia)	Bisphosphonate	Bone Metastases	IV	90 mg/3-4 weeks
Zoledronate (Zometa) (Reclast)	Bisphosphonate	Bone Metastases Osteoporosis	IV SQ IV	4 mg/3 - 4 weeks 120 mg/4 weeks 5 mg/year
Denosumab (Xgeva) (Prolia)	RANK-L monoclonal antibody	Bone Metastases Osteoporosis	SQ SQ	120 mg/3-4 weeks 60 mg/6 months
Sunitinib (Sutent)	Tyrosine kinase inhibitor	Antineoplastic, antiangiogenic: GIST, RCC, pNET	Oral	37.5 – 50 mg/day
Sorafenib (Nexavar)	Tyrosine kinase inhibitor	Antineoplastic, antiangiogenic: HCC, RCC	Oral	400 mg twice daily
Bevacizumab (Avastin)	VEGF monoclonal antibody	antiangiogenic: mCRC, NSCLC, Glio, mRCC	IV	10 mg/kg every 2 weeks
Sirolimus (Rapamune)	mTOR kinase inhibitor	Immunosuppressant; prevention of renal transplant rejection	Oral	5 mg/day

Abbreviations: IV intravenous; SC subcutaneous; GIST gastrointestinal stromal tumor; RCC renal cell carcinoma; pNET pancreatic neuroendocrine tumor; HCC hepatocellular carcinoma; mCRC metastatic colorectal carcinoma; NSCLC non-squamous non-small cell lung carcinoma; Glio Glioblastoma; mRCC metastatic renal cell carcinoma.

Dental Management of Patients About to Initiate Antiresorptive (or Antiangiogenic) Drug Therapy

- The objective for this group of patients is to minimize the risk of developing MRONJ via preventive dental treatment prior to the initiation of antiresorptive or antiangiogenic drug therapy, especially when being use in conjunction with the treatment of cancer.

  - Medical oncologists should evaluate and manage patients scheduled to receive IV antiresorptive or antiangiogenic therapy similar to those patients scheduled to initiate radiation therapy to the head and neck. The osteoradionecrosis prevention protocols are guidelines that are familiar to most oncologists.
  - The patient must be informed about the potential risk incurred by not receiving recommended preventive dental treatment before the initiation of antiresorptive therapy.
- Therefore if systemic conditions permit, initiation of antiresorptive therapy should be delayed until dental health is optimized. This decision must be made in conjunction with the treating physician and dentist and other specialists involved in the care of the patient.
- Dental factors that are known to increase the risk for ONJ such as periodontal disease with alveolar bone loss, pockets of occult infection, bleeding on probing and mobility, unsalvageable teeth and root fragments, caries, periapical pathology, edentulism, and denture stability should be addressed:
  - It is preferable to complete of any necessary oral surgery prior to initiation of antiresorptive therapy. Non-restorable teeth and those with a poor prognosis (e.g., those with 3+ mobility) should be extracted:
    - Consider periodontal stabilization splints for teeth with grade 1+ or 2+ mobility in patients with good oral hygiene, and consider extraction of such teeth in patients with poor oral hygiene that is not likely to improve). Other necessary elective dentoalveolar surgery should also be completed at this time.
    - Based on experience with osteoradionecrosis, it appears advisable that antiresorptive or antiangiogenic therapy should be delayed, if systemic conditions permit, until the extraction site has mucosalized and there is adequate osseous healing (i.e., a minimum of at least 14 days, with at least 30 days being preferable).
  - Dental prophylaxis, caries control and restorative dentistry are critical to maintaining functionally sound dentition. This level of care must be continued indefinitely.
  - Patients with full or partial dentures should be examined for areas of mucosal trauma, especially along the lingual flange region.
- It is critical that patients be educated about:
  - the potential risks for, and signs and symptoms of MRONJ;
  - the importance of smoking cessation;
  - reporting any dental pain, swelling or exposed bone to their dentist; and
  - the importance of maintaining good dental hygiene and regular (periodic) dental examinations.

(Continued on the next page)

Table 2: Risk Factor Stratification for MRONJ

(Adapted and modified from: Nicolatou-Galitis O, et al. Medication-related osteonecrosis of the jaw: definition and best practice for prevention, diagnosis, and treatment. Oral Surg Oral Med Oral Pathol Oral Radiol. 2019 Feb;127(2):117-135.)

Low MRONJ Risk	High MRONJ Risk
Patients are considered "low risk" for MRONJ if: • they have received, or are currently receiving a low-dose bisphosphonate or denosumab for ≤ 3 years (as is used for the treatment of osteoporosis or osteopenia), AND • they do not have any significant comorbidity for MRONJ such as: - concurrent use of systemic corticosteroids, angiogenesis inhibitors, or chemotherapy for cancer; - history of radiotherapy (for cancer treatment) involving the head or neck; - significant immunosuppression due to drugs and/or disease (e.g., cancer, hematological disorders, inadequately controlled or brittle diabetes, AIDS, status post-bone marrow, stem cell, organ transplant receiving antirejection drugs); - severe periodontal disease, periosteal mucosal trauma or ulceration (such as from improperly fitting dentures), or exposed bone in the oral cavity; - tobacco use (smoking).	Patients are considered "high risk" for MRONJ if: • they have received, or are currently receiving a high-dose bisphosphonate or denosumab (as is used for the treatment / management of cancer-related conditions), OR • they have received, or are currently receiving a low-dose bisphosphonate or denosumab for > 3 years (as is used for the treatment of osteoporosis or osteopenia), OR • they have received, or are currently receiving a low-dose bisphosphonate or denosumab for ≤ 3 years (as is used for the treatment of osteoporosis or osteopenia), AND have any significant comorbidity for MRONJ (as described in column on the left).

Dental Management of Patients with a History of, or Current use of Drug(s) Associated with MRONJ

- General Considerations:
  - It is unacceptable to deny dental care to a patient solely because the patient has a history of, or is currently receiving an antiresorptive drug.
  - Informed Consent: When invasive dental care is necessary in a patient at risk for MRONJ, it is recommended that written informed consent be obtained from the patient that includes documentation of a discussion of MRONJ and the benefits and risks of the proposed dental treatment and any alternative therapies.

- Dental Treatment for Patients at "Low Risk" (see Table 2) for MRONJ
  - All restorative, prosthodontic, non-surgical endodontic, and routine periodontic procedures can be performed as needed.
    - Patient education in maintaining good oral hygiene and having regular (periodic) dental care (i.e., a regular recall schedule) is of vital importance in preventing dental disease that may require surgical dental treatment.
  - Surgical procedure involving bone (e.g., extractions, implants, apicoectomy,

periodontal surgery) may be performed:

- These patients may be at slightly increased risk of developing ONJ compared to the general populations, therefore surgical dental treatment that involves bone should be carefully considered on a case-by-case basis, based on the risks and individual patient needs.
- For patients receiving zoledronate (Reclast), 5 mg every year, or denosumab (Prolia) 60 mg every 6 months for the treatment of osteoporosis or osteopenia, the recommended optimum timing of any surgical dental treatment is at 2 months after the last drug dose.
- Also see: "Recommendations to Reduce the Risk of ONJ" (below).

- Dental Treatment for Patients at "High Risk" (see Table 2) for MRONJ
  - All restorative, prosthodontic, non-surgical endodontic, and routine (non-surgical) periodontic procedures can be performed as needed.
    - Patient education in maintaining good oral hygiene and having regular (periodic) dental care (i.e., a regular recall schedule) is of vital importance in preventing dental disease that may require surgical dental treatment.
  - Although no oral or maxillofacial surgical procedures are absolutely contraindicated, treatment plans that minimize periosteal and/or intrabony exposure or injury are strongly preferred. Less invasive (non-surgical) procedures are recommended over more invasive (surgical) procedures:
    - As an alternative to extraction whenever possible, non-restorable teeth may be treated by removal of the clinical crown and endodontic treatment of the remaining roots.
    - Any extractions or dentoalveolar surgeries that are required due to bona fide dental or medical emergencies are appropriate.
    - Placement of dental implants should be avoided, particularly in patients that have received, or are receiving high-dose antiresorptive drugs to treat/manage cancer-related conditions.
  - Also see: "Recommendations to Reduce the Risk of ONJ" (below).

- Recommendations to Reduce the Risk of ONJ
  - If extractions or bone surgery is necessary, a conservative surgical technique is preferable. After an extraction, sharp bony edges should be smoothed to facilitate primary tissue closure of wounds whenever possible.
  - Any indicated extractions should be done per quadrant and closely observed for adequate healing before proceeding with any additional extractions / surgery in other quadrants; radiographic assessments of extraction site bone remodeling may also be necessary.
  - Periprocedural Prophylactic Antibiotics:
    - Use of an antimicrobial mouthwash is recommended, especially when periosteal or medullary bone exposure is anticipated or observed: 0.12% chlorhexidine solution, twice per day for 4 to 8 weeks depending on the patient's healing progress.
    - It does <u>not</u> appear that systemic prophylactic antibiotics reduce the risk of MRONJ, or are indicated in conjunction with routine, non-surgical dental treatment that does not involve osseous injury.

- There is conflicting evidence and varying recommendations regarding the use of systemic prophylactic antibiotics before and after dental treatment that involves direct osseous injury to help reduce the risk of MRONJ. It appears that the use of systemic prophylactic antibiotics to help reduce the risk of MRONJ in patients undergoing oral (including periodontal or periapical) surgery that involves osseous injury may be particularly beneficial in situations where an active infection is present at the surgical site (e.g., the presence of pain, inflammation, swelling, or a fistula with active pus drainage).
  - Whenever possible, systemic antibiotics should be started 1 day before the surgical procedure and maintained for at least 7 days or longer (i.e., until adequate wound healing is observed).
  - Some systemic prophylactic antibiotic (adult dose) regimens recommended in the current literature include:
    - penicillin VK, 500 mg every 6 hours, OR
    - amoxicillin 500 mg + metronidazole 500 mg every 8 hours

    OR for penicillin-allergic patients,
    - levofloxacin, 500 to 750 mg every 24 hours, OR
    - doxycycline, 100 mg every 12 hours.
- "Drug Holidays": There is currently no clear or convincing evidence that interrupting antiresorptive drug (i.e., bisphosphonate or denosumab) therapy alters the risk of ONJ in patients following tooth extraction or that support the benefits of a "drug holiday" for osteoporosis patients receiving bisphosphonate therapy. However, a theoretical benefit for a "drug holiday" may still apply for those patients receiving antiresorptive drug therapy and are considered to be at the highest risk for ONJ. Nevertheless, interrupting or discontinuation of antiresorptive therapy should be a medical decision based primarily on the risk of experiencing skeletal-related events (e.g., bone fractures) secondary to low bone density, not the potential risk of developing MRONJ. When considering an antiresorptive "drug holiday", the increased risk of skeletal-related events during the drug holiday must be balanced with any possible (currently unproven) benefit from the reduction in development of ONJ on a individual patient basis and in consultation with the patient's oncology care providers.

Clinical Presentation and Dental Management of a Patient with MRONJ

- MRONJ may remain asymptomatic for weeks, months, or years, or it may result in pain or exposed bone.
- Signs and symptoms of MRONJ that may occur before the development of clinically detectable osteonecrosis include pain, tooth mobility, mucosal swelling, erythema, and ulceration.
  - These lesions are most frequently symptomatic when surrounding tissues become inflamed or there is clinical evidence of infection.
  - Some patients may also present with complaints of altered sensation (paresthesia) in the affected area.
  - Chronic maxillary sinusitis secondary to osteonecrosis with or without an oral-antral fistula can be the presenting symptom in patients with maxillary involvement.
- The typical radiographic findings of ONJ seen in intraoral and panoramic radiographs are:
  - increased trabecular density, incomplete healing of extraction sockets, sequestrum

formation, thickening of the mandibular canal or sinus floor cortication, and periosteal bone formation.

- Patients may be considered to have MRONJ if all of the following characteristics are present:
    1. Current or previous treatment with antiresorptive agents; current or recent treatment with antiangiogenic agents listed in Table 1;
    2. Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than eight weeks; and
    3. No history of radiation therapy to the jaws or obvious metastatic disease to the jaws.
- Patients with suspected MRONJ should be referred to, and managed by Oral Medicine and/or Oral Surgery with frequent appointments for follow up. A summary of the AAOMS staging and treatment recommendations for MRONJ is shown in Table 3.

Table 3: Staging and Treatment Strategies for
Medication-Related Osteonecrosis of the Jaw (MRONJ)

From: American Association of Oral and Maxillofacial Surgeons (AAOMS) Medication-Related Osteonecrosis of the Jaw—2014 Update

MRONJ† Staging	Treatment Strategies‡
At risk category No apparent necrotic bone in patients who have been treated with either oral or IV bisphosphonates	• No treatment indicated • Patient education
Stage 0 No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms	• Systemic management, including the use of pain medication and antibiotics
Stage 1 Exposed and necrotic bone, or fistulae that probes to bone, in patients who are asymptomatic and have no evidence of infection	• Antibacterial mouth rinse • Clinical follow-up on a quarterly basis • Patient education and review of indications for continued bisphosphonate therapy
Stage 2 Exposed and necrotic bone, or fistulae that probes to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage	• Symptomatic treatment with oral antibiotics • Oral antibacterial mouth rinse • Pain control • Debridement to relieve soft tissue irritation and infection control
Stage 3 Exposed and necrotic bone or a fistula that probes to bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone,(i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla) resulting in pathologic fracture, extra-oral fistula, oral antral/oral nasal communication, or osteolysis extending to the inferior border of the mandible of sinus floor	• Antibacterial mouth rinse • Antibiotic therapy and pain control • Surgical debridement/resection for longer term palliation of infection and pain

† Exposed or probable bone in the maxillofacial region without resolution for greater than 8 weeks in patients treated with an antiresorptive and/or an antiangiogenic agent who have not received radiation therapy to the jaws.

‡ Regardless of the disease stage, mobile segments of bony sequestrum should be removed without exposing uninvolved bone. The extraction of symptomatic teeth within exposed, necrotic bone should be considered since it is unlikely that the extraction will exacerbate the established necrotic process.

CANCER, LEUKEMIA, LYMPHOMA

(Adapted in part from: Little, Falace, Miller, Rhodus: "Dental Management of the Medically Compromised Patient", C.V. Mosby, 2013, Chapter 26.)

Overview:

- In order to effectively diagnose, prevent and treat oral complications of cancer (including leukemia or lymphoma) therapy, the oral health professional must have a working knowledge of the potential impact of cancer and cancer therapy on oral health.
- Dental treatment planning for the patient with cancer begins with the establishment of the diagnosis. Planning involves:
    1. Pre-cancer treatment evaluation and preparation of the patient.
    2. Oral health care during cancer therapy, which includes hospital and out-patient care.
    3. Post-cancer treatment management of the patient, including long-term considerations.

  Cancers that are amenable to surgery and do not affect the oral cavity require few (if any) treatment plan modifications. However, certain cancers (including oropharyngeal cancers, leukemia, multiple myeloma, and most lymphomas) affect oral health either directly because of surgery, or indirectly due to chemotherapy or immunosuppression.
- Detailed information about the complexities of the dental management of the patient with cancer is beyond the scope of this guide. The oral health professional should consult additional references such as: Hupp WS, Migliorati CA, Brennan M (eds.). "Clinician's Guide to The Dentist's Role in the Management of the Cancer Patient." American Academy of Oral Medicine, Edmonds, WA, 2011.

Treatment of Cancer:

- Curing cancer requires eliminating all cancer cells and can involve any of several modalities including:
    - Surgery
    - Radiation therapy (radiotherapy)
    - Chemotherapy (using cytotoxic, antineoplastic drugs)
    - Hormonal therapy (for selected cancers, e.g., prostate, breast, endometrium)
    - Immunotherapy (e.g., monoclonal antibodies, interferons, and other biologic response modifiers and tumor vaccines)
    - Differentiating drugs (e.g., retinoids)
    - Targeted drugs that exploit the growing knowledge of cancer cellular and molecular biology (e.g., cancer cell enzyme inhibitors [e.g., tyrosine kinase inhibitors, mTOR inhibitors], apoptosis-inducing drugs, angiogenesis inhibitors [e.g., VEGF inhibitors]).

  Often, modalities are combined to create a treatment program that is appropriate for the patient and is based on patient and tumor characteristics as well as patient preferences.

- Palliative care is care given to improve the quality of life of patients who have a serious or life-threatening disease, such as cancer. Palliative care is also called comfort care, supportive care, and symptom management. The goal of palliative care is not to cure the patient's cancer or to achieve remission, rather to prevent or treat, as early as possible, the symptoms and side effects of the disease (and any treatment including surgery, radiotherapy and chemotherapy if it is provided), in addition to the related psychological, social, and spiritual problems.

- For example, palliative cancer surgery is used to relieve symptoms and preserve the patient's quality of life for as long as possible, and may be a reasonable alternative when cure is unlikely or when an attempt at cure produces adverse effects that are unacceptable to the patient. Palliative tumor resection may be indicated to control pain, to reduce the risk of hemorrhage, or to relieve obstruction of a vital organ (e.g., intestine, urinary tract). Similarly, palliative chemotherapy or radiotherapy may be used for the same purposes in some patients with cancer.
- Note that palliative care is different from hospice care. Although they share the same principles of comfort and support, palliative care begins at diagnosis and continues during cancer treatment and beyond. In contrast, when a person has a terminal diagnosis (usually defined as having a life expectancy of 6 months or less) and is approaching the end of life, he or she might be eligible to receive hospice care.

Staging of Cancer:

- Staging describes the severity of a patient's cancer based on the size and/or extent of the original tumor and whether or not cancer has metastasized. Staging is important in that it helps select and plan appropriate cancer treatment and can be used in estimating the patient's prognosis.
- The TNM Classification is an anatomically based system that records the primary and regional nodal extent of the tumor and the absence or presence of metastases. Each individual aspect of TNM is termed a category:
  - T: describes the primary tumor size
  - N: describes the regional lymph node involvement
  - M: category describes the presence or otherwise of distant metastatic spread

  The definition of each category depends on the site and histology of the cancer. In selecting the best treatment for patients, the use of the TNM system alone can generate a large number of different subcategories. To simplify the description the categories can, therefore, be grouped together as an anatomical stage classification and given a Roman numeral stage (e.g., stage I, II, III, and IV). The TNM staging for oral cancer is shown in Figure 1 (next page).
  - Other TNM parameters:
    - X: category cannot be assessed.
    - G (1–4): the grade of the cancer (1=well differentiated [low grade], 2=moderately differentiated [intermediate grade], 3=poorly differentiated [high grade]; 4=undifferentiated [high grade].
    - S (0–3): elevation of serum tumor markers (grading depends on the serum level of specific marker under consideration [e.g.,alpha-fetoprotein, beta-2-microglobulin, carcinoembryonic antigen, etc.]).
    - R (0–2): extent of residual tumor after surgery (0=No residual tumor, 1=microscopic residual tumor, 2=macroscopic residual tumor).
    - L (0–1): invasion into lymphatic vessels (0=none, 1=positive).
    - V (0–2): invasion into veins (0=none, 1=microscopic, 2=macroscopic).
    - C (1–5): a modifier of the certainty (quality) of the last mentioned parameter (i.e., can be used to assist a third-party in making decisions as to whether a classification is reliable or less certain).

- TMN prefix modifiers:
  - c: stage given by clinical examination of a patient. (The c-prefix is implicit in absence of the p-prefix).
  - p: stage given by pathologic examination of a surgical specimen.
  - y: stage assessed after neoadjuvant chemotherapy and/or radiation therapy.
  - r: stage for a recurrent tumor in a patient that had some period of time free from the disease.
  - a: stage determined at autopsy.
  - u: stage determined by ultrasonography or endosonography. (Clinicians often use this modifier although it is not an officially defined one).

Figure 1: TNM Staging for Oral Cancer

T - Tumor	
TX	No available information on primary tumor
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor less than 2 cm in diameter
T2	Tumor 2-4 cm in diameter
T3	Tumor greater than 4 cm in diameter
T4	Tumor invades adjacent structures. This classification is further classified as T4a and T4b depending on structures involved and resectable (T4a) versus unresectable (T4b) nature of the lesion.
N - Node	
Nx	Nodes not assessed
N0	No palpable nodes
N1	Ipsilateral palpable nodes (3 cm or less in diameter)
N2	Contralateral or bilateral nodes (3-6 cm in diameter). This group is further subdivided into N2a, N2b, and N2c categories.
N3	Fixed palpable nodes (greater than 6 cm in diameter)
M - Metastasis	
MX	Distant metastasis not assessed
M0	No distant metastasis
M1	Clinical or radiographic evidence of metastasis

Stage	TNM classification
Stage I	T1 N0 M0
Stage II	T2 N0 M0
Stage III	T3 N0 M0, or T1, T2, or T3 N1 M0
Stage IV	
Stage IVA	T4a N0 or N1 M0, or T1, T2, T3, or T4a N2 M0
Stage IVB	Any T N3 M0, or T4b any N M0
Stage IVC	Any M1 lesion

- Some forms of cancer use specific staging systems:
  - Hodgkin and non-Hodgkin lymphomas are most frequently staged using the Ann Arbor System (see: Table 1 [next page]).
  - Multiple myeloma is frequently staged using the Durie-Salmon system or the International Staging System (not shown).
  - Chronic lymphocytic leukemia is frequently staged using the Rai system or the Binet system (not shown).

Table 1: Ann Arbor Staging of Hodgkin and Non-Hodgkin Lymphomas

Stage	Definition
I	Involvement of a single lymph node (LN) region (I) or of a single extranodal organ or site (IE)
II	Involvement of two or more LN regions, on the same side of the diaphragm (II) or localized involvement of an extralymphatic organ or site and one or more LN region on the same side of the diaphragm (IIE)
III	Involvement of LN regions on both sides of the diaphragm (III), which may be accompanied by involvement of the spleen (III S) or by localized involvement of an extralymphatic organ (III E) or both (IIISE)
IV	Noncontiguous involvement of one or more extralymphatic site with or without LN involvement
Annotation	**Definition**
A	No B symptoms
B	At least one of the following within the last 6 months:
	a. Weight loss >10%
	b. Unexplained persistent or recurrent fever
	c. Drenching night sweats
X	Bulky disease (≥ 6 cm in diameter or mass > 1/3 of mediastinal) diameter
E	Extension to a single extralymphatic organ adjacent to a known involved site

Dental Implications of a Patient with:

- Newly Diagnosed (or Recurrent) Cancer, Leukemia, or Lymphoma Who has Not Yet Started Treatment.
  - Pre-cancer treatment dental care should include oral hygiene instructions, the encouragement of a noncariogenic diet, calculus removal, prophylaxis and fluoride treatment, and elimination of all oral sources of irritation and infection.
    In children undergoing chemotherapy, mobile primary teeth and those expected to be lost during chemotherapy should be extracted, and gingival opercula should be evaluated for surgical removal to prevent entrapment of food debris.
  - Guidelines for extracting questionable teeth before chemotherapy, and/or radiation therapy (radiotherapy) that will involve the head and neck (i.e., oral/maxillofacial region) are presented in Figure 2 (next page).

(CONTINUED ON THE NEXT PAGE)

Figure 2: Guidelines for Tooth Extraction in Patients Scheduled to Receive Head and Neck Irradiation (Including the Oral/Maxillofacial Region) or (Cytotoxic, Antineoplastic) Chemotherapy

From: Little, Falace, Miller, Rhodus: "Dental Management of the Medically Compromised Patient", C.V. Mosby, 2013, p. 479.

Indicators of Extraction

- Pocket depths 6 mm or greater, excessive mobility, purulence on probing
- Presence of periapical inflammation
- Broken-down, nonrestorable, nonfunctional, or partially erupted tooth in a patient who is noncompliant with oral hygiene measures
- Patient lack of interest in saving tooth/teeth
- Inflammatory (e.g., pericoronitis), infectious, or malignant osseous disease associated with questionable tooth

Extraction Guidelines

- Extraction should be performed with minimal trauma, with timing as follows:
  - At least 2 weeks,* ideally 3 weeks, before initiation of radiation therapy
  - At least 5 days (in maxilla) before initiation of chemotherapy
  - At least 7 days (in mandible) before initiation of chemotherapy
- Trim bone at wound margins to eliminate sharp edges.
- Obtain primary closure.
- Avoid intraalveolar hemostatic packing agents, which can serve as a nidus for microbial growth.
- Transfuse if the platelet count is less than 50,000/mm^3.
- Delay extraction if the white blood count is less than 2000/µm or the absolute neutrophil count is less than 1000/µm or expected to be this level within 10 days; alternatively, prophylactic antibiotics (cephalosporin) can be used with extractions that are mandatory.

* In *select* circumstances in which healing will not be compromised, a minimum of 10 days is acceptable. Biologic modifiers that promote healing (e.g., vitamin C) may be useful in these circumstances. Alternatively, if these time recommendations cannot be met before initiation of chemotherapy, a root canal procedure can be performed to reduce the number of viable microbes; then the extraction can be performed after the white blood cell count returns to sufficient levels.

What to Include in a Medical Consultation

- Prior to starting cancer treatment, consultation with the patient's physician (preferably their oncologist) is recommended in order to determine:
  - the type of cancer, the stage, a summary of the anticipated treatment, and the anticipated date of any surgery and/or the start of any chemotherapy and/or

radiotherapy.

- Inform the oncologist of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient.
- Determine if the patient's cancer treatment may/will include the use of any drugs known to increase the risk of medication-related osteonecrosis of the jaws (MRONJ), such as zoledronic acid/zoledronate, pamidronate, angiogenesis inhibitors (e.g., bevacizumab, sunitinib, sorafenib, etc.), or RANKL inhibitors (e.g., denosumab [Xgeva]).

- Example:

  "Mr. X is dental patient of the ULSD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

  (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here).

  Mr. X reports a history of (cancer, leukemia, lymphoma) that was diagnosed (in/on date).

  Can you please provide

  1. The specific diagnosis of this patient's (cancer, leukemia, lymphoma), as well as its current stage and sites(s) involved.
  2. A summary of the treatment plan (e.g., surgery, chemotherapy, radiotherapy, etc.) for the patient's (cancer, leukemia, lymphoma), as well as anticipated start date(s).
  3. Due concerns regarding the increased risk of medication-related osteonecrosis of the jaws (MRONJ), can you please inform us if this patient's cancer treatment is likely to include any drugs associated with an increased risk of MRONJ, such as zoledronic acid/zoledronate, pamidronate, angiogenesis inhibitors (e.g., bevacizumab, sunitinib, sorafenib, etc.), or denosumab (Xgeva).

  Thank you for your assistance in the care of our mutual patient.

Dental Implications of a Patient with:

♦ A History of Radiotherapy Involving the Oral/Maxillofacial Region.

- Radiation therapy (radiotherapy) is used in more than half of all patients with cancer:
  - either as an adjuvant (i.e., used after primary treatment, such as surgery) or neoadjuvant treatment (i.e., given before primary treatment such as surgery);
  - as a definitive treatment alone;
  - in combination with chemotherapy;
  - as an organ-sparing therapy (i.e., to treat a cancerous organ in such a way to avoid complete removal of the organ and preserve the remaining organ function);
  - to palliate cancer symptoms.
- The most significant chronic, long-term oral complications seen in patients who have received radiotherapy for head/neck/oral cancer include: salivary gland hypofunction (dosages in excess of 3,000 cGy are the most damaging, especially if shielding or medication is not provided to the patient during delivery of radiation) leading to severe xerostomia (less than 0.2 mL/min unstimulated salivary flow); oral mucosal atrophy; mucositis; cheilitis; glossitis; glossodynia; dysgeusia; dysphagia; submucosal and muscle fibrosis (resulting

in trismus); a severe form of (usually cervical) caries called radiation caries; and osteoradionecrosis of the jaws.

- Osteoradionecrosis (ORN): is a condition characterized by exposed bone that fails to heal (present for 6 months) after high-dose radiation to the jaws. ORN results from radiation-induced changes (hypocellularity, hypovascularity, and ischemia) in the jaws. Most cases result from damage to tissues overlying the bone as opposed to direct damage to the bone. Accordingly, soft tissue necrosis usually precedes ORN and is variably present at the time of diagnosis.
  - ORN rarely occurs in patients irradiated with total doses below 5,000 cGy and usually develops in patients exposed to total radiation doses over 6,400 cGy. The risk for ORN also appears to be greater in patients who received concurrent chemotherapy and radiotherapy.
  - Risk is for ORN is significantly greater in the mandible (compared to the maxilla), particularly in the buccal cortex of the premolar, molar, and retromolar regions.
  - Risk for ORN is greater in patients with a history of oral mucosal trauma and those that undergo a traumatic dental procedure (e.g, extraction), (although ORN can also occur spontaneously). Nonsurgical procedures that are traumatic (e.g., curettage) or cause a reduction of blood supply to the region (use of vasoconstrictors) can result in ORN.
  - Risk is ORN greater for dentate patients than edentulous patients and when periodontal disease is present.
  - Risk for ORN is greater in patients with heavy tobacco and/or alcohol use.
  - The risk for ORN remains throughout a patient's lifetime.
- If the dentist is unsure of the amount of radiation received and invasive procedures are planned, the patient's radiation oncologist should be contacted to determine the total dose to the head and neck region before initiating care.
  - Clinicians should be aware that risk of ORN increases with increasing dose to the jaws (e.g., 7,000 cGy is a greater risk than 6,500 cGy). Patients determined to be at risk should be provided the appropriate preventive measures.
- Patients who have received neck irradiation (at a total dose of 4,500 cGy or more) are more likely to develop carotid artery atheromas (calcified atherosclerotic plaques) after treatment than are risk-matched control patients who have not undergone irradiation. These lesions can be detected by panoramic radiography and constitute a risk factor for stroke that warrants referral of the patient to the physician for evaluation.
- Patients with a history of head and neck cancer must be periodically monitored for recurrence. As such, a careful and comprehensive head/neck/intraoral soft tissue examination should be performed for all patients at follow-up dental visits.
  - The local recurrence rate for oral cavity squamous cell carcinoma is ~ 30%, while the occurrence of second primary cancers after treatment for laryngeal cancer has been estimated at 17% to 18%.
  - An understanding of soft tissue changes as a result of fibrosis from previous surgeries or radiotherapy helps differentiate these changes from recurrent cancer. The distinction may be subtle since both can present as tissue induration.

What to Include in a Medical Consultation:

- A medical consultation from the patient's radiation oncologist is indicated for any

patient with a history of (or a possible history of) radiotherapy to the maxillofacial region.

- Inform the radiation oncologist of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient.
- It is important to obtain adequate information to determine the patient's risk for osteoradionecrosis of the jaws from the patient's radiation oncologist.

- Example:

  "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

  (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

  Mr. X reports a history of treatment of (insert condition [e.g., oral squamous cell carcinoma]) in (date[s]) that included radiotherapy involving the maxillofacial region. Can you please (provide us with / confirm):

  1. The specific diagnosis, stage and site(s) of this patient's cancer at the time they presented for treatment.

  In order to assist us in determining this patient's risk for oral complications resulting from cancer treatment, including osteoradionecrosis of the jaws, can you please provide us with:

  2. A summary of the patient's radiotherapy, and other cancer treatment, that includes the total radiation dose to the head and neck region, as well as the total radiation dose and diagram(s) of any field(s) that involved the maxilla, mandible, and major salivary glands.

  Thank you for your assistance in the care of our mutual patient."

- Note: If the current status of the patient's cancer is unknown, you should send a medical consult to the physician/oncologist who is currently following this patient's cancer (i.e., they are periodically re-evaluating the patient for any signs/symptoms or recurrence), and request a summary of the current status of the patient in this regard.

Dental Implications of a Patient with:

♦ Cancer, Leukemia or Lymphoma that is Currently Receiving Chemotherapy.

- Most cytotoxic, antineoplastic chemotherapeutic agents used to treat cancer will cause:

  - breakdown of the mucous membranes,
  - depression of the bone marrow, (resulting in anemia, leukopenia, and thrombocytopenia and subsequent immunosuppression and impaired hemostasis),
  - gastrointestinal changes (diarrhea, malabsorption), and altered nutritional status,
  - alopecia, and
  - may sometimes cause cardiac and pulmonary toxicities/dysfunctions.

- Accordingly, patients receiving chemotherapy may manifest:
  - mucositis: erythema and ulceration of the oral mucosa,
  - oral infections: bacterial, viral (e.g., HSV), fungal (e.g., candidiasis)
  - excessive bleeding / impaired hemostasis with minor trauma,
  - xerostomia, and
  - neurotoxicity (e.g., dysgeusia, and [particularly with vincristine and vinblastine] odontogenic pain that mimics irreversible pulpitis).
- Whether a patient is receiving inpatient or outpatient chemotherapy, the dental healthcare provider should be familiar with the patient's WBC count and platelet status before dental care. In general, routine dental procedures can be performed if :
  - the total WBC (granulocyte) count is greater than 2,000/mm^3,
  - the absolute (total) neutrophil count is greater than 500/mm^3,
  - the platelet count is greater than 50,000/mm^3, and
  - the patient feels capable of withstanding dental care.

  For outpatient care, this is generally at least 17 days after chemotherapy, or a few days before the next chemotherapy cycle.
- For patients who require invasive dental treatment where the risk for a post-operative infection is of concern due to immunosuppression secondary to the cancer (e.g., acute leukemia) and/or chemotherapy, the use of prophylactic antibiotics to prevent post-operative infection is dictated by WBC and neutrophil counts. Prophylactic antibiotics are often recommended if:
  - the total WBC count is less than 2,000/mm^3, or
  - the absolute neutrophil count is less than 500/mm^3.

  It is important to note that there is no direct evidence that antibiotic prophylaxis is effective under these circumstances, but it is often recommended. The potential adverse effects of antibiotics should be kept in mind in making the decision to use them. No standard antibiotic regimen is recommended for prophylaxis for the prevention of a post-operative infection in patients receiving chemotherapy. The antibiotic(s), duration, and dosage to be used for prophylaxis should be established in consultation with the oral medicine faculty and the patient's oncologist.

What to Include in a Medical Consultation:

- Most patients currently receiving cytotoxic, antineoplastic chemotherapy (as well as radiotherapy involving the oral/maxillofacial region) are usually NOT candidates for elective dental treatment.
  - Any urgent (emergency) dental treatment needs for these patients are best addressed in a hospital setting (i.e., ACB GPR and graduate OS clinics).
- Please see Dr. Migliorati for assistance regarding the dental treatment and/or content of any medical consultation(s) for a patient with cancer/leukemia/lymphoma that is currently receiving chemotherapy, or radiotherapy involving the oral/maxillofacial region.

➧ For a summary of oral and maxillofacial complications of (antineoplastic, cytotoxic) chemotherapy and head/neck radiotherapy, see Table 3.

Dental Implications of a Patient with:

- A History of Cancer, Leukemia or Lymphoma that has Previously Received or Completed Chemotherapy, or Radiotherapy that did NOT Involve the Oral/Maxillofacial Region.
  - It is important that dental healthcare providers have some knowledge and understanding of the prognosis of their patients who have been diagnosed with cancer as this will have implications when considering the patient's dental treatment plan.
    - For example, the dental treatment plan for a patient with a poor prognosis who is receiving palliative cancer therapy, or for a patient with a prognosis of less than 6 months, may include removal of symptomatic teeth with active infection, simple restorative dentistry, and dental prophylaxis, and should not include placement of extensive fixed prosthesis and dental implants.
  - Various terms are used to describe the response to cancer treatment (Table 2). The disease-free interval often serves as an indicator of cure and varies with cancer type.
    - For example, lung, colon, bladder, large cell lymphomas, and testicular cancers are usually "cured" if a 5-year disease-free interval occurs. However, breast and prostate cancers may recur long after 5 years, an event defining tumor dormancy; thus, a 10-year disease-free interval is more indicative of cure.

Table 2: Definitions of Response to Cancer Treatment

Term	Definition
Cure	Treatment has successfully eradicated all traces of the patient's cancer and there is long-term (usually at least 5 years or longer) absence of symptoms or signs of cancer. However, a cure does not mean that the patient will never have cancer again. Although patients who appear to be cured may still have viable tumor cells that may eventually cause relapse (recurrence), or a second primary cancer. It is also possible that another cancer (i.e., a new [different] primary cancer) will develop in the patient at some point in the future.
Complete Remission (Complete Response)	Disappearance of all clinical evidence (signs and symptoms) of cancer. (Complete remission is not synonymous with cure)
Partial Remission (Partial Response)	Greater than 50% reduction in size of tumor mass or masses, sometimes leading to significant palliation and prolongation of life but with inevitable regrowth of the tumor.
Stable Disease	Neither improvement nor worsening.
Disease-free Survival (Disease-free Interval)	Interval of time between the disappearance of the tumor and relapse.
Progression-free Survival	Interval of time from the initiation of treatment to the time of overt progression of the cancer in a surviving patient.
Survival Time	Interval of time from cancer diagnosis to death.

- Metastatic spread of a carcinoma to the jaws usually occurs by the hematogenous route. Although metastases to a jawbone may arise from primary carcinomas of any anatomic site, carcinomas of the breast, lung, thyroid, prostate, and kidney give rise to the majority of metastases involving the maxilla and/or mandible.
  Furthermore, an increased risk of second primary cancers of the head and neck has been identified for survivors of soft tissue sarcoma, neuroblastoma, and leukemia.
  Also, squamous cell carcinomas are the most common second primary solid malignancy after allogeneic hematopoietic stem cell transplantation (HSCT).
  - As such, a careful and comprehensive head/neck/intraoral soft tissue examination should be performed for all patients at follow-up dental visits.
- For cancers that frequently cause hypercalcemia and/or metastasize to bone (e.g., multiple myeloma, breast, lung, and prostate cancers), intravenous (IV) bisphosphates (e.g., Zometa [zoledronic acid/zoledronate] and Aredia [pamidronate]) are frequently used as an adjunct to antineoplastic chemotherapy for the treatment of bone metastases of solid tumors and osteolytic lesions of multiple myeloma.
  - Because of the very long (~ 10 to 12 years) half-life of bisphosphonates, recovery of normal osteoclast function and bone turnover after discontinuance is very gradual and the risk for medication-related (drug-induced) osteonecrosis of the jaw (MRONJ) in patients treated with IV bisphosphonates for cancer therapy is prolonged for many years.
  - Among cancer patients treated with zoledronate, the cumulative incidence of MRONJ is low (range = 0.7% - 6.7%), but is still between 50 to 100 times higher than cancer patients treated with placebo.
    See the section on, "Bisphosphonates- and Medication-related Osteonecrosis of the Jaws" in this guide for more information.

What to Include in a Medical Consultation:

- After cancer therapy, consultation with the patient's oncologist is recommended to determine:
  - the type of cancer, the stage at the time of diagnosis, and the treatment provided;
  - current stage of the cancer, and current status (i.e., cure, complete remission, partial remission, recurrence, etc.);
  - any history of recurrences (and treatment regimens for recurrences).
- Inform the oncologist of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient.
- If the patient with a history of multiple myeloma, breast, lung, or prostate cancer is unsure if they have received IV bisphosphates (e.g., Zometa [zoledronic acid/zoledronate] and Aredia [pamidronate]), their oncologist should be consulted in order to ascertain if the patient has received either of these drugs.

- Example:
  "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each using local anesthesia (2% lidocaine

containing 1:100,000 epinephrine).

(Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here).

Mr. X reports a history of (cancer, leukemia, lymphoma) that was first diagnosed (date). Can you please provide

1. The specific diagnosis of this patient's (cancer, leukemia, lymphoma), as well as its current stage and sites(s) involved.
2. The current status of the patient's (cancer, leukemia, lymphoma), and a summary of any treatment provided (e.g., surgery, chemotherapy, radiotherapy, etc.).

If the patient reports a history of multiple myeloma, breast, lung, or prostate cancer and is unsure if they have received IV bisphosphates then you should also ask:

Due concerns regarding the increased risk of medication-related osteonecrosis of the jaws, can you please inform us if this patient received zoledronic acid/zoledronate or pamidronate (as well as its dosage and duration) in conjunction with the treatment of their malignancy?

Thank you for your assistance in the care of our mutual patient.

(Table 3 Starts on the Next Page)

Table 3: Oral/Maxillofacial Complications of
(Antineoplastic, Cytotoxic) Chemotherapy and Head/Neck Radiotherapy

Complication	Onset	Comments
Mucositis	Starts at about second week	Mucositis is an inflammatory process that results from oral mucosal tissue damage due to chemotherapy and/or radiotherapy; results in oral pain and mucosal atrophy forming ulcerations; odynophagia and decreased oral intake; decreased oral hygiene; and altered speaking ability. • Standard-dose chemotherapy: 40% incidence of mucositis (all grades); starts at 7^{th} to 10^{th} day of chemotherapy and usually resolves within 1 to 2 weeks after the last dose of chemotherapy. • High-dose chemotherapy: 70 - 80% incidence of grade 3 to 4 oral mucositis; typically peaks at 7^{th} to 10^{th} day of chemotherapy and resolves 14 to 18 days after the last dose of chemotherapy. • Radiotherapy-induced: usually begins to manifest itself within 2 to 3 weeks of the start of treatment (if the dose is ~ 200 cGy per week). By week 5, frank erythema, ulceration, and pseudomembrane formation are usually present. After the completion of radiotherapy, mucosal healing begins, symptoms gradually decrease, and typically ulcerations are dramatically improved within 4 to 6 weeks.
Oral/Gastrointestinal Ulceration	Starts at about second week	[C]; Oral and gastrointestinal mucosal ulcerations are common findings in many patients receiving chemotherapy and are frequently caused by the direct effect of cytotoxic chemotherapeutic drugs on the mucosal cells. In patents receiving chemotherapy, the development of oral and gastrointestinal mucosal ulcerations are usually an extension (progression) of the mucosal atrophy and break-down associated with the development of oral mucositis.
Taste Alterations (Dysgeusia)	Starts at about second week	Dysgeusia occurs in many patients receiving radiotherapy, probably as a result of damage to the microvilli of the taste cells and may cause decreased oral intake, decreased appetite, nausea and gagging. Dysgeusia is more frequent, severe, and of longer duration with radiotherapy (lasts ~ 3 to 4 months) versus chemotherapy. Patients receiving chemotherapy typically complain of bitter taste in the mouth, unpleasant odors, and aversions to certain foods that usually resolves within a few days after the last dose of chemotherapy.
Hyposalivation and Xerostomia	Starts at about one week	[R]; Symptoms are more severe with radiation induced- (versus chemotherapy induced-) hyposalivation and may be permanent with radiation doses > 30 Gy to the major salivary glands. Usually a 50 - 60% reduction in salivary flow occurs in the first week after radiotherapy. Severe hyposalivation (defined and an unstimulated salivary flow less than 0.2 mL/minute) results in severe xerostomia; mucositis; cheilitis; glossitis; fissured tongue; glossodynia; dysgeusia; dysphagia; and a severe form of caries (i.e., radiation caries).

Neutropenia and Secondary Infections (Fungal, Bacterial, Viral)	Starts at about one week	[C]; Occurs due to the myelosuppressive effects of chemotherapy (and/or total body irradiation) on the bone marrow. The risk of infection is primarily related to the (absolute) neutrophil count. Patients with mild or moderate neutropenia generally are able to mount an adequate response to infections. However, in patients with severe neutropenia (< 500 mm^3) and/or a total white blood count < 2,000 mm^3, the immune system is less able to manage these infections, and can be potentially life-threatening. The most frequent opportunistic infection of the oral cavity in patients undergoing cancer therapy (in whom hyposalivation and immunosuppression are common) is due to Candida albicans. Recurrent orofacial herpes simplex virus (HSV) infections often develop during chemotherapy if antivirals are not prophylactically prescribed.
Thrombocytopenia and Bleeding	Starts at about 6 to 10 days	[C]; Occurs due to the myelosuppressive effects of chemotherapy (and/or total body irradiation) on the bone marrow. Most common in patients treated with high doses of chemotherapy (and/or those with being treated for a hematologic malignancy). Severe bleeding generally does not develop until the platelet count is below 10,000 to 20,000/mm^3.
Radiation Caries	Delayed onset	[R]; Patients who have not shown any degree of carious activity for years may develop decalcification, dental decay, and varying degrees of tooth disintegration after irradiation known as radiation caries; appears to be attributable to the lack of saliva (xerostomia) and to changes in the chemical composition of dental hard tissues; a pattern of cervical decay is most common. Studies have indicated that minimal tooth damage (and increased caries risk) with less than a 30 Gy tooth-level radiations dose; there is 2 to 3 times increased risk of caries with a 30 - 60 Gy tooth-level radiation dose (likely related to salivary gland involvement / hyposalivation); there is 10 times increased risk of tooth damage / caries when the tooth-level dose is > 60 Gy indicating radiation-induced damage to the mineralized tissues of teeth in addition to salivary gland damage.
Hypersensitive Teeth, Pulpal Pain and Necrosis	Acute and delayed onset	[R]; Teeth may become hypersensitive during and following radiotherapy. This could be related to the decreased secretion of saliva and the lowered pH of secreted saliva. With high-dose radiotherapy, pulpal tissue can demonstrate long-term fibroatrophy after irradiation. Patients may exhibit hypersensitivity, pulpal pain, and necrosis. Patients receiving chemotherapy (particularly vincristine and vinblastine) may sometimes experience odontogenic pain that mimics irreversible pulpitis due to neurotoxicity associated with these drugs; pain is more frequently described in the molar region and can be bilateral.
Osteoradionecrosis	Delayed onset	[R]; Osteoradionecrosis (ORN) occurs when osteocytes and the microvascular system of the jaws are irreversibly injured by radiotherapy. ORN rarely occurs in patients irradiated with total doses below 50 Gy and usually develops with total doses over 64 Gy. ORN is more common in mandible, less common in maxilla. Clinical manifestations of ORN may include pain, orofacial fistulas, exposed necrotic bone, pathologic fracture and suppuration. The risk for ORN remains throughout a patient's lifetime.

Trismus	Delayed onset	[R]; Trismus can result from high-dose radiotherapy exposure to the TMJ region, including the masseter/pterygoid muscles, mainly due to fibrosis of muscles of mastication.
Increased Risk of Carotid Atheroma	Delayed onset	[R]; Patients who have received neck irradiation of :: 45 Gy are more likely to develop carotid artery atheromas (calcified atherosclerotic plaques) after treatment than are risk-matched control patients who have not been irradiated. These lesions can be detected by panoramic radiography and are a risk factor for stroke that warrants referral of the patient to their physician for evaluation.
Alternations in Growth and Development in Children	Delayed onset	Craniofacial deformities and dental anomalies are common in patients who receive chemotherapy and/or cranial/maxillofacial radiotherapy as children, particularly if given before age 5 years. The most common anomalies reported are deficient mandibular development, dental agenesis, arrested root development, microdontia, and enamel dysplasia. Chemotherapy received in early childhood can have neurologic toxic effects to the brain that can include deficits in cognitive, intellectual and neuropsychological functions that can persist into adulthood.

[C] = limited to, or more prominent with chemotherapy
[R] = limited to, or more prominent with radiotherapy

CARDIOVASCULAR DISEASE:

- ARRHYTHMIA
- CONGESTIVE HEART FAILURE
- CORONARY ARTERY DISEASE, ANGINA PECTORIS, and MYOCARDIAL INFARCTION

ARRHYTHMIA

- Arrhythmia denotes an alteration of the normal site or rate of electrical impulse generation within the heart or an alteration of the impulse's orderly spread through the cardiac conducting system.

Dental Implications of a Patient with an Arrhythmia:

- The stress and anxiety of dental treatment or excessive amounts of epinephrine may induce life-threatening arrhythmias in susceptible patients.
- Patients with existing arrhythmia are at increased risk for serious complications such as angina, myocardial infarction, stroke, heart failure, or cardiac arrest.
- Patients with an implanted pacemaker or defibrillator are at (low) risk for possible malfunction caused by electromagnetic interference if in close proximity to some dental equipment (e.g., ultrasonic scaler [Cavitron]).
- In patients who are taking a nonselective beta blocker, excessive amount of epinephrine may cause a dangerous elevation in blood pressure.
- Patients with atrial fibrillation who are taking warfarin (Coumadin) are at increased risk for excessive postoperative bleeding.
- Patients who are taking digoxin (Digitalis, Lanoxin) are at increased risk for arrhythmia if epinephrine is used; digoxin toxicity is also a potential problem.

What to Include in a Medical Consultation:

- A medical consultation is indicated for any patient with a diagnosed or suspected arrhythmia.
- Inform the physician of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient's disease. Also, inform the physician that we plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.
- It is important to determine or confirm the type and severity of the arrhythmia, and current medical status of the patient's arrhythmia (i.e., Is their arrhythmia adequately medically controlled at this time or is it still symptomatic or refractory despite treatment?).

- Example:

  "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

1. The patient reports a history of (e.g., atrial fibrillation, PSVT, an unspecified "arrhythmia" and is unable to provide any additional information). Please summarize the specific diagnosis and severity of this patient's arrhythmia and any other cardiovascular disease that is currently under medical management.
2. Please summarize the current status and adequacy of medical control of this patient's arrhythmia/cardiovascular disease.
3. Please provide your assessment of this patient's overall cardiovascular risk in relation to their ability to safely tolerate the proposed dental procedures, as well as any specific medical management precautions or recommendations you may have as it relates to their dental treatment.
4. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

- For patients taking Coumadin (warfarin): See the section on,"Anticoagulant and Antiplatelet Therapy" for more information about what you need to add to this medical consultation).

ASA Classification for the Patient with Arrhythmia

Classification	ASA Risk Category
Low Risk: no medications required for treatment, no or infrequent arrhythmia symptoms • Asymptomatic paroxysmal arrhythmias • Young, active individuals with sinus bradycardia	II
Moderate Risk: require chronic antiarrhythmic medications or treatment, and are currently asymptomatic • Moderate risk arrhythmias (essentially all others that are not classified as low risk or high risk) • First-degree AV block or Mobitz type I second-degree AV block	III
High Risk: any untreated, symptomatic arrhythmia, or arrhythmia that remains symptomatic despite treatment (refractory arrhythmia), or a patient that presents with an abnormal pulse rate and / or rhythm without medical evaluation • High risk arrhythmias: symptomatic ventricular arrhythmia; supraventricular arrhythmia with uncontrolled ventricular rate • Untreated Mobitz type II second-degree AV block, or third-degree AV block	IV

Dental Management of a Patient with Arrhythmia:

- For High-risk Arrhythmia (ASA IV: high-grade atrioventricular [AV] block, symptomatic ventricular arrhythmia, supraventricular arrhythmia with uncontrolled ventricular rate):

- Elective dental care should be deferred. Dental treatment should be limited to urgent care only such as treatment of acute infection, bleeding, or pain; preferably in a hospital dental clinic. If treatment is necessary, it should be provided in consultation with the physician.
- Management may include establishment of an IV line; sedation; monitoring of electrocardiogram, pulse oximeter, and blood pressure; oxygen; and avoidance or cautious use of vasoconstrictors.

- For Intermediate- and Low-risk Arrhythmia (ASA II or III):
  Elective dental care may be provided with the following management considerations:
  - Provide oral sedative premedication and/or inhalation sedation if indicated.
  - Assess and record pretreatment vital signs.
  - Provide profound local anesthesia and adequate postoperative pain control (analgesics); limit the quantity of vasoconstrictor used (see: Box 1).

Box 1: Dose Reduction Guidelines for the Use of Local Anesthetic Containing a Vasoconstrictor

- Limit the initial dose of a local anesthetic containing a vasoconstrictor to a maximum of:
  - 0.036 mg of epinephrine (two 1.8 mL cartridges of 2% lidocaine with 1:100,000), or
  - 0.18 mg of levonordefrin (two 1.8 mL cartridges of 2% mepivacaine with 1:20,000 levonordefrin)

  within 30–45 minutes.
- Assess and record the patient's pulse rate and blood pressure prior to, and 5 minutes after, administering local anesthetic, especially when containing a vasoconstrictor. Additional precautions include:
  - Avoiding the use of epinephrine impregnated gingival retraction cord (aluminum potassium sulfate impregnated gingival retraction cord is a safe alternative).
  - Avoiding the use of local anesthetic with vasoconstrictors for direct hemostasis to control local bleeding
  - Avoiding the use of local anesthetic with vasoconstrictors for intraligamentary or infrabony infiltrations.
- If, during the dental procedure, additional local anesthetic is necessary and 0.036 mg of epinephrine has already been administered at least 30–45 minutes ago, options include:
  - Administer a local anesthetic without a vasoconstrictor (e.g., 3% mepivacaine, 4% prilocaine), or
  - Check blood pressure and pulse, and if within acceptable limits, administer additional local anesthetic with up to 0.018 mg of epinephrine; recheck blood pressure and pulse 5 minutes after injection.

- If the patient is taking warfarin (Coumadin), the INR should be 2.5 or less prior to performance of invasive dental procedures (see section on,"Anticoagulant and Antiplatelet Therapy" for more information).
- For patients with an implanted cardiac pacemaker or defibrillator, avoid the use of electrosurgery and keep ultrasonic scalers and other devices that may cause electromagnetic interference as far from the patient as possible during use; antibiotic prophylaxis is not recommended for these patients.

- For patients who are taking digoxin, avoid the use of epinephrine because of the increased risk of inducing arrhythmia; be observant for signs of digoxin toxicity (e.g., hypersalivation). Also, an increased gag reflex and an increased tendency for nausea and vomiting may be seen in patients taking digoxin

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CONGESTIVE HEART FAILURE (CHF)

- Heart Failure (or Congestive Heart Failure [CHF]) is a symptom complex, not a disease entity, that can result from a variety of cardiac disorders. The syndrome is characterized by inability of the heart to pump blood sufficiently to keep pace with the body's circulatory demands.

Dental Implications of a Patient with CHF:

- CHF is a symptom complex, not a disease entity, that occurs secondary to other systemic illness (e.g., hypertension, coronary artery disease). Therefore it is important to note that the underlying systemic illness responsible for causing the congestive heart failure needs to be addressed when considering any dental treatment restrictions and considerations for the patient.
- Providing dental treatment to a patient with symptomatic or uncontrolled CHF may result in worsening of symptoms, acute heart failure, arrhythmia, myocardial infarction, or stroke.
- Patients with CHF may have difficulty breathing and may not tolerate a supine chair position.
- In patients who are taking a non-cardioselective beta blocker (e.g., propranolol) excessive amounts of epinephrine may cause a dangerous elevation in blood pressure.
- The use of epinephrine in patients who are taking digoxin may cause arrhythmia.

What to Include in a Medical Consultation:

- A medical consultation is indicated for any patient with suspected, undiagnosed CHF by history, or with NYHA Class II, III or IV CHF.
- Inform the physician of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient's disease. Also, inform the physician that we plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.
- It is important to:
  - identify the underlying causative factors responsible for the patient's CHF (e.g., coronary artery disease, valvular disease, hypertension).
  - determine the current severity (NYHA classification), and status of the patient's CHF (i.e., their CHF adequately medically controlled at this time, or is are they still symptomatic or refractory despite treatment?).

New York Heart Association (NYHA) Classification of Congestive Heart Failure

Class	Clinical Presentation
I	No limitation of physical activity. No dyspnea, fatigue, or palpitations with ordinary physical activity.
II	Slight limitation of physical activity. These patients have fatigue, palpitations, and dyspnea with ordinary physical activity but are comfortable at rest.
III	Marked limitation of activity. Less than ordinary physical activity results in symptoms, but patients are comfortable at rest.
IV	Symptoms are present at rest, and any physical exertion exacerbates the symptoms.

- Example:

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

1. Mr. X reports having congestive heart failure with current signs and symptoms consist with NYHA Class (I, II, III, IV) disease. Please summarize the specific diagnosis and severity of this patient's CHF/cardiovascular disease that is currently under medical management.
2. Please summarize the current status and adequacy of medical control of this patient's cardiovascular disease.
3. Please provide your assessment of this patient's overall cardiovascular risk in relation to their ability to safely tolerate the proposed dental procedures, as well as any specific medical management precautions or recommendations you may have as it relates to their dental treatment.
4. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

Dental Management of a Patient with CHF:

1. Overview:
   - The patient's degree of cardiovascular compromise (and resulting symptoms) is a major consideration in evaluating their ability (or risk) to safely undergo routine dental procedures (see: Table: "Summary of Dental Treatment Considerations for Patients with Congestive Heart Failure"). Patients with:
     - Severe or significantly symptomatic CHF (i.e., NYHA Class III or IV, or ACC/AHA stage D or significantly symptomatic stage C patients):
       - Are usually not acceptable candidates for elective, invasive dental treatment. Dental treatment should usually be limited to emergency (urgent) care only such

as treatment of acute infection, bleeding, or pain; preferably in a hospital dental clinic. If urgent dental treatment is necessary, it should be provided in consultation with the physician.

- Well controlled, asymptomatic, mild to moderate CHF (i.e., NYHA class I or II CHF or ACC/AHA Heart Failure stages A, B, and some [well-controlled, minimally symptomatic] stage C patients):
  - Can usually can undergo routine dental care after appropriate medical coordination and consultation have taken place.

Summary of Dental Treatment Considerations for Patients with Congestive Heart Failure

NYHA CHF Classification	ASA Classification	Dental Treatment Considerations*
I	II	• None* - Okay for elective, routine dental care.
II	III	• Patient is usually at acceptable risk for most elective dental treatment in a dental office setting, including routine, uncomplicated oral surgery. • Require consultation with physician prior to dental treatment. • Limit dose of local anesthetic containing a vasoconstrictor.‡
III	III	• Elective, invasive dental treatment is usually contraindicated; patient may be able to have noninvasive or minimally invasive dental treatment in a dental office setting. • Require consultation with physician prior to any dental treatment, and should consider invasive or surgical dental treatment in a special care facility (e.g., hospital dental clinic). • Use of local anesthetic containing a vasoconstrictor may be contraindicated (consult with physician).

IV	IV	• Elective dental care is generally contraindicated. • Require consultation with physician prior to any dental treatment and are best treated conservatively (emergency or minimally invasive treatment only) in a special care facility (e.g., hospital dental clinic). Use of local anesthetic containing a vasoconstrictor is usually contraindicated.

* Congestive heart failure is a symptom complex, not a disease entity, that occurs secondary to other systemic illness. Therefore it is important to note that the underlying systemic illness responsible for causing the congestive heart failure needs to be addressed when considering any dental treatment restrictions and considerations for the patient.

‡ See: Box 1

2. General Considerations for Dental Patients with CHF:
   - Address and appropriately manage the underlying, causative factors responsible for the patient's CHF.
   - Keep appointment duration as short as possible. Also, morning appointment are probably preferable for most patients as they may become more fatigued as the day

progresses.

- Record pretreatment vital signs. Continuous (automated) monitoring of blood pressure, pulse and blood oxygen saturation during dental treatment is advantageous.
- A semisupine or upright chair position may be needed for patients with a history of orthopnea.
- Assess the patient's level of anxiety or fear related to dental treatment and utilize appropriate stress and anxiety reduction protocols as indicated:
  - e.g.: triazolam, 0.125 to 0.5 mg the night before appointment, and 0.125 to 0.5 mg 1 hour before treatment and N_2O-O_2, inhalation sedation during procedure (when not otherwise medically contraindicated), or low-flow oxygen (2-4 L/min) via nasal cannula.
- Provide profound local anesthesia:
  - For patients with severe, uncompensated or uncontrolled CHF (e.g., NYHA class IV or ACC/AHA stage D), the use of vasoconstrictors in local anesthetics is usually contraindicated.
  - For most other patients with CHF, it is advisable to follow the vasoconstrictor dose reduction guidelines in Box 1.
- Watch for orthostatic hypotension, make position or chair changes slowly, and assist in and out of chair.
- An increased gag reflex and an increased tendency for nausea and vomiting may be seen in patients taking cardiac glycosides (e.g., digoxin).

CORONARY ARTERY DISEASE, ANGINA PECTORIS, and MYOCARDIAL INFARCTION (MI)

- Coronary artery disease (CAD): is cause by the accumulation of atherosclerotic plaques and/or scar tissue on the walls of the coronary arteries. Symptoms may include: chest pain on exertion (angina pectoris [see below]), which may be relieved by rest; weakness and/or shortness of breath on exertion; jaw pain, back pain, or arm pain, especially on left side, either during exertion or at rest; palpitations; dizziness, light-headedness, or fainting.
- Angina Pectoris: is a syndrome of episodic, paroxysmal, substernal or precordial chest pain resulting from the inability of diseased coronary vessels to provide adequate blood for myocardial oxygenation. It typically occurs on exertion and is relived by rest and/or the use of nitroglycerin. However, in severe cases, angina can occur with minimal exertion or even at rest.
- Acute Myocardial Infarction (MI): refers to irreversible myocardial injury, occurring as a result of prolonged ischemia. The result is coagulative necrosis of the myocardial fibers, with loss of the normal conductive and contractile properties of the affected myocardial tissue. Infarction most frequently involves the left ventricle, due to its greater work load as compared with the other heart chambers. The most common long-term sequella of MI are congestive heart failure, and arrhythmias.

Dental Implications of a Patient with CAD, Angina Pectoris and/or a History of MI:

- The stress and anxiety of a dental visit could precipitate an anginal attack, myocardial infarction, or sudden death.
- For patients who are taking a non-cardioselective beta blocker (e.g., propranolol), the use of excessive amounts of epinephrine could precipitate a dangerous elevation in blood pressure.
- Patients with a history of MI may have some degree of (congestive) heart failure.
- Patients who are taking low-dose aspirin (::; 325 mg/day) and/or other platelet aggregation inhibitor (e.g., clopidogrel [Plavix]) may demonstrate impaired hemostasis but is (almost) never of sufficient magnitude to be clinically significant in regards to dental treatment including oral surgical procedures.
- Patient who are taking warfarin (Coumadin) (or to a lesser degree, direct-acting oral anticoagulants) may experience excessive postoperative bleeding.

What to Include in a Medical Consultation for a Patient with Angina Pectoris:

- A medical consultation is indicated for any patient with suspected or undiagnosed angina by history. A medical consult is also indicated for any patient diagnosed with vasospastic angina or angina with current symptoms that are consistent with CCS Class III or IV disease.
  - Inform the physician of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient's disease. Also, inform the physician that plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.
  - It is important to determine or confirm the severity of the patient's angina, and current medical status of the angina (i.e., Is their angina adequately medically controlled, or is it still symptomatic or refractory despite treatment?).

  - Example:

    "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

    (Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

    1. Mr. X reports they currently experience symptoms of angina pectoris that are consistent with Class (I, II, III, IV) disease according to the Canadian Cardiovascular Society (CCS) Functional Classification of Angina Pectoris. Please summarize the specific diagnosis and severity of this patient's cardiovascular disease that is currently under medical management.
    2. Please summarize the current status and adequacy of medical control of this patient's cardiovascular disease.
    3. Please provide your assessment of this patient's overall cardiovascular risk

in relation to their ability to safely tolerate the proposed dental procedures, as well as any specific medical management precautions or recommendations you may have as it relates to their dental treatment.

4. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

- You may also have to add additional questions for a patient taking warfarin (see section on,"Anticoagulant and Antiplatelet Therapy" for more information).

What to Include in a Medical Consultation for a Patient with a History of MI:

- A medical consultation is indicated for any patient with a history of MI.
- Inform the physician of the most invasive dental treatment that the patient may require; use words, 'oral surgery' or 'extractions' when requesting information about the patient's disease. Also, inform the physician that we plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.
- It is important to determine or confirm the patient's current post-MI cardiovascular status and stability including the presence of other significant cardiovascular pathology and increased surgical risk including such as: congestive heart failure; arrhythmia; angina; hypertension.

- Example:

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

Mr. X reports a history of ischemic heart disease with subsequent myocardial infarction on (date[s]). His/Her current cardiovascular functional status is consistent with Class (I, II, III, IV) disease according to the (select the most appropriate assessment based on the patient's history and clinical presentation), Canadian Cardiovascular Society (CCS) Functional Classification of Angina Pectoris or New York Heart Association (NYHA) Classification of Congestive Heart Failure.

1. Please summarize the specific diagnosis and severity of this patient's cardiovascular disease that is currently under medical management.
2. Please summarize the current status and adequacy of medical control of this patient's cardiovascular disease.
3. Please provide your assessment of this patient's overall cardiovascular risk in relation to their ability to safely tolerate the proposed dental procedures, as well as any specific medical management precautions or recommendations you may have as it relates to their dental treatment.

4. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.
   Thank you for your assistance in the care of our mutual patient."

- You may also have to add additional questions for a patient taking warfarin (see section on,"Anticoagulant and Antiplatelet Therapy" for more information).

Canadian Cardiovascular Society (CCS)
Functional Classification of Angina Pectoris

Class	Definition	Specific Activity Scale
I	No limitation of ordinary physical activity; Exercise tolerance 7 - 8 METs: Ordinary physical activity, (e.g., walking and climbing stairs) does not cause angina. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.	Ability to ski, play basketball, light jog (5 mph), or shovel snow without angina.
II	Slight limitation of ordinary activity; Exercise tolerance 5 - 6 METs: Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold, in wind, or when under emotional stress, or only during the few hours after awakening. Walking more than 2 blocks on the level and climbing more than 1 flight of ordinary stairs at a normal pace and under normal conditions.	Ability to garden, rake, roller skate, walk at 4 mph on level ground, and have sexual intercourse without stopping.
III	Marked limitation of ordinary physical activity; Exercise tolerance 3 - 4 METs: Angina occurs on walking 1 to 2 blocks on level ground or climbing 1 flight of stairs at a normal pace in normal conditions.	Ability to shower or dress without stopping, walk 2.5 mph, bowl, make a bed, and play golf.
IV	Inability to perform any physical activity without discomfort; anginal symptoms may be present at rest; Exercise tolerance 1 - 2 METs.	Inability to perform activities requiring 2 or fewer METs* without discomfort or stopping.

* Activities requiring 2 or fewer metabolic equivalents (METs) include: lying or sleeping (80 kcals/hour or 1.0 METS); desk work (110 kcals/hour or 1.5 METS); driving (120 kcals/hour or 1.6 METS); fishing (130 kcals/hour or 1.8 METS); sitting (100 kcals/hour or 1.4 METS); standing (140 kcals/hour or 2 METS); walking 2 mph (150 kcals/hour or 2 METS).

(Continued on next page)

ASA Risk Classification for Angina Pectoris

Classification	ASA Risk Category
• CCS* Class I or II Angina	II
• CCS* Class III Angina • Vasospastic Angina	III
• CCS* Class IV Angina • Unstable Angina	IV

* CCS = Canadian Cardiovascular Society

ASA Risk Classification for Myocardial Infarction (MI)

Classification	ASA Risk Category
• Stable post-MI status* and more than 30 days post-MI	III
• Unstable post-MI status* or • Between 8 and 30 days post-MI	IV
• Acute MI (:::; 7 days post-MI)	IV

* As determined by medical (cardiology) consultation.

Dental Management of a Patient with Angina Pectoris and/or a History of MI:

- Unstable Angina (ASA IV: major risk), or
- Recent Myocardial Infarction (< 30 days post-MI) (ASA IV: major risk)
  - Elective dental care should be deferred. Dental treatment should be limited to urgent care only such as treatment of acute infection, bleeding, or pain; preferably in a hospital dental clinic and after consultation with the patient's physician.
  - Management may include establishment of an IV line; sedation; monitoring of electrocardiogram, pulse oximeter, and blood pressure; oxygen; avoidance or cautious use of vasoconstrictors; and prophylactic nitroglycerin.

- Stable Angina (ASA II or III: intermediate risk), or
- Past Myocardial Infarction (> 30 days ago or longer without symptoms) (ASA III: intermediate risk)

  Elective dental care may be provided with the following management considerations:

- Appropriate patient monitoring:
  - Record pretreatment vital signs.
  - Continuous (automated) monitoring of blood pressure, pulse and blood oxygen saturation during dental treatment is advantageous.
  - If patient becomes fatigued or has an abnormal change in pulse rate or rhythm, discontinue treatment and reschedule.
- Stress reduction measures:
  - Keep appointment duration as short as possible. Also, A.M. appointment are probably preferable for most patients as they may become more fatigued as the day progresses.
  - Consider the use of N_2O-O_2 inhalation sedation and/or premedication with oral anti-anxiety medications such as benzodiazepines (e.g., triazolam, 0.125 to 0.5 mg the night before appointment, and 0.125 to 0.5 mg 1 hour before treatment).
- Ensure adequate oxygenation:
  - Oxygen by nasal cannula at 2 to 4 L/min (if not already using N_2O-O_2 inhalation sedation or not contraindicated by severe COPD).
  - A semisupine or upright chair position may be needed for patients with a history of orthopnea.
- Use of pre-treatment nitrates:
  - If dental treatment predictably precipitates angina, then consider premedication with nitroglycerin (0.3 mg to 0.6 mg sublingual tablet) prior to initiating dental treatment.
  - Patient should bring own supply of nitroglycerin to appointment for use if necessary. This should be placed in easy reach of the patient in case a dose is necessary during dental treatment.
- Provide profound local anesthesia:
  - For high-risk post-MI patients the use of vasoconstrictors in local anesthetics is usually contraindicated and should be discussed with the patient's physician.
  - For post-MI patients that are not considered high-risk for complications, it is advisable to follow the vasoconstrictor dose reduction guidelines in Box 1.
- Concerns for patients taking aspirin and/or antiplatelet drug (e.g., clopidogrel [Plavix], ticlopidine [Ticlid], prasugrel [Effient], ticagrelor [Brilinta]):
  - The American College of Chest Physicians, American Heart Association/American College of Cardiology and American Dental Association all recommend that low dose aspirin (::; 325 mg/day) and/or antiplatelet drug therapy <u>should not be interrupted</u> for routine invasive dental procedures including uncomplicated oral surgery.
    - The risk of discontinuing (single or dual [e.g., aspirin + clopidogrel]) antiplatelet drug therapy far outweigh the low risk of postoperative oral bleeding complications resulting from dental procedures.
    - For patients with intravascular coronary artery stents, premature discontinuation (after < 1 year) of dual antiplatelet therapy strongly increases the risk of a catastrophic event of stent thrombosis leading to myocardial infarction and/or death.
    - The risk of postoperative bleeding complications following routine dental

treatment procedures, including uncomplicated multiple extractions, in patients single or dual antiplatelet drug therapy is low to negligible, especially when appropriate local hemostatic methods are used.

- Concerns for patients taking warfarin (Coumadin):
  - If patient is taking warfarin (Coumadin) for anticoagulation, pretreatment prothrombin time (PT) should evaluated. If the PT time is ;:: 2.5 times the control value or the international normalized ratio (INR) is ;:: 3.5, this may result in significantly abnormal hemostasis and greatly complicate moderate- or high-risk invasive dental procedures. The patient's physician should be consulted to as to the possibility of adjusting the patient's anticoagulant dose to bring the PT/INR within desired limits prior to these dental procedures.
- Ensure adequate post-treatment pain control with analgesics as indicated:
  - Among patients receiving antithrombotic therapy (e.g., aspirin, clopidogrel, warfarin) after myocardial infarction (MI), the use of NSAIDs was associated with increased risk of bleeding and excess thrombotic events, even after short-term (3 days or less) NSAID use and are generally not recommend for use in this at-risk patient population. (Olsen AS, et al. JAMA. 2015;313(8):805-814.) Additionally, concurrent administration of non-COX-selective NSAIDs may interfere with aspirin's cardioprotective effect of blocking the formation of TXA_2 and inhibiting platelet aggregation.
- Avoid anticholinergic drugs (scopolamine or atropine).

CEREBROVASCULAR DISEASE

Clinical Manifestations:

- Transient Ischemic Attack (TIA)
- Cerebrovascular Accident (CVA)

Background:

- A cerebrovascular accident (CVA), or "stroke" is a neurologic deficit caused by sudden interruption of oxygenated blood to the brain. Focal necrosis of brain tissue is the end result. The interruption of blood supply most commonly is caused (65% to 80% of cases) by thrombosis of a cerebral vessel. Other common causes of the interruption of cerebral blood flow include cerebral embolism and intracranial hemorrhage.
- Transient ischemic attack (TIA): A TIA is a "mini stroke" caused by a temporary disturbance in blood supply to a localized area of the brain. It often causes numbness of the face, arm, or leg on one side of the body (hemiplegia), weakness, tingling, numbness, or speech disturbances that usually last less than 10 minutes. Approximately one-third of patients with untreated TIA's will eventually suffer a major stroke (CVA). Most commonly, a major stroke (CVA) is preceded by one or two TIAs within several days of the first attack.

General Considerations:

- Atherosclerotic lesions at the carotid bifurcation frequently are calcified and have been shown to be detectable on the panoramic dental radiographs of neurologically asymptomatic patients. Identifying a calcified carotid artery atheroma on a panoramic radiograph is of major clinical importance. Patients with such calcifications may be at a significantly increased risk of experiencing CVA, and should be referred to an appropriate physician for confirmation of the findings and determination of the extent of disease.
  - The UFCD Radiology Division has a specialized referral/consultation form to send to the physician of a patient that demonstrates radiographic evidence of a calcified carotid artery atheroma.

Dental Implications of a Patient with a History of Cerebrovascular Disease

- Dental treatment could precipitate or coincide with another CVA or TIA.
- Patient taking anticoagulant drugs used to prevent cerebral thrombosis (especially warfarin [Coumadin]) are at increased risk for excessive postoperative bleeding.
- After a stroke, loss or difficulty in speech, unilateral paralysis of the orofacial musculature, and loss of sensory stimuli of oral tissues may occur.
  - The tongue may be flaccid, with multiple folds, and deviate on extrusion.
  - The gag reflex may be diminished or impaired, increasing the risk for aspiration.
  - Dysphagia is common.
  - Patients with right-sided brain damage may neglect the left side. Thus, food and debris may accumulate around teeth, beneath the tongue, or in alveolar folds.

- Patients may need to learn perform oral hygiene tasks or clean dentures with only one hand.

What to Include in a Medical Consultation:

- A medical consultation is indicated for any patient with a history of CVA, (or TIA and is not under the active care of a physician)*.
- Inform the physician of the most invasive dental treatment that the patient may require; use words, "oral surgery" or "extractions" when requesting information about the patient's disease. Also, inform the physician that we plan to use a local anesthetic containing a vasoconstrictor (e.g., 2 % lidocaine with 1:100,000 epinephrine) unless it is specifically contraindicated due to an increased risk of an adverse cardiovascular event.
- It is important to:
  - determine or confirm the specific diagnosis (TIA, CVA) and timing (dates) of the patient's cerebrovascular disease, including hospitalizations.
  - obtain an assessment of the patient's current post-CVA status and stability. This would entail a summary of any residual neurologic deficits or disabilities* including: motor, sensory, cognitive, memory and behavioral deficits, (a specific assessment for dysphagia, impairment of the gag reflex, and increased risk for aspiration may be beneficial).
  - identify the presence of continued risk factors for CVA, including: hypertension, diabetes, smoking, hyperlipidemia, hypercholesterolemia, cardiovascular disease, etc.

* NOTE: By definition, patients who experienced a TIA should not have any residual neurological deficits beyond ~ 24 hours (otherwise this would classified as a CVA), therefore, DO NOT ASK ABOUT THE PRESENCE OF RESIDUAL NEUROLOGICAL DEFICITS IN PATIENT WITH A HISTORY OF TIA ONLY.

- Example:

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

The patient reports a history of a CVA on (date[s]).

1. Please provide a summary of this patient's current post-CVA status and stability, as well as the presence of any residual neurologic deficits or disabilities, including dysphagia, impairment of the gag reflex, and increased risk for aspiration.
2. Please identify the presence of any continued risk factors for CVA, and indicate if they are adequately medically controlled at this time.
3. Please indicate any specific precautions or recommendations regarding the proposed dental treatment for this patient.
4. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

- May also have to request the date and results of a recent INR for a patent taking warfarin (see section on,"Anticoagulant and Antiplatelet Therapy" for more information).

Dental Management of the Cerebrovascular Disease Patient

- In general, a standard evidence-based protocol for dental management of post-stroke patients is not available, and current recommendations are based primarily on intuitive extrapolations from the medical literature.
  - A 2010 study by Elad S., et al. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;110:145-150.) has indicated that dental treatment may be safely administered in patients a few weeks after a CVA as long as these patients are kept under optimal medical surveillance (monitoring).
- Major issues to be considered when treating patients at risk for or after a stroke include:

1. Control of the Underlying Disease and Stroke Risk Factors:
   - Atherosclerosis and thromboembolic events are the main etiologies for ischemic stroke, as can be observed from he present group of patients. Other etiologies of stroke are evident, such as vasculitis and hypercoagulability disorders.
     The dentist should assure that the underlying disease is controlled to minimize the risk for repeated stroke. Good communication (consultation) with the physician regarding the status of the underlying disease and risk factors for stroke are a key requirement for the treatment of such a patient.
     The dentist's treatment approach should consider the systemic risks once the plan of dental treatment has been decided. In addition to minimizing the risk for recurrent strokes, any underlying disease (e.g., (hypertension, atrial fibrillation) should be addressed according to accepted practice.

2. Optimal Medical Surveillance (Monitoring):
   - Pre- and intraoperative vital signs should also be monitored and recorded. Continuous (automated) monitoring of blood pressure, pulse and blood oxygen saturation (using a pulse oximeter) during dental treatment is advantageous.

3. Stress Reduction Protocol and Local Anesthesia:
   - Keep appointment duration as short as possible. Also, A.M. appointment are probably preferable for most patients as they may become more fatigued as the day progresses.
   - Stress and anxiety reduction protocols as necessary for the patient: e.g.: triazolam, 0.125 to 0.5 mg the night before appointment, and 0.125 to 0.5 mg 1 hour before treatment and N_2O-O_2, inhalation sedation during procedure, or low-flow oxygen (2-4 L/min) via nasal cannula.
   - Use of epinephrine-containing local anesthetics is not contraindicated if optimal medical monitoring is utilized, but they should be used judiciously. It is advisable to limit the initial dose of a local anesthetic containing a vasoconstrictor to a maximum of 0.036 mg of epinephrine (two 1.8 mL cartridges of 2% lidocaine with 1:100,000), or 0.18 mg of levonordefrin (two 1.8 mL cartridges of 2% mepivacaine with 1:20,000 levonordefrin).
     - Assess and record the patient's pulse rate and blood pressure prior to, and 5 minutes after, the administration of a local anesthetic containing a vasoconstrictor.

- Additional precautions include:
  - Avoiding the use of epinephrine impregnated gingival retraction cord (aluminum potassium sulfate impregnated gingival retraction cord is a safe alternative).
  - Avoiding the use of local anesthetic with vasoconstrictors for direct hemostasis to control local bleeding.
  - Avoiding the use of local anesthetic with vasoconstrictors for intraligamentary or infrabony infiltrations.
- If, during the dental procedure, additional local anesthetic is necessary and 0.04 mg of epinephrine has already been administered, options include:
  - Administer a local anesthetic without a vasoconstrictor (e.g., 3% mepivacaine, 4% prilocaine)
  - Check blood pressure and pulse, and if within acceptable limits, administer additional local anesthetic with up to 0.02 mg of epinephrine; recheck blood pressure and pulse 5 minutes after injection.

• Ensure adequate post-treatment pain control with analgesics as indicated

4. Bleeding / Hemostasis Concerns:
   • Patients receiving daily aspirin therapy (325 mg qd) to prevent thromboembolic complications, and/or other platelet inhibitor drugs, (e.g., clopidogrel [Plavix], dipyridamole [Persantine], ticlopidine [Ticlid]) may demonstrate mild impaired hemostasis but should not be of sufficient magnitude to be clinically significant in regards to dental treatment including oral surgical procedures.
   • If patient is taking warfarin (Coumadin) for anticoagulation, pretreatment prothrombin time (PT) should evaluated. If the PT time is ;: 2.5 times the control value or the international normalized ratio (INR) is ;: 3.5, this may result in significantly abnormal hemostasis and greatly complicate moderate- or high-risk invasive dental procedures. The patient's physician should be consulted to as to the possibility of adjusting the patient's anticoagulant dose to bring the PT/INR within desired limits prior to these dental procedures. (See the section on, "Dental Management of the Patient Receiving Anticoagulants" for more information).
     - Aspirin and other nonsteroidal antiinflammatory agents (NSAIDs) may increase postoperative bleeding in patients taking warfarin or other oral anticoagulants

5. Neurologic Deficit Considerations:
   • When neurologic deficits exist, the dentist should be aware of difficulties with communication, mobility, and oral function (mastication and swallowing).
   • Be especially cautious to prevent aspiration and/or unintentional swallowing of dental materials/implements by patients if there is loss of protective reflexes, such as swallowing and gag reflexes, or cognitive impairment.
     - Though many stroke victims are adequately managed in an outpatient environment, some may require airway protection through intubation in the operating room
   • Adjustment of the patient's head position is advised to assure an open airway, and if possible, it is advised to treat the patient in an upright position.
   • High-speed suction (evacuation) should be utilized to prevent aspiration of any water/irrigation used during dental treatment.

- The use of rubber dam, effective oral evacuation, and facilitative head positioning alleviate patient's fear of choking and reduce the risk of aspiration.
- Dental staff should demonstrate an empathetic and supportive approach in understanding the patient's physical and emotional limitations and allocate extra time for communication and clinical procedures. Effective communication techniques for the stroke patient include:
  - Face the patient when speaking to them
  - Use slower, more deliberate, less complex pattern of speech
  - Do not wear a mask when talking to the patient (it may impede comprehension)
  - Do not raise voice (talk loudly) or use "baby talk"
  - Ask yes / no questions - simple and brief
  - Give frequent, accurate, and immediate feedback
  - Use simple drawings to explain procedures
  - Do not underestimate or overestimate the patient's abilities
  - Be positive (stroke patients have feelings of grief, loss, and depression)

Dental Treatment Planning Modifications for Patients with Cerebrovascular Disease:

- Technical modifications may be required for patients with residual physical deficits that may make adequate oral hygiene difficult, if not impossible. For these patients, extensive bridgework is not a good choice. However, fixed prostheses may be more desirable than removable because of difficulty of daily placement and removal. If the patient is edentulous, or wearing a non-fitted denture, dental implant retained dentures should be considered to secure denture position and function.
- Individualized treatment plans are important. All restorations should be placed with ease of cleansability in mind. Hygiene may be facilitated by an electric toothbrush, a large-handled toothbrush, or a water irrigation device. Flossing aids also should be prescribed. Frequent professional prophylaxis is advisable.

CIRRHOSIS

Overview:

- Cirrhosis is the end result of irreversible hepatocellular injury that leads to both fibrosis and nodular regeneration throughout the liver. Cirrhosis is a serious and (in almost all cases) irreversible disease and represents the consequences of a sustained wound-healing response to chronic liver injury from a variety of causes including toxins (e.g., alcohol), chronic viral infection, cholestasis, and metabolic disorders. The clinical features of cirrhosis result from hepatic cell dysfunction, portosystemic shunting, and portal hypertension.
- Up to 40% of patients with cirrhosis have compensated cirrhosis and demonstrate no clinical symptoms. Individuals with compensated cirrhosis may be diagnosed as a result of incidental findings during routine laboratory tests, during surgery, or at autopsy. (In contrast, patients with decompensated cirrhosis have symptomatic complications related to cirrhosis, including those related to hepatic insufficiency [jaundice or hepatic encephalopathy], and those related to portal hypertension [ascites or variceal hemorrhage]).
- The etiology of cirrhosis varies both geographically and socially. Although alcohol has long been regarded as the principal cause of cirrhosis in the United States and elsewhere in the Western world, it is now being recognized that chronic viral hepatitis with or without concomitant alcohol consumption accounts for more than half of the cases of cirrhosis.

Dental Implications of a Patient with Cirrhosis:

- Cirrhosis has a number of significant implications for a patient receiving dental treatment. Major considerations include:
  1. The unpredictable hepatic metabolism of drugs administered or prescribed in dental treatment.
     - Cirrhosis (and liver disease in general) may have complex effects on drug clearance, biotransformation, and pharmacokinetics. Pathogenetic factors include alterations in absorption, plasma protein binding, intrinsic clearance and hepatic extraction ratio, liver blood flow and vascular shunting, biliary excretion, enterohepatic circulation, and renal clearance.

       Patients with cirrhosis may have an unpredictable hepatic metabolism of drugs that can lead to atypical effects of administered or prescribed dental medications. However, the hepatic reserve appears to be large and liver disease has to be severe before important changes in drug metabolism take place. The ability to eliminate a specific drug may or may not correlate with liver's synthetic capacity for substances such as albumin or clotting factors, which tends to decrease as hepatic function declines.
  2. The potential for impaired hemostasis and bleeding diathesis due to thrombocytopenia and/or reduced hepatic synthesis of coagulation factors,
  3. The increased risk of infection, or spread of infection (including oral infections), and spontaneous bacterial peritonitis (SBP).

What to Include in a Medical Consultation:

- A medical consult with the patient's physician is mandatory for a patient with a history of cirrhosis. The following information should be requested:
  a. (If not already known), establish the underlying etiology of cirrhosis: (e.g., alcoholism,

viral hepatitis, etc.)

b. Obtain results of most recent lab studies including:
   - hepatic function panel, or a comprehensive metabolic panel (CMP)
   - complete blood count (CBC) with differential (including platelet count)
   - PT / INR
c. Determine if the patient's cirrhosis is currently symptomatic (uncompensated) or compensated (i.e., demonstrates no clinical symptoms)
d. Determine history or presence of complications of cirrhosis including:
   - ascites, encephalopathy, spontaneous bacterial peritonitis (SBP), cardiomyopathy, portal hypertension, esophageal varies, coagulopathy, etc.
e. (If not already known), obtain a list of patient's current medications.

- Example:
  "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).
  (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)
  Based on Mr. X's history of cirrhosis, would you please provide the following:
  1. A copy of the patient's most recent labs results including:
     - hepatic function panel, or a comprehensive metabolic panel (CMP)
     - complete blood count (CBC) with differential (including platelet count)
     - PT / INR
  2. Your assessment of the current status and stage of this patient's cirrhosis, as well as the history or presence of significant complications of cirrhosis (e.g., ascites, SBP encephalopathy, cardiomyopathy, portal hypertension, esophageal varices, etc.).
  3. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.
  4. Your assessment of this patient's overall risk in relation to their ability to safely tolerate the proposed dental procedures, as well as any specific medical management precautions or recommendations you may have as it relates to their dental treatment.

  Thank you for your assistance in my care of our mutual patient."

Dental Management of a Patient with Cirrhosis:

- Patients with uncompensated cirrhosis and/or those with profound hepatic dysfunction* should have all invasive dental treatment performed in a hospital dental clinic.
  * The presence of <u>one or more</u> of the following profound in a patient with cirrhosis would usually be indicative of profound hepatic dysfunction in this context:
    - INR greater than 1.7 attributable to hepatic failure
    - Serum aminotransferase (AST, ALT) levels elevated greater than 4 times normal
    - Serum bilirubin elevated above 2.0 mg/dL
    - Serum albumin less than 3.5 g/dL
    - Ascites or encephalopathy attributable to hepatic failure
    - Platelet count < 50,000 mm^3 (secondary to splenomegaly due to portal hypertension)

- Patients with compensated cirrhosis without profound hepatic dysfunction and that are adequately medically controlled (as confirmed by medical consultation with the patient's physician) may have invasive dental treatment performed in the DMD-student clinics with careful attention to the following potential complications:
    - Impaired hemostasis
    - Unpredictable/impaired hepatic metabolism of certain drugs (e.g., analgesics)
    - Increased risk for, and spread of, oral infections
    - Delayed healing

CORTICOSTEROID USE and ADRENAL INSUFFICIENCY

Background:

- Primary Adrenal Insufficiency (Addison's disease)
  a. Primary adrenal insufficiency produces signs and symptoms that relate to a deficiency of aldosterone and cortisol.
  - The most common complaints are weakness, fatigue, abdominal pain (due to ileus), and hyperpigmentation of the skin and mucous membranes. Hypotension, anorexia, salt craving, myalgia, hypoglycemia, and weight loss are additional commonly associated features.
    - If a patient with Addison's disease is challenged by stress (e.g., illness, infection, surgery), acute adrenal insufficiency (or an adrenal crisis) may be precipitated.
      - This medical emergency evolves over a few hours and manifests as severe exacerbation of the patient's condition, including sunken eyes, profuse sweating, hypotension, weak pulse, cyanosis, nausea, vomiting, weakness, headache, dehydration, fever, dyspnea, myalgias, arthralgia, hyponatremia, and eosinophilia.
      - If not treated rapidly the patient may develop hypothermia, severe hypotension, hypoglycemia, confusion, and circulatory collapse (shock) that can result in death.

- Corticosteroids and Secondary Adrenal Insufficiency / Unresponsiveness:
  a. Pharmacologic (supraphysiologic) doses of exogenous corticosteroids produce hypothalamic-pituitary-adrenal (HPA) axis suppression via a negative feedback mechanism, i.e., they inhibit pituitary ACTH secretion, thereby reducing ACTH-mediated production of corticosteroids and androgens in the adrenal cortex.
  b. The development of adrenal unresponsiveness (and potential adrenal insufficiency), and the time required for recovery of adrenal function depend primarily on the duration of corticosteroid therapy and, to a lesser extent, on dosage, frequency (i.e., higher doses and divided daily doses [versus a single dose each day] are more suppressive), and timing (i.e., a morning dose is less suppressive) of administration, as well as on the potency and biologic (tissue) half-life of the specific corticosteroid (Table 1).
    - For example, some reports indicate that HPA unresponsiveness may occur with as little as approximately 5 to 7 days with daily administration of doses equivalent to 20 to 30 mg of prednisone/day, or take up to 30 days to occur with lower daily doses.
    - Once corticosteroid administration has ceased, the HPA axis regains its responsiveness, and normal ACTH and cortisol secretion eventually resumes. The time required to regain normal adrenal responsiveness is thought to range from days to months. However, studies from a large review (Glick, M: Glucocorticosteroid replacement therapy: a literature review and suggested replacement therapy. Oral Surg Oral Med Oral Pathol. 67, 1989, 614–620.) demonstrated a return to stress stimulation of HPA function within 14 days, despite the fact that supraphysiologic doses were given for a month or longer.
  c. When corticosteroids are employed on a long-term basis, they are often administered on alternate days to minimize suppression of the HPA axis. Giving a glucocorticoid every other day between 6 and 9 AM mimics the normal diurnal pattern of corticosteroid secretion. Such a regimen appears to lessen suppression of the adrenal cortex and permits increased endogenous corticosteroid production in response to stress. Unfortunately, alternate-day (q.o.d.) therapy may not adequately control symptoms in some cases, especially in patients with rheumatoid arthritis and ulcerative colitis.
  d. A tapered dosage schedule often is implemented for the discontinuation of corticosteroid usage, but this approach may not be necessary in many cases.

Table 1: Corticosteroids and Their Relative Potency

From: Katzung BG: Basic and Clinical Pharmacology, Appleton & Lange, 10th ed. (2006), p. 641.

Agent	Activity[1]			Equivalent Oral Dose (mg)	Forms Available
	Anti-Inflammatory	Topical	Salt-Retaining		
Short- to medium-acting glucocorticoids					
Hydrocortisone (cortisol)	1	1	1	20	Oral, injectable, topical
Cortisone	0.8	0	0.8	25	Oral
Prednisone	4	0	0.3	5	Oral
Prednisolone	5	4	0.3	5	Oral, injectable
Methylprednisolone	5	5	0	4	Oral, injectable
Meprednisone[2]	5		0	4	Oral, injectable
Intermediate-acting glucocorticoids					
Triamcinolone	5	5[3]	0	4	Oral, injectable, topical
Paramethasone[2]	10		0	2	Oral, injectable
Fluprednisolone[2]	15	7	0	1.5	Oral
Long-acting glucocorticoids					
Betamethasone	25–40	10	0	0.6	Oral, injectable, topical
Dexamethasone	30	10	0	0.75	Oral, injectable, topical
Mineralocorticoids					
Fludrocortisone	10	0	250	2	Oral
Desoxycorticosterone acetate[2]	0	0	20		Injectable, pellets

[1]Potency relative to hydrocortisone.
[2]Outside USA.
[3]Acetonide: Up to 100.

(Continued on the next page)

Table 2: Recommendations for Corticosteroid Supplementation During Dental Treatment*

Procedure	Corticosteroid Target Dose for Patients With Primary Adrenal Insufficiency†	Corticosteroid Target Dose for Patients With Secondary Adrenal Insufficiency‡
Routine (Non-surgical) Dentistry	• Daily therapeutic dose (taken within 2 hours of the procedure).	• Daily therapeutic dose (taken within 2 hours of the procedure).
Minor Surgical Stress (This includes a few simple extractions, soft tissue biopsy or surgery, performed under local anesthesia)	• 25 mg hydrocortisone (or equivalent), preoperatively on the day of surgery.	• Daily therapeutic dose (taken within 2 hours of the procedure).
Moderate Surgical Stress (This includes multiple extractions, quadrant periodontal surgery, extraction of bony impactions, osseous surgery, osteotomy, bone resections, implant placement, or oral cancer surgery using local anesthesia)	• 50 - 75 mg hydrocortisone (or equivalent) preoperatively on day of surgery and up to 1 day after. • Return to preoperative corticosteroid dose on postoperative day 2.	• Daily therapeutic dose (taken within 2 hours of the procedure).
Major Surgical Stress ! (This includes any surgical procedures involving general anaesthesia, surgical procedures lasting more than 1 hour, or procedures associated with significant blood loss)	• 100 - 150 mg of hydrocortisone (or equivalent) preoperatively on the day of surgery. • After preoperative dose, 50 mg hydrocortisone IV every 8 hours after the initial dose for the first 48 to 72 hours after surgery.	• Daily therapeutic dose (taken within 2 hours of the procedure).

* Guidelines based on patient's adrenal insufficiency status; however, requirements could increase if the patient's health is poor, if concurrent fear/anxiety or infection that is poorly managed is present, and if major surgery is being performed. Frequent monitoring of blood pressure during the first 8 hours postoperatively is recommended.

† This includes patients with primary adrenal failure due to Addison's disease, with congenital adrenal hyperplasia, or with secondary adrenal insufficiency due to hypopituitarism.

‡ Supplemental corticosteroid doses can be provided if signs or symptoms of adrenal insufficiency (e.g., hypotension, abdominal pain, fatigue) appear.

! Major surgery should be performed with the consideration for the need of steroid supplementation based on the overall health status of the patient. In addition, inadequate pain and anxiety control in the perioperative period increases the risk of adrenal crisis. Performance of major surgical procedures in a hospital environment is recommended to afford adequate patient monitoring during the postoperative phase.

(Continued on the next page)

Dental Implications of Patients with Adrenal Disease and/or Taking Corticosteroids:

Patients who are taking corticosteroids present several potential problems to the dentist including:

- Increased Risk of Infection and Delayed Wound Healing: Data largely based on animal models have suggested that patients taking corticosteroids may be at an increased risk of developing post-operative dental infections, as well as have delayed wound healing, since corticosteroids alter (decrease) the host's normal inflammatory response in a dose-related manner, and also reduce the activity of fibroblasts (i.e., the higher the dose of a corticosteroid the greater the risk for infection and delayed wound healing).

  Recent studies in humans have suggested that patient taking corticosteroids do not appear to be at a significantly higher risk of post-operative infection and delayed wound healing (including neuroregeneration) as compared to other patients, and that prophylactic antibiotics should not be administered, unless other indications are present. (Dan AE, et al. Corticosteroid administration in oral and orthognathic surgery: a systematic review of the literature and meta-analysis. J Oral Maxillofac Surg. 2010 Sep;68(9):2207-20; Ahmed AU, et al. Impact of Preoperative Immunosuppressive Agents on Postoperative Outcomes in Crohn's Disease. Dis Colon Rectum. 2014 May;57(5):663-74.)

  Nevertheless, the risk of post-operative infection can be reduced by employing atraumatic and aseptic surgical techniques. When concerns about post-operative infection remain (such as in patients taking very high dose corticosteroids that might mask [obscure] signs and symptoms inflammation due to a post-operative infection), patients can take bactericidal broad-spectrum antibiotics on the day of oral surgery and post-operatively (i.e., as long as needed until sufficient wound healing has occurred to minimize the risk of infection [typically 7 to 10 days]). Follow-up appointments should be arranged to assess for appropriate wound healing.

- Acute Adrenal Insufficiency (Adrenal Crisis) and the Need for Supplemental Corticosteroids: The two major factors influencing the recommendation for supplemental corticosteroids are the type of adrenal insufficiency and the level and type of stress.
  - Currently, only dental patients with primary adrenal insufficiency are recommended to receive corticosteroid supplementation, and this recommendation applies only when surgery is being performed and/or in the management of a dental or systemic infection (see: Table 2). Routine (non-surgical) dental procedures do not stimulate cortisol production at levels comparable with those that occur at the time of surgery and do not require supplementation, even in patients with controlled primary adrenal insufficiency.
  - Patients with secondary adrenal insufficiency and those who take daily or alternate-day corticosteroids have enough exogenous and endogenous cortisol to handle routine dental procedures and surgery, if their usual steroid dose (or parenteral dose equivalent) is taken the morning (or at least within 2 hours) of the procedure.

  Risk assessment for primary or secondary adrenal insufficiency should be determined by performing a thorough medical history and physical examination:
  - A past or present history of tuberculosis, histoplasmosis, or HIV infection increases the risk for primary adrenal disease (insufficiency) in that opportunistic infectious agents may attack the adrenal glands.
  - In addition, adrenal crisis is more likely in patients with malignancy or major traumatic injury, or in adrenally deficient patients who have a severe infection,

discontinue corticosteroid treatment, or simply do not take their corticosteroid before a stressful surgical procedure.

- Although biochemical testing (i.e., ACTH stimulation test) can be helpful in identifying those who may have primary adrenal insufficiency, it is generally not recommended for patients taking glucocorticoids. In the latter, test results do not necessarily reflect how patients will react clinically or whether an adverse reaction will occur.
  - In primary adrenal insufficiency, a low ACTH stimulation test result (levels below 18 µg/dL achieved after administration of 250 mg of cosyntropin) demonstrating inadequate adrenal cortical function indicates that supplemental steroids should be provided if surgical procedures are planned.

- Patients with hyperadrenalism or who take corticosteroids for prolonged periods have an increased likelihood of having hypertension, diabetes, osteoporosis, and peptic ulcer disease.
  - Because osteoporosis has a relationship with periodontal bone loss, implant placement and bone fracture, periodic measures of periodontal bone loss are indicated, and measures should be instituted that promote bone mineralization and avoid extensive neck manipulation if osteoporosis is severe.

Dental Evaluation Patients with Adrenal Disease and/or Taking Corticosteroids:

- In evaluating the dental treatment risk and appropriate management of patients with adrenal disease, the dentist must consider the type and degree of adrenal dysfunction, and the level of invasiveness and physiologic stress of the dental procedure planned.
  1. Obtain the diagnosis of adrenal or non-adrenal disease that requires systemic corticosteroid use.
  2. Determine the current dose (and duration) of the systemic corticosteroid being taken.
  3. Evaluate the patient's risk for acute adrenal insufficiency; evaluate and determine whether primary adrenal insufficiency or secondary adrenal insufficiency exists.
  4. Obtain a medical consultation if the condition is poorly controlled (e.g., acute infection), if clinical signs and symptoms point to an undiagnosed adrenal problem, or if the patient's adrenal diagnosis is uncertain.

Dental Management Patients with Adrenal Disease and/or Taking Corticosteroids:

- Administer supplemental corticosteroids (if indicated):
  - For patients with primary adrenal insufficiency, provide steroid supplementation for patients during surgical procedures or infection (Table 2).
  - For patients with secondary adrenal insufficiency who are undergoing surgical procedures verify they have taken their usual daily therapeutic dose of corticosteroids (Table 2).
- Schedule invasive dental treatment or surgery in the morning, when corticosteroid levels usually are highest.
- Blood pressure should be taken at baseline and monitored during dental appointments.
  - Monitoring of blood pressure throughout the procedure is critical for recognition of the development of an adrenal crisis. During surgery, blood pressure should be evaluated at 5-minute intervals and before the patient leaves the office. A systolic blood pressure

below 100 mm Hg or a diastolic pressure at or below 60 mm Hg represents hypotension. A diagnosis of hypotension dictates that the clinician must take corrective action. This would include proper patient positioning (i.e., head lower than feet), fluid replacement, administration of vasopressors, and evaluation for signs of adrenal dysfunction versus hypoglycemia.

- Blood glucose levels should be determined and invasive procedures should be performed during periods of good glucose control.
  - A fasting state can contribute to hypoglycemia which can mimic features of an adrenal crisis, (but does not require corticosteroids for resolution).
- Blood and fluid volume loss exacerbate hypotension, thereby increasing the risk for development of adrenal insufficiency-like symptoms. Thus, methods of reducing blood loss are important in this setting.
- Inhibitors of corticosteroid production (e.g., ketoconazole metyrapone, aminoglutethimide) should be discontinued at least 24 hours before surgery, with the consent of the patient's physician.
- Provide adequate pain control during the operative and postoperative phases of care.
  - Clinicians should ensure good post-operative pain control by administering long-acting local anesthetics (e.g., bupivacaine) at the end of the procedure, as well as post-operative regular analgesic dosing. (Inadequate pain control during the post-operative period increases the risk of adrenal crisis).
  - Post-operative analgesics should <u>not include aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs)</u> in patients taking corticosteroids due to the increased risk of gastrointestinal bleeding and perforation with concurrent use.
- Provide proper stress reduction, (since anxiety can increase cortisol demand).
  - Use of nitrous oxide-oxygen, intravenous or oral benzodiazepine conscious sedation is helpful, since plasma cortisol levels are not reduced by these agents.
  - General anesthesia <u>increases</u> corticosteroid demand for these patients. Barbiturates also should be used cautiously because these drugs enhance the metabolism of cortisol and reduce blood levels of cortisol
- Patients undergoing surgery should be closely monitored for blood and fluid loss (leading to hypovolemia), hypotension and hypoglycemia during the post-operative period.
  - Patients who take anticoagulants are at increased risk for post-surgical bleeding and hypotension. Also, the action of oral anticoagulants can be potentiated (resulting in increased risk of bleeding) by the intravenous administration of high-dose methylprednisolone.
  - If hypotension appears during monitoring, intravenous fluids are to be given and additional doses of corticosteroid considered if fluid replacement fails to rectify the blood pressure. Patients are returned to their usual corticosteroid dosage as soon as their vital signs are stabilized.
- Patients should be instructed about recognizing the early signs and symptoms of acute adrenal insufficiency during the post-operative period so that corrective measures can be taken as soon as possible should this occur.
  - Communicate with the patient at the end of the appointment and within 4 hours post-operatively to determine whether features of weak pulse, hypotension, dyspnea, myalgias, arthralgia, abdominal pain, fatigue, and fever are present. Signs and symptoms of acute adrenal crisis dictate transport to a hospital for emergency care.

DIABETES MELLITUS

Definition:

- Type 1 diabetes mellitus (DM) is a syndrome with disordered carbohydrate metabolism and inappropriate hyperglycemia due to an absolute deficiency of endogenous insulin secretion resulting in end-organ complications including accelerated atherosclerosis, coronary artery disease, neuropathy, nephropathy, and retinopathy.
  - Represents 5-10% of cases of DM
  - Peak incidence during puberty, but can occur at any age
- Type 2 diabetes mellitus is a syndrome with disordered carbohydrate metabolism and inappropriate hyperglycemia due to either a relative deficiency of endogenous insulin secretion and/or a combination of insulin resistance and inadequate insulin secretion to compensate, resulting in end-organ complications including accelerated atherosclerosis, neuropathy, nephropathy, and retinopathy.
  - Represents 90-95% of cases of DM
  - Risk factors increase over the age of 45 years and include genetic predisposition, obesity and sedentary lifestyle
  - High risk ethnic groups include Black Americans, Latinos and Native Americans

Dental Implications of a Patient with Diabetes:

- Oral Complications of DM include:
  - Increased risk of oral infections: candidiasis (including median rhomboid glossitis, denture stomatitis and angular cheilitis), and periapical abscesses.
  - Wound healing and post-operative infections in patients with DM: A growing body of surgical literature supports a relationship between perioperative glycemic control and postoperative complications, including infections.
    - Both low (< 80 mg/dL) and high (>150 mg/dL [HbA1c > 6.9%) mean 24-hour serum glucose concentrations were associated with significantly increased rates of perioperative infection.
    - Patients with serum glucose concentrations less than 80 mg/dL may represent “brittle” diabetic patients or those who received excessive doses of insulin in the operating room during surgery or soon thereafter, overshooting the target serum glucose concentrations.
    - No significant difference in infection rates were seen in patients with only mildly elevated serum glucose concentrations of 111 to 149 mg/dL.
  - Increased incidence and severity of gingival inflammation, periodontal abscesses and chronic periodontal disease
  - Increased incidence and severity of caries
  - Salivary gland dysfunction resulting in xerostomia and possible asymptomatic bilateral parotid swelling
  - Glossodynia and burning mouth syndrome
  - Dysgeusia
- Dentists treating patients with type 2 DM should review their panoramic radiographs carefully for evidence of carotid artery atheroma formation.
  - Patients with atheromatous lesions must be referred to their physicians for further evaluation and treatment, because the modification of atherogenic risk factors and the surgical removal of atheromas in certain patients have been shown to reduce the likelihood of stroke.

What to Include in a Medical Consultation:

A. The following patients would be considered at increased risk for the development of diabetes and should be advised to speak with their physician about an <u>evaluation for pre-diabetes</u> at their next physical examination (if there is no history of any previous evaluation of the patient for this condition):
   - Patients ::: 45 years of age, particularly those with a body mass index (BMI) :::25 kg/m^2.
   - Screening should be considered in younger individuals with a BMI ::: 25 kg/m^2 and who have one (or more) of the following risk factors:
     - a family history of diabetes
     - gestational diabetes or a baby weighing > 9 lbs.
     - not Caucasian
     - dyslipidemia
     - hypertension

B. The following patients should be referred to a physician for the <u>evaluation of possible undiagnosed diabetes:</u>
   - Patients with signs and symptoms suggestive of diabetes.
     Type 1diabetes:
     - Cardinal symptoms (common): polydipsia, polyuria, polyphagia, weight loss, loss of strength
     - Other symptoms: recurrence of bed wetting, repeated skin infections, marked irritability, headache, drowsiness, malaise, dry mouth

     Type 2 diabetes:
     - Usual symptoms: slight weight loss or gain; urination at night, vulvar pruritus, blurred vision, decreased vision, paresthesias, loss of sensation, impotence, postural hypotension

     Oral signs and symptoms of that may occur secondary to diabetes include: increased severity and rate of progression of periodontal disease, candidiasis, burning mouth syndrome, xerostomia, increased incidence and severity of caries, "ketone breath", and chronic oral ulcers.
   - Example of what to include in the medical consult:
     - "Mrs. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

       (Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

       Mrs. X presents with the signs and symptoms suggestive of possible undiagnosed diabetes mellitus including, [list symptoms here].

       1. Please evaluate and treat this patient with regard to my findings that suggest possible undiagnosed diabetes.
       2. Please indicate any medications that you prescribe, and any additional specific precautions or recommendations regarding the proposed dental treatment for Mrs. X.
       3. A copy of the lab test results and your office visit note for this patient are greatly appreciated.

       Thank you for assisting me in my care of our mutual patient."

C. For patients known to have diabetes mellitus, determine the following:

- Time since diagnosis (age of onset) of diabetes
- Type of diabetes
- Type of therapy required:
  - Control of diet
  - Oral hypoglycemic agents (types and dose)
  - Insulin therapy (types and regimen)
- Adequacy of control:
  - Date and results of most recent hemoglobin A_{lc} (HbA1c)
  - History and frequency of hypoglycemic episodes (and hospitalizations)
  - History and frequency of ketoacidosis
  - Method and frequency of self-monitoring of blood glucose
  - Frequency of physician visits for evaluation of diabetes status and control
- Presence of chronic complications of diabetes:
  - Cardiovascular; neurologic; renal (microalbuminuria, nephropathy); retinal; infectious; etc.
- Example of what to include in the medical consult:
  - "Mrs. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

    (Insert a summary of the patient's current medical history [including type 1 or type 2 diabetes mellitus], significant past medical problems, and list of all current medications here)

    1. Please provide a copy of the most recent lab test results for this patient (including glycosylated hemoglobin [HbA1c]).
    2. A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.
    3. Please provide your assessment of the degree of medical control of this patient's diabetes.
    4. Please indicate any systemic complications in this patient attributable to diabetes, any changes to the medications that they are taking, as well as any additional specific precautions or recommendations regarding the proposed dental treatment.

    Thank you for assisting me in my care of our mutual patient."

CONTINUED ON NEXT PAGE

ASA Risk Categories for the Patient with Diabetes Mellitus*

Clinical Criteria	Risk for Dental Treatment
Type 2 diabetes with: • Good metabolic control on stable medical regimen that does not require insulin • No history of ketoacidosis or frequent episodes of hypoglycemia • No chronic complications of diabetes • HbA1c not greater than 7.0% and FBG ≤ 200 mg/dL	ASA II Low risk for dental treatment
Type 1 or 2 diabetes with: • Adequate metabolic control on stable medical regimen that requires insulin • No recent symptoms of uncontrolled diabetes • No recent history of ketoacidosis or frequent episodes of hypoglycemia • Few, only minor, chronic complications of diabetes (that would not increase the risk for complications from dental treatment) • HbA1c = 7.1 to 9.0% and FBG ≤ 200 mg/dL	ASA III Moderate risk for dental treatment
Type 1 or 2 diabetes with: • Poor metabolic control of diabetes • Frequent symptoms of uncontrolled diabetes • Frequent occurrences of ketoacidosis and/or hypoglycemia • Multiple chronic complications of diabetes (e.g., chronic kidney disease, recent MI, recent CVA, symptomatic angina, CHF, inadequately controlled hypertension, neuropathy, retinopathy, etc.) • HbA1c > 9.0% or FBG > 200 mg/dL	ASA IV High risk for dental treatment

* The presence of other common co-morbid systemic conditions associated with diabetes mellitus (e.g., cardiovascular disease [hypertension, status post-myocardial infarction, angina pectoris, congestive heart failure], status post-cerebrovascular accident, chronic kidney disease/renal failure, etc.) must always be evaluated and taken into consideration when assessing the risk of the patient for dental treatment.

Dental Management of the Diabetic Patient

1. Controlled type 2 diabetic patient (that does not require insulin) (ASA II):
   a. All dental procedures can usually be performed
   b. No special precautions needed unless complications of diabetes are present:
      - Patient's with concurrent systemic complications of diabetes (e.g., cardiovascular disease, renal disease, etc.) will require specific dental treatment modifications and precautions to address these additional risk factors.
   c. Check patient's blood glucose prior to initiating dental treatment (see "2-d" below), or at minimum verify, that patient has had adequate caloric intake (eaten something) in conjunction with taking their hypoglycemic drugs prior to initiating dental treatment.
   d. Patients with type 2 diabetes are disproportionately at increased risk of experiencing stroke, because hyperglycemia and other risk factors associated with diabetes accelerate development of cervical carotid artery atheromas. Therefore, dentists treating patients

with type 2 diabetes must review their panoramic radiographs carefully for evidence of atheroma formation. Patients with atheromatous lesions must be referred to their physicians for further evaluation and treatment, because the modification of atherogenic risk factors and the surgical removal of atheromas in certain people have been shown to reduce the likelihood of stroke.

2. Controlled type 1 or type 2 diabetic patient (that requires insulin) (ASA III):
   a. Usually all dental procedures can be performed.
      - Note: Patients with concurrent systemic complications of diabetes (e.g., cardiovascular disease, renal disease, etc.) will require specific dental treatment modifications and precautions to address these extra risk factors, in addition to those listed below.
   b. Morning appointments are usually best
   c. Advise patient to take usual insulin dosage and normal meals on day of dental appointment; confirm when patient comes for appointment (Some sources recommend having the patient take half (50%) of their usual insulin dose prior to dental treatment, and then taking the remainder of their insulin dose after dental treatment, provided that normal oral intake of nutrition (food) will not be impaired as a result of dental treatment).
   d. Evaluate the patient's blood glucose chairside just prior to initiating dental treatment:
      - If patient's blood glucose is less than 70 to 90 mg/dL, have the patient eat (i.e, give carbohydrates) prior to dental treatment to help avoid a hypoglycemic reaction during dental treatment (this is especially important for long appointment [more than ~ 2 hours], and/or if the patient is not going to be able to resume their normal oral intake of nutrition for some time after dental treatment [e.g., due to residual effects of local anesthesia, post-operative pain, etc.]).
      - If patient's blood glucose is greater than 200 mg/dL then:
        - defer elective dental treatment (and possibly refer patient to physician for evaluation), OR
        - have patient take a hypoglycemic drug (e.g., insulin) if appropriate
   e. Advise patient to inform you or your staff as soon as they become aware of symptoms of insulin reaction (hypoglycemia) that occur during dental visit.
   f. Have approximately 15 grams of a fast-acting oral carbohydrate such as glucose tablets, cake icing, sugar, candy, soft drinks or juice available and give to patient if symptoms of an insulin reaction (hypoglycemia) occur.

   If extensive dental surgery is needed:
   a. Consult with physician concerning dietary needs during postoperative period when oral intake a food may be compromised due to post-surgical pain or other orally-related factors.
   b. Consider perioperative prophylactic antibiotics to help prevent postoperative infection for patients marginally controlled and/or "brittle" diabetes (i.e., very difficult to control, HbA1c > 9%] or prone to frequents swings between hyperglycemia and hypoglycemia) and/or those who have chronic states of oral disease / infection.

VIRAL HEPATITIS (B & C)

Definition:

- Viral hepatitis is classified according to causative viral agent. Currently there are 5 different agents associated with a diagnosis of viral hepatitis. These agents are: Hepatitis A virus (HAV), Hepatitis B virus, (HBV), Hepatitis C virus (HCV), Hepatitis D virus (HDV), Hepatitis E virus (HEV).

- Hepatitis B:
  - Hepatitis B virus (HBV) is transmitted both parentally and via sexual contact. Viral concentrations of HBV are high in blood and serum and moderate in semen and saliva.
  - Those at increased risk are recipients of blood transfusion/products, undergoing hemodialysis, share needles, have sexual contact with an infected person or those who have occupational exposure (such as healthcare workers). HBV can also be transmitted perinatally from infected mother to child.
  - Chronic hepatitis B develops in 1% to 2% of immunocompetent adult patients with acute hepatitis B, but in as many as 90% of infected neonates and infants and a substantial proportion of immunocompromised adults with acute hepatitis B.
  - Such patients are at increased risk for the development of cirrhosis (approximately 40%) and hepatocellular carcinoma (approximately 1% to 3%).
  - Diagnosis: Laboratory diagnostic criteria for HBV include IgM antibody to hepatitis B core antigen (anti-HBc) or hepatitis B surface antigen (HBsAg). Additional tests which may show abnormally elevated results include AST, ALT and bilirubin. In those who recover from the acute episode HBsAg will no longer be detected in the serum. Immunity is indicated by presence of IgG anti-HBc, and/or anti-HBsAg. Recovery from HBV is indicated by presence of antibodies to hepatitis B surface antigen (anti-HBsAg).
  - Treatment:
    - In most cases of acute HBV infection treatment is mainly supportive with > 90% of adults spontaneously clearing the infection.
    - Treatment is recommended in patients with HBeAg-positive or HBeAg-negative chronic hepatitis and in patients with compensated cirrhosis and HBV DNA > 2000 IU/mL and those with decompensated cirrhosis and detectable HBV DNA by PCR regardless of the serum ALT level.
    - Medications for hepatitis B have been improving continually and are usually effective at reducing viral loads markedly or even to undetectable levels. Currently, seven therapeutic agents are approved by the FDA for the treatment of chronic hepatitis B, including two formulations of interferon (interferon-alpha and pegylated interferon-alpha) and five nucleoside or nucleotide analogs (lamivudine, telbivudine, abacavir, entecavir, and tenofovir). Among the approved analogs, both entecavir and tenofovir have potent antiviral activity as well as very low rates of drug resistance. Treatment with these agents reduces HBV DNA levels to undetectable or nearly undetectable levels in most treated persons.
    - In chronic carriers there is a risk for development of hepatocellular carcinoma and ultrasound evaluations are recommended every 6 months.

- Hepatitis C:
  - Hepatitis C virus (HCV) is mainly transmitted via shared needles, blood transfusion/products (before screening for this virus in the blood supply prior to June 1992, when sensitive tests for anti-HCV were introduced for blood screening), perinatally and via hemodialysis. HCV can also be transmitted sexually and through saliva although both are ineffective means of disease transmission. Additionally, healthcare workers are at risk for contraction of HCV.
  - Interestingly most infections (up to 70%) are asymptomatic.
  - Progression to chronic infection is common, 50% to 84%.
  - 74% to 86% have persistent viremia; spontaneous clearance of viremia in chronic infection is rare.
  - 15% to 20% of those with chronic HCV will develop cirrhosis over a period of 20 to 30 years; in most others chronic infection leads to hepatitis and varying degrees of fibrosis.
  - 0.4% to 2.5% of patients with chronic infection develop hepatocellular carcinoma.
  - 25% of patients with chronic infection continue to have an asymptomatic course with normal liver function tests and benign histology.
  - Hepatitis C is the main indication for liver transplantation in the U.S. Recurrent infection occurs in almost all patients with progressive fibrosis and cirrhosis; up to 20% progress to cirrhosis within 5 years post-transplant.
  - Diagnosis: A diagnostic criterion for HCV is presence of HCV antibodies in addition to one or more of the following: elevation of ALT for 6 months or more, positive anti-HCV for 6 months or longer, liver biopsy consistent with chronic hepatitis. Typically antibodies are detected using Enzyme Immunoassay (EIA) whose results are confirmed with Recombinant Immunoblot Assay (RIBA).

    HCV genotyping can distinguish among genotypes 1, 2, 3, 4, 5, and 6, which is helpful in selecting drug therapy since HCV treatment responses vary with the genotype. The highest sustained virologic response (SVR) rates are observed for genotype 2 and the lowest rates observed for genotypes 1 and 4. Genotypes 1, 2, 3, and 4 predominate in the US and Europe (genotype 1 is especially common in North America [60% to 75% of Hep C infections in the US]).
  - Treatment:
    - The primary goal of treatment for chronic HCV is a sustained virologic response (SVR) (SVR is regarded as a cure) and thus prevention of disease progression. SVR (defined as HCV RNA <15 IU/mL at least 12 to 24 weeks after completion of antiviral therapy) is associated with reduction of both all-cause and liver-related mortality from HCV. A combination of peginterferon and ribavirin, given for up to 48 weeks, was previously the mainstay of treatment for all genotypes of HCV, but has been superseded by direct-acting antiviral drugs (DAAs).
    - The introduction of (all orally-administered) DAAs has drastically changed HCV treatment options and improved SVR rates to greater than 95%. Recommendations for the treatment of HCV in adults are changing constantly as new therapies are approved for use. Selection of a specific HCV drug treatment regimen (and duration) is dependent on a number of factors including the patient's HCV genotype, the presence or absence of cirrhosis, and history of previous attempts at treatment of HCV.

- Examples of recommenced DAA treatment of HCV in treatment-naive genotype 1a patients without cirrhosis include:
  - Daily elbasvir (50 mg) + grazoprevir (100 mg) [Zepatier] for 12 weeks and in those who do not have baseline NS5A RAVs (amino acid substitutions at 28, 30, 31, or 93 that confer resistance to elbasvir).
  - Daily ledipasvir (90 mg) + sofosbuvir (400 mg) [Harvoni] for 12 weeks.
  - Daily ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 500 mg [Viekira Pak] for 12 weeks.
  - Daily simeprevir (150 mg) + sofosbuvir (400 mg) for 12 weeks.
  - Daily sofosbuvir (400 mg) + elpatasvir (100 mg) [Epclusa] for 12 weeks.
  - Daily daclatasvir (60 mg) [Daklinza] + sofosbuvir (400 mg) [Solvaldi] for 12 weeks.
- Notable Adverse Effects:
  - Peginterferon alfa-2a can cause anemia (2 -14%), lymphocytopenia (3 - 14%), neutropenia (21 - 40%), thrombocytopenia (5 - 8%), flu-like symptoms, alopecia, nausea, vomiting, diarrhea, loss of appetite, abdominal pain, headache, arthralgia, myalgia, fatigue, dizziness, pruritus, fever, psychiatric disturbances (e.g., major depression in 20% - 40% of patients), and other side effects.
  - Ribavirin can cause neutropenia (8 - 40%), hemolytic anemia (10 - 13%), nausea, vomiting, diarrhea, loss of appetite, headache, asthenia (weakness, disability), dizziness, pruritus, and other side effects.
  - DAAs most common adverse effects are usually limited to fatigue, headache and nausea in ~ 10 - 15% of patients.

Dental Implications of a Patient with Hepatitis B and/or C:

- Since HBV, HCV (and human immunodeficiency virus [HIV]) are transmitted in a similar manner, many patients have coinfection. HBV, HCV, (and/or HIV coinfection) significantly complicates the medical management of the diseases and enhances the probability of the patient's experiencing hepatic dysfunction.
- HBV and HCV are transmissible via infected blood or saliva. Clinicians should comply with the current CDC, OSAP (Organization for Safety and Asepsis Procedures) and ADA infection control recommendations with every patient, regardless of the presence or absence of bloodborne disease.
- The presence of opportunistic infections such as oral candidiasis in patients with hepatitis may signal immunosuppression secondary to progression of the disease.

What to Include in a Medical Consultation:

- Patients with non-specific histories of "hepatitis", or histories or clinical findings of jaundice or scleral icterus should have laboratory testing to determine the presence of active viral hepatitis or chronic carrier infectivity:
  - A positive HBV surface antigen (HbsAg) test is indicative of infectious acute or chronic hepatitis B.
  - A positive anti-HVC (ELISA, RIBA) positive, and positive qualitative HCV-RNA (PCR) tests are indicative of infectious acute or chronic hepatitis C.
    - A possible indicator of current HCV activity or the patient's response to anti-viral therapy is the quantitative HCV-RNA (PCR) test, sometimes referred to as hepatitis C titer or "viral load".

NOTE: For patients who are already diagnosed with chronic hepatitis B and/or chronic hepatitis C the above tests are not necessary and do not need to be requested from the patient's physician.

- Example 1 (history of unspecified viral hepatitis):

  "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

  (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

  Mr. X reports a history of unspecified viral "hepatitis" on (date) (include any details the patient can provide, e.g., associated with a blood transfusion, etc.).

  1. Please confirm/rule-out the presence of HCV infection and/or HBsAg-positive status in this patient.
  2. Please include a copy of the results of the most recent viral hepatitis serology screening panel for this patient for our records.

  Thank you for your assistance in the care of our mutual patient."

- Patients with active or chronic viral hepatitis need to be evaluated to determine the degree of hepatic dysfunction:
  - Request the results of most recent lab studies including:
    - hepatic function panel, or a comprehensive metabolic panel (CMP)
    - complete blood count (CBC) with differential (including platelet count)
  - Note: Patients with severe hepatic dysfunction or cirrhosis (as indicated by an abnormal hepatic function panel) may also have clinically significant impaired hemostasis (indicated primarily by an elevated PT/INR due to abnormal synthesis of prothrombin-dependent clotting factors, and/or thrombocytopenia secondary to splenomegaly).
  - Patients with significant hepatic dysfunction may require the dose reduction (or contraindication) of hepatotoxic drugs and/or drugs metabolized by the liver.

- Patients currently being treated for chronic HCV infection with peginterferon alfa-2a (Pegasys) and ribavirin (Copegus) should have laboratory testing prior to invasive dental treatment including:
  - Request the results of the most recent:
    - CBC with differential and platelet count (to rule out anemia, neutropenia, lymphopenia, and/or thrombocytopenia that may occur as a result of treatment with these drugs).
    - hepatic function panel, or a comprehensive metabolic panel (CMP) (due to potential hepatic damage/dysfunction secondary to HCV infection and/or hepatotoxicity of these drugs).

- Example 2 (history of untreated hepatitis C, or currently receiving antiviral drug treatment for hepatitis C):

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

1. Please provide a summary of the current status, severity/stage, and medical management of this patient's HCV infection.
   Please include copies of the results of most recent lab tests (i.e., quantitative HCV-RNA [viral load], hepatic function panel or CMP, and CBC with differential [including platelets], etc.).
   A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.
2. Please indicate any specific precautions or recommendations you may have as it relates to this patient's planned dental treatment.

Thank you for your assistance in the care of our mutual patient."

- Patients with a history of completed treatment for chronic HCV infection with antiviral drugs should have laboratory testing prior to invasive dental treatment to confirm a sustained viral response (SVR) to treatment of HCV infection rule-out the presence of hepatic dysfunction secondary to HCV infection by requesting the results of the most recent:
  - quantitative HCV-RNA (PCR) test.
  - hepatic function panel, or a comprehensive metabolic panel (CMP)

- Example 3 (history of completed treatment for hepatitis C):

"Mr. X is dental patient of the ULSD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

Mr. X states (he/she) completed antiviral drug treatment for hepatitis C on (date). Please confirm Mr. X has a sustained viral response (SVR) to antiviral drug treatment for hepatitis C, as well as comment on the presence of any remaining secondary hepatic damage/dysfunction.

Please include copies of the results of most recent lab tests including quantitative HCV-RNA [viral load], and well as hepatic function panel or CMP.

A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.

Thank you for your assistance in the care of our mutual patient."

Dental Management of a Patient with Hepatitis B and/or C:

Diagnosis	Dental Treatment Recommendations
Active hepatitis B and/or hepatitis C are not candidates for elective dental treatment.	• Elective dental treatment should be deferred until the resolution of active disease. • Emergency dental treatment should be performed in a hospital dental clinic (ACB).
Chronic hepatitis B and/or hepatitis C with significant hepatic dysfunction *	• Elective and emergency dental treatment should be performed in a hospital dental clinic (ACB).
Chronic hepatitis B and/or hepatitis C without significant hepatic dysfunction	• May receive elective dental treatment without any special precautions. - Clinicians should comply with the current CDC, OSAP, and ADA infection control recommendations with every patient, regardless of the presence or absence of bloodborne disease). • Patients with clinically significant anemia, neutropenia, lymphopenia, and/or thrombocytopenia secondary to treatment with antiviral drugs including peginterferon alfa-2a (Pegasys), or ribavirin (Copegus), may require dental treatment modification(s) depending of the specific type and severity of the hematologic abnormality (e.g, pre- and post-procedural antibiotic prophylaxis, measures to address impaired hemostasis, postponement of invasive dental treatment, etc.).

* The presence of one or more of the following abnormalities when attributable to liver disease would be indicative of significant hepatic dysfunction:
- INR greater than 1.7 attributable to hepatic failure
- Serum aminotransferase (AST, ALT) levels elevated greater than 4 times normal
- Serum bilirubin elevated above 2.0 mg/dL
- Serum albumin less than 3.5 g/dL
- Signs of ascites or encephalopathy attributable to hepatic failure
- Platelet count < 50,000 mm^3 (secondary to splenomegaly due to portal hypertension)

HIV/AIDS

Background:

- The current policy of UFCD is to follow 'standard precautions' of the CDC for handling body fluids as if every patient has a bloodborne pathogen. This includes personal protective equipment as well as sterilization of all instruments and the use of disposables when appropriate.
- Patients who report HIV positive status will likely be part of the U of L 550 (previously WINGS) medical clinic and Ryan White CARE Act dental benefits program and will have the appropriate medical information and current lab tests available for review (see below). Dental and dental hygiene students will only be assigned patients who have demonstrated a stable medical condition; other patient will be assigned to the GPR or community-based dental clinics.
- Occasionally, a new patient who is HIV-positive will desire to be treated at the UFCD and not have copies of their required medical information and current lab tests at hand. An application for the dental benefits program will need to be completed, as well as a medical consultation, before comprehensive dental treatment can be initiated.

Overview of HIV Monitoring During Antiretroviral Therapy (ART):

(Reference: Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2018 Recommendations of the International Antiviral Society–USA Panel. JAMA. 2018;320(4):379-396.)

- Antiretroviral therapy (ART) is the cornerstone of prevention and management of HIV infection.
- ART should be initiated as soon as possible after diagnosis of HIV is made (i.e., preferably immediately after diagnosis, unless patient is not ready to commit to starting therapy).
  - Samples for HIV-1 RNA level; CD4 cell count; HIV genotype for nucleoside reverse transcriptase inhibitor (NRTI), nonnucleoside reverse transcriptase inhibitor (NNRTI), and protease inhibitor (PI); laboratory tests to exclude active viral hepatitis; and chemistries should be drawn before beginning ART, but treatment with ART may be started before test results are available.
- Within 6 weeks of starting ART, adherence and tolerability of therapy should be assessed, along with the patient's HIV RNA level. HIV RNA suppression may take up to 24 weeks, or faster with integrase strand transfer inhibitor (InSTI)-based ART regimens.
- Once the HIV RNA level is below 50 copies/mL, monitoring is recommended every 3 months until suppressed for at least 1 year. After that year, HIV RNA monitoring can be performed every 6 months if the patient maintains consistent medication adherence.
  - Of note, when monitoring intervals are extended and ART therapy fails, HIV resistance to ART has more time to emerge.
- Once viral suppression occurs with ART, CD4 cell counts usually increase. CD4 cell counts are recommended every 6 months until they are above 250/mm^3 for at least 1 year with concomitant viral suppression. <u>Afterward, CD4 cell counts need not be measured unless ART (virologic) failure occurs</u> (defined below) or the patient has an immunosuppressive condition or treatment, such as steroid treatments or chemotherapy.
  - HIV RNA testing is used to detect if ART is failing. When HIV RNA level is above 50 copies/mL, repeating measurement of HIV RNA level within 4 weeks and reassessing for medication adherence and tolerability is recommended.
  - Virologic failure is defined as HIV RNA level above 200 copies/mL on at least 2 consecutive measurements.

What to Include in a Medical Consultation:

Example:

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

Due to (his/her) HIV-positive status, please provide copies of the following:

1. Most recent lab tests including: CBC with differential, CD4+ count, HIV RNA (viral load).
2. Current medication list.
3. Current TB status and any pertinent test results (e.g., PPD, CXR, QuantiFERON-TB).
4. Most recent progress note or summary of last office visit for this patient.

Thank you for your assistance in my care of our mutual patient."

Evaluation of UFCD Dental Patients with HIV:

- The completed (returned) medical consult results must be reviewed with one of the Oral Medicine Faculty before invasive treatment begins and/or continues. The DMD or DH student is responsible for checking with the patient at each visit regarding any new lab tests, medications, or other disease related issues. While most patients with HIV are now being tested for HIV RNA (viral load) every 6 or 12 months, this test may be indicated 'early' due to oral findings suggesting virologic failure (i.e., their HIV is not well-controlled and is progressing), (and the patient may be deferred from elective care until their HIV/medical status becomes stable).
  - Oral manifestations of progressing HIV disease / virologic failure include candidiasis, angular cheilitis, linear gingival erythema, ANUG, ANUP, Kaposi's sarcoma, enlarged parotid glands and xerostomia, recurrent aphthous or herpetic ulcers, papilloma, oral hairy leukoplakia.

*** All oral surgery for HIV-positive patients will be performed at the ACB (unless approved otherwise by oral surgery faculty).

Indicators of HIV Disease Status:

- The CD4 cell count should be above 200/mm^3 without significant recent decline. If possible, reviewing a series of the patient's previous CD4 cell count results is helpful to characterize the patient's disease progression over time.
- HIV-1 RNA or viral load for patients receiving ART should be (optimally) 'non-detectable', or (at least) below 50 copies/mL.
- Complete blood count (CBC): Prophylactic antibiotics need to be considered when the absolute neutrophil count is below 500/mm^3. The test should have been within 30 days, and should be obtained prior to oral or periodontal surgery to determine the need for prophylactic antibiotics.
- Platelet (PLT) count should be obtained prior to extensive oral or periodontal surgery and/or any time bleeding control may be difficult to achieve. A platelet count of at least 50,000/mm^3 is necessary for elective surgery. This count changes quickly and the test should be no longer that

30 days old. If obvious bruising and poor hemostasis are noted, defer treatment until the test can be repeated.

- Many HIV patients are also infected with viral hepatitis and/or have HIV-related liver failure (see the "Hepatitis" section of this document).
  - An INR greater than 1.7 (usually associated with elevated ALT and AST levels) that is not attributable to any other factors (e.g., warfarin, vitamin K deficiency, hereditary deficiency in factors VII, X, V and II, etc.) is highly suggestive of significant hepatic function failure, and the patient should not receive invasive dental treatment in the DMD-student clinics.
- Oral manifestations of progressing HIV disease include candidiasis, angular cheilitis, linear gingival erythema, ANUG, ANUP, Kaposi's sarcoma, enlarged parotid glands and xerostomia, recurrent aphthous or herpetic ulcers, papilloma, oral hairy leukoplakia.

Dental Management Considerations:

- Patients with HIV can receive almost any dental care needed and desired after the possibility of significant immunosuppression, neutropenia, or thrombocytopenia has been ruled out.
- In planning invasive dental procedures, attention must be paid to the prevention of infection and excessive bleeding in patients with severe immunosuppression, neutropenia, and thrombocytopenia.
  - This may involve the use of prophylactic antibiotics in patients with CD4+ cell counts below 200/mm^3 or severe neutropenia (neutrophil count < 500/mm^3). White blood cell and differential counts, as well as a platelet count, should be ordered before any surgical procedure is undertaken.
  - Patients with severe thrombocytopenia (platelet count < 50,000/mm^3) may require special measures (e.g., platelet replacement) before surgical procedures (including scaling and curettage) are performed.
- Care in prescribing any medications needed for dental treatment must be exercised due to the risk for potentially serious adverse interactions or effects with drugs the patient may be taking for the management of HIV/AIDS, or its complications (e.g., Pneumocystis pneumonia, candidiasis, herpes simplex virus or cytomegalovirus infection, or other opportunistic disease), including toxic drug reactions, hepatotoxicity, immunosuppression, anemia, and other potential problems. Most often, consultation with the patient's physician is beneficial in this context.

HYPERTENSION

Definition:

- Hypertension (HTN) is defined as a persistent elevation in blood pressure that is considered to be higher than normal. More specifically, in 2003, the Seventh Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) defined hypertension as a systolic blood pressure greater than or equal to 140 mm Hg or a diastolic blood pressure greater than or equal to 90 mm Hg as recorded during two or more readings on two or more occasions (office visits) (Table 1)

Table 1: Classification and Follow-up of Blood Pressure Measurement for Adults Aged 18 Years or Older*

Adapted from: The Seventh Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (The JNC 7 Report), JAMA, 2003(289);2560-72.

Classification †	Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)	Follow-up Recommended for Dental Patient
Normal	< 120	< 80	Recheck at recall (within 1 year)
Pre-hypertension	120 - 139	80 - 89	Recheck within 1 month; if still elevated have patient evaluated by physician within 1 month
Stage 1 Hypertension	140 - 159	90 - 99	Recheck within 2 weeks; if still elevated have patient evaluated by physician within 2 weeks
Stage 2 Hypertension	;::: 160	;::: 100	Have patient evaluated by physician immediately (or within 1 week depending on severity and clinical situation)

* Not taking antihypertensive drugs and not acutely ill.

† When systolic and diastolic pressures fall into different categories, the higher category should be selected to classify the individuals blood pressure. Isolated systolic hypertension is defined as a systolic blood pressure of 140 mm Hg or more and a diastolic blood pressure of less than 90 mm Hg.

‡ Based on the average of two or more seated blood pressure readings taken on each of two or more office visits.

When Should Vital Signs (Including Blood Pressure) be Taken on a Dental Patient?

- Blood pressure, pulse rate, respiratory rate, and temperature must be taken at every initial patient visit, annual recall exam, and emergency patient visit.
- Blood pressure and pulse rate must be taken for every patient before local anesthetic is administered.
- For patients currently diagnosed with hypertension, blood pressure and pulse rate must be taken at each clinic visit.

Anxiety, Pain and Blood Pressure:

- When measuring a patient's blood pressure, the clinician needs to be aware that many factors that can effect blood pressure, including:
  - Stress and anxiety.
  - Pain.
  - Patient positioning (e.g., standing, sitting, or supine): Whenever possible, the patient should be seated in a chair with their feet on the floor and arm supported at heart level. The patient's back and arm need to be supported fully to enhance muscle relaxation and therefore improve blood pressure measurement accuracy. If the patient's legs are crossed at the knee, the blood pressure measurement may be falsely elevated.
  - The time of day (i.e., blood pressure is usually at its lowest during the morning, rising throughout the day until falling again in the evening).
  - Recent physical activity before measurement.
  - Increased or decreased blood volume, such as that caused by hemorrhage, or dehydration.

Dental Implications of a Patient with Hypertension:

- Patients with hypertension are generally considered to be at an increasing for risk of adverse events during dental treatment approximately in proportion to the severity of hypertension and the presence of end-organ complications.
- Orthostatic hypotension may be a problem for patients taking antihypertensive medications.
- The potential exists for adverse interactions between sympathomimetic vasoconstrictors used in some dental local anesthetic preparations and some antihypertensive agents including non-cardioselective beta-adrenergic blockers, alpha-adrenergic blockers, adrenergic neuronal blockers, and methyldopa.
- Some patients may present with xerostomia of varying severity, secondary to, or exacerbated by, their antihypertensive medications, particularly diuretics.
- Patients taking ACE inhibitors or beta-adrenergic blockers may complain of taste disturbances, present with lichenoid reactions of the oral mucosa; ACE inhibitors are also reported to cause a drug-induced cough.
- Diuretics (especially thiazide-type) and direct-acting vasodilators have been implicated in causing lichenoid or lupus-like oral mucosal changes.
- Patients taking calcium channel blockers may present with drug-induced gingival hyperplasia.

Medical Management and Treatment of Hypertension:

- The panel members appointed to the Eighth (2014) Joint National Committee for the Management of High Blood Pressure in Adults (JNC 8) used rigorous evidence-based

methods developing recommendations for the treatment of hypertension based on a systematic review of the literature. The JNC 8 recommendations for starting (initiating) the use of antihypertensive drugs in adults are summarized in Box 1.

Box 1: Recommendations for the Initiation of Pharmacologic Treatment to Lower Blood Pressure

From: 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults
Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8) JAMA. 2014 Feb 5;311(5):507-20.

- In the general population < 60 years old, pharmacologic treatment to lower blood pressure should be initiated in patients with:
  - a systolic blood pressure ;::: 140 mm Hg or a diastolic blood pressure ;::: 90 mm Hg
- In the general population ;::: 60 years old, pharmacologic treatment to lower blood pressure should be initiated in patients with:
  - a systolic blood pressure ;::: 150 mm Hg, or a diastolic blood pressure ;::: 90mm Hg
- In patients ;::: 18 years old with chronic kidney disease or diabetes, pharmacologic treatment to lower blood pressure should be initiated in patients with:
  - a systolic blood pressure ;::: 140 mm Hg, or a diastolic blood pressure ;::: 90mm Hg

Definition of Adequately Controlled Hypertension:

- The objective of the treatment of hypertension should be to lower the patient's blood pressure to"goal" levels with minimal adverse effects for the patient (Table 2). It may not be possible in all cases to reduce a patient's blood pressure to what would be considered an optimum level, instead a compromise may be necessary in that the patient's blood pressure will be reduced to a level that is as low as can be achieved using an acceptably tolerated therapeutic regimen.

Table 2: Goal Blood Pressure for Patients Diagnosed with Hypertension

From: 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults
Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8) JAMA. 2014 Feb 5;311(5):507-20.

Indication	Systolic Blood Pressure	Diastolic Blood Pressure
Age < 60 years	< 140 mm Hg	< 90 mm Hg
Age ;::: 60 years	< 150 mm Hg	< 90 mm Hg
All ages with diabetes or chronic kidney disease	< 140 mm Hg	< 90 mm Hg

What to Include in a Medical Consultation:

- Before sending a medical consultation that involves an evaluation for possible hypertension, or the degree of control of hypertension, in a patient, it is imperative that

you:

- (If applicable) Confirm the patient is compliant with their hypertension treatment regimen. (Are they taking all their drugs correctly as prescribed?)
- Assess the patient for severe pain and/or situational anxiety related to dental treatment that may be contributory to the patient's elevated blood pressure, or the primary causative factor (as is frequently the case in isolated office hypertension, also called "white-coat" hypertension).
    - Situational anxiety related to dental treatment should be assessed by utilizing Corah's Dental Anxiety Scale/Survey (CDAS), (a copy of the CDAS is included the end of this section that may be printed and given to the patient).
        - Note: CDAS is designed to be completed by the patient as a written survey (and not to be conducted orally, as this may result in decreased validity of the assessment).

The results of the assessment, and presence or absence for situational anxiety related to dental treatment using CDAS should be included in the patient's axiUm treatment record, and also should be included in the medical consult to the patient's physician when requesting an evaluation for possible hypertension.

- Its is also important to remember that comprehensive pain control requires an ability to manage fear and anxiety. Therefore, patients with significant situational anxiety related to dental treatment, as indicated by a CDAS score of 13 or higher, will need to have this problem addressed as part of their dental treatment plan, and will often require the use of pharmacologic means of anxiety control (e.g., nitrous oxide - oxygen sedation).

Information you should provide to the patient's physician should include:

- specifying the most invasive dental procedure(s) you anticipate performing on the patient (e.g., extractions, osseointegrated implants, periodontal surgery, etc.);
- indicating the type of local anesthesia (and sedation if applicable) you anticipate using (e.g., 2% lidocaine containing 1:100,000 epinephrine), oral conscious (enteral) sedation [e.g., triazolam], I.V. sedation [e.g., midazolam and fentanyl]);
- a report of the patient's in-office blood pressure reading(s), and the presence of any factors that could effect the patient's blood pressure (e.g., pain, significant anxiety related to dental treatment [assessed using the CDAS].

Situation 1: The patient has not been previously diagnosed with hypertension and presents with an abnormally elevated blood pressure.

- "Mr. X is dental patient of the ULSD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine). (Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)
  Mr. X presents today with blood pressure of xxx/xx mm Hg, RAS x 2, taken at the beginning and end of a x hour appointment using a (indicate BP cuff size [e.g., regular adult, large adult]) BP cuff. (Also include the date(s) and value(s) of any other blood pressure readings for the patient that may be in the chart from previous, recent dental appointments). Mr X gives no previous history of a diagnosis of hypertension. Mr. X (is/is

not) experiencing acute dental pain at this time, and (does/does not) have significant anxiety related to dental treatment (as indicated by a CDAS score of x/20).
Please evaluate this patient for possible hypertension. A COPY OF THE OFFICE NOTES of your evaluation of this patient, and treatment plan (if indicated) for Mr. X would be greatly appreciated.
Thank you for your assistance in my care of our mutual patient."

Situation 2: The patient has been previously diagnosed, and is currently being treated, for hypertension and presents with blood pressure that is higher than typical goal blood pressure (i.e., equal or higher than 140/90 mm Hg, [or 130/80 mm Hg for patients with diabetes or chronic kidney disease]).

- "Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).
(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)
Mr. X presents today with blood pressure of xxx/xx mm Hg, RAS x 2, taken at the beginning and end of a x hour appointment using a (indicate BP cuff size [e.g., regular adult, large adult]) BP cuff. (Also include the date(s) and value(s) of any other blood pressure readings for the patient that may be in the chart from previous, recent dental appointments). Mr. X (is/is not) experiencing acute dental pain at this time, and (does/does not) have significant anxiety related to dental treatment (as indicated by a CDAS score of x/20).
Please evaluate Mr. X in regards to the degree of control, and effectiveness, of his/her current treatment of hypertension. A COPY OF THE OFFICE NOTES of your evaluation of this patient would be greatly appreciated. Also, please indicate Mr. X's goal blood pressure.
Thank you for your assistance in my care of our mutual patient."

Table 3: ASA Dental Risk Classification for Hypertension in Adult Patients

Classification	ASA Risk Category
• Well-controlled hypertension, defined as: - a systolic blood pressure < 140 mm Hg, (or < 150 mm Hg if ;::: 60 years old or has diabetes or chronic kidney disease) and a diastolic blood pressure < 90 mm Hg.	II
• Hypertension under medical management but not well-controlled, defined as: - a systolic blood pressure ;::: 150 mm Hg (or ;::: 140 mm Hg if < 60 years old or has diabetes or chronic kidney disease) , or a diastolic blood pressure ;::: 90 mm Hg.	III
• Untreated or inadequately treated hypertension, defined as: - a systolic blood pressure > 180 mm Hg or a diastolic blood pressure > 110 mm Hg.	IV

Table 4: Dental Treatment Guidelines for Adult Patients Based on Presenting Blood Pressure

Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)	Dental Treatment Recommendations [1]
♦ 139	♦ 89	• May proceed with all dental treatment. • For patients under pharmacologic management for hypertension: limit initial dose of local anesthetic containing a vasoconstrictor.[2]
140 - 159	90 - 99	• Elective dental treatment should be limited to selective, minimally invasive dental procedures.[4] • Emergency dental procedures approved. • Limit initial dose of local anesthetic containing a vasoconstrictor.[2] • Consider if referral of patient to a physician for evaluation and/or management of hypertension is indicated.
160 - 179	100 - 109	• Elective dental treatment should be deferred pending better control of hypertension. • Emergency dental procedures approved with monitoring of blood pressure every 5 - 10 minutes during treatment. • Limit initial dose and reduce total dose of local anesthetic containing a vasoconstrictor and avoid any additional vasoconstrictor exposure.[3] • Refer patient to a physician for evaluation / management of hypertension.
;::: 180	;::: 110	• All elective dental treatment is contraindicated. • Emergency, palliative dental treatment only, preferably in a hospital dental clinic setting with periodic (automated) monitoring of pulse and blood pressure during treatment. • Whenever possible, contact patient's physician to consult regarding proposed emergency dental treatment and to arrange follow-up for evaluation of patient's hypertension. • Using local anesthetic containing a vasoconstrictor is usually considered to be contraindicated.

1. When systolic and diastolic pressures fall into different categories, the higher category should be selected to classify the individuals dental treatment restrictions.

2. Limit the initial dose of local anesthetic containing epinephrine to a maximum of 0.036 mg (i.e., 2 carpules of 2% lidocaine with 1:100,000 epinephrine). (Local anesthetic containing levonordefrin should be avoided). Re-assess pulse rate and blood pressure prior to, and 5 minutes after, administering any additional local anesthetic, especially one containing a vasoconstrictor.

3. In addition to #2 (above), do not use epinephrine-impregnated gingival retraction cord; do not use local anesthetic containing a vasoconstrictor for direct hemostasis, or intraligamentary or infrabony infiltrations.

4. Selective dental care would include minimally invasive dental treatment such as (but not limited to) dental prophylaxis, nonsurgical periodontal therapy, and simple restorative procedures.

Dental Management of a Patient with a History of Hypertension:

Dental treatment guidelines for adult patients with hypertension are primarily based on an evaluation of their blood pressure at the time they present for dental treatment, and are summarized in Table 4. Other dental management considerations for the dental patient with hypertension include:

- Reduce stress and anxiety prior to and during dental treatment. For patients with significant anxiety, consider the use of nitrous oxide-oxygen inhalation sedation and/or premedication with oral anti-anxiety medications such as benzodiazepines (e.g., triazolam, 0.125 to 0.5 mg the night before appointment, and 0.125 to 0.5 mg 1 hour before treatment).
- Local Anesthesia: Profound local anesthesia is critical for pain and anxiety control and is especially important for patients with hypertension or other cardiovascular disease to decrease the release of endogenous catecholamines (adrenaline). Profound pain control of adequate duration is less likely to be achieved when a vasoconstrictor has been excluded from a local anesthetic solution. If the patient experiences pain during treatment, an exaggerated stress response is observed. Consequently, the cardiovascularly impaired patient is more at risk from endogenously released catecholamines than from exogenous epinephrine administered in a proper manner.
  - Local anesthetics containing a vasoconstrictor are usually <u>not recommended</u> for use in patients uncontrolled or poorly controlled (ASA IV) hypertension (Table 4-6). This is defined as any patient with a systolic blood pressure ;::180 mm Hg and/or a diastolic blood pressure ;::110 mm Hg.
  - For patients with controlled hypertension, (especially those taking a non-cardioselective beta-blocker [e.g., propranolol]) it is advisable to limit the initial dose of a local anesthetic containing a vasoconstrictor (i.e., epinephrine) to a maximum of 0.036 mg of epinephrine (two 1.8 mL cartridges of 2% lidocaine containing 1:100,000) within 30–45 minutes. <u>Levonordefrin should be avoided in patients with hypertension because of its comparative excessive alpha-1 stimulation</u>.
  - Assess and record the patient's pulse rate and blood pressure prior to, and 5 minutes after, administering local anesthetic, especially when containing a vasoconstrictor. Additional precautions include:
    - Avoiding the use of epinephrine impregnated gingival retraction cord (aluminum potassium sulfate impregnated gingival retraction cord is a safe alternative).
    - Avoiding the use of local anesthetic with vasoconstrictors for direct hemostasis to control local bleeding.
    - Avoiding the use of local anesthetic with vasoconstrictors for intraligamentary or infrabony infiltrations.
  - If, during the dental procedure, additional local anesthetic is necessary and 0.036 mg of epinephrine has already been administered at least 30–45 minutes ago, options include:
    - Administer a local anesthetic without a vasoconstrictor (e.g., 3% mepivacaine, 4% prilocaine), or
    - Check blood pressure and pulse, and if within acceptable limits, administer additional local anesthetic with up to 0.018 mg of epinephrine; recheck blood pressure and pulse 5 minutes after injection.
- Avoid stimulating the gag reflex in patients with a history of hypertension.
- Avoid significant potential interactions between drugs used to treat hypertension and drugs commonly used in dental treatment.

(A copy of Corah's Dental Anxiety Scale/Survey [CDAS] and a Specific Dental Stressors Survey appear on the next 2 pages)

Box 2: Scoring the Corah's Dental Anxiety Survey (CDAS)

Anxiety Rating (Total possible = 20 points):

- 6 - 8 = mild anxiety
- 9 - 12 = moderate anxiety (but may have specific stressors [e.g., local anesthetic injection] that could be discussed and managed)*
- 13 - 14 = severe anxiety
- 15 - 20 = very severe anxiety (or phobia)

* If the patient scores greater than 8 points on the CDAS, then a Specific Dental Stressors Survey should be helpful in identifying the specific aspects of dental treatment that cause the most fear and anxiety for the patient.

DENTAL CONCERNS ASSESSMENT*

Date_____

Thank you for taking the time to fill out the front and back of this questionnaire. This only has to be filled out one time and will help us best serve you during your dental visit. Whether you are/are not anxious about going to dental visits, we ask you to complete the questionnaire. Your absolute comfort at all of your appointments is important to us and we strive to understand your needs and give you the most comfortable appointment possible.

Patient First Name _____ **Middle** _____ **Last** _____

Norman Corah's Anxiety Scale Dental Questionnaire

For Patients Age 15 and Older

When going to the dentist for a check-up, how do you feel about it?

Scale
1 ☐ I look forward to it as a reasonably enjoyable experience.
2 ☐ I don't care one way or another.
3 ☐ I am a little uneasy about it.
4 ☐ I am afraid that it would be unpleasant and painful.
5 ☐ I am very frightened of what the dentist would do.

When you are waiting in the dentist's office for your turn in the chair, how do you feel?

Scale
1 ☐ Relaxed.
2 ☐ A little uneasy.
3 ☐ Tense.
4 ☐ Anxious.
5 ☐ So anxious that I sometimes break out in a sweat or almost feel physically sick.

When you are in the dentist's chair waiting while the dentist gets the drill ready to begin working on your teeth, how do you feel?

Scale
1 ☐ Relaxed.
2 ☐ A little uneasy.
3 ☐ Tense.
4 ☐ Anxious.
5 ☐ So anxious that I sometimes break out in a sweat or almost feel physically sick.

Imagine you are in the dentist's chair to have your teeth cleaned. While you are waiting and the dentist or hygienist is getting out the instruments which will be used to scrape your teeth around the gums, how do you feel?

Scale
1 ☐ Relaxed.
2 ☐ A little uneasy.
3 ☐ Tense.
4 ☐ Anxious.
5 ☐ So anxious that I sometimes break out in a sweat or almost feel physically sick.

(Over)

DENTAL CONCERNS ASSESSMENT*

Date_____

Please rank your concerns or anxiety on the accompanying scale.
Please fill in any additional concerns.

		Level of Concern or Anxiety			
		Low	Moderate	High	Don't Know
1	Sound or vibration of the drill	1	2	3	4
2	Not being numb enough	1	2	3	4
3	Dislike the numb feeling	1	2	3	4
4	Injection ("Novocain")	1	2	3	4
5	Probing to assess gum disease	1	2	3	4
6	The sound or feel of scraping during teeth cleaning	1	2	3	4
7	Gagging, for example during impressions of the mouth	1	2	3	4
8	X-rays	1	2	3	4
9	Rubber dam	1	2	3	4
10	Jaw gets tired	1	2	3	4
11	Cold air hurts teeth	1	2	3	4
12	Not enough information about procedures	1	2	3	4
13	Root canal treatment	1	2	3	4
14	Extraction	1	2	3	4
15	Fear of being injured	1	2	3	4
16	Panic attacks	1	2	3	4
17	Not being able to stop the dentist	1	2	3	4
18	Not feeling free to ask questions	1	2	3	4
19	Not being listened to or taken seriously	1	2	3	4
20	Being criticized, put down, or lectured to	1	2	3	4
21	Smells of the dental office	1	2	3	4
22	I am worried that I may need a lot of dental treatment	1	2	3	4
23	I am worried about the cost of the dental treatment I may need	1	2	3	4
24	I am worried about the number of appointments and the time that will be required for necessary appointments and treatment; time away from work, or the need for childcare or transportation	1	2	3	4
25	I am embarrassed about the condition of my mouth	1	2	3	4
26	I don't like feeling confined or not in control	1	2	3	4
27	Other:				

*Developed by J.H. Clarke and S. Rustvold, Oregon Health Sciences University School of Dentistry, 1993 (Revised 1998)

Signature _____ Print _____

Name of Adult Patient, Parent or Legal Guardian completing this form

INFECTIVE ENDOCARDITIS

Definition:

- Infective endocarditis (IE) is defined as an infection of the endocardial surface of the heart, which may include one or more heart valves, the mural endocardium, or a septal defect. Although it might result from a bacteremia originating from any source and representing almost any microorganism, it is of interest to dentistry as it relates to oral flora as a potential source for bacteremia and endocarditis.
- We currently follow the **2007 AHA/ADA Antibiotic Prophylaxis Guidelines for the Prevention of Infective Endocarditis** summarized in ***Boxes 1* & *2***, and ***Table 1*** as follows:

Box 1: Cardiac Conditions Associated with the Highest Risk of Adverse Outcome from Endocarditis for Which Prophylaxis with Dental Procedures Is Recommended

- Prosthetic cardiac valves (including transcatheter implanted prostheses and homografts).
- Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords.*
- Previous infective endocarditis.
- Congenital heart disease (CHD)‡:
  - Unrepaired cyanotic CHD, including palliative shunts and conduits.
  - Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first six months after the procedure†.
  - Repaired CHD with residual hemodynamic defect at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization).
- Cardiac transplantation recipients who develop cardiac valvulopathy (e.g., valve regurgitation due to a structurally abnormal valve).
- Ventricular Assist Device (VAD)*

---

* Condition is not specified in the 2007 AHA/ADA Antibiotic Prophylaxis Guidelines for the Prevention of Infective Endocarditis but appears to be prudent based on later expert panel recommendations.

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

† Prophylaxis is recommended because endothelialization of prosthetic material occurs within six months after the procedure.

Box 2: Dental Procedures for Which Endocarditis Prophylaxis Is Recommended for Patients in Box 1

All dental procedures* that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa. This includes procedures such as biopsies, suture removal, and placement of orthodontic bands.

* The following procedures and events do not need prophylaxis:

- routine anesthetic injections through noninfected tissue
- taking dental radiographs
- placement of removable prosthodontic or orthodontic appliances
- adjustment of orthodontic appliances
- placement of orthodontic brackets
- shedding of deciduous teeth
- bleeding from trauma to the lips or oral mucosa

Table 1: Infective Endocarditis Prophylactic Antibiotic Regimens for a Dental Procedure

Situation	Agent	Regimen: Single Dose 30 to 60 Minutes Before Procedure	
		Adults	Children‡
Oral	Amoxicillin	2 g	50 mg/kg orally
Unable to take oral medications	Ampicillin **OR** Cefazolin or ceftriaxone	2 g IM or IV 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillins or ampicillin – Oral	Cephalexin *† **OR** Clindamycin **OR** Azithromycin or clarithromycin	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone† **OR** Clindamycin	1 g IM or IV 600 mg IM or IV	50 mg/kg IM or IV 20 mg/kg IM or IV

IM indicates Intramuscular; IV, intravenous.

‡ Total children's dose should not exceed adult dose.

* Or other first- or second- generation oral cephalosporin in equivalent adult or pediatric dosage.

† Cephalosporins should not be used in individuals with history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.

Dental Implications of a Patient with at Increased Risk for Endocarditis

- Patients with a mechanical prosthetic heart valve will be taking an anticoagulant such as warfarin (Coumadin) resulting in impaired hemostasis. (See: "Anticoagulant Therapy" for more information).
- Patients at increased risk for endocarditis may have other comorbid cardiovascular disease such as congestive heart failure, hypertension, or arrhythmias that could have implications regarding dental treatment.
- If a series of dental procedures is required, it may be prudent to observe an interval of time (at least 9 to 14 days) between procedures to both reduce the potential for the emergence of resistant organisms and allow repopulation of the mouth with antibiotic susceptible flora.
- An antibiotic for prophylaxis should be administered in a single dose before the procedure. If the dosage of antibiotic is inadvertently not administered before the procedure, or if unanticipated manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa occurs during the procedure**,** the dosage may be administered up to 2 hours after the procedure. However, administration of the dosage after the procedure should be considered only when the patient did not receive the pre-procedure dose.

- If a patient is already receiving antibiotic therapy for several days or longer with an antibiotic that is also recommended for IE prophylaxis for a dental procedure, it is prudent to select an antibiotic from a different pharmacologic class rather than to increase the dosage of the current antibiotic. If possible, it would be preferable to delay a dental procedure until at least 10 days after completion of the antibiotic therapy. This may allow time for the usual oral flora to be reestablished.

Box 3: Antibiotic Prophylaxis for Nonvalvular Prosthetic Devices and Indwelling Vascular Access Devices

The following devices DO NOT require antibiotic prophylaxis prior to dental treatment:

- **implantable cardiac pacemakers or cardioverter defibrillators**
- **implantable vagus nerve, spinal, or dorsal column stimulator**
- **intra-aortic balloon pumps**
- **arterial (e.g., aortic) vascular stents or grafts**
- **prosthetic vascular patches or conduits**
- **cardiac (coronary artery) stents or peripheral vascular stents**
- **cerebrospinal fluid shunts (VAS, VPS, LPS)**
- **inferior vena cava filter (e.g., Greenfield filter)**
- **arteriovenous shunts or fistulas for hemodialysis**
- **subcutaneous implantable drug delivery pumps**
- **breast, penile, or intraocular lens implants**
- **peripheral arterial catheters**
- **peripheral venous catheters (short)**
- **peripherally inserted central venous catheters (PICC)**
- **tunneled central venous catheters**
- **non-tunneled central venous catheters**
- **midline catheters**
- **totally implantable catheters**
- **pulmonary artery catheters**
- **umbilical catheters**

For patients with any of these implanted devices:

- ► The evidence for any significant hematogenous infections in such patients with oral microorganisms is extremely limited or nonexistent.
- ► Equally, there is no evidence that antibiotic prophylaxis is effective in the prevention of infections in these patients.
- ► Antibiotic prophylaxis is not routinely recommended for these patients who undergo dental or other invasive procedures.
- ► If the attending physician requests antibiotic prophylaxis for such patients before dental treatment, the dentist can state that there is no medical reason for such a practice and request that the physician provide the prophylaxis.

What to Include in a Medical Consultation:

- The current AHA/ADA guidelines are reasonably specific and proscriptive concerning those patients for which antibiotic prophylaxis for the prevention of infective endocarditis should be considered prior to dental treatment. However, patients with a history of surgical correction of congenital heart disease (CHD) may, in some cases, require a medical consultation with the patient's physician (preferably a cardiologist).

  Example:

  Mr. X is dental patient of the UFCD and has been diagnosed with (*e.g., dental caries, periodontal disease, partial edentulism, etc.*). Treatment will consist of (*e.g., extractions, periodontal surgery, etc.*) performed over approximately (*n*) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

Mr. X gives a history of a surgically repaired (*ASD, VSD, CHD, etc*.) on (*date*). I need to determine the presence of any residual hemodynamic defect at the site, or adjacent to the site, of any prosthetic patch or prosthetic device used in the repair. If the repair is completely healed and no foreign body exists in the circulation, then no antibiotic prophylaxis will be required according to current (2007) AHA guidelines regarding antibiotic prophylaxis for the prevention of infective endocarditis.

Please provide your assessment of the post-cardiac surgery status and infective endocarditis risk of this patient, including your recommendation as to the need for antibiotic prophylaxis prior to invasive dental treatment, as well as any additional pertinent medical information you may have in this regard?

Thank you for your assistance in my care of our mutual patient.

Note: All medical consultations regarding the need for antibiotic prophylaxis for the prevention of infective endocarditis, or implanted prosthetic devices, **must be countersigned by the faculty supervising the procedure** before they are sent to the patient's physician.

PREGNANCY

- Implications for Dental Treatment:
  - Baseline information before treating a pregnant woman includes:
    - determining her due (delivery) date, and
    - any previous high-risk pregnancies or complications of the current pregnancy (as well as any other medical problems that may have existed before the pregnancy).
  - Blood pressure should be taken at each visit to screen for pre-eclampsia/hypertension, (BP should be < 140/90 mm Hg).
  - If the patient has nausea/vomiting of pregnancy (NVP) (emesis gravidarum or 'morning sickness'), she should be advised to rinse her mouth immediately after vomiting rather than brushing, as the enamel can be softened by stomach acid and more susceptible to abrasion.
  - From the middle of the second trimester onward, supine hypotension syndrome (aortocaval compression syndrome) should be avoided by positioning the patient on her left side (i.e., left lateral position) with minimal compression of the vena cava by the gravid uterus.

- Timing of Dental Treatment:
  - Emergency dental treatment can be performed during all trimesters of pregnancy.
  - Elective dental treatment should be performed during the second or early in the third trimester, although complex treatment plans should be deferred until after delivery.
  - All patients should be encouraged to perform impeccable oral hygiene throughout the term of the pregnancy to ensure against pregnancy-related oral pathology, and to reduce the impact of periodontal disease on the fetus.
  - Dental prophylaxis should be performed in the second trimester, and repeated in the third trimester if there have been any periodontal problems (e.g., pregnancy gingivitis or pyogenic granuloma).

- Radiographs:
  - Radiographs should be used selectively and only when necessary and appropriate to aid in a specific diagnosis and treatment of the patient. ('Routine' radiographs for 'screening' purposes only are contraindicated during pregnancy).
  - Bitewing, panoramic, or selected periapical films are recommended for minimizing patient radiation dose with appropriate lead shielding (i.e., abdominal and thyroid collar).

- Local Anesthetics:
  - Lidocaine containing epinephrine or prilocaine are generally considered to be the safest of the local anesthetics for use during pregnancy (FDA PR Category "B") .
  - Articaine, bupivacaine, and mepivacaine are also typically safe, but are usually not preferred for use during pregnancy (FDA PR Category "C").
  - Although both the local anesthetic and the vasoconstrictor cross the placenta, subtoxic threshold doses have not been shown to cause fetal abnormalities.

- Antibiotics:
  - Penicillins (including amoxicillin), erythromycin (except in estolate form), cephalosporins, metronidazole, and clindamycin are generally considered to be safe to use during pregnancy.

- The use of tetracyclines, including doxycycline, are contraindicated during pregnancy.

Analgesics:

- The analgesic of choice during pregnancy is acetaminophen.
- Aspirin and nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided during pregnancy.
- The safety of opioids (e.g., codeine, hydrocodone, oxycodone) during pregnancy is unclear. Maternal use of opioids may be associated with birth defects, poor fetal growth, stillbirth, preterm delivery, as well as the possibility of adverse respiratory effects. Therefore, it is best to avoid opioids during pregnancy or use them with caution only if needed.
  - Consultation with the patient's physician is recommended before prescribing opioids during pregnancy.

• Anxiolytics:

- Benzodiazepines, zaleplon, and zolpidem should be avoided during pregnancy.
- A single, short-term exposure to nitrous oxide–oxygen (N_2O–O_2) for less than 35 minutes is not thought to be associated with any human fetal anomalies during pregnancy, including low birth rate. The following guidelines are recommended if N_2O–O_2 inhalation sedation is used during pregnancy:
  - The second and third trimester are considered the safer periods use of N_2O–O_2 inhalation sedation because organogenesis occurs during the first trimester.
  - Use of N_2O–O_2 should be minimized to a single exposure of less than 35 minutes during pregnancy.
  - At least 50% oxygen should be delivered to ensure adequate oxygenation at all times.
  - Appropriate oxygenation (oxygen flush) should be provided to avoid diffusion hypoxia at the termination of administration.
  - Repeated and prolonged exposures to nitrous oxide are to be prevented.

Dental Patients with PROSTHETIC JOINTS

Background:

In December, 2012 the American Academy of Orthopaedic Surgeons (AAOS), and the American Dental Association (ADA) published, "Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures - Evidence-based Guideline and Evidence Report". This report is available at: http://www.aaos.org/Research/guidelines/PUDP/PUDP_guideline.pdf

The AAOS/ADA's clinical practice recommendations for the use of antibiotic prophylaxis for patients with prosthetic joint replacement(s) undergoing dental procedures are based on a collaborative evidence-based clinical practice guideline that focuses on the possible linkage between prosthetic joint (i.e., orthopaedic implant) infection and patients undergoing dental procedures. AAOS and ADA staff methodologists and the physician/dentist work group systematically reviewed the available literature and subsequently wrote the following recommendations based on a rigorous, standardized process commensurate with IOM standards.

Recommendation 1 states that, "The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures". Recommendation 1 is supported by "limited" evidence. Its key points are:

- Practitioners consider changing the longstanding practice of prescribing prophylactic antibiotics for patients who undergo dental procedures.
- The evidence shows that dental procedures are unrelated to prosthetic joint infections.
- Subsequent antibiotic prophylaxis does not reduce the risk of prosthetic joint infections.
- High strength evidence suggests that antibiotic prophylaxis reduces the incidence of post-dental procedure related bacteremia.
- There is no evidence that bacteremia increases the risk of prosthetic joint infections (PJI).

A panel of experts convened by the ADA Council on Scientific Affairs in 2014 (2014 Panel) developed an evidence-based clinical practice guideline (CPG) on the use of prophylactic antibiotics in patients with prosthetic joints who are undergoing dental procedures. This CPG is intended to clarify the "Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures: Evidence-based Guideline and Evidence Report," which was developed and published by the AAOS and the ADA in December, 2012 (2012 Panel). The 2014 Panel chose to use the literature selected by the 2012 Panel as the foundation of this CPG. In addition, the 2014 Panel updated the literature search and screening process to identify additional evidence.

The report of the 2014 (ADA Council on Scientific Affairs) Panel was published in January, 2015. They determined that the use of prophylactic antibiotics prior to dental procedures in patients with prosthetic joints is no longer warranted for most people. This report (Sollecito TP, et al. The use of prophylactic antibiotics prior to dental procedures in patients with prosthetic joints. JADA 2015; 146: 11-68.e8) is available here:
http://jada.ada.org/article/S0002-8177(14)00019-1/fulltext?nav=rotatorJanmain

This report recommends that, "In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic

joint infection… For patients with a history of complications associated with their joint replacement surgery who are undergoing dental procedures that include gingival manipulation or mucosal incision, prophylactic antibiotics should only be considered after consultation with the patient and orthopedic surgeon. In cases where antibiotics are deemed necessary it is most appropriate that the orthopedic surgeon recommend the appropriate antibiotic regimen and when reasonable write the prescription."

In October, 2016 the AAOS and ADA published, "Appropriate Use Criteria For the Management of Patients with Orthopaedic Implants Undergoing Dental Procedures" (www.aaos.org/poiudpauc/). The 2016 AAOS/ADA Appropriate Use Criteria (AUC) attempts to define clinical situations in which antibiotic prophylaxis in certain at-risk dental patients could reduce a theoretical risk of post-surgical prosthetic joint infection.

The 2016 AAOS/ADA AUC was developed to include an interactive on-line decision support tool to facilitate the treatment of defined "high risk" and "immune compromised" patients who are on the more severe end of the clinical spectrum of disease, and assist clinicians in making a decision as to whether or not a patient with a prosthetic joint should receive antibiotic prophylaxis prior to dental treatment. This online AUC decision support tool is available here:
www.orthoguidelines.org/go/auc/default.cfm?auc_id=224995&actionxm=Terms

Dental Treatment of UFCD Patients with Prosthetic Joint(s):

Based on the evidence presented in these most recent AAOS and ADA publications, it would appear that antibiotic prophylaxis prior to invasive (bacteremic) dental treatment is usually not indicated for the majority of dental patients with prosthetic joints, and should only be considered for those who patients with a history of previous periprosthetic or deep prosthetic joint infection that required surgical intervention and/or those that are severely immunocompromised.

The AAOS/ADA AUC decision support tool should be consulted at:
www.orthoguidelines.org/go/auc/default.cfm?auc_id=224995&actionxm=Terms
and should serve as the foundation for making a determination regarding the appropriateness of antibiotic prophylaxis for a patient with a prosthetic joint undergoing a bacteremic dental procedure.

The AAOS/ADA note that ideally, their AUC are evidence-based, but in the absence of sufficient evidence, may be derived from a "consensus of expert opinion" and "accepted practice". Therefore, any decisions regarding the use of antibiotic prophylaxis prior to invasive (bacteremic) dental treatment for the prevention of prosthetic joint infection should not be made in the context of any one clinical guideline, but should be made on an individual basis, based upon:

- each patient's own unique medical and dental indications;
- the best evidence in the medical/dental literature;
- the clinician's own experience and best clinical judgment; and
- the patient's needs and preferences.

PSYCHIATRIC and COGNITIVE DISORDERS

General Considerations:

- Drug Interactions: It is imperative to check for any potential, significant interactions between drugs a patient with a psychiatric or cognitive disorder may be taking and those used or prescribed for dental treatment as serious or potentially life-threatening drug interactions may occur. Examples include:
  - Narcotic analgesics with monoamine oxidase inhibitors
  - NSAIDs with lithium
  - Vasoconstrictors (epinephrine, levonordefrin) with tricyclic-antidepressants

Dental Implications of a Patient with:

- Affect Disorders (e.g., Depression, Bi-Polar Disorder):
  - Patients with major depressive disorders that are not under good medical control often have poor oral hygiene because of a mood-induced disinterest in performing oral hygiene procedures. The effects of the poor oral hygiene may be compounded by reduced salivary flow, and patients may complain of dry mouth (xerostomia), which is frequently exacerbated by side-effects of medications the patient may be taking to treat their depression.
    - A majority of the antidepressant, antipsychotic, and mood-stabilizing medications have been shown to cause xerostomia (which affects approximately 18% of patients), stomatitis and glossitis, and a smaller percentage of these medications have been identified as causing sialadenitis, gingivitis, and edema and discoloration of the tongue. SSRI antidepressants have been implicated in causing movement disorders that includes bruxism.
    - The mood-stabilizing agent lithium has been shown to cause xerostomia and dysgeusia.
    - Valproic acid (valproate sodium) and carbamazepine have been associated with xerostomia and glossitis, as well as blood dyscrasias (leukopenia and anemia).Valproic acid (valproate sodium) taken in higher doses (~ 50 mg/kg/day or more) is associated with an increased risk for thrombocytopenia and thrombocytopathia.
  - Patients with major depressive disorders (especially those that are not under good medical control) have a high risk of developing rampant dental caries due to decreased whole-mouth and parotid gland salivary output, xerostomia secondary to drugs used to treat depression, high Lactobacillus count, a preference for diets high in carbohydrates, and often have poor oral hygiene. Patients often respond to their xerostomia and carbohydrate cravings by drinking large quantities of cariogenic sugared beverages. Additionally, lithium and valproate sodium can cause an intense craving for carbohydrates.
  - Patients with a major depressive disorder also are at high risk of developing periodontitis, hypothesized to be the result of the neglect of oral hygiene, and the increased incidence of smoking seen in these patients.
  - Complaints of glossodynia, various facial pain syndromes, TMJ disorder, and bruxism are common in patient with major depressive disorders.

- Psychotic Disorders (e.g., Schizophrenia):
  - Patients with psychotic disorders (as well as some other psychiatric disorders) may engage in painful self-destructive acts. Acts of orofacial mutilation such as eye gouging, pushing sharp objects into the ear canal, lip biting, cheek biting, tongue biting, burning of oral tissues with the tip of a cigarette, or mucosal injury with a sharp or blunt object have been reported.
  - Many conventional antipsychotic drugs (e.g. phenothiazines [such as chlorpromazine] and butyrophenones) can cause profound hyposalivation and exacerbate or cause xerostomia leading to and a worsening in the severity and progression of periodontal disease and caries.
  - Patients who are taking conventional antipsychotic drugs may develop muscular problems (dystonia, dyskinesia, or tardive dyskinesia) that can affect the oral and facial regions.
    - Conventional antipsychotic medication–induced movement disorders are associated with spasms of the jaw muscles that can cause dislocation of the temporomandibular joint, an impaired gag reflex and an increased incidence of death from obstructive asphyxia. The unceasing mandibular movements associated with tardive dyskinesia can cause the dislodging of complete removable prostheses, orofacial pain from mucosal ulcers and fatigue of the masticatory muscles.
  - Some drugs used in the treatment of schizophrenia (e.g., clozapine) can cause agranulocytosis, leukopenia, or thrombocytopenia.
  - Routine dental treatment of the schizophrenic patient should not be attempted unless the patient is under medical management. Even then, these patients may be difficult to manage in regards to the delivery of dental treatement.

- Eating Disorders (Anorexia, Bulimia):
  - Bulimia nervosa is the episodic uncontrolled ingestion of large quantities of food followed by recurrent inappropriate compensatory behavior in order to prevent weight gain such as self-induced vomiting, diuretics or cathartics, or strict dieting or vigorous exercise.
  - Anorexia nervosa in characterized by a weight loss of at least 15% of expected body weight, a devastating fear of weight gain, relentless dietary habits that prevent weight gain, and a disturbance in the way in which body weight and shape are perceived by the patient.
  - The dentist may be the first person to become aware of an eating disorder in a patient by finding a pattern of erosion of the teeth consistent with regurgitation of stomach contents. This should lead to referral and medical diagnosis and treatment. However, patients often deny this is a problem.
    - The erosive pattern involves the lingual surfaces of the teeth, primarily the maxillary teeth as the tongue protects the mandibular teeth. This particular type of erosion is known as perimolysis. In some cases the erosion also can affect the occlusal surfaces of molar and premolar teeth where the process can be accelerated by attrition. Severe erosion can cause increased tooth sensitivity to touch and to cold temperature. Dental caries may be more prevalent in these patients.
  - Patients with anorexia nervosa may be more difficult to identify and deal with in a dental practice. About 40% to 50% of the patients with anorexia nervosa are also bulimic and may show the dental signs of bulimia. Young patients who appear to be anorexic should be confronted concerning the weight loss. If no symptoms or history of serious medical diseases such as cancer or diabetes mellitus are noted the possibility of self-starvation should be discussed with the patient. The serious medical complications, including death (mortality rate

is as high as 15% to 18%), of anorexia nervosa need to be discussed in a straightforward manner. Again when young patients are involved their parents need to be informed, Every attempt should be made to refer these patients to a physician for evaluation and treatment.
- The major role of the dentist in the management of patients with bulimia nervosa is to deal with the results of their diet (dental caries), and the effects of chronic vomiting on the teeth (erosion).
- Bulimic patients should not be treatment planned for complex restorative procedures until the gorging and vomiting cycle has been broken. in a few cases, full coverage may be required in an attempt to save teeth. Once the patient is stable and wants to have the teeth with severe erosion restored this can be done. The dentist and patient need to be aware that relapse is common and complex restorations may fail with recurrence of chronic vomiting.

- Alzheimer's Disease (AD) and other Dementias:
  - Dental treatment planning, oral care, and behavioral management for persons with AD must be designed with consideration of the current stage, severity and progressive nature of the disease, and should involve family members whenever possible.
    - Restoration of oral health is best completed as early as possible in the AD process, because the patient's ability to cooperate diminishes as functional and cognitive abilities decline.
  - The ability of the patient to perform oral hygiene tasks (e.g., brushing and flossing) will decrease with the increasing severity of AD.
  - Patients with AD have a greater incidence of dry mouth, mucosal lesions, candidiasis, plaque and calculus buildup, periodontal disease, and smooth surface (root) and coronal caries, and in later stages of the disease, an increased risk for aspiration pneumonia.
  - Antipsychotics, antidepressants, and anxiolytics are used frequently for behavioral disturbances in patients with AD, and may contribute to xerostomia and increased risk for caries.
    - Antipsychotic drugs sometimes taken by patients with AD can cause agranulocytosis, leukopenia, or thrombocytopenia.
    - Additional adverse effects of antipsychotic drugs include muscular problems such as dystonia, dyskinesia, or tardive dyskinesia in the oral and facial regions.
  - Changes in oral environment (e.g., prostheses) may be disturbing for patients with later stage AD.

- Parkinson's Disease (PD):
  - Dental treatment plans for a patient with PD needs to carefully consider the progressive, degenerative nature of the disease, and should involve family members whenever possible.
    - Restoration of oral health is best completed as early as possible in the PD process, because the patient's ability to cooperate diminishes as functional and cognitive abilities decline.
  - The dentist must address the adverse effects of muscle tremor and rigidity on the patient's ability to perform home oral hygiene, as well as its effect during delivery of dental treatment.
    - Tremor and rigidity of the orofacial musculature may induce orofacial pain, temporomandibular joint discomfort, cracked teeth and dental attrition and may create difficulties in controlling and retaining dentures
    - The ability of the patient to perform oral hygiene tasks (e.g., brushing and flossing) will

decrease with the increasing severity of PD.

- Excess salivation, and drooling with decreased swallowing frequency may be associated with PD; conversely xerostomia may occur due to some drugs (e.g., anticholinergics, amantadine, dopaminergics, levodopa) used to treat PD.
- Levodopa and dopamine agonists may cause tardive dyskinesia; manifestations include uncontrolled, purposeless chewing movements and bruxism.

Medical Consultation Indications:

- A medical consultation is usually indicated for a patient with a psychiatric or cognitive disorder IF there is any question or uncertainty regarding any one (or more) of the following concerns:

  a. Is the patient's psychiatric disorder currently under adequate medical control? (I.e., are they experiencing any significant unresolved signs or symptoms of their psychiatric disorder at this time?)

  b. Will the patient's psychiatric or cognitive disorder significantly effect or complicate our ability to safely and effectively provide dental care to the patient and/or impair the patient's ability to follow or understand instructions?

  c. Does the patient's psychiatric or cognitive disorder effect their ability to make informed consent decisions regarding their dental treatment.

What to Include in a Medical Consultation:

- Example:

  "Mr./Ms. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each using local anesthesia (2% lidocaine containing 1:100,000 epinephrine). (Insert a summary of patient's current medical history, significant past medical problems, and list of all current medications here)

  1) Please provide us with this patient's current psychiatric diagnosis as well as a summary of their status and stability under current medications and treatment (i.e., are they experiencing any significant unresolved signs or symptoms of their psychiatric disorder at this time)?
  2) Please comment on any implications or considerations this patient's psychiatric disorder might have as it pertains to our proposed dental treatment.

  If the attending oral medicine faculty is unable to determine, or uncertain regarding, the patient's ability to make informed consent decisions about their dental treatment then add the following:

  3) In your opinion, do you will feel this patient will be able to make informed consent decisions regarding their dental treatment?

  Thank you for your assistance in my care of our mutual patient."

RENAL DISEASE

Definition:

- Renal disease results in the kidneys inability to function as a filter to eliminate metabolic (nitrogenous) waste via the urine, maintain the bodies fluid, acid/base and electrolyte balance, reabsorb protein, secrete the hormones renin and angiotensin which are responsible for the control of blood pressure and erythropoietin which modulates red blood cell maturation.
  Chronic renal failure (CRF) (end-stage renal disease [ESRD], chronic kidney disease [CKD]) is a progressive decrease in renal function, typically characterized by a glomerular filtration rate (GFR) less than 60 mL/min for at least 3 months or longer, with subsequent accumulation of nitrogenous waste products in the blood, electrolyte abnormalities, and anemia.

National Kidney Foundation (NKF) Stages of Chronic Kidney Disease (Renal Failure)

Stages of CKD[a]		
Stage	**Description**	**GFR (mL/min/1.73 m²)**
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	89-60
3A	Mild to moderate ↓ GFR	59-45
3B	Moderate ↓ GFR	45-30
4	Severe ↓ GFR	30-15
5	Kidney failure	< 15 or dialysis

CKD, chronic kidney disease; GFR, glomerular filtration rate.

[a]Adapted from the Renal Association. http://www.renal.org/whatwedo/InformationResources/CKDeGUIDE/CKDstages.aspx. Accessed November 16, 2013.

Dental Implications of a Patient with Chronic Renal Failure:

- Advanced renal disease will result in uremia that is fatal if not treated.
- The failing kidneys do not excrete sodium properly which results in fluid retention, edema, hypertension and cardiovascular disease.
- The inability of the kidney to eliminate nitrogenous waste products results in azotemia, metabolic acidosis, and electrolyte imbalances.
- Decreased erythropoietin production and blood loss contributes to anemia. Uremia increases the propensity towards bleeding due to decreased platelet aggregation and adhesiveness.
- Host defenses may be compromised due to decreased production of white blood cells, nutritional deficiencies and immunosuppressive therapy.
- Bone disorders (renal osteodystrophy) resembling hyperparathyroidism may be noted in the skeleton and mandible.
- Oral complications are related to uremic odor, mucosal ulceration and pain, xerostomia, secondary infection and bleeding.

What to Include in a Medical Consultation:

1. For Patients with Chronic Renal Failure Only:
    a. Determine cause of renal failure and concurrent/contributing conditions (e.g., diabetes).
    b. Determine presence of symptoms of uncontrolled renal failure including: easy fatigability, lethargy, pruritus, nausea, vomiting.
    c. Rule out uncontrolled hypertension (or symptomatic hypotension).
    d. Obtain a medical consult to determine the following:
        - Current status (severity) of renal failure and status of patient with present treatment including results current :
            - Basic or comprehensive metabolic panel (BMP or CMP) with estimated GFR
            - Complete blood count (CBC) with differential (including platelets)

- Example:

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each, using local anesthesia (2% lidocaine containing 1:100,000 epinephrine).

(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

1. Please provide a summary of the current status and severity/stage of this patient's chronic kidney disease.
   Please include the results of most recent lab tests (i.e., BMP or CMP with estimated GFR, CBC with differential [including platelets], etc.).
   A COPY OF YOUR LAST OFFICE VISIT NOTE for this patient will be greatly appreciated.
2. Please provide your assessment of this patient's overall risk in relation to their ability to safely tolerate the proposed dental procedures, as well as any specific medical management precautions or recommendations you may have as it relates to their dental treatment.

Thank you for your assistance in the care of our mutual patient."

2. For Patients With CRF and on Hemodialysis:
    a. Determine / obtain items 1a, 1b, 1c, 1d (above).
    b. Determine the type of vascular access (indwelling catheter, fistula or graft).
    c. Determine the timing (schedule) of hemodialysis.

3. For Patients on Peritoneal Dialysis:
    a. Determine / obtain items 1a, 1b, 1c, 1d (above).
    b. Determine type of peritoneal dialysis (chronic cycling or chronic ambulatory).
    c. Determine the timing (schedule) of dialysis.

4. For Patients after Renal Transplantation:
    a. Determine cause of renal failure and date(s) of transplant surgery.
    b. Determine present status of transplanted kidney (function?, rejection?).
    c. Determine present medications.

ASA Risk Classification for Patients with Chronic Kidney Disease

Classification	ASA Risk Category
• National Kidney Foundation (NKF) Stage 1 or 2 CKD	II
• NKF Stage 3 or 4 CKD • Status-post renal transplant with no signs of rejection and satisfactory renal function	III
• Status-post renal transplantation with signs of rejection and/or renal function impairment / insufficiency • NKF Stage 5 CKD (or receiving dialysis)*	IV

* Patients with CKD who are receiving dialysis who are clinically stable, and do not have other significant poorly controlled co-morbid complicating medical conditions (e.g., hypertension, diabetes mellitus), may effectively be considered as ASA III from a non-surgical dental treatment risk perspective if appropriate management precautions are followed.

Dental Management of a Patient with Chronic Renal Failure:

NOTE: As a general guideline, patients diagnosed with chronic renal failure, especially those receiving hemodialysis or peritoneal dialysis, who require invasive dental treatment should be treated in a hospital dental clinic (ACB).

Under Conservative Care for CKD:

a. Consultation with physician advised:
   - Avoid dental treatment if CKD is poorly controlled or advanced
   - Screen for the presence of a bleeding disorder and/or anemia before surgery (CBC with platelet count)

b. Monitor blood pressure closely during treatment (~ every 5 to 10 minutes).

c. Pay meticulous attention to good surgical technique and evaluate the need for antibiotic prophylaxis to prevent post-operative infection:
   - Patients with CKD and clinically significant lymphopenia may require the use of antibiotics to prevent post-operative wound infection. The need for, and selection of, prophylactic antibiotics in patients with CKD requires careful consideration and should be done in consultation with the patient's physician. The drug levels may be affected by altered excretion through the kidneys or the dialysis process, requiring dosage adjustments to avoid adverse effect. Potassium-containing penicillins may be satisfactory for prophylactic use but should be used with caution for extended courses because they may lead to high levels of potassium that can cause cardiac arrhythmias. The aminoglycosides, tetracyclines, and cephalosporins should usually be avoided owing to their nephrotoxicity.

d. Drug administration in patients with CKD:
   - Most drugs administered or prescribed in dentistry are eliminated from the body via renal

excretion. Excretion of drugs by the kidney involve may filtration, secretion, and reabsorption depending on the specific drug. In addition to modulating the rates of excretion of drugs, the kidney accumulates certain drugs. For drugs normally eliminated in an unchanged form, reduced glomerular filtration and tubular secretion associated with renal insufficiency or failure may lead to toxic plasma drug levels with normally safe dosages (particularly if the drug does not undergo hepatic metabolism, has a low (narrow) therapeutic index, or a long half-life).

- For example, vancomycin is an antibiotic that used in the treatment of severe infections with pathogens such as Staphylococcus and Streptococcus. Following intravenous administration, vancomycin is poorly metabolized and is mainly excreted unchanged in urine. Excretion of vancomycin is dependent on the kidney, and is correlated with creatinine clearance and GFR. The serum elimination half-life of vancomycin in adults with normal renal function averages 4-7 hours. In one study of patients with severe CKD with creatinine clearances less than 10 mL/min, the average elimination half-life of vancomycin was 146.7 hours (range: 44.1-406.4 hours).

The kidney is also capable of metabolizing certain drugs. Renal insufficiency may affect the metabolism of drugs not only by decreasing the rates of excretion in the urine, but also by a number of nonrenal mechanisms.

- For drugs commonly used in dentistry, tables and drug dose references (e.g., Lexicomp) containing schedules for drug dose modification are available for use in patients with CKD, and provide a useful guide for drug administration or prescription.
  - These references use the patient's (estimated) GFR as the basis for determining the necessity and method of modification of drug dose regimens in patients with CKD. Generally, two different methods are used to adjust drug regimens in patients with CKD:
    1. The amount of drug administered is reduced, but the dosing interval is held constant.
       - For example in an adult patient with a GFR > 50 mL/min, a normal dose of codeine (e.g., 30 mg) may be administered every 4 hours. If the patient's GFR is 10 – 50 mL/min, then the dose of codeine should be reduced to 75% of the normal dose (e.g., 22.5 mg) administered every 4 hours, and if GFR is < 10 mL/min, then the dose of codeine should reduced to 50% of the normal dose (e.g., 15 mg) administered every 4 hours.
    2. The amount of drug administered per dose is held constant, but the dosing interval is lengthened.
       - For example, in an adult patient with a GFR > 50 mL/min, a dose of amoxicillin (e.g., 500 mg) may be administered every 8 hours (which is the normal dose interval). If the patient's GFR is 10 – 50 mL/min, then the dose interval of amoxicillin should be lengthened to every 8 to 12 hours, and if GFR is < 10 mL/min, then the dose of amoxicillin should be administered every 24 hours.
  - Some drugs, particularly those that are potentially nephrotoxic, should not be used in patients with CKD.
    - For example, tetracycline antibiotics (with the exceptions of doxycycline and perhaps minocycline) can exacerbate renal impairment in patients with pre-existing kidney disease, and clinicians should not administer these drugs to patients with renal impairment.
  - Aspirin and NSAIDs may be contraindicated in patients with CKD:
    - Aspirin and NSAID use may compromise existing renal function by reducing renal blood flow which may cause renal decompensation.

- Patients with impaired renal function, dehydration, heart failure, liver dysfunction, those taking diuretics, ACE inhibitors, and the elderly are at greater risk of renal toxicity due to aspirin and NSAIDs.
- NSAIDs (and aspirin) are generally not recommended for use in patients with renal insufficiency or chronic kidney disease (CKD).
  - Short-term use (a few days) of NSAIDs for management of dental pain may be acceptable for many patients with CKD.
  - NSAIDs may also be used if the patient already has end-stage renal disease with no residual renal function, however, the antiplatelet effect of NSAIDs may exacerbate the risk of a bleeding diathesis in patients with uremia undergoing surgical procedures.

e. Bleeding risk / impaired hemostasis:
- Patients with severe renal failure (end-stage renal disease [ESRD], stage V chronic kidney disease [CKD]) are at increased risk for intra- and post-operative bleeding.
- General measures to improve hemostasis in patients with ESRD include:
  1. Elimination uremic toxins: Uremic toxins contribute to platelet dysfunction. Both hemodialysis and peritoneal dialysis are effective in clearing toxins, and thus in preventing perioperative bleeding.
     - For patients receiving hemodialysis that includes the use of unfractionated heparin (UFH), it is advisable to wait a long enough to minimize any residual effects of UFH on hemostasis prior to surgery (typically at least 6 hours; UFH effective half-life [$T_{1/2}$] mean: ~ 1.5 hours; range: ~ 1–2 hours).
       - The aPTT test is used to monitor the effect of UHF on hemostasis.
  2. Correction of anemia:
     - Erythropoietin (EPO) can be used to correct anemia associated with ESRD and thereby improve platelet function. Two to six weeks may be needed from the time of administration of EPO to the obtainment of an adequate hematocrit level.
  3. Avoidance of antiplatelet and anticoagulant drugs prior to surgery.
- Specific measures used to improve hemostasis in patients with ESRD include:
  1. Desmopressin acetate (DDAVP): (0.3 mg/kg IV or SC), onset of action is 30 – 60 minutes, with a duration of 6 – 12 hours, (or 300 µg intranasally given 1 to 2 hours before dental treatment).
  2. Plasma cryoprecipitate: (1 unit/10 kg), onset of action is within 1 hour, with a duration of 12 – 24 hours.
  3. Conjugated estrogen: (IV: 0.6 mg/kg/day; oral: 50 mg/day), the underlying mechanism of action in the prevention of bleeding is not fully understood. L-arginine (a precursor of nitric oxide) is believed to be inhibited, thereby improving platelet aggregation.
     - Onset of action after 24 hours, with a peak after 5 – 7 days, and persists for 2 weeks.

  In circumstances where the above measures have failed some reports recommend:
  - Tranexamic acid (10 mg/kg IV) is anti-fibrinolytic lysine analog that stabilizes hemostatic clots.

f. Manage orofacial infections aggressively with bacterial culture and sensitivity test and appropriate antibiotics.

g. Consider hospitalization for severe infection or major procedures.

Receiving Peritoneal Dialysis:

Same as conservative care recommendations (above)

Receiving Hemodialysis:

Same as conservative care recommendations plus:

a. Concerns for patients at increased risk for bacterial endocarditis:
   Although the current AHA antibiotic prophylaxis recommendations for the prevention of endocarditis may serve as a guide, specific recommendations and prophylactic antibiotic dose regimens for use in patients receiving hemodialysis who are going to receive invasive dental treatment and are best considered on an individual basis in consultation with the patient's physician.
b. Avoid use of blood pressure cuff or IV medications in arm with vascular access site.
c. Avoid dental treatment on day of dialysis if possible (especially within first 4 hours afterward due to a potential* for increased bleeding due to heparin use with hemodialysis; defer dental treatment until later on in the day after dialysis, or until the morning of the day after dialysis. (*Heparin administered during hemodialysis does not usually cause any clinically significant impaired hemostasis and its effects lasts only 3-4 hours after infusion. Situations involving prolonged post-operative bleeding in dental patients with CKD are most often related to quantitative and qualitative defects in platelets rather than to heparinization).
d. Consider screening for hepatitis B, hepatitis C, and HIV before any treatment or treat as potentially infectious. (The increased risk of these infections diseases in patients receiving hemodialysis as been declining in recent years due to increased testing and surveillance. However CKD patients are still to be considered to be at increased risk for infectious diseases due to renal failure-related immunosuppression. For example the incidence of tuberculosis in patients with CKD has been reported to be ten times greater than in the general population.)
   In patients with chronic active hepatitis B or C, impaired hepatic function may contribute to impaired hemostasis, and decrease the metabolism of drugs used in dental treatment.

Status-Post Renal Transplant:

- These patients will be on immunosuppressive drugs for the remainder of their lives (e.g., corticosteroids, azathioprine, cyclosporine, tacrolimus), thus susceptibility to infection is the primary concern.
  - Consultation with physician/transplant coordinator is needed to confirm satisfactory renal function without signs of rejection.
  - Elective dental treatment as needed can usually be performed.
  - Frequent periodontal recall and prophylaxis.
  - Daily antibacterial mouth rinses (0.12% chlorhexidine).
  - Avoid NSAIDs (due to increased bleeding with corticosteroids and potentiation of nephrotoxicity of cyclosporine and tacrolimus).
  - Consider antibiotic prophylaxis to prevent post-operative infection after invasive dental procedures.
  - Consider need for supplemental corticosteroids for surgical dental treatment
  - Screen for head and neck cancers (increased risk secondary to immunosuppression).

SEIZURE DISORDER / EPILEPSY

Definition:

- A seizure is a sudden, uncontrolled paroxysmal disturbance of central nervous system function secondary to aberrant cerebral cortical electrical activity that is characterized by varying combinations of impaired consciousness, abnormal motor function and/or inappropriate behavior, sensory disturbances, and autonomic dysfunction. The term "epilepsy" is used to describe any disorder characterized by recurrent seizures.

Dental Implications of a Patient with Epilepsy:

- Consideration of dental treatment setting (i.e., DMD-student clinic vs. ACB) based on pre-treatment evaluation and assessment of degree of adequacy of seizure control.
  - Modifications to dental treatment may be required depending on level of seizure control.
- Clinically significant leukopenia (that can result in an increased risk of infections and delayed wound healing), and/or anemia, can occur in patients taking phenytoin, carbamazepine, or valproic acid (valproate sodium).
- Impaired hemostasis: Patients taking higher doses (~ 50 mg/kg/day or more) of valproic acid (valproate sodium) are at increased risk for a dose-related elevation in liver enzymes, thrombocytopenia, and thrombocytopathia (due to inhibition of the secondary phase of platelet aggregation), which may be reflected in prolonged bleeding time and/or frank hemorrhaging.
- Oral conditions associated with drugs used to control seizures:
  - Gingival hyperplasia: 40% to 50% of patients taking phenytoin for more than 3 months will exhibit some degree of gingival hyperplasia
  - Xerostomia
- Patients may injure themselves during a generalized tonic-clonic seizure; maxillofacial or dental injuries, lacerations, shoulder dislocations, and even fractures may result.

What to Include in a Medical Consultation:

1. For patient's taking phenytoin, carbamazepine, or valproic acid (valproate sodium, divalproex) it may be prudent to obtain the results of a current CBC with differential [including platelets] to assess possible anemia, leukopenia, or thrombocytopenia secondary to these drugs prior to invasive dental treatment with a significant risk for bleeding and/or infection.
2. IF the following information cannot be adequately obtained from the patient (or a family member) during the medical history interview, ONLY THEN should the patient's physician be consulted in order to help determine the following:
   - Type(s) of seizures (e.g., tonic-clonic, absence, etc.)? (Ask the patient or a family member to describe what usually happens to them [signs, symptoms, duration] when they are having a seizure).
   - Ask the patent about the frequency of their seizures under current medication(s), and the date of their last seizure?
   - Ask the patient if they have a known seizure prodrome and/or aura?
   - Ask the patient if they have any known factors that precipitate or trigger a seizure (e.g., stress)?
   - Determine the presence of any underlying pathology responsible for the seizure disorder (if

known*) (e.g., neoplastic disease, history of head trauma, history of CNS infections [e.g., bacterial meningitis], etc.)?

* Note: Frequently patients will be diagnosed with idiopathic epilepsy or seizures (i.e., no identifiable cause can be found).

Dental Management of a Patient with Epilepsy:

- Avoid any factors known to precipitate (trigger) the patient's seizure (e.g., stress).
- Do not treat patients who are experiencing any of their known prodromal seizure symptoms.
- Patients with poorly controlled seizures (i.e., more frequent than one per month) or those with stress-triggered seizures may require additional anticonvulsant or sedative medications (i.e., benzodiazepines) prior to treatment as determined after consultation with the patient's physician.
  - Patients with a poorly controlled tonic-clonic seizure disorder should be considered for dental treatment in a hospital dental clinic (refer to the ACB for dental treatment).
  - Nitrous oxide sedation has been known to induce seizures in some patients with epilepsy and should be used initially with caution.
- If significant leukopenia or thrombocytopenia is present, invasive dental treatment, whenever possible, should be deferred until blood counts have returned to normal.
- Minimize the risk of aspiration and injury if a seizure occurs during dental treatment:
  - Rubber mouth props may prove useful in preventing aspiration of foreign objects and/or injury to the patient if a seizure occurs during dental treatment. Also, a rubber dam is preferable to multiple intraoral cotton rolls for isolation. Any instruments placed in the mouth (e.g., rubber dam clamps, rubber mouth props, etc.) should all have dental floss leads attached to prevent, or assist in recovery if aspirated.

TUBERCULOSIS

Definition:

- Tuberculosis (TB) is a chronic, recurrent infection most commonly caused by Mycobacterium tuberculosis that most commonly manifests itself as pulmonary disease.
- Infection with M. tuberculosis may also result in extrapulmonary disease, which can affect the pleura, lymph nodes, genitourinary tract, bone, meninges, peritoneum, or pericardium.
- High risk patients include those who are immunocompromised by illness or medication, prison inmates and workers, injection drug users, homeless people, recent immigrants from endemic regions, and anyone who lives or has close contact with TB patients.
- Screening tests are appropriate for anyone in a high risk category, including the PPD skin test (also called a tuberculin skin test [TST]) and chest x-ray. The chest x-ray is used to confirm lung lesions after a positive TST.
  - Many patients from the Caribbean, Central America, and Europe will have had the BCG vaccine which will make the PPD test false-positive.
- Sputum culture tests are performed to confirm an active TB infection as well as therapeutic responses to antibiotic therapy for TB.
- Treatment of active TB includes secluding the patient to limit further exposure to others, and multiple antibiotic medications for 6 or 9 months. These medications may include isoniazid hydrochloride (INH), rifampin, streptomycin, ethambutol, and pyrazinamide.
- Post-TB-exposure prophylaxis and inactive TB infection will likely include treatment with INH for 6 to 9 months.
- Signs and symptoms of active pulmonary tuberculosis include:
  - Cough: is nearly universal; typically, it is initially dry but then progresses with increasing volumes of purulent secretions and the variable appearance of blood streaking or gross hemoptysis.
  - Fever and night sweats: peaks as high as 104.0 to 105.80 F, typically occurring in the evening; however, although most patients with TB complain of feeling "feverish", a substantial proportion do not have fever when assessed.
  - Weight loss
  - Malaise
  - Lymphadenopathy
  - Non-pleuritic chest pain

Dental Implications and Evaluation of a Patient with (a history of, or active) TB:

- Dental evaluation is directed at the identification of patients with active TB.
  - While CDC guidelines clearly state that the overall risk borne by dental health care workers for exposure to a patient with active TB disease is probably quite low, no patient with active tuberculosis will be treated at the UFCD due to the special treatment facilities required that provide engineering controls such as TB isolation rooms. Standard face masks do not protect against TB transmission.
- Assess each patient for a history of TB as well as symptoms suggestive of active TB during all initial medical histories and at periodic updates.
  - The patient should be questioned about the presence of signs and symptoms suggestive of TB (i.e., fever, chills, night sweats, bloody sputum production, weight loss).

- Record dates and results of prior tuberculin skin tests (TSTs) or QuantiFERON-TB tests*
- Patients with a history of TB should be asked about:*
  - the degree of disease involvement
  - the type and duration of therapy received
  - the current status of disease activity

* A medical consult with the patient's physician is necessary to obtain and/or confirm this information.

What to Include in a Medical Consultation:

- Medical consultation is required for any patient who reports:
  - any history of active or suspected TB,
  - an exposure to a person with TB,
  - any HIV-positive patient (See the section on "HIV-AIDS" in this document for the evaluation of TB status in HIV-positive patients).
- Include language such as:

  This patient reports previous (suspected, exposure to, treatment of, chemoprophylaxis for) TB on (date[s]). Please indicate the patient's current TB status, including date and results of any pertinent test results including (select the appropriate test(s) as applicable to patient's TB history, e.g., chest x-ray, PPD, QuantiFERON-TB).

  Please confirm this patient is currently negative for active TB.

  (This information should be no older than one year, or more recent if the patient currently shows symptoms suggestive of TB).

Dental Treatment Risk Categories for a Patient with (a history of, or active) TB

High Risk (infectious / active disease): ♦ Patients with known active, sputum-positive tuberculosis and/or symptoms of active tuberculosis ♦ Patients with oral manifestations of tuberculosis
Moderate Risk (infected but not infectious): ♦ Patients with positive tuberculin skin tests but no evidence of active disease ♦ Patients with chest x-ray findings suggestive of prior tuberculosis involvement but no evidence of active disease ♦ Patients with inadequately treated tuberculosis but no evidence of active disease
Low Risk: ♦ Patients with known tuberculosis who have been adequately treated with no evidence of active disease ♦ Patients with a history of exposure to tuberculosis but negative skin tests and no evidence of disease

Dental Management of a Patient with (a history of, or active) TB:

- Patients with a medical history or symptoms indicative of undiagnosed, active TB should be referred promptly for medical evaluation to determine possible infectiousness.
  - Such patients should not remain in the dental school any longer than required to evaluate

their dental condition and arrange a referral.
- While in the dental school, the patient should be isolated from other patients and staff as much as possible, wear a surgical mask when not being evaluated, or be instructed to cover their mouth and nose when coughing or sneezing.
- Elective dental treatment should be deferred until a physician confirms that a patient does not have infectious TB, or if the patient is diagnosed with active TB, until confirmed the patient is no longer infectious.
- If urgent dental care is provided for a patient who has, or is suspected of having active TB disease, the care should be provided in a facility (e.g., hospital) that provides airborne infection isolation (i.e., using such engineering controls as TB isolation rooms, negatively pressured relative to the corridors, with air either exhausted to the outside or HEPA-filtered if recirculation is necessary).
  - Standard surgical face masks do not protect against TB transmission.
- Patients with recently diagnosed clinically active TB may be treated in the dental school after receiving antibiotic therapy for at least several (usually ~ 3 or more) weeks, and the patient has been confirmed by their physician to be non-infectious.

- Patients Reporting a Past History of TB:
  - Approach patient with caution; obtain good history of disease and its treatment duration; appropriate review of systems is mandatory.
    - The patient should give history of periodic chest radiographs and physical examination to rule out reactivation or relapse.
  - Consult with physician and postpone treatment if there is:
    1. Questionable history of adequate treatment time (less than 6 months)
    2. Lack of appropriate medical follow-up since recovery
    3. Signs or symptoms of relapse (active TB)
  - If present status is free of clinically active TB, then treat as normal patient.

- Patients with a Positive TST (or Recent Conversion to a Positive TST):
  - A person who has a positive TST should be viewed as having been infected with tuberculosis (unless due to BCG vaccine history, or until medically proven otherwise).
  - The patient should give a history of being evaluated for active TB by physical examination and chest radiograph. In the absence of clinically active TB, a regimen of prophylactic isoniazid may be started for 6 months to a year to prevent clinical disease.
  - Once patient is under medical treatment and confirmed to be absent of clinically active TB by a physician, they can be treated in a normal manner. No special precautions are required.

USE of VASOCONSTRICTORS in LOCAL ANESTHETICS

Background:

- A vasoconstrictor is included in the anesthetic solution to delay systemic absorption that increases the duration and profoundness of the local anesthesia. The preponderance of data in regard to epinephrine-containing local anesthetics shows that blood pressure and heart rate are minimally affected by the typically low doses and short-term use of the drug in dentistry.
- Clinical studies on local anesthetics containing vasoconstrictors (e.g., epinephrine) have consistently shown negligible influences on blood pressure in hypertensive patients (when used with appropriate precautions).
- Furthermore, the exogenous epinephrine contained in anesthetic solution may actually help prevent the release of excessive endogenous epinephrine (adrenaline). Patients experiencing pain due to less-than-profound anesthesia during dental treatment results in physiologic stress and has been associated with increased release of endogenous epinephrine (adrenaline).
  - If the patient experiences pain during dental treatment due to inadequate anesthesia, an exaggerated physiologic stress response may occur that places the patient at increased risk for an adverse cardiovascular event.
- Profound pain control of adequate duration is less likely to be achieved when a vasoconstrictor (epinephrine) has been excluded from a local anesthetic solution, and will significantly decrease the duration of profound anesthesia as well as treatment "working time". This will necessitate the administration of additional amounts of local anesthetic and increase the risk of complications including toxicity.
- Without the use of a epinephrine-containing local anesthetic, we will usually not be able to achieve profound anesthesia of long enough duration for the vast majority of our DMD-students to accomplish the procedures indicated for our patients in the General Dentistry Clinic.

Implications in Dental Treatment

- Local anesthetics containing a vasoconstrictor (epinephrine, levonordefrin) are absolutely contraindicated in a patient with a sulfite (e.g., sodium metabisulfite) allergy, since sulfites are used as an anti-oxidant preservative in local anesthetic preparations containing vasoconstrictors.

- The use of local anesthetic containing a vasoconstrictor is usually considered to be absolutely contraindicated in patients with:

  - Severe Cardiovascular Disease (defined as):
    - Unstable or severe (CCS-IV) angina pectoris
    - Recent (within 30 days) myocardial infarction
    - Recent (within 30 days) coronary artery bypass surgery
    - Symptomatic or significant arrhythmias:
      e.g., Untreated Mobitz type II second-degree AV block or third-degree AV block, symptomatic ventricular arrhythmias in the presence of underlying heart disease, supraventricular arrhythmia with uncontrolled ventricular rate.
    - Untreated or uncontrolled severe hypertension defined as:
      systolic BP :: 180 mm Hg and/or diastolic :: 110 mm Hg

- Uncompensated or uncontrolled congestive heart failure
- Uncontrolled hyperthyroidism
- Sulfite sensitivity (and/or systemic steroid-dependent asthma [?])
- Pheochromocytoma

- Patients in which a dose reduction* of the maximum amount of local anesthetic containing epinephrine would usually be indicated includes:

  - Patients with significant cardiovascular disease‡, but not severe enough to be considered an absolute contraindication to the use of local anesthetic containing vasoconstrictors:
    - e.g., adequately controlled hypertension, stable angina, controlled arrhythmias, etc.
      - ‡ This would be particularly applicable for patients with cardiovascular disease who are also taking sympathomimetic drugs (e.g., albuterol; aminophylline; dopamine; metaproterenol; methylphenidate; phentermine; phenylephrine; pseudoephedrine; salmeterol; theophylline; etc.).
  - Patients with a history of stroke (CVA)
  - Patients taking:
    - Tricyclic antidepressants (e.g., amitriptyline, doxepin, imipramine, etc.)
    - Non-cardioselective beta-adrenergic blockers (e.g., propranolol, nadolol, etc.)
    - Phenothiazines (e.g., chlorpromazine, thioridazine, trifluoperazine, etc.)
    - MAO inhibitors (e.g., phenelzine, tranylcypromine, etc.)

  * Dose reduction of local anesthetic with epinephrine is defined as:
    - Limiting total epinephrine dose to 0.04 mg or 2.2 cartridges of 2% lidocaine with 1:100,000 epinephrine or equivalent.
    - Do not use epinephrine impregnated gingival retraction cord (aluminum potassium sulfate impregnated gingival retraction cord is a safe alternative).
    - Do not use local anesthetics containing vasoconstrictors for:
      - Direct hemostasis
      - Intraligamentary or intrabony infiltrations
    - Additional considerations:
      - Check blood pressure and pulse before and 5 minutes after the administration of a local anesthetic containing a vasoconstrictor.
      - If, during the dental procedure, additional local anesthetic is necessary and 0.04 mg of epinephrine has already been administered, options include:
        - Administer a local anesthetic without a vasoconstrictor (e.g., 3% mepivacaine, 4% prilocaine).
        - Check blood pressure and pulse, and if within acceptable limits, administer additional local anesthetic with up to 0.02 mg of epinephrine; recheck blood pressure and pulse 5 minutes after injection.

Medical Consultations for Patients Taking a Non-cardioselective Beta-adrenergic Blocker (e.g., propranolol, sotalol, nadolol, pindolol, labetalol, etc.)

Concurrent use of a non-cardioselective beta-adrenergic blocker [NCSBB] (e.g., propranolol,

sotalol, nadolol, pindolol, labetalol, etc.) and a local anesthetic containing epinephrine can result in a serious adverse drug reaction in that propranolol blocks the beta-2 vasodilatory effects of epinephrine, leaving the alpha-1 vasoconstrictive effects functioning unopposed, leading to hypertension with a concomitant reflex bradycardia. For patients being treated with a non-cardioselective beta-adrenergic blocker [NCSBB] (e.g., propranolol, nadolol, etc.) we recommend the following medical consult be sent to the prescribing physician.

"Mr. X is dental patient of the UFCD and has been diagnosed with (e.g., dental caries, periodontal disease, partial edentulism, etc.). Treatment will consist of (e.g., extractions, periodontal surgery, etc.) performed over approximately (n) appointments of 2 to 3 hours duration each.
(Insert a summary of the patient's current medical history, significant past medical problems, and list of all current medications here)

(For a patient taking a NCSBB for treatment of cardiovascular disease (e.g., hypertension, arrhythmia):
The use of 2% lidocaine with 1:100,000 epinephrine for local anesthesia is indicated and preferred for Mr. X's dental treatment. Mr. X reports that are currently taking propranolol, (n) mg/day. Propranolol is a non-cardioselective beta-blocker and has been reported in the medical literature to enhance the pressor response to epinephrine, potentially resulting in hypertension with a concomitant reflex bradycardia. Therefore, would you please consider switching Mr. X from propranolol to a cardioselective beta-blocker in order to reduce the risk for a potentially serious adverse drug interaction between propranolol and epinephrine during dental treatment?
Thank you for your assistance in the care of our mutual patient."

(For a patient taking a NCSBB for treatment of a non-cardiovascular condition (e.g., anxiety):
The use of 2% lidocaine with 1:100,000 epinephrine for local anesthesia is indicated and preferred for Mr. X's dental treatment. Mr. X reports that are currently taking propranolol, (n) mg/day. Propranolol is a non-cardioselective beta-blocker and has been reported in the medical literature to enhance the pressor response to epinephrine, potentially resulting in hypertension with a concomitant reflex bradycardia. Therefore, please let us know if it would be permissible to instruct Mr. X to discontinue propranolol 24 hours prior to dental treatment in order to reduce the risk for a potentially serious adverse drug interaction between propranolol and epinephrine during dental treatment? The patient can resume taking propranolol that evening.
Thank you for your assistance in the care of our mutual patient."

APPENDIX

American Society of Anesthesiologists (ASA)
Physical Status Classification System
** MODIFIED FOR DENTISTRY **

(F. John Firriolo, DDS, PhD -- Rev.: 01/04/2019)

In 1962 the American Society of Anesthesiologists adopted what is now commonly referred to as the ASA Physical Status Classification System. The system was designed primarily as method of estimating the medical risk for patients who were to receive general anesthesia for a surgical procedure, but since its introduction the classification system has been used for all surgical patients regardless of anesthetic technique (for example, general anesthesia, regional anesthesia, or sedation). The most recent verison of the ASA Physical Status Classification System was approved by the ASA on October 15, 2014 and continues to be a valuable method for determining surgical and anesthesia risk prior to the actual procedure.

The current ASA Physical Status Classification System is as follows:

ASA I:	A patient without systemic disease; a normal healthy patient.
ASA II:	A patient with mild systemic disease.
ASA III:	A patient with severe systemic disease that limits activity but is not incapacitating.
ASA IV:	A patient with an incapacitating systemic disease that is a constant threat to life.
ASA V:	A moribund patient not expected to survive 24 hours with or without operation.
ASA VI:	A declared brain-dead patient whose organs are being removed for donor purposes.
ASA E:	Emergency operation of any variety; E precedes the number, indicating the patient's physical status (for example, ASA E-III)

This system has been modified and adopted for use in a typical outpatient dental treatment setting (and the "ASA E" category is not used for this purpose).

The ASA classification system is quite easy to employ in dentistry. This is especially the case when a patient has but one isolated medical problem (see examples provided with each ASA category). However, many patients will have a history of multiple diseases, in which case determination of the appropriate ASA classification might be more complex. In these situations the dentist must weigh significance of each disease and their summative effect on the patient's risk for dental treatment, and then choose the appropriate ASA category.

The ASA physical status classification system is not meant to be inflexible; rather, it is meant to function as a relative value system based on a dentist's clinical judgment and assessment of the relevant clinical data that are available. The degree of risk for medical complications associated with dental treatment represented by these patients increases with the ASA category (I < II < III) as do the indications and need for treatment modification to help minimize the risk of medical complications associated with dental treatment.

When the dentist is unable to determine the clinical significance of one or more disease entities, consultation with the patient's physician or other medical or dental colleagues is recommended. In all cases, however, the ultimate decision either to treat or to postpone treatment must be made by the treating dentist. The ultimate responsibility rests solely in the hands of the dentist who treats or does not treat the patient.

ASA I

ASA I patients are considered to be normal and healthy. Physiologically and psychologically, these patients should be capable of tolerating the stress involved in the proposed dental treatment with no added risk of serious complications. Healthy patients with minimal or no anxiety towards dental treatment are classified ASA I. Treatment modifications are usually not necessary for patients in this group.

Review of their medical histories, physical evaluation (including vital signs), and any other parameters that have been evaluated indicate no significant abnormalities.

The ASA I dental patient should NOT have any:

- medical problem(s) that could result in potential serious medical complications secondary to physiologically stressful or invasive dental treatment;

- medical problem(s) that could result in an adverse reaction or potential medical complication due to drugs we may administer as part of dental treatment, such as antibiotics, local anesthetics, vasoconstrictors, N_2O, or analgesics such as narcotics or NSAIDs;

- medical problem(s) that places them at an increased risk for metastatic infections (e.g., bacterial endocarditis) and would require the use of pre-operative antibiotic prophylaxis;

- medical problem(s) or take any medication(s) that places them at an increased risk for post-treatment infection due to immunosuppression and/or delayed wound healing;

- any medical problem(s) or take any medication(s) that could result in clinically significant impaired hemostasis;

- any medical or behavioral problem(s) (including severe anxiety towards dental treatment) that requires the use of pharmacologic agents (e.g., N_2O sedation, benzodiazepines or other oral anti-anxiety drugs) for stress / anxiety reduction during dental treatment;

- any medical, psychiatric or cognitive problem(s) that would impair their ability to follow or understand instructions and/or make them unable to provide legal consent to treatment and make informed consent decisions;

- current (active) drug or alcohol dependence or abuse;

- history of severe (e.g., anaphylactic) allergic reactions (especially to drugs or materials that may be encountered as part of dental treatment).

An ASA I classification represents a “green flag” to proceed with all planned dental treatment.

ASA II

ASA II patients have no functional limitations and have a well-controlled disease of one body system, or are healthy (ASA I) patients who demonstrate significant anxiety and fear toward dentistry. These patients are generally somewhat less stress tolerant than ASA I patients; however, they still represent a minimal risk during invasive dental treatment. Routine, invasive treatment is in order with consideration given toward possible treatment modifications or special considerations as warranted by the particular condition.

An ASA II classification represents a "yellow flag" (i.e., proceed with caution) regarding dental treatment. Elective, invasive dental treatment is warranted with little increase in risk to the patient during the procedure. Consideration should be given to possible treatment modifications. Examples of such modifications include the use of sedative/anxiolytic techniques, limiting the duration of treatment, limiting the use of vasoconstrictors in local anesthetic, and so forth.

Examples of ASA II patients include (but are not limited to) those with:

- Well-controlled hypertension (defined as a systolic blood pressure of < 140 mm Hg, or a diastolic blood pressure < 90mm Hg).

- Canadian Classification System (CCS) Class-I angina pectoris*
  * No limitation of ordinary physical activity: Ordinary physical activity, (e.g., walking and climbing stairs) does not cause angina. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.

- New York Heart Association (NYHA) Class-I congestive heart failure (CHF)*.
  * Defined as no limitation of physical activity. No dyspnea, fatigue, or palpitations with ordinary physical activity.

- An asymptomatic paroxysmal cardiac arrhythmia (that does not require chronic medication).

- Well-controlled mild intermittent or mild persistent asthma and mild exacerbations (attacks).

- Mild COPD (emphysema, chronic bronchitis) (i.e., dyspnea only on significant exertion; FEV_1 > 65% of predicted; SaO_2 [on room air] > 95%).

- National Kidney Foundation (NKF) Stage-II (mild) chronic kidney disease (defined as a GFR 60 - 89 mL/min/1.73 m^2).

- Well-controlled hyperthyroid or hypothyroid disorders who are under medical management and currently have normal thyroid function (euthyroid).

- Well-controlled type 2 diabetes mellitus defined as:
  - good metabolic control on stable medical regimen that does not require insulin, and
  - no history of ketoacidosis or frequent episodes of hypoglycemia, and
  - no chronic complications of diabetes, and
  - HbA1c ::: 7.0%.

- "Well controlled" asthma defined as:
  - Asthma symptoms on 2 or less days per week;
  - two or less nighttime awakenings per month due to asthma symptoms;
  - no interference with or limitation of normal daily activities due to asthma;
  - use of a short-acting beta-2-selective agonist inhaler (e.g., albuterol) on 2 or less days per week due to acute asthma symptoms; and
  - PEF or FEV_1 greater than 80% personal best or % predicted.

- Healthy, pregnant women (during their [uncomplicated] pregnancy).

- The potential for drug-induced (e.g., warfarin) impaired hemostasis that can be corrected by drug dose modification prior to invasive dental treatment.

- Well-controlled tonic-clonic seizure disorder (i.e., no seizure activity within the past year).

- A history of severe allergic (e.g., anaphylactic) reactions (especially to drugs or materials that may be encountered as part of dental treatment).

- Severe dental fear/anxiety (as indicated by a score of 13 or higher on Corah's Dental Anxiety Scale/Survey) or significant psychiatric illness (e.g., severe major depression, schizophrenia, etc.).

- Current smoker and/or social alcohol drinker. (The quantity of current smoking or alcohol use is not specified by the ASA.)

ASA III

ASA III patient have systemic disease that limits activity but is not incapacitating, have a controlled disease of more than one body system or one major system (e.g., cardiovascular, hepatic renal), and no immediate danger of death. At rest ASA III patients will not exhibit signs and symptoms of distress, but will do so when stressed either physiologically or psychologically. (An example of this would be the patient with angina pectoris who, while in the waiting room is asymptomatic, but develops chest pain when seated in the dental chair).

The ASA III classification represents an "orange flag" (i.e., approach with increased caution) regarding dental treatment. Elective, invasive dental care may or may not be contraindicated (based on the level of invasiveness of the procedure and the anticipated risk for medical complications), and this patient does represent a greater risk for medical complications during treatment. Implementation of various treatment modifications will generally be required for these patients.

Examples of ASA III patients include (but are not limited to) those with:

- Hypertension under medical management but not at goal blood pressure (defined as a systolic blood pressure of ≥ 150 mm Hg [or ≥ 140 mm Hg if < 60 years old or has diabetes or chronic kidney disease] , or a diastolic blood pressure ≥ 90mm Hg).

- Vasospastic angina or Canadian Classification System (CCS) Class II or Class-III angina pectoris*
  * CCS Class II is defined as slight limitation of ordinary activity. Symptoms occurs when:
    - Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold, in wind, or when under emotional stress, or only during the few hours after awakening.
    - Walking more than 2 blocks on the level and climbing more than 1 flight of ordinary stairs at a normal pace and under normal conditions.
  * CCS Class III is defined as marked limitation of ordinary activity. Symptoms occurs when walking 1 to 2 blocks on level ground or climbing 1 flight of stairs at a normal pace in normal conditions.

- New York Heart Association (NYHA) Class II or Class-III congestive heart failure (CHF)*.
  * NYHA Class II is defined as slight limitation of physical activity. These patients have fatigue, palpitations, and dyspnea with ordinary physical activity but are comfortable at rest.
  * NYHA Class III is defined as marked limitation of activity. Less than ordinary physical activity results in symptoms, but patients are comfortable at rest.

- An arrhythmia that requires chronic antiarrhythmic medication(s) and/or treatment (e.g., implanted permanent pacemaker and/or defibrillator), and are currently asymptomatic; first-degree atrioventricular (AV) block, or Mobitz type I second-degree AV block.

- Moderate COPD (emphysema, chronic bronchitis) (i.e., dyspnea on exertion; SaO_2 (on room air): 90 - 95%; FEV1 40% to 65% of predicted; hypoxemia [PaO_2 < 85 mm Hg] but no CO_2 retention).

- Stress-induced asthma attacks, or "not well controlled asthma" defined as having one or more of the following:
  - Asthma symptoms more than 2 days per week.
  - One to three nighttime awakenings per week due to asthma symptoms.
  - Some interference with / limitation of normal daily activities due to asthma.
  - Use of a short-acting beta-2-selective agonist inhaler (e.g., albuterol) more than 2 times per day due to acute asthma symptoms.
  - PEF or FEV_1 60% to 80% personal best or % predicted.

- National Kidney Foundation (NKF) Stage-III (moderate) (defined as a GFR 30 - 59 mL/min/1.73 m^2) or Stage-IV (severe) (defined as a GFR 29 - 15 mL/min/1.73 m^2) chronic kidney disease (and not receiving peritoneal or hemodialysis).

- Compensated cirrhosis (i.e., laboratory tests and/or liver biopsy indicative of cirrhosis but with NO clinical signs/symptoms) [e.g., gastroesophageal varices, jaundice, ascites, hepatic encephalopathy, or coagulopathy]).

- A history of transient ischemic attacks (TIA) and/or cerebrovascular accident (CVA) (stroke) more than 3 months ago and with unresolved or inadequately controlled continued risk factor(s) for CVA (e.g., unresolved or inadequately controlled hypertension, atrial fibrillation, diabetes mellitus, hypercoagulable disease, etc.).

- The potential for drug-induced (e.g., warfarin) impaired hemostasis that cannot be corrected by drug dose modification prior to invasive dental treatment (due to increased medical risk).

- Type 2 diabetes mellitus that requires insulin, or type 1 diabetes mellitus, with:
  - no symptoms of uncontrolled diabetes, ketoacidosis or frequent episodes of hypoglycemia within the past year; and
  - few, only minor, chronic complications of diabetes (that would not increase the risk for complications from dental treatment); and
  - HbA1c = 7.1% to 9.0%.

- Symptomatic hyperthyroid or hypothyroid disorders.

- HIV-positive, but without Stage 3 disease (AIDS) ($CD4^+$ T-lymphocyte count is ≥ 200 µL and percentage is ≥ 14; negative for any AIDS-defining conditions).

- Active hepatitis.

- Current (active) drug or alcohol dependence or abuse.

- Morbid obesity (body mass index [BMI] ≥ 40).

ASA IV

ASA IV patients have at least one severe disease that is poorly controlled or at end-stage with a possible risk of death. Patients in this category have a severe medical problem of greater importance to the patient than the planned dental treatment. As a general rule, elective, invasive dental care should be postponed until such time as the patient's medical condition has improved to at least an ASA III classification.

An ASA IV classification represents a "red flag"; a warning indicating that the risk involved in treating the patient is too great to allow elective, invasive dental treatment to proceed.

The management of dental emergencies, such as infection or pain, should be treated as conservatively as possible until the patient's condition improves. When possible, treatment should be noninvasive, consisting of the prescription of medications such as analgesics for pain and antibiotics for infection. In situations in which it is felt that immediate intervention is required (incision and drainage, extraction, pulpal extirpation), it is suggested that the patient receive such care within the confines of an acute care facility (i.e., a hospital). Although a hospitalized patient can still be at risk, his or her chance of survival will perhaps be increased should an acute medical emergency arise.

Examples of ASA IV patients include (but are not limited to) those with:

- Canadian Classification System (CCS) Class-IV angina pectoris* or unstable angina pectoris.
  * Defined as the inability to perform any physical activity without anginal symptoms (e.g, retrosternal chest discomfort or pain), anginal symptoms may be present at rest.

- Recent (within 3 months) myocardial infarction (MI), transient ischemic attack (TIA), cerebrovascular accident (CVA) (stroke), coronary artery bypass surgery or angioplasty with stents.*
  * If the patient has been evaluated by their physician and specifically determined to be medically stable and at an acceptable (low) level of risk to receive invasive dental treatment using local anesthesia containing a vasoconstrictor, then the patient may be reclassified as ASA III.

- Severe, symptomatic valvular heart disease.

- Significant (severe) arrhythmia, including: symptomatic, refractory ventricular arrhythmia; supraventricular arrhythmia with uncontrolled ventricular rate; untreated Mobitz type II second-degree AV block, or third-degree (complete) AV block.

- New York Heart Association (NYHA) Class-IV congestive heart failure (CHF)*.
  * Defined as symptoms (e.g., dyspnea, fatigue, or palpitations) present at rest, and any physical exertion exacerbates the symptoms.

- Active pulmonary tuberculosis.

- Untreated or inadequately treated hypertension defined as a blood pressure greater than 180 mm Hg systolic or 110 mm Hg diastolic in an adult patient.

- National Kidney Foundation (NKF) Stage-V chronic kidney disease (defined as a GFR < 15 mL/min/1.73 m^2) or requiring peritoneal or hemodialysis.

- Uncontrolled or poorly controlled tonic-clonic seizure disorder (defined as one or more tonic-clonic seizure per month).

- Severe COPD (emphysema, chronic bronchitis) defined as having one or more of the following:
  - Requiring chronic ambulatory oxygen supplementation and/or confined to wheelchair due to dyspnea
  - SaO_2 (on room air) < 90%
  - FEV_1 < 40% of predicted
  - CO_2 retention ($PaCO_2$ > 45 mm Hg)

- "Very poorly controlled" (or uncontrolled) asthma defined as having one or more of the following:
  - Asthma symptoms occurring throughout the day.
  - Four or more nighttime awakenings per week due to asthma symptoms.
  - Very significant interference with / limitation of normal daily activities due to asthma.
  - Use of a short-acting beta-2-selective agonist inhaler (e.g., albuterol) several times per day due to acute asthma symptoms.
  - PEF or FEV_1 less than 60% personal best or % predicted.

- Decompensated or advanced cirrhosis defined as having one or more of the following:
  - INR > 1.7 attributable to hepatic failure
  - Serum aminotransferase (AST, ALT) > 4 times normal values
  - Serum bilirubin > 2.0 mg/dL
  - Serum albumin < 3.5 g/dL
  - Ascites, encephalopathy, jaundice or esophageal varices attributable to hepatic failure

- Poorly controlled (especially type 1) diabetes mellitus defined as having one or more of the following:
  - HbA1c > 9.0%
  - Frequent occurrences of ketoacidosis and/or hypoglycemia
  - Multiple chronic systemic complications attributed to diabetes (e.g., chronic kidney disease, recent MI, recent stroke, symptomatic angina, CHF, inadequately controlled hypertension, neuropathy, retinopathy, etc.)

- Severe immunosuppression due to systemic disease (e.g., AIDS) or drugs (e.g., patients receiving antineoplastic cytotoxic chemotherapy, post-solid organ, -stem cell or -bone marrow transplant patients receiving high-dose anti-rejection drugs).

- Impaired hemostasis due to a known systemic bleeding disorder (e.g., thrombocytopenia, Von Willebrand's disease, hemophilia), or due to systemic disease (e.g., cirrhosis, renal failure).

- Severe, symptomatic anemia (e.g., hemoglobin < 11 g/dL and/or those with dyspnea, tachycardia or SaO_2 [on room air] < than 90%).

NOTE: As a general rule ASA IV patients should not any receive invasive dental treatment in the DMD-student general dentistry clinic and should be referred for treatment elsewhere (e.g., GPR program, faculty practice, etc.). ASA IV patients may be able to receive non-invasive dental treatment (e.g., removable denture fabrication) by a DMD-student general dentistry clinic after receiving approval from oral medicine faculty.

ASA V

ASA V patients are moribund and are not expected to survive more than 24 hours with or without the planned surgery or other medical intervention.

ASA V patients are almost always hospitalized, terminally ill patients. They might be considered in many institutions to be "DNR" (do not resuscitation) patients. Elective dental treatment is definitely contraindicated; however, emergency care, in the realm of palliative treatment (i.e., relief of pain), may be necessary.

Examples of ASA V patients include those who are terminally ill and not expected to survive more than 24 hours with or without medical intervention, such as those ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction (e.g., renal failure, heart failure, respiratory failure).

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In addition to the references cited in the text of this document, the following sources were also used in its compilation.

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