Red & White
Oral Precancerous and Cancerous Lesions

Iowa Dental Association
2008 Annual Session
Michael D. Rohrer, DDS, MS
Professor and Director, Division of Oral & Maxillofacial Pathology
University of Minnesota

Estimated New Cancer Cases and Deaths, US, 2008

	New Cases	Deaths
All sites	1,437,180	565,650
Oral/pharyngeal	35,310	7,590

Oral Cancer Outnumbers Many Others

- Cervical
- Stomach
- Liver
- Larynx
- Brain
- Bone & Joint
- Testes

WHITE AND RED LESIONS

DIFFERENTIAL DIAGNOSIS FOR RED & WHITE LESIONS

- Hyperkeratosis (traumatic or other)
- Squamous Cell Carcinoma
- Verrucous Carcinoma
- Physical and Chemical Injury
- Candidiasis
- Lichen Planus
- Geographic Tongue
- HIV Manifestations

WHITE PATCHES

LEUKOPLAKIA

DANGER SIGNALS!!

- NO CAUSE
- CAUSATIVE AGENT CARCINOGEN
- LOCATION
- ULCERATION, INDURATION, REDNESS (ERYTHROPLAKIA)

DANGER SIGNALS!!

- NO CAUSE

  This is the single MOST IMPORTANT danger signal

Practice according to the "M/S System"

What would you do for your

Mother or Sister?

HYPERKERATOSIS-VARIATIONS

- SOLAR CHEILITIS
- NICOTINE STOMATITIS
- SNUFF DIPPERS POUCH

IDIOPATHIC LEUKOPLAKIA

A clinical white lesion that does not rub off and cannot be determined to be a specific disease.

W.H.O. and M.D.R.

IDIOPATHIC LEUKOPLAKIA

MUST BE BIOPSIED!

What I've learned from consulting on malpractice cases

- **Document well**
- **(Digital) pictures are easy and great**
- **If you see a lesion, have a good reason <u>not</u> to have it biopsied (follow my Danger Signals)**
- **Lawyers want to see a biopsy report**
- **Document patient's compliance with follow-up**

What I've learned from consulting on malpractice cases

If something goes wrong in treatment, a patient will want to blame someone - the person who might have missed the lesion in an early stage is a good target

What I've learned from consulting on malpractice cases

- **Do a head & neck and oral exam at *<u>EACH</u>* visit**
- **DOCUMENT THIS**

WHICH PATHOLOGISTS SHOULD YOU USE?

- **Oral Pathologists**
- **Ones you trust**
- **Ones you know the best**

What do I do if the dx is hyperkeratosis/hyperplasia ?
Keep an eye on it - biopsy it periodically
What do I do if the dx is dysplasia?
Excise the entire lesion and keep an eye on it for recurrence

LEUKOPLAKIA

35% of excised lesions recur

Silverman, Gorsky, Lozada
Cancer 53:563-568, 1984

LEUKOPLAKIA

MALIGNANT TRANSFORMATION

Non-smokers	**24%**
Smokers (continuous)	**16%**
Smokers (quit)	**12%**

Silverman, Gorsky, Lozada
Cancer 53:563-568, 1984

LEUKOPLAKIA

In the absence of tobacco as an irritating, causative agent, there may be a more lethal initiating or potentiating factor.

Silverman, Gorsky, Lozada
Cancer 53:563-568, 1984

PUNCH BIOPSY

Advantages

- **Easy**
- **Good specimen**
- **Doesn't twist**
- **No suture**

Acuderm, Inc.

Ft. Lauderdale, FL

5mm or 6mm

Toll Free 800-327-0015

LEUKOPLAKIA

Need for continued observation no matter how long the white patch has been present and seemingly benign

Silverman, Gorsky, Lozada
Cancer 53:563-568, 1984

Pain & Cancer

Some have the impression that if it's painful, it's not cancer

WRONG!

LEUKOPLAKIA PAIN

50% of patients with leukoplakia at the time of diagnosing their malignant transformation had complaints of pain.

Silverman, Gorsky, Lozada
Cancer 53:563-568, 1984

ERYTHROPLAKIA 91% are either:

- **Invasive carcinoma**
- **Carcinoma *in situ***
- **Severe epithelial dysplasia**

Shafer & Waldron
Cancer 36:1021-1028, 1975

The persistence of erythroplastic lesions for more than 14 days without obvious cause requires biopsy.

Mashberg, *et al.*
Cancer 32:1436-1445, 1973

SPECKLED ERYTHROPLAKIA

ALMOST ALWAYS CARCINOMA *IN SITU* OR SQUAMOUS CELL CARCINOMA

Asymptomatic, early squamous cell carcinoma

90.5% had a red component
62% had a white component
78% of these were patchy or stippled

Mashberg, *et al.*
Cancer 32:1436-1445, 1973

ERYTHROPLAKIA

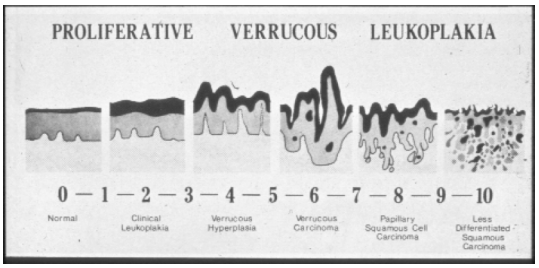
>90% dysplasia or squamous cell carcinoma

DANGER SIGNALS!!

- NO CAUSE
- CAUSATIVE AGENT CARCINOGEN
- LOCATION
- ULCERATION, INDURATION, REDNESS (ERYTHROPLAKIA)

Proliferative Verrucous Leukoplakia (PVL)

What is this and how will it affect my practice?



PROLIFERATIVE VERRUCOUS LEUKOPLAKIA (PVL) (1)

- High risk oral white lesion
- Progression from hyperkeratosis to squamous cell carcinoma
- HPV (subtype 16/18) may be a causative factor

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA (PVL) (2)

University of Minnesota Study (Rohrer & Betterman)

- Females 2:1 Males
- Each subsequent biopsy is likely to be a higher grade (even if from another location)
- Gingiva is the most likely location
- Smoking plays no or a minor role

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA (PVL) (3)

- No absolutely predictive histologic pattern
- No test to perform to prove likely progression (aneuploidy? ki67? p16?)
- Must be re-evaluated very frequently and totally removed if recurs

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA (PVL) (4)

- High rate of "field cancerization"
- >50% defeloped further SCC in other parts of the oral cavity
- Supports hypothesis of an infectious agent, such as HPV

Gagan, J.V., *et al.*
Oral Oncology (2004):40;440-443

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA (PVL) (5)

- Development of at least one additional squamous cell carcinoma
  - 90% females
  - Most frequent location = gingiva and palate (80%)

Gagan, J.V., *et al.*
Oral Oncology (2004):40;440-443

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA (PVL) (6)

- Very low frequency of SCC in PVL in the typical "high risk" locations despite frequency of PVL in those sites
- 84% females
- Only 21% smokers

Gagan, J.V., *et al.*
Oral Oncology (2004):40;440-443

What's the relationship of Human Papilloma Virus to oral cancer?

- Not really sure, but there's a lot of activity and lots of speculation
- HPV is now accepted as the causal agent of cervical cancer
- HPV appears to be involved in the etiology of cancer of the oral cavity

"HPV appears to play an etiologic role in many cancers of the oropharynx and possibly a small subgroup of cancers of the oral cavity. The most common HPV type in genital cancers (HPV16) was also the most common in these tumors."

Herrero, R *et al.*
Journal of the National Cancer Institute
December 2003; 95:1772-83

"These results support the idea of systemic susceptibility, and infection through a common agent such as HPV, contributing to the cause of squamous cell carcinoma."

Postma, TC and Van Heerden WF
Anticancer Research
July-August 2003 (4):3509-12

"Our results suggest an association of oral carcinogenesis and infection with the high-risk HPV types 16 and 18."

Ostwald, C *et al.*
Med Microbiol Immunol (Berlin)
August 2003; 192:145-8

"These results strongly suggest that HPV-16 may be involved in the early stages of the development of some oral carcinomas."

Sugiyama, M *et al.*
Oral Surg Oral Med Oral Pathol Oral Radiol Endod
May 2003; 95:594-600

Aneuploid Dysplastic Oral Leukoplakia

- **"ploidy" is nuclear DNA content**
- **Diploid - normal nuclear content**
- **Tetraploid - double the normal amount of DNA and # of chromosomes**
- **Aneupoid - amount of DNA not an exact multiple of the diploid number**

What about new ways of detecting potentially malignant lesions earlier?

Critical Evaluation of Diagnostic Aids for the Detection of Oral Cancer*

M Lingen, J Kalmar, T Karrison & P Speight

Oral Oncology 2008 Jan;44(1):10-22

University of Chicago, Ohio State University, University of Sheffield

*** A position paper of the American Academy of Oral and Maxillofacial Pathology**

True Positive and True Negative Requires a "GOLD STANDARD"

GOLD STANDARD for tissue diagnosis is a scalpel biopsy

Screening vs. Case-Finding

•Case-finding - a diagnostic test for a patient who has abnormal signs or symptoms (Class I)

•Screening - checking for a disease in a person who is symptom free (Class II)

Evidence of chemiluminescence enhancing intraoral examinations?

Literature was only for gynecological examinations until 2004

Only 6 articles in the literature

MOST RECENT

Efficacy of the ViziLite System in the Identification of Oral Lesions

Oh, ES and Laskin, DM

J Oral Maxillofac Surg 2007 Mar;65(3):424-6

School of Dentistry, University of North Carolina, Chapel Hill, NC

32 clinically undiagnosable lesions were examined with Oral CDx
2 were "atypical" and were biopsied
Neither was premalignant or malignant

Conclusions: "Although the acid rinse accentuated some lesions, the overall detection rate was not significantly improved. The chemiluminescent light produced reflections that made visualization more difficult and thus was not beneficial."

Vizilite® **My opinion at this time**

•Extra time and care using the system ARE VALUABLE

•Evidence of aiding detection of premalignant lesions is quite sparse

•Unclear what added benefit there is to practitioner

•Cannot discriminate indolent lesions from biologically worrisome

VELscope®

My opinion at this time

•Best use is in determining margins for excisions of premalignant lesions

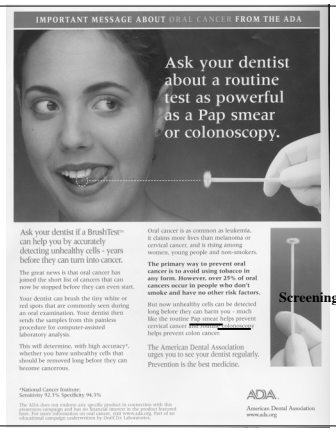
•Could be useful in screening if shortcomings cited in the literature can be corrected

Biopsy versus other methods of analyzing oral tissues

Brush "Biopsy"

exfoliative cytology (1)

- **PROS**
  - **No anesthesia**
  - **Patient acceptance**
- **CONS**
  - **Negative results are not biopsied**
    - **? trust ?**
    - **No research on negatives**



Screening exams

The Brush Test® is a "case-finding" test, not a "screening test"

Brush Test®

exfoliative cytology

- **PROS**
  - **No anesthesia**
  - **Patient acceptance**
- **CONS**
  - **Negative results are not biopsied**
    - **? trust ?**
    - **No research on negatives**
    - **Negative results were not tested against the "gold standard"**

Brush Test®

exfoliative cytology

- **PROS**
  - **No anesthesia**
  - **Patient acceptance**
- **CONS (continued)**
  - **No diagnosis**
  - **"Positive" or "Atypical" results <u>still need to be biopsied</u>**
    - **delayed diagnosis**
    - **extra cost**

Brush Test®

exfoliative cytology

- **PROS**
  - **No anesthesia**
  - **Patient acceptance**
- **CONS (continued)**
  - **Extremely high number of false positives**

Brush Test®

exfoliative cytology

- **PROS**
  - **No anesthesia**
  - **Patient acceptance**
- **CONS (continued)**
  - **No ability to detect dysplasia by architecture**
  - **No baseline histology if future biopsies are done**

Brush Test®

exfoliative cytology

Shows promise

Study needed with a large cohort of Class II subjects with brush and biopsy of ALL subjects

Brush Test® may be beneficial:

1. **Multiple lesions, particularly in someone with no history of oral cancer**
2. **Non-compliant patient who is unlikely to come back for a follow-up exam or accept an immediate biopsy**

Judicious use in these scenarios may be clinically useful

Brush "Biopsy"

exfoliative cytology (5)
ADA Council on Scientific Affairs

All Oral CDx "atypical" or "positive" results must be confirmed by incisional biopsy and histology to completely characterize the lesion.

Brush "Biopsy"

exfoliative cytology (6)
ADA Council on Scientific Affairs

Persistent lesions, even with negative results, must receive adequate follow-up evaluations.