Therapeutic Agents & Treatment Strategies for the Management of Selected Oral Conditions

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Footnote Key:

1. These medications are all contraindicated in microbial diseases. If given to patients with microbial diseases, microbial proliferation is usually enhanced, and systemic dissemination is possible. Candidosis is a common side effect.

2. Systemic steroids are contraindicated or must be used with caution in numerous systemic conditions. Consultation with the patient's physician is recommended before prescribing. Tapering of prednisone is not necessary with 5-7 day burst therapy. Tapering of prednisone is not necessary with alternate day therapy (QOD) if the dosage does not exceed 20 mg QOD. To reduce the possibility of adrenocortical suppression, it is important that prednisone be taken in harmony with diurnal adrenocortical steroid levels. To accomplish this, prednisone should be taken 1-1/2 hours after normal arising time. Alternate day AM (QOD) dosage also reduces the possibility of adrenocortical suppression.

3. Whenever topical mouth rinses or ointments are prescribed, the manner in which the medication is used is very important. The patient should be advised that the medications are effective on contact and that they should avoid anything by mouth (NPO) for 1/2-1 hour after using them to prolong medication contact time.

4. Baseline hematology laboratory studies to include platelets are necessary to monitor possible bone marrow suppression.

5. Hepatotoxicity has been reported. **OPRM Faculty**

*** Denotes prescription items that must be extemporaneously compounded by a pharmacist.** Usually a specialty "compounding pharmacy" is a better choice as they have more experience and knowledge regarding product formulation.

Extemporaneously Compounding Medications for Intraoral Conditions

- Few products available in the U.S - ?? limited product demand
- Problems:
  - Difficulty with insurance payments, XIX & Medicare will not reimburse for the full cost
  - Expensive – Dental Pharmacy can mail Rxs to patients living in Iowa – at significantly less cost to patient patients and the products are formulated correctly for improved efficacy
  - "I can do that" - generalized lack of knowledge – many pharmacies incorrectly compound intraoral products causing mucosal irritation, reduced efficacy
- Make sure products are not flavored or sweetened (especially with sucrose) unless necessary!

I. CHRONIC NON-MICROBIAL MUCOSITIS

(aphthous stomatitis, erosive lichen planus, mucous membrane pemphigoid, pemphigus, erythema multiforme)

Avoid: Magic mouth rinse, miracle mouth rinse, 1, 2, 3 mouth rinse, special mouth rinse, etc.
DON'T bother!! WHY: Dilution effect from mixing commercial products renders them ineffective

Typical Miracle Mouthrinse Formulation: 1:1:1 w/wo hydrocortisone

- *1 Part Nystatin 100,000U/mL suspension……diluted down to final concentration of 33,300U/mL*
  - Considered to be a poor antifungal at full strength

- *1 Part Benadryl (diphenhydramine) 12.5mg/5mL solution…….diluted down to final concentration of 0.83 mg/mL*
  - Recently experimented with 25mg/10ml x 1 min. rinse with little effect

- *1 part Mylanta® suspension……as coating agent*
  - Older formulations used Kaopectate® which was then formulated with an attapulgite clay to coat the mucosa. Kaopectate now contains bismuth subsalicylate, which can cause a grayish-black discoloration of the tongue and is contraindicated in patients with hypersensitivity to salicylates. Mylanta® contains aluminum & magnesium hydroxide and simethicone and is used in most current versions of the rinse.

- *Hydrocortisone powder…….added at 0.25 mg/mL of final product*
  - Considered lowest potency topical corticosteroid
  - Triamcinolone – mid potency

Baseline initiatives to allow therapies to work:

- *Decrease common possible irritants – Avoid:*
  - Pyrophosphates, cinnamic aldehyde
  - Menthols, phenols, etc.
- *Maintain "salivary pellicle"*
  - Avoid sodium lauryl sulfate (SLS) in dentifrices
  - Avoid EtOH if possible
- *Maintain saliva*
  - Xerogenic agents
  - Hydration
- *Manage bugs*
  - Bacteria
  - Fungi

Mouthrinses[1,3]

***RX*:** **Dexamethasone 0.5 mg/5mL oral solution**[1] (Hickma)
Disp: 240 mL
Sig: Rinse with 5 mL for 1 min. and expectorate QID, PC (after meals) and HS (before retiring). NPO 1\2 hr

- **NOT as efficacious as triamcinolone rinse**

- Commercial product covered by insurance companies
- Specify Hickma/Roxane brand, others are elixirs (5% - 40% EtOH)
- Use correct strength to avoid toxicity
- Biologic half-life 36-54 hours

❋***RX*:** **Triamcinolone acetonide (micronized) 0.1 OR 0.2% aqueous suspension**[1]
Disp: 240 mL
Sig: Rinse with 5 mL for 1 min. and expectorate QID, PC (after meals) and HS (before retiring). NPO 1\2 hr.

- TAC is >>> stronger than commercial dexamethasone
- Use the 0.2% for more severe cases
- Better effect if made with micronized powder at Dental Pharmacy vs. commercial in Kenalog® inj. (also much less expensive $26.96 from Dental Pharmacy vs. $200 w/ Kenalog®)

❋***RX*:** **Triamcinolone acetonide (micronized) 0.1 OR 0.2% in sugar-free nystatin 100,000 U/mL suspension**
Disp: 240 mL
Sig: Rinse with 5 mL for 1 min. and expectorate QID, PC (after meals) and HS (before retiring). NPO 1\2 hr.

- Use in patients predisposed to candidosis
- Commercial nystatin suspension is 30-50% sucrose
- We make a sugar-free nystatin suspension at the COD
- ($36.10 at DP)

❋***RX*:** **Triamcinolone acetonide (micronized) 0.1 OR 0.2% in sugar-free amphotericin-B 15mg/mL suspension**
Disp: 240 mL
Sig: Rinse with 5 mL for 1 min. and expectorate QID, PC and HS. NPO 1\2 hr.

- Use in patients predisposed to candidosis when other therapies have failed
- Much more efficacious than nystatin suspension
- Use amphotericin-B 25 mg/mL if needed
- ($69.95 at Dental Pharmacy)

Ointment [1, 3]

RX: **Triamcinolone acetonide 0.1% OR 0.5% ointment**
Disp: 15 gm
Sig: Apply thin film to inner surface of dentures or medication trays up to QID, NPO 1/2 hr.

- We usually use higher potency steroids in trays

- Low 0.1% to medium potency 0.5% strength ($18)
- Use 0.1% strength on lips and dermis
- Still fluorinated and can thin lips or dermis long term Choose desonide instead for chronic use
- Seat trays for 30 min., then rinse mouth

RX: **Clobetasol 0.05% OR fluocinonide 0.05% ointment**
Disp: 15 gm
Sig: Apply thin film to inner surface of dentures or medication trays BID. Seat for 30 minutes

- High potency steroids, commercial products
- Instruct patients to expectorate & rinse mouth thoroughly after use
- Commercial clotrimazole ointments $70-150 for 15 g tube

Occlusive Ointment [1, 3]

Note: Orabase Maximum Pain Reliever Paste® (Colgate) with 20% benzocaine is no longer on the market.

- Similar products such as Oral Pain Reliever 20% Paste® (CVS Health) contain 20% benzocaine and are made in an oral adhesive base but do not have the same ingredients as the original Orabase.®

❋***RX:*** **Triamcinolone acet. 0.5% ointment 1:1 with Oral adhesive base**
Disp: 20 gm
Sig: Apply thin film to dried mucosa BID-QID, PC & HS Do not rub in. NPO 1/2 hr.

- Lower potency mixture due to 1:1 dilution
- Prescribe ointments to mix with oral adhesive bases
- Rubbing may cause the product to become grainy & lose elasticity
- Base is VERY difficult to find (CVS-OTC)

RX: **Triamcinolone 0.1% Dental Paste®**
Disp: 5 gm tube
Sig: Apply thin film to dried mucosa QID. Do not rub in. NPO 1/2 hr.

- Commercially available but cost to patient without insurance is $80 per 5 gram tube!
- Low concentration of triamcinolone
- Good "bandage" effect, useful in pediatric patients

❋***RX:*** **Clobetasol 0.03%, 0.06% or 0.1% in Jelene compounded ointment 1:1 with Oral adhesive base**
Disp: 20 gm
Sig: Apply thin film to dried mucosa BID. Do not rub in. NPO 1/2 hr.

- Allows for various concentrations of clobetasol, including higher concentrations than obtained by mixing commercial products 1:1 with oral adhesive base
- Consistency is a problem for some people

Combined Anti-inflammatory & Antimycotic Topical Agents [1]

❋***RX:*** **Clobetasol 0.05%, clotrimazole 2% in Jelene oint.**
Disp: 15 g
Sig: Apply thin film inner surface of dentures or medication trays BID. Seat for 30 minutes. Rinse mouth thoroughly after use.

- Compounded from drug powders (not a 1:1 mixture)
- Allows for 2x commercial strength of clotrimazole
- Can customize strengths of both agents
- Ointment formulation is more occlusive than creams

Systemic and Intralesional Steroids

RX: **Prednisone 5 mg, 10 mg, 20 mg tabs[1, 2]**
Disp: #
Sig: 40mg PO q A.M. (1-1/2 hrs after normal arising time) x 5 days followed by 10 mg QOD A.M. x 10 days

- Short bursts ≤ 3 weeks don't require taper
- Best taken with food

- Dose range 40-80 mg per day, depending on professional judgment; generally, for severe acute cases such as erythema multiforme or initial therapy for long term unmanaged pemphigus, lichen planus or pemphigoid
- When daily dose is 30 mg or greater patients may experience insomnia, headache or irritability

RX: **Triamcinolone acetonide injectable 40 mg/mL (Kenalog®) diluted to 10 mg/mL or use Kenalog 10 mg/mL strength**[1]
Directions: Inject 10-40 mg (shake syringe immediately before use)

- Of value in management of solitary lesions recalcitrant to topical or systemic steroids

- Best mixed with lidocaine with epinephrine as the diluent
- Area should be anesthetized before injection of triamcinolone acetonide suspension if local anesthetic is not used.

II. MUCOUS MEMBRANE PEMPHIGOID

Anti-Collagenase Agents

RX: **Doxycycline or minocycline 100 mg tabs/caps**
Disp: #30
Sig: Take QD or BID with food and plenty of water.
- Avoid taking HS – esophageal irritant
- Use as an adjunct to steroid therapy in patients
- Avoid taking with antacids, iron, calcium tablets
- Nicotinamide has similar actions but requires close monitoring by a specialist

III. APHTHOUS STOMATITIS

Pathophysiology: Immunologic
- L*ocation: nonkeratinized, unattached mucosal surfaces*
  - Typically, buccal vestibule, lateral or ventral tongue, floor of mouth
- *Heals in a predictable manner*
  - Types: minor, major, herpetiform
- *Precipitating Factors:*

Diet	Trauma	Stress	Genetics
Medications	Sodium Lauryl Sulfate (SLS)	Chemicals	Estrogen shifts

Primary Prevention Factors:
- Relate to maintenance of salivary pellicle or impeding the recognition of antigens to the immune system

Table 1. Clinical features of minor, major, and herpetiform recurrent aphthous stomatitis (RAS)

	MINOR RAS	MAJOR RAS	HERPETIFORM RAS
Gender predilection	Equal	Equal	Female
Morphology	Round or oval lesions Gray-white pseudo-membranes Erythematous halo	Round or oval lesions Gray-white pseudo-membranes Erythematous halo	Small, deep ulcers that commonly converge Irregular contour
Distribution	Lips, cheeks, tongue, floor of mouth	Lips, soft palate, pharynx	Lips, cheeks, tongue, floor of mouth, gingiva
Number of ulcers	1–5	1–10	10–100
Size of ulcers	<10mm	>10mm	2–3mm
Prognosis	Lesions resolve in 4–14 days No scarring	Lesions persist >6 weeks High risk of scarring	Lesions resolve in <30 days Scarring uncommon

Adapted from Wallace A, Rogers HJ, Hughes SC, et al. Management of recurrent aphthous stomatitis in children. *Oral Medicine*. 2015;42(6):564–572.

Pharmacotherapeutic Management Choices:

- *Topical Route*
  - Treatment of choice: triamcinolone acetonide rinse – globally alters course of disease, increases healing rates
  - Steroid ointments, pastes
- *Systemic Route*
  - Prednisone - for difficult cases, large +/or multiple ulcerations, use with topicals
- *Over-The-Counter Products*
  - 20% benzocaine products help with pain
- *Inappropriate Chronic Treatment*
  - Cautery agents - do not affect course of disease (Debacterol®, silver nitrate, polyphenol sulfonic acid complex, laser)
  - Tetracycline rinses, oral antibiotics etc.
- *Sodium Lauryl Sulfate (SLS) Free Dentifrices*
  - Sodium lauryl sulfate (aka: sodium dodecyl sulfate, SDS) is a surfactant (foaming agent) found in most commercially available toothpastes and gels
    - Causes dose-dependent epithelial desquamation
    - Note: All SLS free products are not appropriate for some patients due to pyrophosphate content
  - Cocamidopropyl betaine (CABP or CPB) - surfactant that is less irritating to tissue than SLS
    - RX: Prevident® 5000+ Dry Mouth, 100 g container (only SLS free Prevident® product)
    - Note: For overdenture abutments use only Prevident gel (56 g tube), not a dentifrice (does not contain surfactants or abrasives)
    - CAPB dentifrices: Biotène® (GSK) Fresh Mint Original Formula, Gentle Mint Formula, Sensodyne®(GSK) products (except Deep Clean which contains SLS)

  - ***Squigle® Enamel Saver Toothpaste*** Our toothpaste of choice
    - Very mild dentifrice – no tartar control agents or irritating flavors (mild mint)
    - Uses poloxamer as surfactant – very mild detergent
    - Can be difficult to find in retail stores, may be obtained online or mailed from Dental Pharmacy

IV. CANDIDIASIS

Topical Suspensions [3]

RX: **Nystatin oral suspension 100,000 U/mL**
Disp: 14 day supply (280 mL)
Sig: Rinse with 5 mL for 1 minute and expectorate P.C. (after meals) and HS (before retiring) NPO 1/2 hr.

- Poor antifungal at any concentration
- Commercial products contain 33-50% sucrose, not recommended for this reason, especially in chronic/recurrent cases like Sjögren's, medicament xerostomia or post radiation xerostomia, ($50)

❋***RX:*** **Nystatin oral suspension 100,000 U/mL Sugar-Free**
Disp: 12-day supply (240 mL)
Sig: Rinse with 5 mL for 1 minute and expectorate P.C. (after meals) and HS (before retiring) NPO 1/2 hr.

- Viscous, will coat tissue
- Compounded at Dental Pharmacy
- Must be refrigerated, shorter shelf life than commercial, but not cariogenic ($35)

❋***RX:*** **Amphotericin-B oral suspension 25mg/mL**
Disp: 12-day supply (240 mL)
Sig: Rinse with 5 mL for 1 minute and expectorate P.C. (after meals) and HS. (before retiring) NPO 1/2 hr.

- Much more effective than nystatin suspension
- Of use for fluconazole-refractory infections or when C. *krusei or* C. *glabrata* are suspected
- May use 15mg/mL strength when combining with triamcinolone acetonide ($58)

Ointment [3]

***RX*:** **Nystatin ointment 100,000 U/g**
Disp: 15 gm
Sig: Apply thin film to inner surfaces of dentures and angles of mouth QID, PC & HS. NPO 1/2 hr.

- Poor antifungal
- Works OK under dentures, but not first line agent
- Bright yellow color may be objectionable for angular cheilitis, ($24)

❋***RX*:** **Clotrimazole 2% in Jelene ointment**
Disp: 30 g
Sig: Swab or apply thin film onto affected area QID, PC and HS, NPO 1/2 hr.

- Useful for debilitated patients who cannot rinse
- Higher concentration (2%) and more occlusive than commercial creams (no commercial oint. available)
- Compounded at Dental Pharmacy

Troches [3]

RX: **Clotrimazole 10 mg oral troches**
Disp: 70 troches
Sig: Dissolve 1 troche in mouth every 3 hours while Awake (5 tabs per day). NPO 1/2 hr. after use.

- Patients with decreased salivary flow should rinse mouth with water prior to use to enhance dissolution

- Compliance problems with 5X daily therapy ($80)
- 1-2 troches QD HS is useful for maintenance or prevention.
- Can also dissolve 2 troches in am, 1 in afternoon and 2 HS to improve compliance
- Contains sucrose, FDA pregnancy category: C

Buccal Tablet

RX: **Miconazole 50mg buccal tablet (Oravig®)**
Disp: 14
Sig: Apply tablet to canine fossa once daily for 14 days

- Approved for patients 16 years and older
- Cost: $1,214/14 tablets, insurance usually will not cover

Angular Cheilitis (with or without atrophic candidosis under the upper denture)

- OTC clotrimazole 1% cream works – explain labeling to patient as it is marketed for athlete's foot
- RX drug of choice is ketoconazole 2% cream-fastest resolution with best best therapeutic result
- RX for clotrimazole 2% ointment (Jelene) – doubles the strength of clotrimazole

Cream [3]

RX: **Clotrimazole 1% cream (Rx, OTC as Lotrimin AF®, g)**
Disp: 15 gm Rx or 12 gm OTC
Sig: Apply thin film to inner surface of denture and angles of mouth QID. NPO 1/2 hr. after use.

- Has slight anti-staph activity
- Available OTC ($7) but labeled for athletes' foot and jock itch which may cause some patients to hesitate.
- Identical to Rx version ($28)

RX: **Ketoconazole 2% cream (Nizoral©,generic**)
Disp: 15gm
Sig: Apply thin film to inner surface of denture and Angles of mouth QID. NPO ½ hr after use.

****RX:*** **Clotrimazole 2% in mupirocin 2% ointment**
Disp: #20 g
Sig: Apply thin film to corners of mouth three times daily (after breakfast, mid-day and at bedtime. NPO for 30 min. after use

- This combination works well if the problem has been persistent or there is redness (secondary to skin staph and strep)
- Use until clear plus 4 days

Systemic [5]

RX: **Fluconazole 100 mg tablets**
Disp: #11-15 tabs
Sig: Take 1 tablet BID for first day, then take 1 tablet daily for 10 – 14 days.

- Potent CYP2C9 inhibitor, moderate CYP3A4 inhibitor, causes QT prolongation

- Loading dose results in steady state concentration in 2 days
- Price of 15 tablets is approximately $65 without insurance, cheaper to break 200 mg tablets in half
- Serious interactions with statin drugs, psych drugs, sulfonylureas, warfarin, some antihypertensives and many other drug classes – always check for interactions
- FDA pregnancy category: X Even single doses in 1st or 2nd trimester can cause miscarriage

Antibacterial Mouth Rinse [3]

RX: **Chlorhexidine 0.12% oral rinse (Peridex®, g)**
Disp: 473 mL
Sig: 10 - 15 mL mouth rinse for 30 seconds and expectorate BID (after breakfast and HS), NPO 1\2 hr.

- 11.6% alcohol content will irritate ulcerations and enhance xerostomia, ($4-14)
- Due to chemical deactivation, separate from toothpaste by 30 min.
- FDA pregnancy category: B

RX: **Alcohol-Free Chlorhexidine (Periogard Alcohol Free®)**
Disp: 473 mL
Sig: 10-15 mL mouth rinse 60-90 seconds and expectorate BID, PC, AM & HS. NPO 1/2 hr.

- Non-alcohol formulation – useful for alcoholics, patients with mucositis, xerostomia, ($18)
- Due to chemical deactivation, separate from toothpaste by 30 min.

V. HERPES & HERPES ZOSTER INFECTIONS

Herpes Labialis (Cold Sores, Fever Blisters)

- Virus remains dormant within the dorsal root ganglia until activated
- Asymptomatic viral shedding occurs for several days before the prodromal period & after lesions heal
- Specific triggers:
  - Sunlight (ultraviolet radiation) UVB
  - Tissue injury & inflammation
  - Physical or emotional stress: malnutrition, fever, colds, influenza, menstruation, exposure to extremes in temperature

Systemic Treatment of Herpes Labialis (Immunocompetent Patients)

RX: **Valacyclovir 1 g tablets (Valtrex®, g)**
Disp: 4 tablets
Sig: 2 tablets at onset of symptoms, then 2 tablets 12 hours after first dose

- Drug of choice -probably most efficacious therapy to date ($20)
- A prodrug of acyclovir which is 3 times more bioavailable than acyclovir, may use in patients ≥ 12 years of age
- *WARNING:* Use with caution in renal disease, has not been studied in pre-pubescent children
- Headache &/or nausea are dose related side effects (15%)

RX: **Famciclovir 500 mg tablets**
Disp: 3 tablets
Sig: Take 3 tablets (1500 mg) at onset of prodome

- Symptom duration decreased by 1.7 days when taken within an hour of onset of prodome
- ($30), not available in all pharmacies
- Best taken within 48 hours of symptom onset
- Can cause headaches, dizziness, GI upset
- Efficacy & safety haven't been established in patients under 18 years of age, adjust dosage in renal impairment
- 2nd line therapy after valacyclovir
- FDA pregnancy category: B

Topical Treatment of Herpes Labialis (Immunocompetent patients)

Ointments and Creams

- *Topicals are MUCH less efficacious than oral (systemic) therapy, prohibitively expensive and **not recommended for use** but included here for completeness.*
- Topical creams and ointments are not appropriate for intraoral use

OTC: **Docosanol 10% cream (Abreva® , g)** ($21)
2 gm tube
Directions: Apply 5 times daily at onset of symptoms until lesions heal

- Recurrent HSV labialis studies (2) demonstrate mean duration of lesions & pain ↓ by ½ to 1 day
- ??? Efficacy compared to other topicals

RX: Penciclovir 1% cream (Denavir®) 5 gram tube ($975)
RX: Acyclovir 5% cream (Zovirax®,g) 5 g tube ($300-900)

- ↓ mean duration of lesions & pain ↓ by 1 day, more efficacious than acyclovir oint.

Oral buccal tablet

RX: **Acyclovir 50 mg buccal tablet (Sitavig®)** ($1,450)
Disp: 2
Sig: Apply tablet to the upper gum region (canine fossa) within 1 hr after onset of prodromal symptoms.
- Single application per episode
- Contraindication: allergy to casein (milk protein)

- Study: mean duration of herpes labialis episodes were decreased by ½ day compared to placebo ($315/2 tablets)
- Patients experienced 35% aborted episodes
- Place on canine fossa and hold in place with slight pressure on the upper lip for 30 sec. to ensure adhesion.
- Apply to ipsilateral to symptoms

Systemic Agents for Primary & Recurrent HSV Gingiviostomatitis (Immunocompetent Patients)

- Acute herpetic gingivostomatitis can occur on both movable and attached oral mucosa. Recurrent infections in healthy patients are usually limited to attached gingival and hard palate
- *It is important to note that the duration of treatment for a primary case of HSV gingivostomatitis vs a recurrent case is different. Recurrent cases require shorter durations of treatment!!!*
- Short term therapy is indicated for patients who get recurrent herpetic after prolonged sun exposure, dental treatment, etc. Therapy must be initiated before exposure to any triggers. Start the day before trigger exposure and continue for a full course of treatment as listed below.

RX: **Valacyclovir 500 mg or 1 g (Valtrex®, g) caplet**
Primary HSV Gingivostomatitis :
Sig: 1 gram BID x *7-10 days*
Recurrent HSV Gingivostomatitis:
Sig: 500mg BID x *3 days* **Or** 1 g once daily x *5 days*

- *WARNING:* Use with caution in renal & hepatic disease
- Approved for 12 years of age and older, limited data in children 2-<12 years of age. Pediatric consult needed for children age 2-6
- Headache & nausea are dose related side effects (15%)

RX: **Famciclovir 250 mg or 500 mg tablets**
Primary Gingivostomatitis HSV:
Sig: 250 mg TID x *7-10 days*
Recurrent Gingivostomatitis HSV:
Sig: 1000 mg BID x *1 day* **Or** 125 mg BID x *5 days*

- Can cause headaches, dizziness, GI upset
- Best taken within 48 hours of symptom onset
- Efficacy & safety haven't been established in patients under 18 years of age

***RX*:** **Acyclovir 400 mg (Zovirax®, g) tablet**
Primary HSV Gingivostomatitis:
Sig: 400 mg 3 times daily for *7-10 days*
Recurrent HSV Gingivostomatitis:
Sig: 400 mg 3 times daily for *5 days*
Or 800mg 3 times daily for *2 days*

- Only effective if initiated very early in recurrence
- *WARNING:* Use with caution in renal impairment, dehydration
- FDA pregnancy category B
- Pediatric consult needed for children ages 2-6.
- Primary gingivostomatitis in children: Acyclovir 20mg/kg PO QID (max of 400 mg per dose) for seven days based on limited data – low level of evidence

Prophylaxis for Recurrent HSV Infections (Immunocompetent Patients)

Prophylaxis for recurrent herpes labialis (RHL) and gingivostomatitis using oral antivirals:

- Long term prophylaxis is indicated if patients have at least six or more herpetic outbreaks per year. Reassess need every 6 – 12 months.

RX: **Valacyclovir 500 mg (Valtrex®, generic)**
Disp: 30 caplets
Sig: Take 500 mg daily
RX: **Famciclovir 500 mg (Famvir®, generic)**
Disp: 30 tablets
Sig: Take 500 mg BID

- Doesn't appear to have large advantage over acyclovir, but regimen is easier
- Regimen for patients with >9 episodes/year is 1 gram QD
- No evidence that famciclovir prevents RHL
- Use valacyclovir

Varicella Zoster Virus (VZV) Infections

- 25-fold decrease in zoster after immunization
- Patients with prior varicella zoster virus infection have a 10% chance of acquiring shingles
- Increased risk of stroke within 6 months of episode, antivirals may have protective effect
- For patients >50 years add prednisone to decrease pain in acute phase of disease
  - Does not decrease incidence of post-herpetic neuralgia
- Trials showing benefit of Rx therapy only in patients treated within 3 days of onset of rash.

RX: **Valacyclovir 1 gram (Valtrex®, generic) tablets**
Disp: 21 caplets
Sig: Take 1 caplet TID for *7 days*

- Agent of choice
- Patients should begin treatment within 48 hours of the onset of symptoms.
- More effective than acyclovir for acute pain cessation and decreasing the frequency of persistent pain.
- *WARNING:* Use with caution in renal impairment

RX: **Famciclovir 500 mg tablets**
Disp: 21 tablets
Sig: Take 1 tablet every 8 hours for *7 days*

- Prodrug of penciclovir, approximately same efficacy and safety as acyclovir
- Patients should begin treatment within 48 hours of onset of symptoms, efficacy after 72 hours is questionable
- *WARNING:* Use with caution in renal function impairment, has not been approved in children <18 years of age
- Equivalent to acyclovir in reduction of acute pain and incidence of PHN

RX: **Acyclovir 800 mg (Zovirax®, generic) tablets**
Disp: 35 - 50 tablets
Sig: Take 1 tablet q 4 hours (5 tablets per day) for *7-10 days*

- Therapy is most effective if started within 48 hrs after the onset of symptoms
- Meta-analysis: acyclovir accelerated by 2-fold pain resolution and reduced incidence of PHN at 3 & 6 months
- Don't use.

VI. LIP CONDITIONS - SUMMARY AND EXAMPLES

NOTE: EVERY PATIENT IS UNIQUE AND WE INDIVIDUALIZE ALMOST ALL THE EXAMPLES GIVEN IN THIS SECTION.

Chapped lips and baseline therapy for other lip problems

- *Moisturizer: Lanolin*
  - Use 3-4 times a day
  - Brand names Lansinoh® or Purelan100® (venture into the breast feeding aisle)
  - Ultra-pure (HPA) brands are less allergenic and more efficacious than generic lanolin products

- *Lip balm:*
  - PROBABLY NOT NECESSARY UNLESS GOING OUT IN THE WIND or SUN
  - Prefer Banana Boat® Aloe with Vitamin E (SPF 45) or Blistex® Complete Moisture® (SPF 15)
    - Use when in sun or wind once or twice if in the sun frequently
    - Put this on immediately after the lanolin

Ulcerative conditions of the lips, including idiopathic, lichen planus, pemphigoid etc.

- *Steroids (ointments on vermilion)*
  - Use only nonfluorinated steroids and limit these steroids ONLY for inflammatory or ulcerative conditions confined to the lipstick portion of the lips
  - Rx: desonide 0.05%. Apply very thin layer to lips twice a day
    - PUT ON AFTER LANOLIN
    - DON'T apply to corners of lips

- *Apply for three weeks or until the ulcer is gone*
  - Do not prescribe these products for use > 3 times per year
    - If ulcer resolves but erythema remains start decreasing the application of the steroid cream, per outline below or until erythema resolves
    - First to once a day x 10-14 days, then every other day x 10-14 days, then every third day x 10-14 days
    - If ulcer resolves without residual erythema steroids may be discontinued completely

- *IF THE ULCER IS STILL THERE IN 3 weeks may consider short term ultrapotent steroid:*
  - 1:1:1 Mixture of clobetasol 0.03% ointment and 2% mupirocin (Bactroban, g) ointment and clotrimazole 2% cream

Conditions of the lips occurring outside the vermilion border

- *NON-STEROIDAL AGENTS IN PERIORAL/CIRCUMORAL REGION*
  - Steroids are NOT indicated for circumoral or perioral dermatitis
  - Likewise angular cheilitis cases (covered below) only rarely requires anti-inflammatory agents

- *Creams are preferred on skin surfaces*
  - In these areas outside the vermilion pimecrolimus or tacrolimus may be used
  - NOTE: Due to the "black box" warning associated with these medications, this handout summary will not cover these. If clinician is familiar with restrictions and limitations they may be mixed and used with mupirocin and clotrimazole similar to the clobetasol 1:1:1 mixture above.

- *Treatment of angular cheilitis*
  - Use 2% clotrimazole cream and 2% mupirocin cream (mixed in 1:1 ratio)
    - Apply to lip first thing in the morning and last thing at night
    - After the morning application wait about a half hour to apply the lanolin or Blistex Complete Moisture if going outside.
  - <u>Don't</u> use the desonide while using this mixture unless consultation for complicating factors is performed. There are numerous cofactors including vertical dimension, obsessive compulsive disorders and perioral rhytides