Patients Undergoing Radiation and Chemotherapy; Dental Care and Concerns

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Objectives

- Understand the medical treatment pathway of head and neck cancer patients
- Be able to discuss with your patients the effects of radiation and chemotherapy on the oral cavity
- Be knowledgeable as to the dental treatment prior to, during and after radiation treatment
- Be able to treat oral complications of radiation treatment (or know when to refer)
- Be able to recognize biological agents in the patients’ list of medications
- Be knowledgeable in the staging and dental treatment of medication-related osteonecrosis of the jaws
Topics – Head and Neck Cancer

- Epidemiology
- Etiology/Pathogenesis
- Risk Factors
- Medical Management
- Dental Management

Internet photos
Epidemiology

- 5th most common cancer worldwide*
- Estimated 9,570 will not survive
- Twice as common in males than females
- Rise in oropharyngeal cancers linked to human papilloma virus (HPV) infections (more favorable prognosis)
- Death rates decreasing over last 30 years
- Average age is 62; >25% occur in younger than 55

American Cancer Society at www.cancer.org
Last Medical Review: 07/16/2014
Last Revised: 01/27/2016
Epidemiology

- Rates vary among countries
  - higher in Hungary and France (did not mention India)
  - less common in Mexico and Japan

- Sites
  - tongue
  - tonsils and oropharynx
  - gums, floor of the mouth, other parts of the mouth

- May develop another cancer in the lung, mouth, throat, or other nearby area

Lifelong Follow-Up Exams

American Cancer Society at www.cancer.org
Last Medical Review: 07/16/2014
Last Revised: 01/27/2016
Effect of Insurance Coverage


- Uninsured patients and patients without Medicaid are more likely to:
  - Present with metastatic disease
  - Not be treated definitively
  - At a higher risk of head and neck cancer specific mortality
Etiology/Pathogenesis

- Multistep process
- Accumulation of mutations (activation of oncogenes) AND the loss of regulatory control (inactivation of tumor suppressor genes, reduced number of function of natural killer cells)
- Mendelian genetics, nonmendelian inheritance (polygenic or multifactorial), exposure to carcinogenic agents
- At least 3 – 6 somatic mutations needed to transform a normal cell into a malignant cell
- Uncontrolled proliferation, ability to recruit blood vessels, ability to spread

Dental Management of the Medically Compromised Patient, 8th edition; James Little, Donald Falace et al; Elsevier/Mosby; 2013
HPV and Cancer

Webinar looks at HPV link to cancer

BY MICHELLE MANCHIR

ADA members can earn one hour of continuing education at no cost by attending a live webinar May 5.

The course, “HPV Infection, Risk Factors and HPV-Related Oropharyngeal Cancer,” will review what is known about oral HPV infection and trends in HPV-related oropharyngeal cancer.

Topics covered include common questions and answers about HPV transmission and HPV-related oropharyngeal cancer; risk factors for oral HPV infection, including the role of oral sex; and new data that helps explain why HPV infections and related cancers are more common in men than in women.

Speakers will include Gypsyamber D’Souza, PhD, a cancer epidemiologist at Johns Hopkins Bloomberg School of Public Health, and Dr. Mark Lingen, a professor of pathology at the University of Chicago Pritzker School of Medicine, whose research dealing with tumor angiogenesis and oral cancer has resulted in more than 100 publications.

The ADA Council on Scientific Affairs, in collaboration with the ADA Science Institute, developed the course.

For more information and to register for the course, scheduled May 5 at 6 p.m. Central time, visit ADA.org/CElive. ADA CE Live is a series of in-person continuing education courses at ADA Headquarters in Chicago.

—manchir@ada.org

ADA News April 4, 2016
Signs and Symptoms

- Asymptomatic
- Palpable mass
- Leukoplakia/Erythroplakia
- Ulcer with raised margins
- Pain
- Hoarseness/Change in voice
- Dysphagia/Odynophagia
- Intractable ulcers
- Bleeding
- Numbness
- Loosening of teeth
- Difficulty opening
- Change in denture fit
## Color Characteristics of Oral Squamous Cell Carcinoma

<table>
<thead>
<tr>
<th>COLOR</th>
<th>% of TOTAL SCCa’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only white lesion</td>
<td>24.8</td>
</tr>
<tr>
<td>White lesions with erythroplakia</td>
<td>60.0</td>
</tr>
<tr>
<td>Other erythroplakic (red) lesions</td>
<td>33.3</td>
</tr>
<tr>
<td>Other</td>
<td>1.9</td>
</tr>
</tbody>
</table>

*Dental Management of the Medically Compromised Patient, 8th edition; James Little, Donald Falace et al; Elsevier/Mosby; 2013*
Pain

The Neurobiology of Cancer Pain; Brian L. Schmidt, DDS, MD, PhD; J Oral and Maxillofacial Surg; 73:S132-S135, 2015

- Different mechanisms responsible for pain
- Tumor size does not generally correlate with pain severity
- Greater pain severity at the oral site (primary) when cervical node metastasis present
- Premalignant and dysplastic lesions rarely painful
- Excision of the oral cancer relieves the pain
- Oral squamous cell carcinoma exhibits genome heterogeneity and manifests in the disparate oral cancer phenotypes
- Greater molecular complexity of oral cancer
- Nervous system responsible for pain but also contributes to carcinogenesis
Adjunctive Screening Tests

- Toluidine blue (TB)

- Transepithelial oral cytology
  - Oral CDx® Brush Test (Oral CDx Laboratories, Inc., Suffern, NY)

- Tissue reflectance or chemiluminescence
  - ViziLite® Plus with TBlue® (Zila, Inc., Fort Collins, CO)
  - Microlux™ (AdDent, Inc., Danbury, CT)
  - Orascoptic DK™ (Orascoptic, A Kerr Co., Middleton, WI)

The ADA Practical Guide to Patients with Medical Conditions, 2nd edition; Lauren Patton, Michael Glick editors; Wiley Blackwell; 2016

Reviewed in ADA chapter
Adjunctive Screening Tests

- Narrow-emission tissue autofluorescence
  - VELscope® Vx (LED Dental, Burnaby, BC, Canada)

- Multispectral technology (autofluorescence and tissue reflectance)
  - Identafi® 3000 (Tirmira, Houston, TX)

- HPV screening
  - OraRisk® HPV test (OralDNA® labs, Quest Diagnostics, Madison, NJ)

The ADA Practical Guide to Patients with Medical Conditions, 2nd edition; Lauren Patton, Michael Glick editors; Wiley Blackwell; 2016
Toluidine Blue Staining

Oral CDx Brush Biopsy

Transepithelial oral cytology

Internet photos
ViziLite®

Microlux

Orascoptic DX

Tissue reflectance or chemiluminescence

Internet photos
Velscope® VX

Narrow-emmision tissue autofluorescence

Identifi® 3000

Internet photos

Multispectral technology
"It is important to note that as a screening tool, it is designed to aid in identifying those patients at increased risk that warrant further evaluation. It is not meant to be a diagnostic tool to replace biopsy, which remains the gold standard for diagnosis."
Adjunctive Screening Tests

Adjunctive techniques for oral cancer examination and lesion diagnosis: A systematic review of the literature; Lauren L. Patton, DDS, FDS RCSEd, Joel B. Epstein, DMD, MSD, FRCD(C) , FDS RCSEd, A. Ross Kerr, DDS, MSD; JADA; Vol 139; pp 896-905; July 2008

- Systematic review of English-based literature

- Evaluated effectiveness of toluidine blue (TB), ViziLite Plus with TBlue (Zila Pharmaceuticals, Phoenix), ViziLite (Zila Pharmaceuticals), Microlux DL (AdDent, Danbury, Conn.), Orascoptic DK (Orascoptic, a Kerr Company, Middleton, WI), VELscope (LED Dental, White Rock, British Columbia, Canada) and Oral CDx (Oral CDx Laboratories, Suffern, N.Y.)

- Abstracted data relating to study design, sampling and characteristics of the study group, interventions, reported outcomes and diagnostic accuracy of adjunctive aids
Adjunctive Screening

- “There is evidence that TB {Toluidine blue} is effective as a diagnostic adjunct for use in high-risk populations and suspicious mucosal lesions.”

- “Oral CDx {brush test} is useful in assessment of dysplastic changes in clinically suspicious lesions; however, there are insufficient data meeting the inclusion criteria to assess usefulness in innocuous mucosal lesions.”

- “Overall, there is insufficient evidence to support or refute the use of visually based examination adjuncts.”

Adjunctive techniques for oral cancer examination and lesion diagnosis: A systematic review of the literature; Lauren L. Patton, DDS, FDS RCSEd, Joel B. Epstein, DMD, MSD, FRCD(C), FDS RCSEd, A. Ross Kerr, DDS, MSD; JADA; Vol 139; pp 896-905; July 2008
Biopsy

- Scapel
- Cutting ring punch
- Biopsy forceps
- Needles/Fine needle aspirate
- Toluidine blue may help guide what portion of the lesion to biopsy
Biopsy Results

A retrospective study of 51,781 adult oral and maxillofacial biopsies; Edwin A. Dovigi, MSc, Elaine Y. L. Kowk, MSc, et al; JADA; Vol 147, No 3; pp 170-176; March 2016

- Oral Pathology Diagnostic Service, San Diego, CA
- Reactive lesions were most prevalent at 74.9%
- Malignant diagnoses comprised 1.97%
- Three most prevalent diagnoses: benign keratosis, chronic apical periodontitis, radicular cyst
- Women: lichen planus (2X that of men), benign fibroma, osteomyelitis, nevi, and inflammatory fibrous hyperplasia
- Men: dentigerous and incisive canal cysts

Internet photo
Laboratory Tests

- No mandated lab tests in the diagnosis of head and neck squamous cell carcinoma (blood biomarkers?)

- Chemotherapy patients
  - complete blood count with white cell differential
  - basic metabolic, renal, and liver panels
  - nutrition status markers
  - virus or tumor markers
Diagnostic Imaging

- Bitewing, periapical, occlusal films
- Panoramic dental radiograph
- Computed tomography (CT) scan
- Cone beam computed tomography (CBCT) scan
- Magnetic resonance imaging (MRI)
- Positron emission technology (PET) scan
- Ultrasound
# Diagnostic Imaging – Panoramic Radiograph

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial screening</td>
<td>Lack of 3D visualization</td>
</tr>
<tr>
<td>Treatment planning for extractions</td>
<td>Early cortical erosion missed</td>
</tr>
<tr>
<td>Planning osteotomies for resection</td>
<td>May underestimate the extent of intrabony involvement</td>
</tr>
</tbody>
</table>
Diagnostic Imaging – CT Scan

**Advantages**

- Excellent bone detail
- Adequate soft tissue enhancement
- Relatively low cost
- Superior (over MRI) for detection of cervical lymphadenopathy??

**Disadvantages**

- Artifacts created by metallic restorations (retromolar pad and buccal mucosa)
- Irregular tooth sockets or periodontal disease may be confused with tumor extension
Diagnostic Imaging - CBCT

- Limited number of reports using CBCT in identifying mandibular tumor invasion
- Inability to produce a contrast-enhanced soft tissue study
- CBCT is $\frac{1}{12}$th the cost ($350) of a CT scan
- CBCT is $\frac{1}{6}$th the radiation dose

The Use of Cone Beam Computed Tomography as an Aid in Evaluating and Treatment Planning for Mandibular Cancer; James J. Closmann, DDS, Brian L. Schmidt, DDS, MD, PhD; J Oral and Maxillofacial Surg; 65:766-771; 2007
# Diagnostic Imaging - MRI

## Advantages
- Superior soft tissue detail
- Lack of ionizing radiation
- Superior for concern of
  - perineural invasion
  - skull base involvement
  - intracranial spread

## Disadvantages
- More sensitive to motion artifact
- May overestimate the extent of bony involvement
- More expensive than CT
- Claustrophobic patients
- Contraindicated
  - cardiac pacemakers
  - ferromagnetic aneurysm clips
Positron Emission Tomography (PET) Scan

- Identify metastasis
- Tumor recurrence
- Aggressive malignant processes
- Can be fused with CT scan
- Increased tracer uptake in highly metabolic tumor sites
- Less sensitive in occult primary tumor identification (50%)
- Sensitive to lesions larger than 6mm
- Postsurgical inflammation and radiation-induced inflammation causing poor specificity
- Diabetics/patients who have eaten
PET Scan / CT Scan
<table>
<thead>
<tr>
<th><strong>T - Tumor</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>No available information on primary tumor</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor less than 2 cm in diameter</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor 2-4 cm in diameter</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor greater than 4 cm in diameter</td>
</tr>
<tr>
<td>T4</td>
<td>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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>N - Node</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Nodes not assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No palpable nodes</td>
</tr>
<tr>
<td>N1</td>
<td>Ipsilateral palpable nodes (3 cm or less in diameter)</td>
</tr>
<tr>
<td>N2</td>
<td>Contralateral or bilateral nodes (3-6 cm in diameter). This group is further subdivided into N2a, N2b, and N2c categories.</td>
</tr>
<tr>
<td>N3</td>
<td>Fixed palpable nodes (greater than 6 cm in diameter)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>M - Metastasis</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Distant metastasis not assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Clinical or radiographic evidence of metastasis</td>
</tr>
</tbody>
</table>
Oral Cancer Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1 N0 M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2 N0 M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3 N0 M0, or T1, T2, or T3 N1 M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td></td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4a N0 or N1 M0, or T1, T2, T3, or T4a N2 M0</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>Any T N3 M0, or T4b any N M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any M1 lesion</td>
</tr>
</tbody>
</table>
**LOCAL:** only in area cancer started (Stage I, II, III no lymph nodes)

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-Year Relative Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>93%</td>
</tr>
<tr>
<td>Regional</td>
<td>48%</td>
</tr>
<tr>
<td>Distant</td>
<td>52%</td>
</tr>
</tbody>
</table>

**REGIONAL:** spread to nearby tissues and lymph nodes (Stage III, IV no metastasis)

**DISTANT:** metastasis (Stage IV)

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-Year Relative Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>78%</td>
</tr>
<tr>
<td>Regional</td>
<td>63%</td>
</tr>
<tr>
<td>Distant</td>
<td>36%</td>
</tr>
</tbody>
</table>

American Cancer Society at [www.cancer.org](http://www.cancer.org)
Last Medical Review: 07/16/2014
Last Revised: 01/27/2016
Patient’s Path to Treatment

- Patient complaint or routine exam
- Suspicious lesion
- Biopsy – Confirmation
- Otolaryngology
- Medical Oncology
- Radiation Oncology
- Tumor Board
- Consults
  - Dental
  - Gastroenterology
  - Nutrition
  - Speech/Swallowing
  - Mental Health
  - Social Services
Patient’s Path to Treatment

- PET/CT scan
- Simulation
- Gastrostomy tube (PEG tube)
- Treatment
- Post treatment surveillance

Internet photos
Pretreatment Evaluation and Considerations

- Rule out oral disease that may exacerbate during cancer therapy
- Provide a baseline for comparison and monitoring sequela of radiation and chemotherapy damage
- Detect metastatic lesions
- Minimize oral discomfort during therapy
Dental Pretreatment

- Patient education
- Oral hygiene instruction
- Noncariogenic diet
- Calculus removal
- Prophylaxis
- Fluoride treatment
- Elimination of sources of irritation or infection (sharp teeth)
- Mouth guard fabrication
- Medical consultation
  - what type of cancer and location
  - proposed total dose of radiation and exact anatomical areas to be irradiated
  - how much radiation to the jaws, teeth, salivary glands
  - timeline
## Guidelines for Tooth Extraction

<table>
<thead>
<tr>
<th>INDICATORS FOR EXTRACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pocket depth $\geq$ 6mm, excessive mobility, purulence on probing</td>
</tr>
<tr>
<td>Periapical inflammation</td>
</tr>
<tr>
<td>Broken-down, nonrestorable, nonfunctional, or partially erupted tooth in a patient who is noncompliant with oral hygiene</td>
</tr>
<tr>
<td>Patient lack of interest in saving tooth/teeth</td>
</tr>
<tr>
<td>Inflammatory, infectious or malignant osseous disease associated with questionable teeth</td>
</tr>
</tbody>
</table>

Dental Management of the Medically Compromised Patient, 8th edition; James Little, Donald Falace et al; Elsevier/Mosby; 2013
# Guidelines for Tooth Extraction

## Extraction Guidelines

<table>
<thead>
<tr>
<th>Extraction performed with minimal trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>- at least 2 weeks, ideally 3 weeks, before initiation of radiation therapy</td>
</tr>
<tr>
<td>- at least 5 days (in maxilla) before initiation of chemotherapy</td>
</tr>
<tr>
<td>- at least 7 days (in mandible) before initiation of chemotherapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trim bone at wound margins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtain primary closure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Avoid intraalveolar hemostatic packing agents (nidus for infection)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Transfuse if platelet count below 50,000/mm³</th>
</tr>
</thead>
</table>

| Delay extraction if white blood cell count is < 2000/um, or absolute neutrophil count is < 1000/um, or expected to be this level in 10 days |

Prophylactic antibiotics (cephalosporin) can be used with mandatory extractions.

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Dental Management of the Medically Compromised Patient, 8th edition; James Little, Donald Falace et al; Elsevier/Mosby; 2013
Dental Care During Cancer Treatment

- Maintenance of oral health
- Previously eliminated oral infections and potential problems
- May delay routine dental care
- Development of dental complications during treatment may interrupt or delay cancer treatments
Dental Care Post Treatment

- Cancer surveillance
- Recall visits every 3 – 6 months
- Re-access of daily oral hygiene
- Caries prevention and restoration
- Feasibility and timing of prosthetic reconstruction
- Tracheostomy
- Electronic voice box
Physical, Functional, Psychological Effects

Early and late physical and psychosocial effects of primary surgery in patients with oral and oropharyngeal cancers: a systematic review; Annelise Mortensen, RN, MHA, Mary Jarden, MScN, PhD; OOOO; Vol 121, No 6; pp 583-594; June 2016

- “Head and neck cancer has been bound to be more emotionally traumatic compared with any other type of cancer, and there is a high prevalence of emotional or psychological distress in patients with head and neck cancer, leading to poorer QOL”.

- “Patients with OPC {oropharyngeal cancer} suffer in the long term from emotional distress, compounded by physical dysfunction and social isolation”.
Early and Late Physical Effects

- **Pain** – decreased at 3 months and 1 year
- **Nutrition** – worst at 6 months up to even 9 years
- **Dysphagia** – persists for months up to 2 years (not experienced at 9 years after diagnosis)
- **Trismus** – even at 2.5 years, 33% reported among the third most burdensome symptoms
- **Voice and speech** – deteriorates first 3 months after surgery with slight improvement at 6 months; improved at by 5th year; affected quality of life more than any other symptom
- **Disfigurement** – 77% concerned with appearance

Early and late physical and psychosocial effects of primary surgery in patients with oral and oropharyngeal cancers: a systematic review; Annelise Mortensen, RN, MHA, Mary Jarden, MScN, PhD; OOOO; Vol 121, No 6; pp 583-594; June 2016
### Early and Late Psychological Effects

- **Social life** – affected for years and significantly for the long term

- **Emotional distress** – slowly improves up to 5 years where worry of recurrence did not interfere with quality of life

- **Lifestyle** – at 9 years postoperatively, 31% were heavy alcohol users and 23% smoked

- **Time factors** – burden of symptoms the most the first 3 months after surgery, diminishing up to 5 years

- **Factors of influence** – tumor size, location, stage of cancer, type of surgery, adjuvant radiotherapy

- **Support groups, family and literature important**

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*Early and late physical and psychosocial effects of primary surgery in patients with oral and oropharyngeal cancers: a systematic review; Annelise Mortensen, RN, MHA, Mary Jarden, MScN, PhD; OOOO; Vol 121, No 6; pp 583-594; June 2016*
# Radiation Effects on Normal Tissues

<table>
<thead>
<tr>
<th>TISSUE</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosa and lamina propria</td>
<td>Atrophy, mucositis, vascular changes, intimal thickening, luminal stenosis, obliteration, decreased blood flow</td>
</tr>
<tr>
<td>Muscle</td>
<td>Fibrosis, vascular changes</td>
</tr>
<tr>
<td>Bone</td>
<td>Decreased number of osteocytes and osteoblasts, decreased blood flow</td>
</tr>
<tr>
<td>Salivary glands</td>
<td>Atrophy of acini (serous), vascular changes, fibrosis</td>
</tr>
<tr>
<td>Pulp</td>
<td>Necrosis (orthovoltage)</td>
</tr>
</tbody>
</table>

Dental Management of the Medically Compromised Patient, 8th edition; James Little, Donald Falace et al; Elsevier/Mosby; 2013
### Complications of Radiation/Chemotherapies

- Nausea and vomiting
- Mucositis
- Taste alteration
- Secondary infections
- Hypersensitive teeth
- Speech and swallowing
- Nutritional status
- Dental and facial skeletal delay
- Skin toxicity
- Xerostomia (R)
- Radiation caries (R)
- Muscular dysfunction (R)
- Osteoradionecrosis (R)
- Pulpal pain and necrosis (R)
- Ulceration (C)
- Bleeding/Impaired hemostasis (C)
- Pain

**Ability to Tolerate Dental Care**
Nausea/Vomiting

- Acute onset
- TREATMENT: Ondansetron (Zofran)
- PREVENTION: Ondansetron (Zofran)
Mucositis

- Starts about the 2nd week
- Direct cytotoxic effects of radiation or antineoplastic agents on rapidly dividing oral epithelium
- Oral mucositis: 15 – 20 Gy; Ulceration mucositis: 30 Gy
- Occurs in up to 40% of chemotherapy patients (may alter chemotherapy doses or radiation schedule)
- Develops on nonkeratinized mucosa and adjacent to metallic restorations
- Generally subsides 1 – 2 weeks following treatment

Mucositis

- Red, raw, tender oral mucosa with epithelial sloughing
- Uncomfortable due to pain, dysphagia, loss of taste, difficulty eating, difficulty performing oral hygiene
- Appears worse near metallic restorations
- Possible to develop secondary infection

Internet photo
Mucositis - Treatment

- Maintain good oral hygiene
- Bland oral rinse with saline and baking soda
- Soft toothbrush
- Topical pain relief
- Analgesics
Mucositis – Topical Pain Relief

- 1-2-3 Mouthrinse (viscous lidocaine, benadryl, Maalox®)
- Kaopectate®
- Dyclonine HCL throat lozenges
- Gelclair® (Helsinn Healthcare S.A., Lugano, Switzerland)
- Caphosol® (EUSAPharma (USA), Inc)
- MuGard™ (Access Pharmaceuticals, Dallas, Tx)

The ADA Practical Guide to Patients with Medical Conditions, 2nd edition; Lauren Patton, Michael Glick editors; Wiley Blackwell; 2016
Mucositis - Prevention

- No effective preventative for radiation induced mucositis
- Ice chips – undergoing 5-fluorouracil, etidronate, high-dose melphalan chemotherapy
- Keratinocyte growth factor-1 (palifermin) - high-dose chemotherapy and total body irradiation
- Peridex has no impact on preventing mucositis
Hypogeusia / Dysgeusia

- Radiation > 60 Gy may lead to permanent loss of taste
- May be related to reduced salivary flow, taste receptor destruction, mucositis
- TREATMENT: Zinc, 220mg BID
- PREVENTION: None
Secondary Infections

- Candida and viral infections
- Radiation and stem-cell transplant patients
- Changes in microbial load of oral mucosa and skin

TREATMENT: Acyclovir or Valacyclovir (Herpes Simplex), Fluconazole, Ketoconazole, Clotrimazole

PREVENTION: Acyclovir or Valacyclovir (Herpes Simplex)
Speech and Swallowing

- Surgical and radiation induced
  - TREATMENT: Maxillary obturators
    - Swallowing maneuvers
    - Speech and swallowing therapy
    - Gastrostomy feeding tube
- PREVENTION: None
Nutritional Status

- Surgery, radiation and/or chemotherapy
- Poor healing
- Immunocompromised
- Independent negative prognostic sign
- TREATMENT/PREVENTION: High-protein, high moisture content nutritional supplements, gastrostomy tube, nutrition counseling
Radiation-Induced Skin Toxicity

- Affects up to 95% of patients
- Within 1 to 4 weeks of radiation
- Persist from 2 to 4 weeks post radiation
- Red, warm, rashy appearance
- 30 Gy – destruction of sweat and sebaceous glands
- PREVENTION: Ointments, creams
- TREATMENT: Routine skin care, ointments, dressings
Xerostomia

- 25 Gy can cause salivary gland degeneration
- Serous glands degenerate faster than mucous glands
- 1st week: 50 – 60% reduction
- 7th week: Flow ≈ 20%
- Oral functional changes

Internet photo
Signs of Hyposalivation

- Sticking of intraoral mirror to the buccal mucosa or tongue
- Frothy saliva
- No saliva pooling in floor of mouth
- Loss of papillae of tongue dorsum
- Altered/smooth gingival architecture
- Glassy appearance to the oral mucosa (especially palate
- Lobulated/deeply fissured tongue
- Cervical caries (> 2 teeth)
- Mucosal debris on palate (except under denture)

Diagnosis and management of xerostomia and hyposalivation; Alessandro Villa, Christopher L Connell, Silvio Abati; Therapeutics and Clinical Risk Management; Vol 11; pp 45-51; 2015
Xerostomia - Treatment

- Sipping water
- Saliva substitutes
- Salivary stimulants
- Mouth rinse
- Sialogogues
- Petrolatum ointment to lips
- Avoid carbonated, acidic, alcohol-based products
### Xerostomia - Treatment

<table>
<thead>
<tr>
<th>TREATMENT MODALITY</th>
<th>EXAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary Substitute</td>
<td>Carboxymethylcellulose with added mucopolysaccharide or glycerate polymer gel base <strong>Biotene ®</strong></td>
</tr>
<tr>
<td>Salivary Stimulant</td>
<td>Sugarless, xylitol-containing</td>
</tr>
<tr>
<td>Mouth Rinse</td>
<td>¼ teaspoon glycerine in 8 oz water</td>
</tr>
<tr>
<td>Sialogogues</td>
<td><strong>Pilocarpine</strong> 5mg three times daily <strong>Cevimeline</strong> 30mg three times daily</td>
</tr>
</tbody>
</table>

**Efficacy and safety of pilocarpine for radiation-induced xerostomia in patients with head and neck cancer: A systematic review and meta-analysis; Cai-Qi Cheng, BS, Hao Xu, BS, et al; JADA; Vol 147, No 4; pp 236-243; April 2016**

The ADA Practical Guide to Patients with Medical Conditions, 2nd edition; Lauren Patton, Michael Glick editors; Wiley Blackwell; 2016

Xerostomia - Prevention

- **Amifostine** - free radical scavenger preventing radiation damage to DNA
- Moderate to severe xerostomia
- Toxicity
- Need for daily injections
- Cost
Oral Moisturizers

pH and Erosive Potential of Commonly Used Oral Moisturizers; Alex J. Delgado, DDS, MS, Vilhelm G. Olafsson, DDS, MS, Terence E. Donovan, DDS; Journal of Prosthodontics; pp 1-5; 2015

- Critical pH for enamel: 5.2 and 5.5
- Critical pH for dentin: 6.7
- Accessed the pH and erosive potential of commercially available oral moisturizers using a pH meter and gravimetric analysis (tap water and citric acid controls)
<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>pH</th>
<th>EROSION POTENTIAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTx2 Spray (Oral Biotech, Albany, OR)</td>
<td>9.09</td>
<td>No loss of tooth structure</td>
</tr>
<tr>
<td>Rain (Xlear Inc., American Fork, UT)</td>
<td>7.10</td>
<td>No loss of tooth structure</td>
</tr>
<tr>
<td>Tap Water</td>
<td>6.99</td>
<td></td>
</tr>
<tr>
<td>Biotene Oral Balance (GlaxoSmithKline, Raleigh-Durham, NC)</td>
<td>6.61</td>
<td>No loss of tooth structure</td>
</tr>
<tr>
<td>Oasis (Oasis Consumer Health, Cleveland, OH)</td>
<td>6.33</td>
<td>Moderate loss of tooth structure</td>
</tr>
<tr>
<td>Dry Mouth Spray (Thayers Natural Remedies, Westport, CT)</td>
<td>6.30</td>
<td>Moderate loss of tooth structure</td>
</tr>
<tr>
<td>Biotene Moisturizing Mouth Spray (GlaxoSmithKline, Raleigh-Durham, NC)</td>
<td>6.11</td>
<td>Considerable loss of tooth structure</td>
</tr>
<tr>
<td>Mouth Cote (Parnell Pharmaceuticals, Inc., San Rafael, CA)</td>
<td>3.03</td>
<td>Considerable loss of tooth structure</td>
</tr>
<tr>
<td>Citric Acid</td>
<td>1.33</td>
<td></td>
</tr>
</tbody>
</table>

pH and Erosive Potential of Commonly Used Oral Moisturizers; Alex J. Delgado, DDS, MS, Vilhelm G. Olafsson, DDS, MS, Terence E. Donovan, DDS; Journal of Prosthodontics; pp 1-5; 2015
Dental Caries

- Related to salivary gland deficit
- Demineralization starts as early as 12 weeks
- Rampant caries
- Progressing rapidly in areas normally immune to caries
- TREATMENT: Routine dentistry
- PREVENTION: Daily oral hygiene
  - Re-call dental exams
  - Fluoride
Radiation Induced Dental Caries

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>PREVENTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amalgam</td>
<td>Topical fluoride</td>
</tr>
<tr>
<td>Fluoride-releasing resin-modified glass ionomer</td>
<td>Mouth rinses</td>
</tr>
<tr>
<td>Composite (anterior teeth)</td>
<td>Remineralizing agents</td>
</tr>
<tr>
<td>Full-coverage crowns</td>
<td>Xylitol-containing products</td>
</tr>
<tr>
<td></td>
<td>Restricted sugar containing foods</td>
</tr>
</tbody>
</table>
Trismus

- Related to radiation fibrosis
- Contraction of masticatory muscles or TMJ
- Limited opening impairs proper oral hygiene, nutrition
- TREATMENT: Physiotherapy with tongue depressors, Analgesics, Anti-inflammatory meds
  - Pentoxifylline and tocopherol (vitamin E)
  - Coronoidectomy
- PREVENTION: Mouth opening exercises (20x TID)
  - TheraBite ® Jaw Rehabilitation System
    - (Craniomandibular Rehab, Inc., Denver, Co)
Trismus

The TheraBite System

Internet photos
Osteoradionecrosis (ORN)

- Exposed, devitalized bone in a radiation field without healing for 3 months without any evidence of tumor recurrence

- Patients may experience
  - pain
  - dysesthesia (disagreeable sensation produced by ordinary stimuli)
  - trismus
  - orocutaneous fistula
  - pathologic fractures
ORN Pathophysiology

1938 – exposure to radiotherapy above a critical dose, local injury, development of an infection (Watson and Scarborough)

1960 – direct damage to the osteocytes, vascular changes noted histologically (Gowgiel)

1970 – radiation, trauma, infection (Meyer)

1983 – hypovascular, hypoxic, hypocellular, bacteria as contaminants (Marx)

2004 – radiation induced fibroatrophic process (Delanian)
ORN Risk Factors

- Radiation
  - type, total dose, fractionation, field
- Location
  - close to the mandible
  - tonsillar region
  - retromolar region
- Dentoalveolar trauma
- Infection (actinomyces)

Most significant predictor of ORN

Internet photos

- Patient age
- Dental status
- Oral hygiene
- Continued smoking/alcohol
- Nutritional status
 Predicting ORN

Patient and treatment-related risk factors for osteoradionecrosis for the jaw in patients with head and neck cancer; Jan-Dirk Raguse, MD, DMD, Jaber Hossamo, MD, et al; OOOO, Vol 121, No 3; pp 215-221; March 2016

- Any comorbidity
- Poor oral hygiene
- Tumor osteotomy in the lower jaw
- Dentoalveolar surgery by a surgeon without specific training
## ORN Staging

### Store and Boysen Classification System

<table>
<thead>
<tr>
<th>STAGE EVENT</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Mucosal defects only</td>
</tr>
<tr>
<td>1</td>
<td>Radiologic evidence of necrotic bone with intact mucosa</td>
</tr>
<tr>
<td>2</td>
<td>Positive radiologic findings with denuded bone intraorally</td>
</tr>
<tr>
<td>3</td>
<td>Clinically exposed bone, verified on imaging techniques, skin fistula and infection</td>
</tr>
</tbody>
</table>

### Marx and Meyers System

<table>
<thead>
<tr>
<th>STAGE EVENT</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt; 2mm of exposed bone with or without pain and with radiological signs of diffuse demineralization</td>
</tr>
<tr>
<td>2</td>
<td>&gt; 2mm of exposed bone</td>
</tr>
<tr>
<td>3</td>
<td>Pathological fracture, oral fistula, fistula or lesion of the inferior border of the mandible</td>
</tr>
</tbody>
</table>
ORN Treatment

- Most cases develop within the first 3 years post radiation completion
- Conservative measures
- Hyperbaric oxygen treatment (HBO)
- PENTOCLO
- Surgery
Hyperbaric Oxygen Treatments

- 20 preoperative dives
- 2.4 atmosphere absolute for 90 minutes
- 10 post operative dives (total cost $9,000 - $16,000)
- Increases oxygen supply in hypoxic tissue
- Stimulates fibroblast proliferation and angiogenesis
- Debate exists over efficacy
Internet photos
Hyperbaric Oxygen Treatments

- Barotraumatic otitis and pneumothorax
- Reduced visual acuity
- Claustrophobia
- Seizures resulting from oxygen toxicity
- Angiogenic effect promoting growth of residual tumor??
- Effective due to the oxygen gradient in affected bone
PENTOCLO Treatment

**FIRST PHASE**
- Lasts 4 – 6 weeks
- Daily treatments
- 2 g amoxicillin-clavulanic acid
- 1 g ciprofloxacin
- 50 mg fluconazole
- 20 mg prednisone
- 20 mg omeprazole

**SECOND PHASE**
- Continued until complete healing (five days a week)
- 800 mg pentoxifylline
- 1 g tocopherol (vitamin E)
- 1600 mg clodronate **** (not approved in the US)
- 20 mg predisone (Sat and Sun)

Patient Discussion of the Dental Concerns with Radiation Treatment

Reviewed with the patient what to expect with radiation of the _________________. Explained to the patient that during the active radiation treatment that they can expect redness and inflammation of the oral tissues. The soreness may make it difficult to swallow or eat foods. The patient may also feel increasing tightness of the oral soft tissues. The effect of radiation treatment to the salivary glands was discussed with the patient. The mouth will start to feel dry as the salivary glands are affected. The use of dental products to help in dry mouth was discussed. Explained the function of saliva to the patient, it was explained that as the salivary flow decreases the risk for development of dental caries increases due to the loss of saliva which acts as a buffer to the acids that cause caries formation. The carious lesions typically start at the gum line so it is very important to keep the teeth clean to prevent caries formation. Fluoride use was discussed. The importance of monitoring the oral tissues for any signs of irritation because radiation therapy affects the blood flow to the soft tissues and bone was emphasized to the patient. The decreased blood flow can lead to ulceration of the soft tissue and possible osteoradionecrosis. Discussed with the patient the development of osteoradionecrosis and discussed the progression that as levels of radiation increase risk of osteonecrosis increases. Discussed the amounts of radiation to the tissues and explained that if any areas of dentition were going to receive more than 60 Gy (and possibly >50 Gy) then those teeth would need to be extracted, along with any nonsalvageable teeth or teeth with poor prognosis. If the patient is wearing any type of removable dentures advise the patient to be very careful of any irritation that can possibly lead to osteoradionecrosis. In 25% of the cases the patient will get areas of spontaneous osteonecrosis in spite of all preventative measures. Reviewed with the patient what would happen in the case of development of osteoradionecrosis. The protocol for treatment is initially patient would be given a mouthrinse and antibiotics to try to heal the soft tissue ulceration. If the area did not resolve with initial treatment it may be necessary to remove the necrotic bone under local anesthetic. If the osteonecrosis does not resolve with conservative measures it may be necessary to treat the patient with hyperbaric oxygen or possibly other medications. The hyperbaric oxygen protocol was reviewed with the patient and that this treatment would only be used in the most severe osteonecrosis situations. Surgery may be required.
Management of the Neck

- Status of the cervical lymph nodes most important prognostic factor
- Overall prognosis decreases by approximately 50% with cervical lymph nodes metastasis
- 40% patients initially found with nodal metastasis
- Occult metastasis occurs in 20 – 45% of patients staged as N0
- Tumor thickness (≤ 5mm, 10%; > 5mm, 46%) only independent predictor of tumor metastasis

Tumor Infiltration Depth as Predictor of Nodal Metastasis in Early Tongue Squamous Cell Carcinoma; Achille Tarsitano, MD; Giacomo Del Corso, DDS, et al; J Oral Maxillofacial Surg; 74:523-527; 2016
Netter’s Head and Neck Anatomy for Dentistry

The ADA Practical Guide to Patients with Medical Conditions, 2nd edition
## Neck Node Levels and Head and Neck Cancer Lymphatic Drainage Patterns

<table>
<thead>
<tr>
<th>LEVEL AND NODAL GROUPS</th>
<th>CANCER SITES OF LYMPHATIC SPREAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>I–Submental and submandibular nodes</td>
<td>Lip; anterior tongue; floor of mouth; gingiva; buccal mucosa</td>
</tr>
<tr>
<td>II–Upper jugulodigastric group</td>
<td>Oral cavity; pharynx; larynx</td>
</tr>
<tr>
<td>III–Middle jugular nodes</td>
<td>Nasopharynx; oropharynx; oral cavity; hypopharynx; larynx</td>
</tr>
<tr>
<td>IV–Inferior jugular nodes</td>
<td>Hypopharynx; subglottic larynx; esophagus</td>
</tr>
<tr>
<td>V–Posterior triangle group</td>
<td></td>
</tr>
<tr>
<td>VI–Anterior compartment group</td>
<td></td>
</tr>
</tbody>
</table>
# Lymphatic Drainage

<table>
<thead>
<tr>
<th>CANCER SITE</th>
<th>METASTASIZE TO LEVELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharynx</td>
<td>II, III, IV</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td></td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>I, II, III</td>
</tr>
<tr>
<td></td>
<td>(Level IV: 3 – 17 %)</td>
</tr>
<tr>
<td></td>
<td>(Level V: 1 – 6 %)</td>
</tr>
</tbody>
</table>
Treatments

- Surgery
- Radiation
- Gamma knife
- Chemotherapy
- Surgery or Radiation for early disease (stage 1-2 disease)
- Combined (stage 3 - 4 disease)
Radiation Treatment

- Extracapsular spread
- Multiple metastatic nodes (more than 3)
- Positive margins
- Perivascular emboli, perineural spread relative indications
- 6 weeks, 30 fractions
Radiation Regimens

- **Hyperfractionation** – increases number of treatment intervals and lowers the individual dose

- **Accelerated fractionation** – increase total radiation dose and decrease the total treatment time

- **Intensity-modulated radiation therapy (IMRT)** – multiple beams with multileaf collimation, 3-D conformational planning, and dose escalation
  - minimize toxicity to organs
  - improves quality of life
“Old Time” Radiation Treatment
Intensity-Modulated Radiation Therapy (IMRT)

- Modulates the intensity of the radiation beam in multiple small volumes
- Higher radiation focused to regions in the tumor
- Minimize dose to surrounding normal critical structures
- Potential to reduce treatment toxicity, even when doses are not increased
- Treat prostate, head and neck, central nervous system cancers

www.radiologyinfo.org
Radiotherapy procedure

www.radiologyinfo.org
Radiation Dose in Tooth Bearing Regions

Dosimetric distribution to tooth-bearing areas in intensity-modulated radiation therapy for head and neck cancer: a pilot study; Sun-Yung Bak, DDS, X. Sharon Qi, PhD, et al; 0000; Vol 121, No 1; pp 43-48; January 2016

- Patients with advanced tumors
- Incidence decreasing for 11.8% (1968) to 5.4% (1992) to 3% (1997)
- Dosimetric distribution dependent on tumor site, arch type (maxilla or mandible), location of teeth in the arch
- Found in mandible with doses of 5000 cGy to 7000 cGy
- Found in maxilla (nasopharyngeal carcinoma) with doses 7000 cGy to 8000 cGy
- Patients receiving concurrent chemotherapy, biological effects on tissues as though receiving an additional 1000 cGy
### Radiation Dose – Base of Tongue

<table>
<thead>
<tr>
<th>TOOTH BEARING AREA</th>
<th>MANDIBLE in cGy (high)</th>
<th>MAXILLA cGy (high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>3363 (3790)</td>
<td>2785 (3619)</td>
</tr>
<tr>
<td>Premolar</td>
<td>4036 (4645)</td>
<td>3568 (4045)</td>
</tr>
<tr>
<td>Molar 1</td>
<td>4672 (5093)</td>
<td>4138 (4477)</td>
</tr>
<tr>
<td>Molar 2</td>
<td>4674 (5695)</td>
<td>4381 (5389)</td>
</tr>
<tr>
<td>Molar 3</td>
<td>6030 (6379)</td>
<td>5100 (7020)</td>
</tr>
</tbody>
</table>

Internet photo

Dosimetric distribution to tooth-bearing areas in intensity-modulated radiation therapy for head and neck cancer: a pilot study; Sun-Yung Bak, DDS, X. Sharon Qi, PhD, et al; 0000; Vol 121, No 1; pp 43-48; January 2016
## Radiation Dose – Tonsil

<table>
<thead>
<tr>
<th>TOOTH BEARING AREA</th>
<th>MANDIBLE in cGy (high)</th>
<th>MAXILLA cGy (high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>3494 (4327)</td>
<td>3886 (4051)</td>
</tr>
<tr>
<td>Premolar</td>
<td>4249 (4852)</td>
<td>4179 (4570)</td>
</tr>
<tr>
<td>Molar 1</td>
<td>5228 (5781)</td>
<td>4882 (5596)</td>
</tr>
<tr>
<td>Molar 2</td>
<td>4831 (5666)</td>
<td>4760 (5200)</td>
</tr>
<tr>
<td>Molar 3</td>
<td>4997 (5287)</td>
<td>4998 (5231)</td>
</tr>
</tbody>
</table>

Dosimetric distribution to tooth-bearing areas in intensity-modulated radiation therapy for head and neck cancer: a pilot study; Sun-Yung Bak, DDS, X. Sharon Qi, PhD, et al; 0000; Vol 121, No 1; pp 43-48; January 2016

Internet photo
## Radiation Dose – Larynx

<table>
<thead>
<tr>
<th>TOOTH BEARING AREA</th>
<th>MANDIBLE in cGy (high)</th>
<th>MAXILLA cGy (high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>1528 (2495)</td>
<td>1416 (2716)</td>
</tr>
<tr>
<td>Premolar</td>
<td>2341 (2623)</td>
<td>981 (1938)</td>
</tr>
<tr>
<td>Molar 1</td>
<td>2276 (2749)</td>
<td>1005 (1320)</td>
</tr>
<tr>
<td>Molar 2</td>
<td>2448 (3009)</td>
<td>714 (1835)</td>
</tr>
</tbody>
</table>

Dosimetric distribution to tooth-bearing areas in intensity-modulated radiation therapy for head and neck cancer: a pilot study; Sun-Yung Bak, DDS, X. Sharon Qi, PhD, et al; 0000; Vol 121, No 1; pp 43-48; January 2016

Internet photo
**Radiation Dose – Nasopharynx**

<table>
<thead>
<tr>
<th>TOOTH BEARING AREA</th>
<th>MANDIBLE in cGy (high)</th>
<th>MAXILLA cGy (high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>3127 (3957)</td>
<td>4046 (4870)</td>
</tr>
<tr>
<td>Premolar</td>
<td>3914 (4588)</td>
<td>4238 (4738)</td>
</tr>
<tr>
<td>Molar 1</td>
<td>2877 (4525)</td>
<td>4481 (4943)</td>
</tr>
<tr>
<td>Molar 2</td>
<td>3389 (4731)</td>
<td>5174 (5914)</td>
</tr>
</tbody>
</table>

Dosimetric distribution to tooth-bearing areas in intensity-modulated radiation therapy for head and neck cancer: a pilot study; Sun-Yung Bak, DDS, X. Sharon Qi, PhD, et al; 0000; Vol 121, No 1; pp 43-48; January 2016
Radiation Dose – Hypopharynx

<table>
<thead>
<tr>
<th>TOOTH BEARING AREA</th>
<th>MANDIBLE in cGy (high)</th>
<th>MAXILLA cGy (high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>2458 (2553)</td>
<td>3298 (3521)</td>
</tr>
<tr>
<td>Premolar</td>
<td>4126 (4353)</td>
<td>4164 (4592)</td>
</tr>
<tr>
<td>Molar 1</td>
<td>3418 (3510)</td>
<td>4410 (4790)</td>
</tr>
<tr>
<td>Molar 2</td>
<td>5043 (6037)</td>
<td>4464 (5406)</td>
</tr>
</tbody>
</table>

Dosimetric distribution to tooth-bearing areas in intensity-modulated radiation therapy for head and neck cancer: a pilot study; Sun-Yung Bak, DDS, X. Sharon Qi, PhD, et al; 0000; Vol 121, No 1; pp 43-48; January 2016
Tooth-Specific Dosimetry

Prospectively-collected, tooth-specific dosimetry correlated with adverse dental outcomes; Alan T. Monroe, MD, Debra Flesher-Bratt, RDH, et al; OOOO; Vol 122, No 2; pp 158-163; August 2016.

- Confirmed a threshold dose near 5000 cGy as a risk factor for ORN (0.1% vs 1.2% above 5000 cGy)

- Individual teeth exceeding this historical threshold clinically unaffected almost 99% of the time

- At patient level, 3-year actuarial risk of ORN (2.5%) and periodontal disease (36.6%)

- At 4 years, actuarial risk of ORN increased to 12%

- Assessed per tooth, 3-year actuarial risk of ORN (0.1%) and periodontal disease (5.1%)
Extractions and Laryngeal Cancer

Establishing a targeted plan for prophylactic dental extractions in patients with laryngeal cancer receiving adjuvant radiotherapy; Courtney Hentz, MD, Aidnag Z. Diaz, MD, MPH, et al; OOOO; Vol 122, No 1; pp 43-49; July 2016

- “With the exception of the posterior molars (particularly in node positive patients), radiation exposure falls below the threshold for pre-radiotherapy tooth extractions (50 Gy) in patient with laryngeal cancer receiving adjuvant radiotherapy.”

- T and N stages laryngeal cancers influence the radiation dose to the mandible

- No significant difference between ipsilateral and contralateral teeth or the parotid glands
Dental Implications

- Antibiotics, antivirals, analgesics do not appear to interfere with radiation
- Radiographic changes after radiation
- Dental implants 84.3% success rate in irradiated bone

**Irradiated patients and survival rate of dental implants:**
A systematic review and meta-analysis; Adhara Nobrega Smith, DDS, Joel Ferreira Santiago Jr, DDS, et al; J Prosthet Dent; April 2016

- Reports of oral malignancy imitating peri-implantitis

Changes on Panographic Images

Mandibular changes on panoramic imaging after head and neck radiotherapy; King Chong Chan, DMD, MSc, Susanne E. Perschbacher, DDS, MSc, et al; 0000; Vol 121, No 6; pp 666-672; June 2016

- Incidental widening of the periodontal ligament space along the mandibular tooth roots
- Bone sclerosis, periodontal disease-like bone loss, bone resorption observer variability
- Absence of adjacent bone destruction
- No treatment required

Internet photo
Hungarian mummy offers clues to cancer mystery

By Michael Casey - Published February 25, 2016 - FoxNews.com

Mummies have long offered up a wealth of medical information, from the role that diet plays in heart disease to the ancient origins of tuberculosis.

Now, a new PLOS One study of 16th century Hungarian mummies concludes that a genetic predisposition to colorectal cancer preceded the advent of modernization. If confirmed, that would mean the role of processed food, physical inactivity and other factors that were not commonplace back then may not play as important a role in causing the cancer as previously thought.

"Colorectal cancer is among the most common health hazards of modern times," Rina Rosenstein of Tel Aviv University's (TAU) Department of Clinical Microbiology and Immunology and a co-author of the study in PLOS One, said in a statement. "And it has a proven genetic background. We wanted to discover whether people in the past carried the APC mutation — how common it was, and whether it was the same mutation known to us today. In other words: Is the increase in the incidence of cancer the result of man's manipulation of nature alone?"
Study: U.S. cancer deaths are mostly preventable

Americans can prevent their risk of dying from cancer simply by maintaining a healthy lifestyle, according to a new study in the Journal of the American Medical Association Oncology. Such lifestyle change would decrease cancer deaths by 67 percent for men and 59 percent for women. Similarly, a healthy lifestyle would drop the discovery of new cancers by 41 percent in women and 63 percent in men.

What does this study mean by a “healthy lifestyle”? Don’t smoke, don’t drink too much, maintain a body mass index between 18.5 and 27.5, and exercise 73 to 150 minutes weekly.

So, maybe it’s time to cut back a drink or two at happy hour and jump on an elliptical.

About 89,500 white women and 46,300 white men participated in the study, which looked at deaths of carcinoma (all cancers except skin, brain, lymphatic, hematologic and nonfatal prostate malignancies). The study only looked at Caucasians to avoid any “racial distributions.”

In 2014, 16.8 percent of Americans were identified as smokers (smoked almost every day or have smoked at least 100 cigarettes in their lifetime), according to the Centers for Disease Control and Prevention.

An estimated 598,490 Americans are expected to die of cancer this year, according to the American Cancer Society.

The study published in JAMA analyzed data from the Nurses’ Health Study, the Health Professionals Follow-up Study and national cancer statistics.

A healthy lifestyle has been shown to reduce the risk of a number of wellness concerns, including memory decline.

A study published by the American Association for the Advancement of Science in January 2015 challenges this new cancer research. It attributes cancer risk to stem cell divisions, not lifestyle, saying the majority of people who get cancer have “bad luck,” although some environmental factors and family genetics can play a role.
Cancer Diagnosis

**Nation**

**NEWS DIGEST**

Crews work to contain oil after train derailment

SEATTLE — Environmental crews worked Saturday to contain a sheen of oil that appeared in the Columbia River near the Washington-Oregon state line after a Union Pacific train derailed and caught fire, but officials said there was no immediate indication of harm to wildlife.

Sixteen of the 96 tank cars on the train derailed Friday near Mosier, Ore., about 70 miles east of Portland. Four burned, sending up a thick plume of black smoke. Firefighters extinguished the flames Saturday.

The Associated Press

**MAN PARTIALLY BURIES BOSSES IN WORK-SITE FIGHT**

A Florida man buried his bosses nearly waist-deep in dirt during an argument at a construction site that ended in a

**MEDICINE**

‘Liquid biopsies’ work well, cancer study finds

Blood tests to analyze tumors may cost less, cause less pain than surgical procedures

CHICAGO — The biggest study to date on new blood tests to detect and analyze cancerous tumors concluded that such “liquid biopsies” are a reliable alternative to conventional biopsies, offering a potentially cheaper and less invasive way of monitoring malignancies.

The study, which involved genetic information from more than 15,000 patients and 50 tumor types, compared tumor samples from liquid biopsies with those from traditional biopsies. In the vast majority of cases, the genetic changes detected by the blood tests agreed with the mutations identified in the tissue biopsies.

The findings suggest that liquid biopsies provide an accurate snapshot of the genomic landscape of the tumor, and a new release that accompanied the data, which was released Saturday at the annual meeting of the American Society of Clinical Oncology in Chicago.

The liquid biopsy test used in the study was Guardant360, which looks for about 70 mutations. It is made by Guardant Health, which also funded the effort.

Liquid biopsies are a hot field, with several companies, including Foundation Medicine, offering the tests or working to develop them. Such tests are designed to pick up in the bloodstream small pieces of DNA shed by cancerous tumors, information that can be used to tailor and monitor the therapies.

Currently, doctors largely use surgical biopsies for information about tumor’s genetic mutations and whether the cancer can be treated with available drugs. But such biopsies are invasive and can be expensive and painful.

Philip Mark of the University of California at Davis, who presented the findings, said that the study indicates that a liquid biopsy can be a “highly informative, minimally invasive alternative to a traditional biopsy, especially when the

Researchers say a blood test to detect cancer mutations produced results that agreed with those of invasive tumor biopsies.

Cancer is in a difficult-to-reach location such as the brain.

He also said at a news briefing that two-thirds of the liquid-biopsy results in the study were “actionable,” meaning patients had mutations that could be treated by drugs.

Laura McCauley

**THE WASHINGTON POST**
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Hallmarks of Cancer Cells

- Sustaining proliferative signaling
- Evading growth suppressors
- Deregulating cellular energetics
- Avoiding immune destruction
- Resisting cell death
- Enabling replicative immortality
- Genome instability & mutation
- Tumor-promoting inflammation
- Inducing angiogenesis
- Activating invasion & metastasis
Patients Undergoing Chemotherapy

- Control tumor with limited toxicity
- Not the same level of immunocompetence as for bacterial infections
- For example, in leukemias cancer populations reach $10^{12}$; a 99.9% reduction results in a residual population of a billion cells or more ($10^7$)
- Combination drug therapy regimen
- Drug resistant cells and cancer stem cells - recurrence
Chemotherapy – Head and Neck Cancer

- Late stage disease
- Recurrent cancer
- **Neoadjuvant** (induction)
- **Concurrent** (at the same time to increase radiosensitivity)
- **Adjuvant** (after surgery)
- Three cycles – day 1, 22, 43
- Cisplatin, 5-fluorouracil (5-FU), or both

“In the euphonic chorus to date, however, head and neck cancer – a disease for which no effective systemic therapies exist once it has metastasized – has lost attention and has had only one FDA-approved drug for standard of care for head and neck cancer in the last 30 years”. **Editorial, The fourth modality: immunotherapy for head and neck cancer hits pay dirt; Dr. R. Bryan Bell; OOOO, Vol 121, No 6; p 575-577; June 2016**
Chemotherapy – Head and Neck Cancer

- Organ preservation
  - bleomycin or peplomycin

- Immunotherapy
  - cetuximab (anti-epidermal growth factor receptor antibody)

- Chemoprevention
  - vitamins, minerals, anti-inflammatory agents, Retinoids
Cancer Treatments

- Surgery
- Radiation
- Chemotherapy
- Immunotherapy

- Changes in immunological, histochemical, biological markers, physics in imaging techniques, delivery techniques (retrograde superselective intra-arterial chemotherapy)
Biological Therapy

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015

- Uses living organisms or a synthetic version of them
- Food and Drug Administration defines biologics as
  “any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment, or cure of disease or injuries of man.”
- Includes artificial valves or genetic therapy
- Biologic drugs include vaccines, blood and blood-derived preparations, antitoxins, growth hormones, human insulin, gene therapy, recombined therapeutic proteins and allergens, new biologics
Biological Therapy - Classes

- Key signaling proteins (cytokines or natural antagonists)
- Monoclonal antibodies
- Fusion proteins (soluble)

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015
Signaling Proteins, Cytokines

- Process information from immediate environment or from integration of several simultaneous signals
- Signals can be hormones, neurotransmitters, or mechanical stimuli
- Signaling molecules bind to receptor proteins to initiate physiological change
- Soluble proteins, peptides, glycoproteins help cell signaling
- Immunomodulators regulate host responses to inflammation and infections
- Examples: Interferon $\alpha$ and $\beta$, interleukin2 (IL-2)
- Suffix (soluble cytokines): $-\text{cept}$ (Etanercept, Abatacept)

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015
Monoclonal Antibodies

- Bind to target cells to send signal arrest (apoptosis), modulate a receptor, interfere with ligand binding
- Organ transplant recipients, act as adjunctive immunosuppressants
- Can be used to deliver agents (radioisotopes, toxins, cytokines)
- Singular molecular species active against a single target antigen
- Highly specific
- Immunotherapy – human antibodies and hybrid cells
- Suffix: -mab (Denosumab, Abciximab)

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015
MAB’s - What’s In a Name?

- Middle of the drug name reflects the disease drug was initially intended to treat
  - **lim**- inflammatory
  - **cir**- cardiovascular
  - **tu**- tumors or neoplastic diseases

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015
Fusion Proteins

- Soluble cytokine receptors or ligands
- Composed of transmembrane proteins connected to another molecule
- Competitively inhibit the binding of a ligand to its specific receptor to prevent unwanted effects
- Half-life can be expanded, cytotoxicity can be enhanced, activity can be increased

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015
Side Effects of Biologics

- Injection/infusion site effects
- Flu-like symptoms
- Hematologic disorders
- Infections
- Immunological reactions
- Cancer
- Hepatotoxicity
- Neurologic disorders
- Periodontal disease

Biological therapy and dentistry: a review paper; Lida Radfar, DDS, MS, Roshanak E. Ahmadabadi, DDS, et al; 0000; Vol 120, No 5; pp 594-601; November 2015
Dental Considerations with Biologics

- Obtain a complete blood count and platelet count
  - neutropenia absolute neutrophil count < 1000 cells/mm³ may require antibiotics
  - platelet count < 50,000/mm³ may require transfusion
- Obtain a PT, PTT, and INR if patient has liver disease
  - INR between 2 and 3.5 considered safe
- Consult with patient’s primary physician for possible discontinuation of biologic agents
  - stop 4 – 5X the drug’s half-live before dental surgical procedures
  - restart when wound healing satisfactory
- No information regarding antibiotic prophylaxis for patients on biologics
Biological Agents

Oral Squamous Cell Carcinoma Presenting in a Patient Receiving Adalimumab for Rheumatoid Arthritis; Anna Beattie, BDentSc, Leo F. A. Stassen, MA, Kumara Ekanayake, MBBCh, MS, BBDS, MSc; J Oral Maxillofacial Surg; 73:2136-2141; 2015

- Target specific steps in proinflammatory pathway
- Tumor necrosis factor-α (TNF-α) inhibitors (adalimumab)
- Interleukin inhibitors (ustekinumab)
- Lymphocyte modulators (alefacept – T lymphocyte modulator, rituximab – B-lymphocyte modulator)

Biopsy Non-healing Sites
Stem Cell Transplantation

- Restore blood-forming stem cells (destroyed by very high doses of chemotherapy or radiation therapy)
- Stem cells provide white blood cells, red blood cells, platelets
- Donors – autologous, allogeneic, syngeneic
- Stem cells do not work directly against cancer
- Multiple myeloma and some types of leukemia (graft-versus-tumor effect)
- Used to treat patients with leukemia and lymphoma

National Cancer Institute at www.cancer.gov
Posted: April 29, 2015
Stem Cell Transplantation – Dental Concerns

- Optimize oral health prior to transplantation
- Graft-versus-host disease (GVHD)
  - allogeneic transplants
  - donor cells recognize host cells as foreign
  - acute GVHD occurs within first 100 days (mild rash to diffuse severe sloughing)
  - chronic GVHD may occur several years after transplantation (resembles lichen planus, affects mainly tongue, labial mucosa, buccal mucosa)
Stem Cell Transplantation – Treatments

- Topical corticosteroids
- Topical anesthetics
- Analgesics as necessary
- Topical fluoride
- Psoralen and Ultra-Violet A (PUVA) therapy

Expect some degree of graft-versus-host disease in most allogeneic bone marrow transplant recipients

The most common oral malignancy is squamous cell carcinoma
Mantel Radiation Fields

Hodgkin Lymphoma Staging

Usually around 30 Gy

Internet photos
Medication-Related Osteonecrosis of the Jaws

- Current or previous treatment with antiresorptive or antiangiogenic agents
- Exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region that has persisted for longer than 8 weeks
- No history of radiation therapy to the jaws or obvious metastatic disease to the jaws
VEGF = vascular endothelial growth factor
RANKL = receptor-activator of nuclear factor kappa beta ligand
PTH = parathyroid hormone
OPG = osteoprotegerin
M-CSF = macrophage colony-stimulating factor
Think Road Repair

Internet photos
# Bisphosphonates

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ROUTE INDICATION</th>
<th>DOSE (mg)</th>
<th>FREQUENCY</th>
<th>RELATIVE POTENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etidronate</td>
<td>Oral Paget Disease</td>
<td>300-700</td>
<td>Daily x 6 months</td>
<td>1</td>
</tr>
<tr>
<td>Alendronate</td>
<td>Oral Osteoporosis</td>
<td>75</td>
<td>Weekly</td>
<td>1,000</td>
</tr>
<tr>
<td>(Fosamax)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risedronate</td>
<td>Oral Osteoporosis</td>
<td>35</td>
<td>Weekly</td>
<td>1,000</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>Oral Osteoporosis</td>
<td>150</td>
<td>Monthly Every 3 months</td>
<td>1,000</td>
</tr>
<tr>
<td>(Boniva)</td>
<td>IV Osteoporosis</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pamidronate</td>
<td>IV Bone Metastasis</td>
<td>90</td>
<td>Monthly</td>
<td>5,000</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>IV Bone Metastasis</td>
<td>4 (Zometa)</td>
<td>Monthly Yearly</td>
<td>10,000+</td>
</tr>
<tr>
<td></td>
<td>Osteoporosis</td>
<td>5 (Reclast)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from University of Miami Division of Oral and Maxillofacial Surgery Position Paper on Drug Induced Osteonecrosis of the Jaws, April 2014
Are there other meds with a similar therapeutic effectiveness?

Denosumab (Prolia, Xgeva)

- human monoclonal antibody
- inhibits osteoclasts
- does not bind to bone (diminished after 6 months)
- does not inhibit angiogenesis
- no soft tissue toxicity
- may cause osteonecrosis of the jaws (ONJ)
- Denosumab induced ONJ may resolve more rapidly with a drug holiday than bisphosphonates
Bisphophonate Radiograph
Why in the Jaws?

- Alveolar crest remodels
  - 10X the rate of the tibia
  - 5X the rate at the inferior border of the mandible
  - 3 – 5X the rate of the bone at the level of the mandibular canal

- Alveolar bone has greater uptake of bisphosphonates and accumulates at higher concentrations

- Alveolar bone depends more on osteoclastic bone resorption/remodeling
Lamina dura cannot remodel and becomes hypermineralized (sclerosis and widened PDL)

Alveolar bone cannot respond with new bone formation

Overlying mucosa is deprived of its supporting blood supply and breaks down

Clinically exposed bone

Also seen over tori
Medical Indications for Bisphosphonates

- Most cancers cannot resorb bone on their own
- They recruit the osteoclast to resorb bone
- The osteoclast does not recognize it is being activated by a pathologic rather than physiologic process
- The cancer spreads into the resorbed bone
Medical Indications for Bisphosphonates

- Stabilizing osteolysis from metastatic deposits of various malignancies in bone
  - multiple myeloma, metastatic breast and prostate cancer
- Reducing the hypercalcemia associated with certain malignancies
- Paget disease of bone (accelerated bone resorption and apposition)
- Osteoporosis
- “off label” for osteopenia
Risk of Developing MRONJ

- **Duration** of continuous therapy
- Concomitant use of **steroids** (increases the toxicity of bisphosphonates)
- History of **methotrexate** use (rheumatology/autoimmune patients)
Laboratory Tests

- C-terminal cross-linking test (CTX)
- Measure of bone remodeling through serum markers

<table>
<thead>
<tr>
<th>VALUE (pg/ml)</th>
<th>RISK FOR OSTEONECROSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>High</td>
</tr>
<tr>
<td>100 – 125</td>
<td>Moderate</td>
</tr>
<tr>
<td>126 – 150</td>
<td>Minimal</td>
</tr>
<tr>
<td>&gt; 150</td>
<td>Clinically Normal Bone</td>
</tr>
</tbody>
</table>

CTX values increase **24 pg/ml** each month
Serum C-Telopeptide Cross-link of Type 1 Collagen

Assessing the utility of serum C-telopeptide cross-link of type 1 collagen as a predictor of Bisphosphonate-related osteonecrosis of the jaw; A systematic review and meta-analysis; Reyes Enciso, PhD, Jill Keaton, DMD, MS, et al; JADA; Vol 147, No 7; p 551-560; July 2016

Meta-analysis of 9 controlled studies

“no significant difference in mean sCTX values between patients with BRONJ and control participants”

second meta-analysis with 4 studies

“no significant difference in risk of having an sCTX value below 150 {pg/ml} for patients with BRONJ compared with control participants”
Dental Risk Factors

- Any condition or procedure that increases the demand for bone turnover/renewal
- Periodontal disease
- Dental abscesses
- Traumatic occlusion
- Invasive dental procedures
- Extractions
- Implant placements
- Periodontal surgery
- Apicoectomies
- Bone grafts
Periodontal Disease Preceding Osteonecrosis

Periodontal disease preceding osteonecrosis of the jaw (ONJ) in cancer patients receiving antiresorptives alone or combined with targeted therapies: report of 5 cases and literature review; Ourania Nicolatou-Galitis, DDS, Evangelia Razis, MD, et al; OOOO; Vol 120, No 6; pp 699-706; December 2015

“The present study suggests that pain, tooth mobility, purulence, periodontal ligament widening, and increased alveolar bone density in patients who receive antiresorptives or angiogenesis inhibitors may be signs of developing osteonecrosis.”
Disease Stage and Mode of Therapy

Patients in stage 1 or 2 more likely better outcomes than state 3 disease

Mandible most common location for MRONJ

Patients receiving operative care 28X more likely positive outcome

Occur mostly in the elderly (mean age 68.9 years)
Disease Stage and Mode of Therapy Are Important Determinants of Treatment Outcomes for Medication-Related Osteonecrosis of the Jaw; Salvatore L. Ruggiero, DMD, MD, Nina Kohn, MBA, MA; J Oral and Maxillofacial Surg; 73:S94-S100; 2015

- Zoledronic acid accounted for 57.3% of exposure cases
- Relationship between Denosumab (Xgeva) and antiangiogenic agents (Sunitinib, Sorafenib, Bevacizumab, Everolimus) and MRONJ
- Least potent or poorly absorbed antiresorptive medications (osteoporosis) have longest exposure times
- Duration of therapy did not have an effect on the outcome of treatment
Manage with antibiotics, antimicrobial rinses, oral hygiene (conservative management)

Bone turnover markers are not endorsed or recommended for determining ONJ risk

Drug holidays have not been validated

Metastatic cancers identified in bone samples (multiple myeloma, metastatic breast cancer)

Soft tissue toxicity a leading hypothesis in pathogenesis of ARONJ (fibroblasts and macrophages)

ARONJ = Antiresorptive Agent-induced Osteonecrosis of the Jaw
Parathyroid hormone has been shown to increase bone healing in periodontal defects, possibly enhance new bone formation around implants, and provide ONJ resolution in humans.

Studies to evaluate the role of biofilms and ARONJ pathophysiology.
## Staging and Treatment 2014 Update

<table>
<thead>
<tr>
<th>STAGING</th>
<th>TREATMENT</th>
</tr>
</thead>
</table>
| AT RISK – no apparent necrotic bone, have received oral or IV bisphosphonates | No treatment  
Patient education                                              |
| STAGE 0 – no clinical evidence of necrotic bone but nonspecific clinical findings, radiographic changes, and symptoms | Systemic management, including use of pain medication and antibiotics |
| STAGE 1 – exposed and necrotic bone or fistulas that probes to bone in patients who are symptomatic and have no evidence of infection | Antibacterial mouth rinse  
Clinical follow-up on quarterly basis  
Patient education and review of indications for continued bisphosphonate therapy |
<table>
<thead>
<tr>
<th>STAGING</th>
<th>TREATMENT</th>
</tr>
</thead>
</table>
| **STAGE 2** – exposed and necrotic bone or fistulas that probes to bone associated with infection as evidenced by pain and erythema in the region of exposed bone with or without purulent discharge | Antibacterial mouth rinse  
Symptomatic treatment with oral antibiotics  
Pain control  
Debridement to relieve soft tissue irritation and infection control |
| **STAGE 3** – exposed and necrotic bone or fistulas that probes to bone in patients with pain, infection, and > 1 if the following: exposed and necrotic bone extending beyond the region of alveolar bone (ie, inferior border and ramus in mandible, maxillary sinus, and zygoma in maxilla) resulting in pathologic fracture, extraoral fistula, oral antral or oral nasal communication, or osteolysis extending to inferior border of the mandible or sinus floor | Antibacterial mouth rinse  
Antibiotic therapy  
Pain control  
Surgical debridement or resection for longer-term palliation of infection and pain |
Antibiotic Regimens

- Pen VK 500mg q6h daily
- Doxycycline 100mg daily
- Extend at least 14 days or until infection signs disappear
- Clindamycin not recommended
- The most common isolated microorganism was Actinomyces spp, Eikenella spp, and Moraxell spp. (Clindamycin not recommended)
Dental Implants and Bisphosphonates

- Oral bisphosphonates, 9 month presurgical drug holiday followed by 3 month postsurgical holiday (includes tooth extractions and periodontal surgery)
- Avoid implant placement in IV bisphosphonate patients (along with tooth extraction and periodontal surgery)
- Drug holidays from IV bisphosphonates do not decrease incidence of MRONJ

Prescribing physician decides whether to discontinue use of antiresorptive/antiangiogenic medications
Cancer Treatment Side Effects

- Oral ulcerations / mucositis
- Bleeding / Impaired hemostasis
- Susceptibility to Infection
- Inability to tolerate dental care
Consultation with a Medical Colleague

Our mutual patient, (Mr/Mrs/Ms, Name and identifiers), presented for a (routine, emergency) dental examination on (specify date). (He, She) presents with (a non-restorable tooth, requiring extraction), or, is in need of (periodontal surgery, routine dental restorations, dental cleaning). The procedure involves minor surgery including gingival and/or bone manipulation under local anesthestic. Hemostasis will be managed by local control measures. I expect healing to be stable and nearly completed by 3 weeks. The patient’s medical history is significant for (list conditions that are concerning for the dental treatment). Please provide pre-, peri-, and post-operative recommendations to include the use of epinephrine, specific antibiotics and analgesics along with dosages. (Ask for pertinent laboratory reports). Given the patients current condition, is the patient medically optimized for surgery at this time? Thank you.

Would the patient be able to undergo a drug holiday for (specify months, or up to 9 months) without compromising his/her medical condition?

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Thank You