Diagnosis and Treatment of Diseases and Disorders Causing Desquamative Gingivitis
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  Dallas, Texas
Desquamative Gingivitis

• A clinical manifestation of several diseases and disorders featuring gingival erythema, sloughing of gingival epithelial tissues and potentially painful erosive gingival lesions.

• Mostly caused by mucocutaneous diseases with the most common being lichen planus, mucous membrane pemphigoid and pemphigus vulgaris. Other causes include hypersensitivity reactions to various oral hygiene products and dental materials.

• Confirmed diagnosis may require histopathological examination and direct immunofluorescence testing.
Phases of Therapy

Diagnostic phase
Control phase
Consolidation phase
Maintenance phase

Modified from:
Brystryn, 1988
Sciubba, 1996
Accuracy of Dentists in Clinical diagnosis of Oral lesions

- 976 oral biopses reviewed
- 43% were incorrect
- Malignant lesions clinically misdiagnosed 5.6%

Incorrect
- General dentists 46%
- Oral Surgeons 42.8%
- Endodontists 42.2%
- Periodontists 41.2%
Diagnostic Phase

- Past history
- Clinical appearance
- Biopsy
  - Histology
  - Direct immunofluorescence
- Indirect immunofluorescence
- Culture/smear
- Ancillary tools?
Biopsy Site Selection

- Choose an area of intact epithelium
- Include perilesional tissue
- Select normal appearing tissue for some immunofluorescence testing
- When possible avoid gingival biopsies
Post-Surgical Management

- Monsel’s Solution (ferric subsulfate)
- Synthetic collagen
- Gelfoam
Shipment

Formaldehyde for histopathologic evaluation

Ambient temperature transport media (Michelle’s solution) for DIF

Obtain each from pathology lab or immunology lab, usually without charge
Control Phase

- Intense therapy to suppress disease in days or weeks
- Efficacy versus safety versus patient acceptance
- Avoid patient disenchantment over multiple daily treatment yet minimal results.
- Prevent side effects such as candidiasis.
Control Phase Alternatives

- **Aggressive** therapy with very high potency topical or systemic corticosteroids
- **Moderate** therapy with high potency topical corticosteroids combined with intralesional injections when indicated
- **Mild** therapy with medium or low potency topical corticosteroids and carrier (Kenalog in Orabase, denture adhesive, patches etc.)
Consolidation Phase

- Maintain required type and dose of medications until bulk of lesions have healed
- Weeks not months
- If lesions are slow to heal intensity of therapy may be inadequate
Therapeutic Endpoints
(Perio Workshop 1996)

Remission
Suppression of symptoms
Maintenance Phase

• Gradually taper **frequency** of medication use and/or **potency** of medication
• Goal is to achieve complete remission or to determine lowest dosage necessary to prevent new lesions
• Sustain periodontal health with frequent recall intervals, oral antimicrobials, etc.
• Determine appropriate recall intervals
Department of Periodontics
Stomatology Center
Baylor College of Dentistry
September 1, 2011
Number of Patients: 7385
# Disease Frequency

**7856 Patients (BCD) (September 2012)**

<table>
<thead>
<tr>
<th>Disease Description</th>
<th>Count (N)</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Erosive lichen planus/ lichenoid drug reaction</td>
<td>1015</td>
<td>12.9%</td>
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<tr>
<td>Xerostomia</td>
<td>839</td>
<td>10.7%</td>
</tr>
<tr>
<td>Chronic candidiasis</td>
<td>767</td>
<td>9.0%</td>
</tr>
<tr>
<td>Aphthae &amp; other ulcerations</td>
<td>521</td>
<td>6.6%</td>
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<tr>
<td>Sjögren’s syndrome</td>
<td>447</td>
<td>5.7%</td>
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<tr>
<td>Allergic reactions</td>
<td>325</td>
<td>4.1%</td>
</tr>
<tr>
<td>Burning mouth syndrome</td>
<td>313</td>
<td>4.0%</td>
</tr>
<tr>
<td>Mucous membrane pemphigoid</td>
<td>213</td>
<td>2.7%</td>
</tr>
<tr>
<td>Hyperkeratosis</td>
<td>176</td>
<td>2.2%</td>
</tr>
<tr>
<td>Migratory glossitis</td>
<td>143</td>
<td>1.8%</td>
</tr>
<tr>
<td>Oral malignancies</td>
<td>74</td>
<td>0.9%</td>
</tr>
<tr>
<td>Pemphigus vulgaris</td>
<td>58</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>4891</strong></td>
<td><strong>62.2%</strong></td>
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</tbody>
</table>
Other Disorders Causing Desquamative Gingivitis

(BCD) (September 2012)

- Graft vs. host disease 33
- Lupus erythematosus 16
- Erythema multiforme 14
- Leukemic/lymphocytic gingivitis 9
- Scleroderma 9
- Psoriasis 8
- Chronic ulcerative stomatitis 8
- Sarcoidosis 8
- Lichen planus/Pemphigoides 7
- Gingival histiocytosis X 4
- Epidermolysis bullosa 4
- Wegener's granulomatosis 3
- Pyostomatitis vegetans 3
- Actinomycosis 2
- Gingival histoplasmosis 2
- Ehlers-Danlos syndrome 2
Mucocutaneous Diseases
Oral Lichen Planus Types

- Papular
- Reticular
- Plaque-like
- Atrophic
- Ulcerative
- Bullous

Reticulated
Erythematous
Erosive

Andreasen 1968
Eisen 1993
ELP Concomitant Findings (BCD)(04/05)

- Skin 12.2%
- Genitalia 1.6%
Vulvo-Vaginal Gingival Lichen Planus Syndrome
EROSIVE LICHEN PLANUS
LABORATORY CONFIRMATION
(September 2012)

Biopsy  
72.6%

Direct IF  
69.5%
Treatment
OLP Treatment Options

- Topical corticosteroids
- Oral retinoids
- Phototherapy
- Prednisone
- Oral cyclosporin 2.5-5 mg.kg/d in 2 divided doses
- Mycophenolate mofetil 0.5-1.0 g 2x daily
- Azathioprine 1-2.4 mg/kg/d in 1-2 divided doses
- Methotrexate 2.5-7.5 mg once weekly
- Griseofulvin microsize 500 mg/d for 2-4 weeks
- Metronidazole 500 mg 2/d for 2 months
- Sulfasalazine 1.5 g/d increase by 0.5 g/d every week for 4-16 weeks. Maximum 4 g/d
- Alefacept
- Tetracycline
- Aloe vera gel or benzydamine rinse
- Topical calcineurin inhibitors
  - Tacrolimus topical (0.03% or 0.1%) 2x daily
  - Pimecrolimus topical 15 2x daily
High Potency Topical Corticosteroids

- 0.25% Desoximetasone (Topicort)
- 0.20% Fluocinolone (Synalar HP)
- 0.05% Fluocinonide (Lidex)
- 0.50% Triamcinolone Acetonide (Aristocort, Kenalog)

Monitor quantity used and do not exceed 15 grams within two weeks
Highest Potency Topical Corticosteroids

• Betamethasone dipropionate (Diprolene) 0.05% gel, cream, ointment
• Clobetasol (Temovate) 0.05% gel, cream, ointment
• Halobetasol (Ultravate) 0.05% cream, ointment
Immune Suppression

- Oral application of fluocinonide resulted in no detectable systemic uptake. (Plemons et al 1990)
- Application of large quantity of topical clobetasol to skin resulted in significant systemic uptake. Effect was dose related. (Allen, 2002)
- Oral use of topical clobetasol 1.5 gm daily for 2 weeks resulted in a small but detectable systemic uptake. (IADR abs.- Ezzo and Plemons, 1993)
- To date no adverse systemic effects have been reported related to oral use of topical corticosteroids
Intralesional Corticosteroids

• Deliver high concentration to diseased site with minimal systemic absorption
• Use alone or in combination with other therapy
• Triamcinolone acetonide injectable (Kenalog 10mg/ml or 40 mg/ml)
• Tuberculin syringe (27 gauge)
• Inject 1mg/cm²
• Repeat at 1-2 week intervals if needed up to 4 times
• Primarily use- buccal, labial mucosa, or tongue
Potential Adverse Effects

• Xerostomia
• Candidiasis
• Epithelial atrophy
• Systemic effects
  – Adrenal suppression
  – Hypertension
  – Blurred vision
  – Elevated blood glucose
  – GI hemorrhage
Steroid Carrier Trays
Disadvantages to Carrier Trays

• Insertion and removal may initiate gingival desquamation
• Risk of increased systemic uptake
• Risk of gingival epithelial thinning
Other Treatments

- Topical tacrolimus (Protopic)- FDA warning
- Topical pimecrolimus (Elidel)- FDA warning
- Plaque control
- Topical cyclosporine A- expense
- Soft “plumper” mouthguards- prevent cheek, lip and tongue irritation
- Replace faulty restorations or restorations causing a contact lichenoid reaction
- Doxycycline monohydrate 100 mg daily for 3 weeks (Ronbeck, 1990)
Potential New Treatment

• Tacrolimus capsule 1mg dissolved in 1000 ml sterile water
  – Rinse with 1 tsp 4 times daily
  – One report describes 20% complete remission, 70% improvement
    » Valeric et al *Arch Dermatol* 2002
    » Gould A. *Am Acad Oral Max-Fac Path* 2012 (Oral presentation)
Alternative Systemic Therapy

- Cyclosporine
- Dapsone
- Azathioprine
- Tetracycline
- Retinoids (Temarotene)
- Griseofulvin
- Psoralen and ultraviolet light
- Others
Periodontal Status in Patients with Chronic Gingival Erosive Lichen Planus

Aristidis Pontikas

Master of Science Thesis

May 2003
Relationship between chronic gingival ELP and periodontal health

1 study documented that effective plaque control improves OLP lesions.
Holmstrup et al 1990

1 study found that presence of OLP had no significant effect on periodontal health
Ramon-Fluixa et al 1999
Materials and Methods

- Periodontal indices were measured in 40 individuals with biopsy confirmed gingival erosive lichen planus
- 40 patients without lichen planus served as age and sex matched controls
- Measurements included Gingival Index, probing pocket depth, clinical attachment level, recession, bleeding on probing, Plaque Index, presence or absence of periodontitis (Machtei et al)
Results

• Individuals with gingival erosive lichen planus were found to have statistically significant increases in;
  – Plaque retention
  – Bleeding on probing
  – Gingival inflammation
Results (Cont.)

– Grade I furcation defects
– Clinical attachment loss
– Gingival recession
– Periodontitis

(2 or more sites with CAL >6mm and 1 or more sites with probing depth >5mm)
Possible Etiology

• Inadequate oral hygiene and plaque induced inflammation
• Effects of drugs causing immune suppression
• Thinning of gingiva associated with use of topical corticosteroids
Conclusions

• Consider lichenoid drug or contact reactions
• Treatment should be progressive:
  – High potency steroids
  – Very high potency steroids
  – Intralesional steroids (less effective on gingiva)
  – Carrier trays for gingival OLP
  – Short term systemic corticosteroids (2 to 3 weeks)
  – Referral or long term systemic corticosteroids?
Conclusions (Cont.)

• Periodontal disease is more frequent and severe in patients with gingival erosive LP
• Ideally gingival LP lesions should be controlled before definitive periodontal Rx
• Patients with gingival lesions can tolerate periodontal RX-lesions will worsen temporarily then improve
• Consider use of low dose doxycycline or local delivery antimicrobial agents
International Oral Lichen Planus Support Group

- Oral lichen planus support group - TAMHSC
- Iolp dallas
- www.tambcd.edu/lichen/
Mucous Membrane
Pemphigoid
Mucous Membrane Pemphigoid (MMP)

- Autoimmune disorder
- Oral &/or other mucous membranes affected
- Mean age of onset = 50
- Females > Males
# MMP

## Clinical Sites (09/2011)

<table>
<thead>
<tr>
<th>Site</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Gingiva</td>
<td>93.0%</td>
</tr>
<tr>
<td>Mucosa</td>
<td>19.8%</td>
</tr>
<tr>
<td>Palate</td>
<td>10.6%</td>
</tr>
<tr>
<td>Tongue</td>
<td>3.1%</td>
</tr>
<tr>
<td>Pharynx</td>
<td>1.1%</td>
</tr>
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</table>
MMP Clinical Sites (September 13, 2012)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gingiva</td>
<td>89.5%</td>
</tr>
<tr>
<td>Mucosa</td>
<td>24.4%</td>
</tr>
<tr>
<td>Palate</td>
<td>10.5%</td>
</tr>
<tr>
<td>Tongue</td>
<td>7.2%</td>
</tr>
<tr>
<td>Pharynx</td>
<td>1.1%</td>
</tr>
</tbody>
</table>
MMP
Diagnosis

- Clinical appearance
- Histopathological examination
- Immunofluorescence
MMP Laboratory Confirmation

- 155 patients
  - DIF 90.6%
  - Histopathology 78.7%
- 11 patients diagnosed by H&E alone
- 5 patients diagnosed by DIF alone
Treatment

• Steroids similar to oral lichen planus
• Plaque control
• Low dose doxycycline?
• Others
  – Dapsone
  – Methotrexate
  – Azathioprine
  – Mycophenolate mofetil (CellCept)
  – Cyclophosphamide
Periodontal Status in Patients with Gingival MMP

- Markedly significant increase in plaque and gingival indices.
- Significant increases in class 1 molar furcation involvement and gingival recession
- Periodontal index not significantly increased

Tricamo, Melissa et al
Periodontal status in patients with mucous membrane pemphigoid: a 5 year follow-up (Schellinck, AE et al 2009)
• 10 of the same MMP and age, sex and smoking matched control patients compared 5 years later.
• MMP patients had higher gingival index and lingual gingival recession
• Both groups exhibited significant increases in attachment loss but no difference between groups
• Conclusion: MMP patients appear at no greater risk of increased progression of periodontal disease.

Non-surgical periodontal therapy

- Removal of plaque and calculus is essential but avoid impingement on biologic width.
  - Recommend **serial full-mouth debridement**, allowing 2-3 weeks between treatment sessions to achieve partial resolution of tissue inflammation and exposure of subgingival calculus.
  - **Hand instruments** may be preferred to insure minimal tissue trauma.
  - Consider use of **subgingival controlled release antimicrobial agents**
# MMP (04/05)

## Results of Treatment, 102 Patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Remission</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Complete</td>
</tr>
<tr>
<td>Topical steroids only</td>
<td>15</td>
</tr>
<tr>
<td>Topical+short term systemic</td>
<td>12</td>
</tr>
<tr>
<td>Topical+long term systemic</td>
<td>6</td>
</tr>
<tr>
<td>Topical+Dapsone</td>
<td>3</td>
</tr>
<tr>
<td>Topical+antibiotics</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total number</strong></td>
<td><strong>41</strong></td>
</tr>
<tr>
<td><strong>percent</strong></td>
<td><strong>40.2</strong></td>
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</table>
Therapy Issues

• It is not known whether asymptomatic lesions should be treated
• Therapeutic endpoints required to prevent progression have not been established
Pemphigus Vulgaris
Pemphigus Vulgaris (BCD) (September 13, 2012)

- Females 69.0% average age 48.1 years
- Males 31.0% average age 44.9 years
- Combined average age 47.1 years
Skin Lesions

- Bullae
- Erosions
- Can lead to fluid loss and electrolyte imbalance
- Septicemia
Oral Sites

- Mucosa: 60.4%
- Gingiva: 43.4%
- Tongue: 35.9%
- Palate: 26.4%
- Lips: 26.4%

- Mucosa only: 11.3%
- Gingiva only: 7.6%
- Tongue only: 5.7%
Treatment

- Topical corticosteroids - rare
  (Endo et al J Periodontol 2005;76:154-160)
- Topical carrier trays for gingival lesions
  (Endo et al J Periodontol 2005, 2007)
- Intralesional steroid injections
- Short and long term systemic corticosteroids
Alternative Treatment

- Methotrexate
- Aziathioprine
- Dapsone
- Mycofenolate mofetil
- IV immune globulin
- Retuximab (monoclonal antibody)
- Plasmophoresis
- Others
Oral Allergic Reactions
Types of Allergic Reactions (BCD)(9/12)

- Lichenoid Drug 59
- Dental Restorative Materials 51
- Cinnamon/Toothpaste 50
- Erythema Multiforme 14
- Foods and others 11
Contact Stomatitis versus Contact Dermatitis

- Allergic/irritant stomatitis requires longer period of contact
- Saliva dilutes or removes sensitizers and may exert a buffer or neutralizing effect
- Mucosal vascularity may induce rapid dispersion and absorption
Contact Hypersensitivity Reactions
327 Patient (September 13, 2012)

• Female 285 (87.2%)
• Male 42 (12.8%)

• Average age
  – Female 48.8 years
  – Male 46.8 years
  – Combined 48.4 years
Signs of Dentifrice Allergy

- Generalized or localized gingivitis
- Mucositis/glossitis
- Cheilitis
- Lip edema
- Perioral dermatitis

Investigations

- Mucosal biopsy=8
- Patch test=13
- Rechallenge=10
Toothpaste Hypersensitivity

- Sensitivity to tarter control and other toothpaste usually involves the flavoring agents, especially cinnamic aldehyde.
- Adverse reactions, although uncommon, should be considered in the differential diagnosis of oral or gingival edema, erythema or ulceration.
- Oral biopsy and patch testing are important in confirming such reactions and the etiologic agent involved.
## Dentifrices

<table>
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<th>Ingredients</th>
<th>Sensitization</th>
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<tr>
<td>Flavoring</td>
<td>Common</td>
</tr>
<tr>
<td>(cinnamic aldehyde)</td>
<td></td>
</tr>
<tr>
<td>Coloring agents</td>
<td>Rare</td>
</tr>
<tr>
<td>Abrasives</td>
<td>Rare</td>
</tr>
<tr>
<td>Soaps or detergents</td>
<td>Rare</td>
</tr>
<tr>
<td>Base materials</td>
<td>Rare</td>
</tr>
<tr>
<td>Preservatives</td>
<td>Common</td>
</tr>
</tbody>
</table>
Flavoring Agents

- Cinnamon oil
- Cinnamic aldehyde
- Menthol (also in peppermint)
- Mint/spearmint
- L-carvone
- Anethole

- Essential oils
  - Eugenol (eucalyptus oil)
  - Peppermint
  - Wintergreen (methyl salicylate)
  - Clove oil
Cinnamon-Induced Contact Stomatitis (BCD)

- 37 patients (32 female, 5 male)
- Age range 20-80 years
- Mean age 48.4 years

Symptoms/Signs

• Symptoms: Burning/soreness 43%
• Signs:
  – Erythema 84%
  – White plaque 24%
  – Fissured tongue 14%
  – Ulcerations 8%
Clinical Sites

- Gingiva 60%
- Oral mucosa 40%
- Tongue 30%
- Lips and perioral 24%
Diagnostic Methods

• Clinical appearance (11)  30%
• Biopsy (18)              49%
• Patch test (14)          38%
Biopsy Findings (18 patients)

- Chronic gingivitis/mucositis (18) 100%
- Granulomatous reaction (5) 28%
- Psoriasiform inflammation (3) 17%
- Lichenoid features (1) 6%
Patch Test Results (14 patients)

• Positive (11) 79%
• Negative (3) 21%
• Allergen:
  – Cinnamic aldehyde (10)
  – Cinnamic acid (1)
Exposure Medium

- Toothpaste (27)  62%
- Food products (8)  19%
- Chewing gum/mints (8)  19%
Treatment

• Discontinue exposure and avoid further contact with the allergen.

• Results:
  – Complete remission: 15 of 16
  – Partial remission: 1
The Role of Dental Restorative Materials in the Etiology of Oral Mucosal Diseases
Allergy to Dental Metals

Nickel  Silver
Mercury  Titanium
Gold    Copper
Chromium  Beryllium
Cobalt
Palladium/Platinum (cross reactive with nickel)
Nickel Allergy

• Nickel is found in bobby pins, needles, pins, metal lipstick holders, watch backs, earring studs, stainless steel (orthodontic bands and wires), metallic dental restorative material.

• Approximately 6% of Americans are allergic to nickel.

• 10% of women are allergic.
Titanium Hypersensitivity

- Titanium is readily dispersed into adjacent tissues and serum
- The material is extremely biocompatible but occasional hypersensitivity has been reported
- Effectiveness of patch testing has not been fully validated
Allergy to Non-Metallic Restorations

Allergic reactions may be more common than previously recognized.

Reactions are most often to residual methyl methacrylate monomer or its degenerative products:
- Formaldehyde
- Benzoyl peroxide
- Butyl phthalate
Allergy to Non-Metallic Dental Restorations (cont.)

• Some reactions are due to irritant effect rather than allergy.

• Auto-polymerizing acrylic resins release more residual chemicals and are more likely to precipitate adverse reactions.

• Typical allergic reactions include surface erythema and lichenoid changes.
Resins, Epoxy and Acrylates

• Found in:
  – Dental composites
  – Pit and fissure sealants
  – Orthodontic adhesives
  – Glazes
  – Root canal sealants
  – Bonding agents
  – Veneers
  – Temporary crowns
The Role of Metallic Dental Restorations in the Etiology of Mucosal and Periodontal Diseases
Patients Evaluated

- Lichen planus 178
- Burning mouth 125
- Allergic stomatitis 54
- Hyperkeratosis 37
- Restoration related gingivitis/periodontitis 44

Total patients 438
Diseases Associated with Metals Allergy

- Gingivitis/periodontitis 9
- Lichenoid reactions 5
- Allergic stomatitis 3
- Burning mouth 1

Total 18

(4.1%)
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