UPDATE ON ORAL CANCER

Kirk Y. Hirata, MD
January 13, 2017
ROAD TO THE PODIUM?

• 1985-90: LLUSM
• 1990-94: Anatomic and Clinical Pathology Residency, UH John A. Burns School of Medicine
• 1994-95: Hematopathology Fellowship, Scripps Clinic, San Diego
• July 1995: HPL - new business, niche?
ORAL PATHOLOGY

- outpatient biopsies, some were from dentists
- s/o inflammation, “benign odontogenic cyst”, etc
- no service to general dentists or oral surgeons
- wife was a dentist, residency at QMC 1990-91
- idea?
ORAL PATHOLOGY

• telephone calls
• lunches (marketing)
• textbooks
• courses, including microscopy
• began to acquire cases
• QMC dental resident teaching once a month
42ND ANNUAL COURSE IN
ORAL PATHOLOGY

4 - 8 DECEMBER 1995

GROSVENOR RESORT
WALT DISNEY WORLD VILLAGE
LAKE BUENA VISTA, FLORIDA

Course Directors
Robert B. Brannon, Col, USAF, DC
Robert K. Goode, Col, USAF, DC

Course Sponsors
Armed Forces Institute of Pathology
American Registry of Pathology

Surgical
Oral and Maxillofacial
Pathology
With Microscopy Workshop

7 - 9 November 1999
Horton Grand Hotel
San Diego, California

Course Directors
Gary L. Ellis, D.D.S.
Gary R. Warnock, CAPT, DC, USN

Jointly Sponsored By
Armed Forces Institute of Pathology
American Registry of Pathology
AFTER 21 YEARS

• established myself in the community as an “oral pathologist”
• QMC Dental Residency Program has been recognized
• 7th edition of Jordan (1999)
• UCSF consultation service
Dr. Richard Jordan  
Professor of Oral Pathology, Pathology & Radiation Oncology  
UCSF Dermatopathology & Oral Pathology Service

I feel fortunate to have joined this group of outstanding dermatopathologists. I believe that my training, experience and expertise in oral and maxillofacial pathology expands the scope and breadth of services that we are able to offer the medical and dental community for their diagnostic pathology needs. I initially trained as a dentist at the University of Toronto that was followed by an internship at the Toronto Western Hospital (now the University Health Network). Following training in anatomic pathology I completed a residency in oral and maxillofacial pathology under the direction of Dr. Jim Main. I also completed a fellowship in oral medicine and then a Master of Science degree in oral pathology. I was fortunate to be able to train with Professor Paul Speight at the University of London were I was awarded a PhD degree in Experimental Pathology. My first faculty position was at the University of Toronto where I practiced oral pathology and oral medicine and developed a research program in oral cancer.

In 2000 I relocated to the University of California San Francisco and have been director of the oral pathology service since 2004. I have published over 130 peer reviewed publications, many invited reviews and I am the author of two leading textbooks, one in oral pathology (Regezi, Sciubba and Jordan. Oral Pathology: Clinical pathologic correlations 6th ed) and the other in oral medicine (Lewis and Jordan. Color Handbook of Oral Medicine 2nd edition).

I am also the Medical Director (working with Dr. Nilsa Ramirez and Dr. Soon Paik) of the NRG Oncology Biospecimen Bank that is based in San Francisco, Columbus OH and Pittsburgh PA supporting phase II and phase III practice changing therapeutic trials for head and neck, breast, colorectal, lung, prostate and brain cancers. Enrolling 5099 patients each year, this biospecimen bank collects, stores, reviews and distributes over 150,000 biospecimens each year as part of the primary trials and translational research.

I am delighted to contribute to the UCSF Dermatopathology and Oral Pathology Service and enjoy providing a high level of diagnostic pathology and expert opinion for clinicians and pathologists for lesions in the head and neck.
LECTURE SCHEDULE

- Survey
- Introduction - statistics
- Etiology
- Leukoplakia - dysplasia
- BREAK
- Carcinoma pathogenesis
- Special types including HPV-related
- Staging
- Treatment and Prognosis
survey of US dentists’ knowledge and opinions about oral cancer
pretested survey mailed to 7,000 randomly selected general dentists
3,200 responded; reminder postcard and second complete mailing
conclusion: recognize that dentists are not as knowledgeable as they could be about cancer prevention and early detection; interested in CE
| TABLE 1 |
|-----------------|-----------------|
| **SELECTED CHARACTERISTICS OF GENERAL PRACTICE DENTISTS (N = 3,200).** | |
| **BACKGROUND CHARACTERISTICS** | **PERCENTAGE*** |
| **SEX** | |
| Male | 86 |
| Female | 14 |
| **TIME OF GRADUATION** | |
| Before 1970 | 22 |
| 1970 to 1979 | 28 |
| 1980 to 1989 | 33 |
| 1990 to 1995 | 17 |
| **TYPE OF PRACTICE** | |
| Solo | 68 |
| Partnership | 12 |
| Employee/Contractor | 14 |
| Other | 6 |
| **INTERVAL SINCE LAST ORAL CANCER CONTINUING EDUCATION COURSE** | |
| Within the Past 12 Months | 13 |
| One to Four Years | 42 |
| Five or More Years | 26 |
| Never Taken a Course | 18 |

* Some groups of percentages do not equal 100 due to rounding.
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### Table 2

**Classification of General Practice Dentists.**

<table>
<thead>
<tr>
<th>KNOWLEDGE OF RISK FACTOR SCORE</th>
<th>KNOWLEDGE OF DIAGNOSTIC PROCEDURES</th>
<th>ALL DENTISTS</th>
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<tbody>
<tr>
<td></td>
<td>LOW SCORE (0-4 ITEMS)</td>
<td>MEDIUM SCORE (5-6 ITEMS)</td>
</tr>
<tr>
<td>Low Score (0-7 Items)</td>
<td>16.1</td>
<td>9.8</td>
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<tr>
<td>Medium Score (8-9 Items)</td>
<td>12.0</td>
<td>11.2</td>
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<tr>
<td>High Score (10-13 Items)</td>
<td>9.2</td>
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<tr>
<td><strong>ALL DENTISTS</strong></td>
<td><strong>37.3</strong></td>
<td><strong>34.6</strong></td>
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<td>BACKGROUND CHARACTERISTICS</td>
<td>HIGH SCORE ON INDEX OF KNOWLEDGE OF ORAL CANCER (P VALUE)</td>
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<tr>
<td>-----------------------------</td>
<td>----------------------------------------------------------</td>
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<tr>
<td></td>
<td>Risk Factors</td>
<td>Diagnostic Procedures</td>
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<td>Time of Graduation</td>
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<tr>
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<tr>
<td>Interval Since Last Oral Cancer Continuing Education Course</td>
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</table>

* NS: Not Significant.
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<thead>
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<th>BACKGROUND CHARACTERISTICS</th>
<th>INDEX OF KNOWLEDGE OF ORAL CANCER</th>
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<td>P Value</td>
<td>Adjusted Odds Ratio</td>
<td>95% Confidence Interval</td>
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<td>1.0*</td>
<td>—</td>
<td>—</td>
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<td>Solo</td>
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<td>1.0*</td>
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<td>Partnership</td>
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<td>1.5</td>
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<td>Before 1970</td>
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<td>1.0*</td>
<td>—</td>
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<td>1970 to 1979</td>
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<td>1.5-2.4</td>
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<td>2.3-3.7</td>
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<td>1990 to 1995</td>
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<td>2.0-3.5</td>
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<td>3.5</td>
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<td>.00000</td>
<td>3.5</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within Last 12 Months</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
<td>1.0*</td>
<td>—</td>
<td>—</td>
<td>1.0*</td>
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<tr>
<td>One to Four Years</td>
<td>0.96</td>
<td>0.8-1.2</td>
<td>.7</td>
<td>0.7†</td>
<td>0.6-0.9</td>
<td>.004</td>
<td>0.9</td>
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<tr>
<td>Five or More Years</td>
<td>1.09</td>
<td>0.8-1.4</td>
<td>.5</td>
<td>0.6†</td>
<td>0.4-0.7</td>
<td>.00001</td>
<td>0.8</td>
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<tr>
<td>Never</td>
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<td>0.8-1.02</td>
<td>.07</td>
<td>0.5§</td>
<td>0.4-0.6</td>
<td>.00000</td>
<td>0.6†</td>
</tr>
</tbody>
</table>

* Reference cells.
† The reflected odds ratio was 1.4.
‡ The reflected odds ratio was 1.6.
§ The reflected odds ratio was 2.0.
## 2003 Lavaman Triathlon

**Waikoloa, HI, April 6, 2003**

<table>
<thead>
<tr>
<th></th>
<th>Name</th>
<th>Age Group</th>
<th>Time (Swim: Bike: Run)</th>
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</thead>
<tbody>
<tr>
<td>61</td>
<td>Trevor Anderson #141</td>
<td>30-34</td>
<td>:26:26 1:13:49 49:18</td>
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<tr>
<td>63</td>
<td>Adam Hodgson #396</td>
<td>25-29</td>
<td>:27:50 1:10:12 52:22</td>
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<td>65</td>
<td>Edward J. Pama #381</td>
<td>30-34</td>
<td>:25:23 1:17:27 47:59</td>
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<td>120</td>
<td>Candes Meijide Gentry #38</td>
<td>25-29</td>
<td>:24:59 1:21:32 52:34</td>
</tr>
<tr>
<td>121</td>
<td>Shawn Rambus #78</td>
<td>25-29</td>
<td>:29:22 1:16:04 57:49</td>
</tr>
<tr>
<td>122</td>
<td>Duane Tamashiro #138</td>
<td>30-34</td>
<td>:32:28 1:18:01 52:57</td>
</tr>
<tr>
<td>123</td>
<td>Kirschen Adler #210</td>
<td>40-44</td>
<td>:25:25 1:18:46 52:44</td>
</tr>
<tr>
<td>124</td>
<td>Tom Solis #370</td>
<td>60-64</td>
<td>:29:36 1:15:17 58:55</td>
</tr>
<tr>
<td>125</td>
<td>Stephen Howard #235</td>
<td>40-44</td>
<td>:26:05 1:21:40 56:12</td>
</tr>
</tbody>
</table>
FIG. 1 – In general, do you feel it is the dental practice's responsibility to screen for any cancers in the head and/or neck region?

- Yes: 94.5%
- No: 2.6%
- Unsure: 3.0%
FIG. 2 – Does your office policy include oral cancer screenings?
FIG. 3 – If it is your office’s policy to screen patients for oral cancer, how often are your patients screened?

- At every appointment: 71.1%
- Our office does not screen for oral cancer: 1.7%
- Less frequently than every other year: 2.1%
- Once a year: 25.1%
FIG. 4 – If it is your office policy to screen patients for oral cancer, what kind of screening do you perform?

- Our office does not screen patients for oral cancer: 2.1%
- A combination of extraoral and intraoral: 70.1%
- Extraoral only (a visual and/or tactile examination of all the tissues in the mouth and throat): 24.8%
- Intraoral only (using an oral cancer screening device): 3.0%
FIG. 5 – If it is NOT your office’s policy to perform oral cancer screenings, what is the main reason?

- Cost: 62.5%
- Time needed for screening: 12.5%
- Don't feel it is our responsibility: 25%
FIG. 6 - Is it your office policy to talk to patients about smoking cessation?

- Yes: 76.0%
- No: 24.0%
FIG. 7 – Is it your office policy to talk to patients about alcohol moderation and/or cessation?

No 66.1%
Yes 33.9%
FIG. 8 – Is it your office policy to talk to patients about the link between HPV (human papillomavirus) and oral cancer?

- No: 51.9%
- Yes: 48.1%
AMERICAN CANCER SOCIETY
2016

• 3% of all cancers in men and 2% of cancers in women
• 36K new cases in the US annually
• ratio of M:F is 2:1, previously was 3:1
• deaths represent 2% of total in men, and 1% in women - 7880 annually, 1.8% decrease from rates between 1991 and 2006
• slight improvement in survival - 63% five-year for period between 1999 and 2005 vs 55% for years between 1984 and 1986
NON-US

• worldwide incidence of oral cancer is 263,000 cases per year
• Indian subcontinent and some Asian countries, oral cancer is the most common type of malignancy accounting for up to 50% of all cases
• high prevalence of smoking, and in Pacific Basin the use of betel nut
Surveillance, Epidemiology, and End Results (SEER) Program

• in the US, incidence rate from 2005 to 2009 was 60 per 100,000 for males aged 65 and older (10 per 100,000, age < 65 years)

• white > black males

• M:F ratio of 2.5:1

• significant increase in oral tongue cancer among young, white women aged 18 to 44 years (not associated with tobacco, alcohol use, or HPV infection)
<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2016</th>
<th>Estimated Deaths 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast Cancer (Female)</td>
<td>246,660</td>
<td>40,450</td>
</tr>
<tr>
<td>2. Lung and Bronchus Cancer</td>
<td>224,390</td>
<td>158,080</td>
</tr>
<tr>
<td>3. Prostate Cancer</td>
<td>180,890</td>
<td>26,120</td>
</tr>
<tr>
<td>4. Colon and Rectum Cancer</td>
<td>134,490</td>
<td>49,190</td>
</tr>
<tr>
<td>5. Bladder Cancer</td>
<td>76,960</td>
<td>16,390</td>
</tr>
<tr>
<td>6. Melanoma of the Skin</td>
<td>76,380</td>
<td>10,130</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>72,580</td>
<td>20,150</td>
</tr>
<tr>
<td>8. Thyroid Cancer</td>
<td>64,300</td>
<td>1,980</td>
</tr>
<tr>
<td>10. Leukemia</td>
<td>60,140</td>
<td>24,400</td>
</tr>
</tbody>
</table>

| Oral Cavity and Pharynx Cancer         | 48,330                   | 9,570                 |

In 2016, it is estimated that there will be 48,330 new cases of oral cavity and pharynx cancer and an estimated 9,570 people will die of this disease.

Number of New Cases per 100,000 Persons by Race/Ethnicity & Sex: Oral Cavity and Pharynx Cancer

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>16.7</td>
<td>6.2</td>
</tr>
<tr>
<td>White</td>
<td>17.4</td>
<td>6.4</td>
</tr>
<tr>
<td>Black</td>
<td>14.4</td>
<td>5.2</td>
</tr>
<tr>
<td>Asian / Pacific Islander</td>
<td>11.1</td>
<td>4.9</td>
</tr>
<tr>
<td>American Indian / Alaska Native</td>
<td>13.2</td>
<td>5.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>17.8</td>
<td>6.6</td>
</tr>
</tbody>
</table>

SEER 18 2009–2013, Age-Adjusted

In the period 2011-2015, oral cancer occurred nearly three times as often in males as in females.

In the period 2011-2015, tongue and throat cancers (malignant neoplasms of the tongue and of the nasopharynx, hypopharynx and oropharynx) were much more likely to occur in males than females.
Percent of New Cases by Age Group: Oral Cavity and Pharynx Cancer

Oral cavity and pharynx cancer is most frequently diagnosed among people aged 55–64.

Median Age At Diagnosis

62

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Oral Cavity and Pharynx Cancer

Percent of Cases by Stage

- Localized (30%) Confined to Primary Site
- Regional (47%) Spread to Regional Lymph Nodes
- Distant (18%) Cancer Has Metastasized
- Unknown (5%) Unstaged

5-Year Relative Survival

- Localized: 83.3%
- Regional: 63.3%
- Distant: 38.0%
- Unstaged: 47.2%

SEER 18 2006–2012, All Races, Both Sexes by SEER Summary Stage 2000

The percent of oral cavity and pharynx cancer deaths is highest among people aged 55–64.

Median Age At Death

67

U.S. 2009–2013, All Races, Both Sexes

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male</th>
<th>Female</th>
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</thead>
<tbody>
<tr>
<td>All Races</td>
<td>3.8</td>
<td>1.3</td>
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<tr>
<td>White</td>
<td>3.7</td>
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<td>1.3</td>
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<td>Asian / Pacific Islander</td>
<td>2.9</td>
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<td>Hispanic</td>
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<td>0.8</td>
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<tr>
<td>Non-Hispanic</td>
<td>3.9</td>
<td>1.4</td>
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</table>

U.S. 2009–2013, Age-Adjusted

New Cases, Deaths and 5-Year Relative Survival

<table>
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<tr>
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<tr>
<td>5-Year Relative Survival</td>
<td>52.7%</td>
<td>53.6%</td>
<td>54.4%</td>
<td>57.0%</td>
<td>58.5%</td>
<td>62.0%</td>
<td>64.8%</td>
<td>66.2%</td>
</tr>
</tbody>
</table>


Based on data from SEER 18 2006–2012. Gray figures represent those who have died from oral cavity and pharynx cancer. Green figures represent those who have survived 5 years or more.

ORAL CANCER

• worldwide: 6th most prevalent cancer
  – developed countries - 8th
  – developing countries - 3rd
  – US - frequency constant; 3% in men, < women

• incidence of oropharyngeal cancer in US has increased annually since since 1973

• SCC accounts for > 90% of all intraoral malignancies
ORAL CANCER

• men in 5th to 8th decade of life
• overall 5-year survival rate has shown little improvement over the past several decades, approximately 50% (blacks < whites)
  – lifestyle habits
  – clinical stage at diagnosis
  – limited access to healthcare
ETIOLOGY

• 50% of cases in American men are attributable to excessive tobacco and alcohol use

• risk increases with larger amount and longer duration of tobacco use - cigarette, cigar, or pipe smoking

• “reverse” smoking, e-cigarettes

• snuff dipping and tobacco chewing - slight increase
ETIOLOGY

• India and SE Asia: smokeless tobacco is combined with betel nut leaf and slaked lime - rates markedly increased

• carcinogens in tobacco act as initiators and promoters in the transformation process

• relative risk declines after cessation of smoking

• carcinogen exposure in chronic marijuana smoking - young patients, includes OPC
ETIOLOGY

• alcohol acts synergistically with tobacco as either a cocarcinogen (increasing the risk) or promoter (decreasing the lag time)
• heavy smoking alone: 2-3x risk
• heavy drinker alone: 2-6x risk
• heavy smoker and drinker: 15x risk
• young adults (age < 46 years): 20x, 5x, 50x risk
ETIOLOGY

- nonusers: older women, spare FOM, earlier stage, lack association with a second primary malignancy
- poor long-term oral hygiene - periodontal disease
- human papillomavirus (HPV) subtypes 16 and 18
- Candida albicans - N-nitrosobenzylmethlamine
- head and neck SCC in sibling or first-degree relative (p16 mutation)
- poor nutritional status
- immunosuppression
ETIOLOGY?

• chronic use of alcohol-based mouthwash
• oral mechanical irritation (jagged teeth, denture)
• syphilitic glossitis, severe iron deficiency (Plummer-Vinson syndrome), lichen planus, and discoid lupus erythematosus
RISK FACTORS FOR ORAL AND PHARYNGEAL CANCERS.

- Use of Any Kind of Tobacco Product
- Heavy Use of Alcohol
- Certain Viruses (Such as Human Papillomavirus)
- Low Consumption of Fruits and Vegetables
- Marijuana Use
- Age Older Than 45 Years
- Black Race
- Male Sex
BETEL HABIT

• 10-20% of the world’s population (WHO estimates 600 million people)

• cultural, early age, habitually chew 16 to 24 hours daily

• Indian subcontinent and Asian countries (SE Asia, Taiwan, Southern China, Polynesia, Micronesia including Guam)

• psychoactive substance - nicotine, alcohol, caffeine, betel nut
BETEL QUID (PAAN)

- quid - leaf wrapped around a mixture of areca nut, slaked lime, possibly tobacco, and sometimes sweeteners and spices
- commercially available, freeze-dried betel quid substitutes (pan masala, gutkha, mawa)
- slaked lime releases alkaloids from the areca nut - feeling of euphoria
BENEFITS OF BETEL NUT

- Controls Cavity
- Control Diabetes
- Anti-Depresent properties
- Symptoms of Schizophrenia
- Controls High blood pressure
ORAL SUBMUCOUS FIBROSIS

- alkaloids also stimulate fibroblasts resulting in oral submucous fibrosis - high risk, precancerous condition
- chronic, progressive scarring of the oral (buccal) mucosa - interincisal distance of 20 mm
- inability to open the mouth (trismus) and generalized oral burning sensation (stomatopyrosis) with intolerance to spicy foods
ORAL SUBMUCOUS FIBROSIS

- dysplasia in 10 to 15% of cases
- carcinoma in 6%
- does not regress with habit cessation
- limited treatment
- 8% rate of malignant transformation (19x risk)
RAISING AWARENESS

• any evidence of health benefits is limited
• WHO classifies betel nut as a carcinogen
• FDA has placed nut on its Poisonous Plants Database
• CDC warns of addiction, oral fibrosis, and cancer
• Taiwan - Betel Nut Prevention Day
WHO DEFINITIONS

- Leukoplakia - persistent white mucosal patch or plaque that cannot be scraped off
- Erythroplakia - persistent red mucosal patch with or without erosion
- Erythroleukoplakia - speckled lesion with features of both
- Verrucous hyperplasia - superficial lesion, white and corrugated
LEUKOPLAKIA

Homogenous

Clinical appearance
- Normal mucosa
- Thin, smooth leukoplakia
- Thick, fissured leukoplakia

Histopathologic features
- Hyperkeratosis
- Acanthosis
- Lymphocytes (variable)

Non-homogenous

Clinical appearance
- Verrucous or nodular leukoplakia
- Erythroleukoplakia (speckled leukoplakia)

Histopathologic features
- Hyperkeratosis
- Verrucous epithelial hyperplasia
- Bulbous rete ridges
- Dysplasia (minimal, mild, or moderate)
- Lymphocytes (variable)

Erythroplakia

Histopathologic features
- Variable hyperkeratosis
- Bulbous rete ridges
- Epithelial atrophy (on right)
- Dysplasia (mild to severe)
- Lymphocytes (moderate numbers), often band-like

LEGEND
- Keratin layer
- Erythema
- Normal epithelium
- Dysplastic epithelial cells
- Lymphocytes
# Precancerous Lesions of the Oral, Pharyngeal, and Laryngeal Mucosa
(Clinical Terms Only)

<table>
<thead>
<tr>
<th>Disease Name</th>
<th>Malignant Transformation Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferative verrucous leukoplakia (PVL)*</td>
<td>★★★★★★</td>
</tr>
<tr>
<td>Nicotine palatinus in reverse smokers†</td>
<td>★★★★★</td>
</tr>
<tr>
<td>Erythroplakia</td>
<td>★★★★</td>
</tr>
<tr>
<td>Oral submucous fibrosis</td>
<td>★★★★</td>
</tr>
<tr>
<td>Erythroleukoplakia</td>
<td>★★★★</td>
</tr>
<tr>
<td>Granular leukoplakia</td>
<td>★★★★</td>
</tr>
<tr>
<td>Laryngeal keratosis</td>
<td>★★★</td>
</tr>
<tr>
<td>Actinic cheilosis</td>
<td>★★★</td>
</tr>
<tr>
<td>Smooth, thick leukoplakia</td>
<td>★★</td>
</tr>
<tr>
<td>Smooth, red tongue of Plummer-Vinson syndrome</td>
<td>★</td>
</tr>
<tr>
<td>Smokeless tobacco keratosis</td>
<td>★</td>
</tr>
<tr>
<td>Lichen planus (erosive forms)‡</td>
<td>★</td>
</tr>
<tr>
<td>Smooth, thin leukoplakia</td>
<td>+/-</td>
</tr>
</tbody>
</table>


*PVL: High-risk, high-recurrence form of oral leukoplakia affecting multiple sites.

†Reverse smoking: Smoking with the lit end of the cigarette in one's mouth.

‡Precancer character is controversial.
GRADES OF EPITHELIAL DYSPLASIA

- CIS - absence of invasion, metastasis cannot occur

MILD → MODERATE → SEVERE/CIS
DENTAL SCREENING

- all patient exams should include a comprehensive history
- systematic visual and tactile examination of not only the oral soft tissues, but also those of the head and neck
- ancillary techniques to aid in the identification of premalignant and malignant oral lesions
ORAL CANCER SCREENING DEVICE

• commercial devices were designed to further assist the dental practitioner
  – identify early tissue changes
  – assess the biological significance of a mucosal lesion
  – explore morphological and biochemical tissue alterations that cannot be observed by normal incandescent light
Toluidine Blue
Viewed with the unassisted eye

Enhanced view using VELscope® Vx device (event later confirmed as oral cancer)

Clinical images courtesy of Dr. Samuel Ng

Enhanced Oral Assessment

AENORMAL
Abnormal loss of fluorescence pattern associated with dysplastic epithelium and underlying stromal disruption.

NORMAL
Tissue produces normal fluorescence pattern.

BLUE EXCITATION LIGHT

Epithelium
- Basement Membrane
- Normal Stroma
- Disruption of Stromal Collagen

Abnormal Epithelial Cells

Normal Epithelial Cells
VELscope Vx
Oral Cancer Screening
ViziLite® Plus
ORAL LESION IDENTIFICATION AND MARKING SYSTEM
Better screening saves lives

A. Normal epithelium absorbs ViziLite illumination and appears dark.
B. Abnormal epithelium reflects ViziLite illumination and appears white.

Lesion under incandescent light
Lesion under ViziLite illumination
How the BrushTest Works

**Step 1: Discover**

Small Red or White Spot is Observed

**Step 2: Sample**

BrushTest Bristles Sample the Spot

**Step 3: Analyze**

Specimen Analyzed by Pathologists

**Step 4: Diagnose**

BrushTest Findings and the Result

People get white or red spots in their mouths from time to time. The majority of spots are caused by everyday trauma such as cheek biting or pizza burns, but some contain unhealthy cells that if left alone could become a problem. If a spot is observed, and there is no clear cause, it needs to be tested by collecting and analyzing cells.

The BrushTest is pressed against the spot and turned; collecting thousands of cells. This is necessary because doctors can’t simply look at a spot and know what caused it to appear, or if it has the potential to cause you any harm. The specimen is then sent to the lab for analysis.

OralCDx Labs has a special process for analyzing each specimen which makes it very accurate. Our imaging system acts like a spell check for cells that brings potential abnormal cells to the attention of our expert pathologists. Then, our pathologists analyze the specimens and issue a result.

The report from OralCDx gives the doctor information that helps determine the cause of the spot so that it can be treated. Just like with a pap smear, the expectation is that the result of the BrushTest will be “negative” for precancer or cancer. Even if unhealthy cells are found, the spot can typically be removed before it can become harmful.
• conclude that these adjunctive aids may not significantly improve the detection and diagnosis of potentially malignant lesions beyond that of conventional and histologic examination

• current level of scientific evidence was insufficient to support recommending the routine use of any of these devices
until then?

increased patient education about the risks for oral cancer

clinical vigilance

suspicious or persistent lesions should be biopsied

histologic examination remains the current gold standard for oral cancer and precancer diagnosis
### Recommendations of the American Dental Association Council on Scientific Affairs Expert Panel on Screening for Oral Squamous Cell Carcinomas,* based on evidence

**Screening for oral cancer** is one component of a thorough hard-tissue and soft-tissue examination that follows patient history and risk assessment.

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>RECOMMENDATION</th>
<th>CLASSIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening During Routine Examinations†</strong></td>
<td>The panel suggests that clinicians remain alert for signs of potentially malignant lesions or early-stage cancers in all patients while performing routine visual and tactile examinations, particularly for patients who use tobacco or who are heavy‡ consumers of alcohol</td>
<td>D</td>
</tr>
<tr>
<td><strong>Follow-up for Seemingly Innocuous Lesions</strong></td>
<td>For seemingly innocuous lesions, the panel suggests that clinicians follow up in seven to 14 days to confirm persistence after removing any possible cause to reduce the potential for false-positive screening results</td>
<td>D</td>
</tr>
</tbody>
</table>
| **Follow-up for Lesions That Raise Suspicion of Cancer and Those That Are Persistent** | For lesions that raise suspicion of cancer or for lesions that persist after removal of a possible cause, the panel suggests that clinicians communicate the potential benefits and risks of early diagnosis. Considerations include the following:  
- even suspicious lesions identified during the course of a routine visual and tactile examination may represent false positives;  
- clinical confirmation (a second opinion) can be sought from a dental or medical care provider with advanced training and experience in diagnosis of oral mucosal disease so as to reduce the potential for a false-positive or false-negative oral cancer screening result;  
- a malignancy or nonmalignancy can be confirmed only via microscopic examination that requires a surgical biopsy;  
- a decision to pursue a biopsy to confirm the presence or absence of malignancy should be made in the context of informed consent | D |
| **Use of Lesion Assessment Devices** | Although transepithelial cytology has validity in identifying disaggregated dysplastic cells, the panel suggests surgical biopsy for definitive diagnosis | D |

* The expert panel was convened in April 2009 to address the benefits and limitations of oral cancer screening and the use of adjunctive screening aids to visualize and detect potentially malignant and malignant oral lesions.
† There is insufficient evidence that use of commercial devices for lesion detection that are based on autofluorescence or tissue reflectance enhance visual detection of potentially malignant lesions beyond a conventional visual and tactile examination. Source: Patton and colleagues.27
‡ Heavy alcohol consumption is defined as follows: for men, consumption of an average of more than two drinks per day; for women, consumption of an average of more than one drink per day. Sources: Pelucchi and colleagues10 and Centers for Disease Control and Prevention.11
SALIVA TEST FOR ORAL CANCER

• SaliMark OSCC (PeriRx, LLC)
• noninvasive, oral diagnostic technology - salivary exRNA biomarker test for oral SCC
• decade of NIH-funded research and prevalidation work at UCLA and MSU
• “signature mutations” (biomarkers) that may be associated with oral cancers
• screening test for early detection (before symptoms) to reduce morbidity and mortality
How to Use the SaliMark™ OSCC Test Score

- Lesion Suspicious For OSCC
  - SaliMark™ OSCC Test

  - Low Risk Test Score < 0.068: Follow Up Within 4 Weeks
  - Moderate Risk Test Score: 0.068 - 0.140: Second Opinion from Specialist*
  - High Risk Test Score: > 0.150: Refer for Consideration of Biopsy

* Specialist decision on biopsy and follow up to be based on quantitative test score, physical examination and risk factors in medical history (smoking, alcohol consumption, age, gender and ethnicity)
BREAK
INTRAORAL CARCINOMA

• in the US, posterior-lateral and ventral surfaces of the tongue and floor of mouth are the most common sites
• gingiva > buccal mucosa > labial mucosa > hard palate
• oral tongue represents an increasingly common site of involvement in young patients
CLINICAL FEATURES

- usually older men who have been aware of a “problem” for 4 to 8 months before seeking professional help (8 to 24 months among lower socioeconomic groups)
- initially pain is usually minimal
- if health care professional does not have a high index of suspicion, then additional weeks or months may lapse
Signs and symptoms of oral cavity and oropharyngeal cancer

Possible signs and symptoms of these cancers can include:

- A sore in the mouth that does not heal (most common symptom)
- Pain in the mouth that doesn’t go away (also very common)
- A lump or thickening in the cheek
- A white or red patch on the gums, tongue, tonsil, or lining of the mouth
- A sore throat or a feeling that something is caught in the throat that doesn’t go away
- Trouble chewing or swallowing
- Trouble moving the jaw or tongue
- Numbness of the tongue or other area of the mouth
- Swelling of the jaw that causes dentures to fit poorly or become uncomfortable
- Loosening of the teeth or pain around the teeth or jaw
- Voice changes
- A lump or mass in the neck
- Weight loss
- Constant bad breath
RADIOGRAPHIC FEATURES

• destruction of underlying bone may be painful or completely painless
• “moth-eaten” radiolucency with ill-defined or ragged margins (similar to OM)
GRADING OF SCC

Well differentiated

Moderately differentiated

Poorly differentiated
PATHOGENESIS (MOLECULAR BIOLOGY)

- development of SCC is driven by the accumulation of mutations and epigenetic changes that alter the expression and function of oncogenes and tumor suppressor genes
  - resistance to cell death
  - increased proliferation
  - induction of angiogenesis
  - ability to invade and metastasize
Figure 2-56 Gene expression in oral cancer.
Cell cycle

Inhibitor proteins (Bcl-2, Bcl-x) Pro-cancer

Inducing proteins (Bax) Anti-cancer

Apoptosis vs. Proliferation

p53 Inhibitor proteins (MDM2) Pro-cancer

Inhibitor proteins Cyclin-dependent kinase inhibitors (p16, p21, p27) Anti-cancer

Inducing proteins Cyclin-dependent kinases (cyclin D1) Pro-cancer
**Figure 2-58** Cancer cell invasion through enhanced cell motility and angiogenesis.
Keratin

Epithelium

Connective tissue

Hyperkeratosis

Verrucous hyperplasia

Verrucous carcinoma

Squamous cell carcinoma
VERRUCOUS CARCINOMA

- locally invasive, nonmetastasizing variant of SCC
- 5% of all oral cancers
- exophytic, warty (bulky) clinical appearance
- buccal > gingiva > tongue > palate > tonsil
- 1 to 10 cm in size
- extends by blunt invasion into soft tissue/bone
VERRUCOUS CARCINOMA

• men, 7th decade
• intense smokers (smokeless tobacco)
• alcohol abuse and HPV not implicated
• difficult mastication (mass), ulcer, pain
• superficial biopsies are often “negative”
• surgical excision is most effective therapy
  +/- radiation therapy
HPV-RELATED SCC

• current epidemic of head and neck cancer
• despite reduction in smoking in US, growing increase in incidence of oropharyngeal cancer since 1970s
• HPV-mediated carcinogenesis is now recognized as the major cause of oral cancer in developed countries (40 to 90% of cases)
• HPV subtypes 16; 18, 31, 33, and 35
HPV-RELATED SCC

- oral DNA carriage in young men is common (15 to 30%)
- HPV-16 most frequent
- younger age at onset, male predominance, strong association with oral sexual behavior
- improved outcomes (not in smokers)
- HPV prevalence in oral cavity cancers is quite variable, outcomes less clear, rarely contain HPV (even when p16 is expressed)
OROPHARYNGEAL CANCER

- subsites include the soft palate, base of tongue, tonsillar region, and posterior pharyngeal wall
- tonsillar region and base of tongue (70-80%) of cases
- tonsillar region is a favored site for HPV-associated carcinomas
- majority of OPC in US are attributed to HPV
OROPHARYNGEAL CANCER

- whites > blacks
- HPV-16 positive: younger individuals without smoking or drinking risk factors
- high rate of lymph node metastasis
- nonkeratinizing SCC histology
- better overall survival - more sensitive to chemoradiation
OROPHARYNGEAL CANCER

• in this posterior location, lesions often go unrecognized for long periods
• by the time of diagnosis, tumor size is typically larger and lymph nodes metastasis is present (higher stage)
• better response to treatment and prolonged survival
PRESENTING SYMPTOMS

- persistent sore throat
- difficulty swallowing (dysphagia)
- pain on swallowing (odynophagia)
- pain is dull or sharp, and frequently referred to the ear
HPV-INDUCED CARCINOMAS

• tumor HPV status is a strong predictor of 5-year survival

• prognostic parameters of conventional staging systems may be modified by HPV infection - AJCC 8th edition

• locoregional recurrence rates are half

• 54% better progression-free and disease-free survival

• distant metastasis may occur at a longer interval

• lowest level risk of a 2nd primary malignancy
<table>
<thead>
<tr>
<th></th>
<th>HPV-Negative Squamous Cell Carcinoma</th>
<th>HPV-Positive Squamous Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location prevalence</td>
<td>All head and neck</td>
<td>Oropharynx mostly</td>
</tr>
<tr>
<td>Etiology</td>
<td>Tobacco, alcohol &gt; other minor</td>
<td>Oncogenic HPV-16 &gt; -18, and other</td>
</tr>
<tr>
<td></td>
<td>contributing</td>
<td>high-risk types &gt;80%</td>
</tr>
<tr>
<td>HPV frequency</td>
<td>25%</td>
<td>Nonkeratinizing SCC</td>
</tr>
<tr>
<td>Morphology</td>
<td>Keratinizing SCC</td>
<td>p53 wild type</td>
</tr>
<tr>
<td>p53 mutation</td>
<td>p53 mutation common</td>
<td>(degraded by E6)</td>
</tr>
<tr>
<td></td>
<td>Positive by IHC</td>
<td>Negative by IHC</td>
</tr>
<tr>
<td>p16 expression</td>
<td>Underexpressed</td>
<td>Overexpressed</td>
</tr>
<tr>
<td></td>
<td>Negative by IHC</td>
<td>Positive by IHC</td>
</tr>
<tr>
<td>Retinoblastoma (Rb)</td>
<td>Rb upregulated</td>
<td>Rb downregulated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(E7 oncoprotein)</td>
</tr>
<tr>
<td>Cyclin D</td>
<td>Cyclin D overexpressed</td>
<td>Cyclin D underexpressed</td>
</tr>
<tr>
<td>Chemo- and radiotherapy</td>
<td>More resistant</td>
<td>More responsive</td>
</tr>
<tr>
<td>3-year survival</td>
<td>57%</td>
<td>84%</td>
</tr>
<tr>
<td>5-year overall survival</td>
<td>40%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>with stage III–IV tumors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SCC IN YOUNGER PATIENTS

• age < 45 years
• no tobacco or alcohol use, HPV negative
• behave aggressively with poor prognosis
• clinical subset with undefined etiology
LIP VERMILION CARCINOMA

- typically found in light-skinned individuals, males (infrequent in nonwhite men and women)
- chronic exposure to UV radiation (sunlight), outdoor occupations
- actinic cheilosis
- site where person holds a cigarette, cigar, or pipe
- 90% are located on the lower lip
LIP CARCINOMA

- crusted, oozing, nontender, indurated ulceration, usually less than 1 cm
- grows slowly, most patients are aware of a “problem” in the area for months
- metastasis is a late event
FLOOR OF MOUTH

- painless, indurated ulcer and/or mass
- FOM are most likely to arise from a preexisting leukoplakia or erythroplakia
- FOM also represents the most common site associated with development of a second primary malignancy
- FOM - midline region near the frenum
GINGIVA/ALVEOLAR

- posterior mandibular mucosa
- least associated with tobacco smoking
- greatest predilection for females
- mimic common benign inflammatory and reactive lesions
- often destroy underlying bone and cause tooth mobility
STAGING
AJCC 8th EDITION

- tumor size and the extent of metastatic spread are the best prognostic indicators
- tumor grade not as important
• Figure 2-77 Composite resection performed for T4, No, Mo squamous cell carcinoma of the anterior floor of mouth. The specimen consists of a monobloc resection of the floor of mouth, mandible, and ipsilateral neck nodes.
HISTOPATHOLOGIC PARAMETERS OF PROGNOSTIC SIGNIFICANCE

- tumor grade - not highly reproducible
- depth of tumor invasion
- lymph-vascular invasion
- perineural invasion
DEPTH OF INVASION

• predictor of biologic behavior and direct therapeutic intervention
• Breslow-type measurement (from BM)
• DOI < 4 mm: 8.3% metastatic rate
• DOI 4 to 8 mm: 35% metastatic rate
• DOI > 8 mm: 83% metastatic rate
• 2 mm: least DOI predictive of cervical LN metastasis
LYMPH-VASCULAR INVASION

PERINEURAL INVASION
EVALUATION OF RESECTION MARGINS

• provide significant information for postsurgical treatment options and prognosis
• less than or greater than 5 mm
• 80% local recurrence rate with positive margin vs 12% (oral cavity) and 18% (oropharynx) with initially free margins
• postoperative radiotherapy for positive margins appears to be ineffective
LYMPH NODE METASTASIS

- enlarged, firm to stone hard, nontender, and not easily movable (fixed)
- presence, number, and size of regional lymph node metastasis are the strongest predictors of survival in oral cavity cancer
- cancer deaths in many patients are the result of uncontrolled regional LN disease
LYMPH NODE METASTASIS

• extracapsular extension (ECE) is associated with a poorer prognosis
  – increased risk for locoregional recurrence
  – distant metastasis
  – shortened survival

• 5-year survival of 33% vs 11% - predicts therapy
**Figure 2-78A**, Computed tomography (CT) demonstrating an enlarged lymph node medial to the left sternocleidomastoid muscle. CT provides an anatomic assessment of this mildly enlarged lymph node. **B**, The positron emission tomography (PET)/CT
**Figure 2-80** Oncologic lymph node levels of the neck. Level I = submental/submandibular nodes; level II = upper jugular nodes; level III = middle jugular nodes; level IV = lower jugular nodes; level V = posterior triangle nodes.

**Figure 2-81** Specimen from a type I modified radical neck dissection. The internal jugular vein is noted on the medial aspect of the sternocleidomastoid muscle. The spinal accessory innervation of the trapezius muscle remains intact in this type of neck dissection.
MULTIPLE PRIMARIES

- patients with head and neck cancer are prone to the development of multiple synchronous and/or metachronous malignancies (27%)
- unfavorable prognostic factor: 5-year survival rate of 17% vs 35%
- field cancerization vs lateral extension of one tumor
DISTANT METASTASIS

• rate of 31% in patients who die of oral cancer after negative neck dissection vs 59% in patients with pathologically staged positive regional lymph node metastasis

• improvements in locoregional tumor control have led to longer survival and thereby opportunity for metastatic cascade to be clinically recognized
**TNM Clinical Staging System for Oral Squamous Cell Carcinoma**

**T—Tumor**
- T1: tumor <2 cm
- T2: tumor 2-4 cm
- T3: tumor >4 cm
- T4: tumor invades deep subjacent structures

**N—Nodes**
- N0: no palpable nodes
- N1: single ipsilateral node <3 cm
- N2A: single ipsilateral node 3-6 cm
- N2B: multiple ipsilateral nodes ≤6 cm
- N2C: contralateral or bilateral nodes ≤6 cm
- N3: node >6 cm

**M—Metastasis**
- M0: no distant metastasis
- M1: distant metastasis

### Table 2-6

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM Designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td>II</td>
<td>T2, N0, M0</td>
</tr>
<tr>
<td>III</td>
<td>T3, N0, M0</td>
</tr>
<tr>
<td>IV</td>
<td>T4, N0, M0</td>
</tr>
<tr>
<td></td>
<td>T4, N1, M0</td>
</tr>
<tr>
<td></td>
<td>T any, N2-3, M0</td>
</tr>
<tr>
<td></td>
<td>T any, N any, M1</td>
</tr>
</tbody>
</table>
Buccal mucosa, floor of mouth, anterior tongue, alveolar ridge, retromolar trigone, hard palate

WORKUP

- H&P\textsuperscript{a,b} including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated
- Biopsy
- Chest imaging as clinically indicated
- CT with contrast and/or MRI with contrast of primary and neck as indicated
- Consider FDG-PET/CT for stage III-IV disease\textsuperscript{c}
- Examination under anesthesia (EUA) with endoscopy, if indicated
- Preanesthesia studies as clinically indicated
- Dental/prosthodontic evaluation,\textsuperscript{d} including Panorex or CT ± contrast as clinically indicated
- Nutrition, speech, and swallowing evaluation/therapy as indicated\textsuperscript{e}
- Multidisciplinary consultation as indicated

CLINICAL STAGING

T1-2, N0 → See Treatment of Primary and Neck (OR-2)

T3, N0 → See Treatment of Primary and Neck (OR-3)

T1-3, N1-3 → See Treatment of Primary and Neck (OR-3)

T4a, any N → See Treatment of Primary and Neck (OR-3)

T4b, any N, or Unresectable nodal disease or Unfit for surgery → See Treatment of Very Advanced Head and Neck Cancer (ADV-1)

Metastatic (M1) disease at initial presentation → See Treatment of Very Advanced Head and Neck Cancer (ADV-2)
Cancer of the Oropharynx

Base of tongue/tonsil/posterior pharyngeal wall/soft palate

WORKUP

- H&P\textsuperscript{a,b} including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated
- Biopsy of primary site or FNA of the neck
- Tumor human papillomavirus (HPV) testing recommended\textsuperscript{c}
- Chest imaging as clinically indicated
- CT with contrast and/or MRI with contrast of primary and neck
- Consider FDG-PET/CT for stage III/IV disease
- Dental evaluation\textsuperscript{d}, including panorex as clinically indicated
- Nutrition, speech and swallowing evaluation/therapy, and audiogram as clinically indicated\textsuperscript{e}
- EUA with endoscopy as clinically indicated
- Pre-anesthesia studies
- Multidisciplinary consultation as clinically indicated

CLINICAL STAGING

- T1-2, N0-1
  - See Treatment of Primary and Neck (ORPH-2)
- T3-4a, N0-1
  - See Treatment of Primary and Neck (ORPH-3)
- Any T, N2-3
  - See Treatment of Primary and Neck (ORPH-4)
- T4b, any N, or Unresectable nodal disease
  - See Treatment of Very Advanced Head and Neck Cancer (ADV-1)
- Metastatic (M1) disease at initial presentation
  - See Treatment of Very Advanced Head and Neck Cancer (ADV-2)
BRONJ

• 2003: a pattern of jaw osteonecrosis began to be recognized
• difficult to treat and associated with certain medications - bisphosphonates (BRONJ)
• 2011 (ADA): antiresorptive-related, due to association with a monoclonal antibody (denosumab) designed to prevent osteoclastic maturation (ARONJ)
# BRONJ

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Route of Administration</th>
</tr>
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<tbody>
<tr>
<td>Pamidronate</td>
<td>Aredia</td>
<td>Intravenous</td>
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<tr>
<td>Alendronate</td>
<td>Fosamax</td>
<td>Oral</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>Boniva</td>
<td>Oral</td>
</tr>
<tr>
<td>Risedronate</td>
<td>Actonel</td>
<td>Oral</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>Zometa, Reclast, Aclasta</td>
<td>Intravenous</td>
</tr>
<tr>
<td>Clodronate</td>
<td>Bonefos</td>
<td>Oral/Intravenous</td>
</tr>
<tr>
<td>Etidronate</td>
<td>Didronel</td>
<td>Oral</td>
</tr>
</tbody>
</table>
MRONJ

• 2014 (AAOMS): medication-related due to discovery that antiangiogenic therapies may also be implicated
• risk is increased if agents are combined with bisphosphonates

<table>
<thead>
<tr>
<th>Antiangiogenic Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tyrosine kinase inhibitors:</td>
</tr>
<tr>
<td>• Sunitinib (Sutent)</td>
</tr>
<tr>
<td>• Sorafenib (NexAVAR)</td>
</tr>
<tr>
<td>Monoclonal antibody inhibiting vascular endothelial growth factor:</td>
</tr>
<tr>
<td>• Bevacizumab (Avastin)</td>
</tr>
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</table>
Medication-Related Osteonecrosis of the Jaw Case Definition

Required characteristics for diagnosis of medication-related osteonecrosis of the jaw (MRONJ):

- Current or previous treatment with antiresorptive or antiangiogenic agent
- Exposed bone in maxillofacial region for longer than 8 weeks
- No history of radiation therapy or obvious metastatic disease to the jaws
MRONJ (Pathogenesis)

- once in the serum, 50% of bisphosphonates are cleared by the kidneys with the remainder going to bone
- osteoclasts and osteoblasts have affinity for medication, incorporated into bone matrix - inhibit osteoclastic function resulting in disruption of the basic cellular unit (BMU)
RISK FACTORS

• advanced patient age (> 65 years)
• steroid use or chemotherapy
• diabetes
• smoking or alcohol
• poor oral hygiene
• duration of drug use > 3 years
CLINICAL FEATURES

• mandible > maxilla
• necrosis followed a dental extraction
• spontaneous, denture pressure, or minor trauma of a torus
• most are painful
• serum C-telopeptide (CTX) - not reliable in predicting risk of MRONJ
TREATMENT

• best therapeutic approach is prevention
• manipulation of bone should be avoided
• osteonecrosis can be minimized with antibiotic prophylaxis
• drug holiday (3 months) is controversial
• annual IV zoledronic acid - surgery in 2 months
• benefits of antiresorptive therapy greatly outweigh the risk of developing MRONJ
ORAL CANCER TREATMENT (NCCN GUIDELINES)

- surgical management
- radiotherapy
- chemotherapy
- radiochemotherapy
- molecular targeted therapy
Cancer of the Oral Cavity

Buccal mucosa, floor of mouth, anterior tongue, alveolar ridge, retromolar trigone, hard palate

CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

- Resection of primary (preferred) ± ipsilateral (guided by tumor thickness) or bilateral (guided by location of primary) neck dissection

ADJUVANT TREATMENT

- No positive nodes and no adverse features
- One positive node without adverse features
- Consider RT

FOLLOW-UP

- Follow-up (See FOLL-A)
- Recurrent or Persistent Disease (See ADV-3)

- Extracapsular spread ± positive margin
- Systemic therapy/RT (preferred) (category 1)

- Adverse features
- Positive margin
- Re-resection or RT

- Other risk features
- RT or Consider systemic therapy/RT

- SLN identification successful
- SLN pN0
- SLN pN+

- Neck dissection

- Definitive RT

- No residual disease
- Residual disease
- Surgery

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

1. See Principles of Surgery (SURG-A).

1. Adverse risk features: extracapsular nodal spread, positive margins, pT3 or pT4 primary, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, vascular embolism (lymphovascular invasion) (See Discussion).
2. See Principles of Systemic Therapy (CHEM-A).
3. Consider re-resection to achieve negative margins, if feasible.
• **Figure 2-86** Intensity-modulated radiation therapy (IMRT) radiation dose (isodose) distribution. Conformal radiotherapy target (*shaded blue*) is shown on an axial planning computed tomography (CT) scan image. Normal parotid glands (*shaded green*) and the spinal cord (*shaded red*) are also shown. Sample isodoses (*bold yellow and light green lines*) are shown conforming around the target while limiting radiation dose to the mandible, parotid glands, and spinal cord.
Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Oral Cavity and Pharynx Cancer

**Percent of Cases by Stage**
- **Localized (30%)** Confined to Primary Site
- **Regional (47%)** Spread to Regional Lymph Nodes
- **Distant (18%)** Cancer Has Metastasized
- **Unknown (5%)** Unstaged

**5-Year Relative Survival**
- Localized: 83.3%
- Regional: 63.3%
- Distant: 38.0%
- Unstaged: 47.2%

SEER 18 2006–2012, All Races, Both Sexes by SEER Summary Stage 2000
SUMMARY

• if oral cancers are diagnosed and treated early, they are eminently curable and the survival rate exceeds 80%

• your responsibility as dental practitioners should be primarily focused on early detection and prevention
Requirements for Ordering/Referring

1. **NPI**
   - The ordering/referring provider's NPI must be for an individual physician/NPP
   - Apply or verify NPI online
     - [https://nppes.cms.hhs.gov/NPPES/Welcome.do](https://nppes.cms.hhs.gov/NPPES/Welcome.do)

2. **Enroll**
   - The physician/NPP must be enrolled in Medicare in either an "approved" or an "opt-out" status
   - Apply or verify enrollment online
     - [https://pecos.cms.hhs.gov/pecos/login.do](https://pecos.cms.hhs.gov/pecos/login.do)

3. **Specialty Type**
   - The physician or NPP must be of a specialty type that is eligible to order and refer
   - [Part B and DMEPOS](https://pecos.cms.hhs.gov/pecos/login.do):
     - Certified Nurse-Midwives;
     - Clinical Nurse Specialists;
     - Clinical Psychologists;
     - Clinical Social Workers;
     - Interns, Residents, and Fellows;
     - Nurse Practitioners;
     - Optometrists (may order/refer only laboratory and X-ray services payable under Medicare Part B and DMEPOS products/services);
     - Physician Assistants; and
     - Physicians (Doctors of Medicine or Osteopathy, Doctors of Dental Medicine, Doctors of Dental Surgery, Doctors of Podiatric Medicine, or Doctors of Optometry)

**Claims with Ordering/Referring Information**

MACs deny the following claims if they lack a valid individual NPI:

- **Claims from clinical laboratories for ordered tests**
- **Claims from imaging centers for ordered imaging procedures**
- **Claims from suppliers of DMEPOS for ordered DMEPOS**
- **Claims from Part A HHAs**

**Part A HHA**

- Doctors of Medicine or Osteopathy; and
- Doctors of Podiatric Medicine
Our Treatment Approach

The Queen’s Head & Neck Institute offers comprehensive and individualized care for people with tumors of the head and neck. It is Hawai’i’s most active treatment center, and is staffed with health professionals who have exceptional expertise and depth of experience.

Head and neck tumors can be devastating to patients. At the Queen’s Head & Neck Institute, our goal is to give individualized treatment that will optimize the chances for cure while preserving quality of life. Our patients are cared for by a comprehensive, multidisciplinary team that will approach treatment from the perspectives of many specialties, with the ultimate goals of successful cancer treatment and preserving quality of life. The Queen’s Head & Neck Institute’s dedicated physicians and health professionals offer Hawai’i’s most advanced surgical techniques, leading edge systemic and targeted therapies, and outstanding rehabilitation services.
Christopher Klem, MD, FACS
Otolaryngology Head and Neck Cancer and Reconstructive Surgeon
MD Anderson Cancer Network® Certified Physician

Christopher Klem, MD, is a Head and Neck Surgeon at the Queen’s Head and Neck Institute. He recently served as the Chief of Otolaryngology – Head and Neck Surgery at Tripler Army Medical Center and retired as a Colonel from the Army after serving 26 years on active duty. Dr. Klem graduated from the Uniformed Services University of the Health Sciences in 1998 and performed his residency training in Otolaryngology – Head and Neck Surgery at Walter Reed Army Medical Center. He served as Clinical Instructor in Otolaryngology at both Walter Reed and the University of Maryland for a year after residency. After completing a two-year fellowship in Head and Neck Oncologic and Microvascular Reconstructive Surgery at MD Anderson Cancer Center in Houston, Texas, Dr. Klem moved to Hawaii and served as an Army physician at Tripler Army Medical Center for 8 years. In 2010, he deployed to Helmand Province in Afghanistan as a Head and Neck Surgeon where he performed more microvascular reconstructive surgeries in a combat zone than anyone ever has. Although he practices the entire spectrum of benign and malignant Head and Neck tumors, Dr. Klem’s special interests include oral cavity cancer, salivary gland tumors, thyroid and parathyroid, and complex microvascular reconstruction. He is recognized as one of the leaders in Head and Neck Clinical Ultrasound and instructs frequently for the American College of Surgeons. Dr. Klem holds appointments as Assistant Professor of Surgery at the University of Hawaii John A. Burns School of Medicine and the Uniformed Services University of the Health Sciences.

Education & Training

Medical School: Uniformed Services University of the Health Sciences
Residency: Walter Reed Army Medical Center
Professional Credentials

Certifications:
Otolaryngology – Head and Neck Surgery

Fellowships: MD Anderson Cancer Center, Head and Neck Oncologic and Microvascular Reconstructive Surgery
Daniel Alam, MD, is a specialist in head and neck reconstructive surgery, including complex microvascular reconstructions to repair major facial injuries and cancer defects. He was the primary microvascular surgeon of the first face transplant procedure in the U.S. at the Cleveland Clinic. Dr. Alam has developed six new surgical procedures over the last five years, from minimally invasive surgeries for facial paralysis to complex facial reconstruction methods. The success rate of microvascular reconstruction in his section at the Cleveland Clinic was unparalleled nationally. Dr. Alam also serves as a Clinical Professor of Surgery at the University of Hawaii John A. Burns School of Medicine.

After graduating from the Johns Hopkins University School of Medicine as valedictorian, Dr. Alam received his surgical training with an internship at Massachusetts General Hospital, followed by residency at the Harvard Medical School’s Combined Hospitals Program in Otolaryngology/Head and Neck Surgery. He then completed a fellowship in facial plastic and reconstructive surgery at the UCLA Medical Center and served on its faculty as a clinical instructor in facial plastic surgery. Before joining Queen’s, Dr. Alam served as the Section Head of Facial Aesthetic and Reconstructive Surgery in the Head and Neck Institute at the Cleveland Clinic and as Professor of Surgery at the Lerner College of Medicine at Case Western Reserve University.

He holds senior-level academic positions in the American Academy of Facial Plastic and Reconstructive Surgery (AAFPRS). He is the director of an AAFPRS-sanctioned Fellowship in Facial Plastic Surgery, and serves on the organization’s board of directors. Dr. Alam is a member of the AAFPRS National Academic Curriculum Committee, leading the section on facial paralysis and rehabilitation. He also serves on the editorial boards of four major journals.

Education & Training
Medical School: Johns Hopkins University School of Medicine
Residency: Harvard Medical School, Combined Hospitals Program in Otolaryngology/Head and Neck Surgery
Professional Credentials
Certifications:
Otolaryngology/Head and neck reconstructive surgery
Fellowships: UCLA Medical Center, facial plastic and reconstructive surgery
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