HPV and Oral Cancer

How do we prevent oral cancer?

Dr. Peter Angeletti

Oral Cancer

- 3% of all cancers in the US are in oral compartment
- 8th most common in men
- 30,000 new cases each year
- 8,000 deaths each year
- 5-year survival rate 52%
Oral Cancer

Rapid rise in oropharyngeal cx in middle aged (40-50) males without traditional risk factors

70% of oropharyngeal cancers in the US are HPV-related squamous cell carcinomas

90% of HPV-related oropharyngeal cancers due to infection with HPV16

An epidemic of HPV-mediated malignancy projected to surpass the incidence rate of cervical cancer by 2020 in US
Tobacco and HPV-related Cancers

Induces HPV Replication 3-5 Fold

Human Papillomavirus

- Non-enveloped
- Circular DNA, 8kb
- Icosahedral capsid
- 50 nm in size
- >200 types
- Lifetime risk > 80%
- >99% of cervical Cx attributed to HPV
Types of Mucosal HPVs

**High-Risk HPVs**
- Examples: High Risk HPVs-16, 18, 31
- Found in the vagina
- Infection can cause cervical cancer

**Low-Risk HPVs**
- Examples: HPV-6 and HPV-11
- Found in the mucosal linings
- Associated with genital warts

**HPV Genome**

- 8 Kb dsDNA
- Replicates Extra-chromosomally utilizing host cell Polymerase α
- LCR - major regulatory region keratin-dependent promoter, origin of replication
- 8 ORFs, complex splicing program

HPV-16
7905 bp
HPV Life Cycle

Squames
Granular
Spinous
Basal Lamina
Fibroblasts

E6, E7, E5

Expansion of The basal layer - benign hyperplasia

“Establishment”
HPV Life Cycle

"Establishment"

Expansion of The basal layer -benign hyperplasia

E6, E7, E5

Squames
Granular
Spinous
Basal Lamina
Fibroblasts
HPV Life Cycle

“Maintenance Phase”

- Low Copy Replication
- Theta Intermediate

Low E1 E2
E6, E7, E5
1-10 Copies/cell

HPV can be maintained indefinitely in basal follicular stem cells.

“Amplification Phase”

- Rolling Circle

100-1000 Copies/cell

E1, E2, E4
E6, E7, E5

E6, E7, E5
HPV Life Cycle

Wart

Squames
Granular
Spinous
Basal Lamina

Fibroblasts

E6, E7, E5
E1, E2, E4
L1, L2
HPV DNA integration and Cancer

HPV Infection and Cancer Incidence
Cervical Lesions

- HPV Pathogenesis may be detected by macroscopic or microscopic cervical lesions
- Cervical cytology used to grade severity of lesions
  - Negative, low grade, high grade

Oral Dysplasia to Cancer

- Normal appearing epithelium
- Hyperplasia
- Mild dysplasia
- Severe dysplasia or carcinoma in situ
- Invasive carcinoma

Carcinogen exposure
- Genetic changes
- Epigenetic aberrations
  - Promoter (methylation status, histone code)
  - Immune escape

Genomic instability

Argiris et al. The Lancet
Volume 371, Issue 9625, Pages 1695-1709 (May 2008)
Examples of Early Oral Cancers

White Lesions

Red Lesions

Ulcerated Lesions

Early Detection is the Key

Outcomes of oral cancer early detection and prevention statewide model in Maryland
Catherine Maybury, MPH1, Alice M. Horowitz, PhD1; Harold S. Goodman, DMD, MPH2
1. School of Public Health, University of Maryland
2. Office of Oral Health, Maryland Department of Health & Mental Hygiene

Table 1: Key findings from Surveys of and Focus Groups with Maryland Health Care Providers and Adults (1992-2000)

- Most oral cancers were detected at a late stage and were diagnosed by physicians, not dentists (4,5).
- Most dentists and dental hygienists reported providing oral cancer examinations, but the majority of respondents did not perform a critical component of the examination—palpation. And, many did not know where to look or what to look for (4,5).
- Most dentists and dental hygienists did not provide oral cancer examinations for edentulous patients (4,5).
- The majority of health care providers know that tobacco and alcohol are risk factors for oral cancer, but do not adequately address tobacco and alcohol use with their patients and many feel inadequate in doing so (4,5).
- The adult public was not knowledgeable about oral cancer prevention and early detection. Only 23% of respondents could identify one early sign of oral cancer and only 21% had heard of an examination for oral cancer (3).
- Only 28 percent of surveyed adults reported ever having had an oral cancer examination (3).
Model Strategy for Oral Cancer Screening

Oral Cancer Literacy
- What everyone needs to know:
  - Risk assessment and risk reduction
  - Risk factors
  - Signs and symptoms
  - Oral cancer exam steps
  - Frequency of oral cancer exam

Provider*
- Provider education
- PQP
- Dental health professionals

Public*
- Educational interventions such as schools/agencies, workplaces, hospitals, faith-based institutions, service organizations, sports and recreation, websites, government, providers

Media*
- Awareness

Policy Makers*
- Funding for research
- Covering of medically necessary dental procedures
- Uniform adult dental coverage that includes preventive services as well as emergency care
- Management/denial of uninsured and undocumented populations
- CMU/CEU
- Medical and dental board licensure and re-licensure
- Oral cancer competency module on licensure exams

Use and provide appropriate screening, referral, follow-up, and treatment

Be Mouthaware and look out for the signs and symptoms of mouth cancer

As mouth cancer can strike in a number of places, including the lips, tongue, gums and cheek, it’s extremely important that we all know what to look out for.

- Ulcers which do not heal within three weeks
- Red & white patches in the mouth
- Lumps or swellings in the mouth or head & neck area
- If in doubt get checked out!
The Pap Smear

Polychromatic Staining using:
- OG6 – Orange
- EA50- Eosin Azure Blue
State of the Art: Oral Cytology

Oral cytology = Oral “Pap Smear”
"Journal of the American Dental Association"

“Oral cytology should be a part of every oral examination in which the dentist detects even the least suspicious lesion”

-recommendations published 30 years ago.

Some of the Problems: Oral Cytology

-10% of all dentists have ever done an oral cytology smear
-42% were ever taught how to do a smear
-96.9 % of dental offices lack necessary materials

**Emerging Best Practices**

*Communication*

- Raising public awareness about signs, symptoms, risk factors & change in demographic of oral cancer

- Evaluating risk profile of patients through a questionnaire and direct conversation

- Assessing readiness to quit smoking/alcohol & refer as indicated

- Inquiring parents about HPV vaccination of their children

- Asking patients about voice changes (hoarseness), lump in throat/neck, swallowing difficulty

- Repeating patient education at every visit

*Emerging Best Practices*

*Examination*

- Screening every patient starting at age 15

- Performing regular & thorough inspection of head, neck & oral tissues

- Informing patients when you are screening for oral cancer

- Documenting all signs/symptoms

- Having a low threshold for referral if signs or symptoms persist

- Instructing patients how to perform self exam between visits
Questions