Commonly prescribed topicals: Perils and pearls of using corticosteroids and antimicrobials in skin conditions

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Disclosure

- Lilly
- AbbVie

Objectives

1. Describe the pharmacodynamics of topical corticosteroids and antimicrobials.
2. Discuss important concepts in selecting appropriate agents to optimize patient outcomes and minimize risks, side effects and complications.
3. Review three case studies of dermatologic conditions and selection of topical therapies.

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Topical Glucocorticosteroids (TCS)
- Usually short-term tx for dermatoses
- Salzberger & Witten (1952)
- Effect vs side effects vs phobia
- Indications (vague)
  - Anti-inflammatory
  - Anti-pruritic
  - Vasoconstriction

TCS Indications

**High potency (I to III)**
- Alopecia areata
- Atopic dermatitis (resistant)
- Discoid lupus
- Lichen plan
- Nummular eczema
- Lichen sclerosis
- Psoriasis
- Hand dermatitis (severe)

**Medium potency (IV and V)**
- Asteatotic eczema
- Stasis dermatitis
- Nummular eczema

**Low potency (VI and VII)**
- Eyelid dermatitis
- Diaper dermatitis
- Perianal inflammation

TCS Mechanism of Action
- Anti-inflammatory effects epidermis
- Anti-proliferative actions epidermis & dermis
### Percutaneous absorption

- Vehicle
- Potency or concentration (vehicle can affect potency)
- Frequency
- Location
- Duration
- Occlusion
- Quality of barrier
- Hydration ↑
- Temperature environment or body ↑

### Choice of TCS Vehicle

- Most alcohol: Foams, Gels, Lotions
- Least alcohol: Creams, Ointment

### Selection of potency

- Vasconstrictor assays & comparative clinical trials
- Duration of inflammatory condition: Acute, Chronic
- Location: Face, intertriginous and genitals - low (2wks), Palms/soles - high/super high
- Age: Infants & elderly
- Condition
- Quality of barrier
- Exceptions
Hypothalamic-pituitary adrenal axis suppression (HPA)

- Can occur with any TCS
- Increases with steroid absorption
- TCS under occlusion
- Higher concentrations of TCS
- Application over large surface areas

Calcineurin inhibitors*

- Pimecrolimus (Elidel)
- Tacrolimus (Protopic)

ALTERNATIVE TO TCSs
Indications: Atopic dermatitis; eczema
Advantage: Do not cause atrophy.
Disadvantages: Not as effective, slower onset, $$$$
SE: burning, stinging, itching

*Black Box Warning: FDA 2006 skin malignancy and lymphoma with long-term use

So what do I prescribe?

- How much?
- Brand or generic?
- Formulation or vehicle?
- What potency?
- How often?
- Refills?

This is so confusing!
Pearls for prescribing TCS

- Control/monitor QUANTITY and REFILLS
- Written instructions: how, when, and when to stop
- Do NOT to share
- Request the pharmacist label the TUBE not the box
- Avoid combination products
- Rotational therapy
- If not responsive (2 weeks) RETHINK diagnosis
- Contraindicated in skin with infection, patients with perioral dermatitis, acne or rosacea

Acute
SHORT courses of HIGH potency
Chronic
Treat with LOW potency
Intermittent better than continuous

Topicals Corticosteroids

<table>
<thead>
<tr>
<th>Category</th>
<th>Potency</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
<td>Super Potency</td>
<td>Clobetasol 0.05%</td>
</tr>
<tr>
<td>Class 2</td>
<td>High Potency</td>
<td></td>
</tr>
<tr>
<td>Class 3</td>
<td>Upper Mid-Potency</td>
<td>Flurandione 0.05%</td>
</tr>
<tr>
<td>Class 4</td>
<td>Lower Mid-Potency</td>
<td>Triamcinolone 0.1%</td>
</tr>
<tr>
<td>Class 5</td>
<td>Moderate Mid-Potency</td>
<td>Fluocinolone 0.05%</td>
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<tr>
<td>Class 6</td>
<td>Mild Potency</td>
<td>Desonide 0.05%</td>
</tr>
<tr>
<td>Class 7</td>
<td>Least Potency</td>
<td>Hydrocortisone 2.5%</td>
</tr>
</tbody>
</table>

Desoximetasone 0.25% cr or 0.05% cr are free of propylene glycol **

Dispensing for BID dosing for 2 weeks

<table>
<thead>
<tr>
<th>Location</th>
<th>Adult Dosage</th>
<th>Child Tube size</th>
<th>Infant Tube size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire face &amp; neck</td>
<td>35 gms</td>
<td>15 gm</td>
<td>15 gm</td>
</tr>
<tr>
<td>One entire hand</td>
<td>14 gms</td>
<td>15 gm</td>
<td>15 gm</td>
</tr>
<tr>
<td>Entire foot (not both)</td>
<td>28 gms</td>
<td>15 gm</td>
<td>15 gm</td>
</tr>
<tr>
<td>One entire arm</td>
<td>42 gms</td>
<td>30 gm</td>
<td>15 gm</td>
</tr>
<tr>
<td>One leg</td>
<td>84 gms</td>
<td>30 gm</td>
<td>30 gm</td>
</tr>
<tr>
<td>Entire body</td>
<td>30gm for one application</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Rule of thumb: Children = ½ adult amount; Infants (6-12 months) = ¼ adult amount
Rule of hands: Area equal to 2 adult hands (palm & fingers) = 1 FTU
### FDA approved TCS in children

<table>
<thead>
<tr>
<th>Class</th>
<th>Generic Name</th>
<th>Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUPER</td>
<td>Clobetasol propionate 0.05% foam</td>
<td>&gt; 12 years</td>
</tr>
<tr>
<td>HIGH</td>
<td>Fluocinonide 0.1% cream</td>
<td>&gt; 12 years</td>
</tr>
<tr>
<td>MED</td>
<td>Mometasone 0.1% cream/ointment</td>
<td>&gt; 2 years</td>
</tr>
<tr>
<td></td>
<td>Fluticasone 0.05% lotion/cream</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td>LOW</td>
<td>Alclometasone 0.05% cream/ointment</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td></td>
<td>Prednicarbate 0.1% cream/ointment</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td></td>
<td>Fluocinolone acetonide 0.01% in peanut oil</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td></td>
<td>Desonide 0.05% hydrogel</td>
<td>&gt; 3 months</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone butyrate 0.1% cream</td>
<td>&gt; 3 months</td>
</tr>
</tbody>
</table>


### Corticosteroids in pregnancy

- Limited data on safety
- Emollient therapy first
- Topicals preferred over systemic
- Mild to moderate potency
- Potential risk: premature rupture of membranes, interuterine growth restriction, gestational DM, osteoporosis, infection and pregnancy-induced hypertension
- Avoid during first trimester if possible

### Localized side effects

- Atrophy
- Bruising, purpura, skin fragility, striae, telangiectasia, pigment abnormality
- Irritation
- Infections (secondary)
- Dermatitis
- Delayed wound healing
- Photosensitization
- Steroid-induced acne & rosacea
- Rebound phenomenon
- Tachyphylaxis
Systemic side effects*

Ocular
Endocrine
Metabolic
Renal & cardiovascular
Misc

*Usually seen in extended use of high potency.

Pearls to reduce steroid side effects

- Use potent steroid to gain QUICK control of disease
- THEN taper to less potent
- Taper instead of abrupt cessation
- Reduce frequency (alternate days, weekend, etc.)
- Use of topical immunomodulators
- Caution on flexural surfaces, face, genitals and intertriginous
- Avoid occlusion
- Employ other topical agents (keratolytics, moisturizers, etc.)
- Avoid combination products

Successful use of topical corticosteroids depends on the correct diagnosis
Atopic Dermatitis

- "Out of place" or strange
- Atopic march
- Most common type of eczema
- "infantile eczema", "atopic eczema"
- 60% cases 1st year, 95% before 4 yrs old

Must have three of the following:
1. Pruritus
2. Typical morphology and distribution
3. Chronically relapsing dermatitis
4. PMH or FHx atopic disease

Therapeutic approach

- Control the Environment
- Emollients (jars & tubes)
- Moisturizers
- Topical corticosteroids
- Topical non-corticosteroids
- Antihistamines

Stasis dermatitis

Frequently in presence of venous insufficiency
- Pruritus
- Eczema
- Hemosiderin staining
- Ankle (medial) involvement
- Varicosities
- Edema

Stasis dermatitis:
- Can develop into secondary infection, cellulitis, ulcers, etc
- Most frequent cause for patients admitted unnecessarily w/misdiagnosis of cellulitis

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Stasis Dermatitis

- Assess underlying etiology
- Topical CCS (Una boot if wet)
- Assess for infection or ulceration
- Compression and elevation

Comparison of Oral and Intramuscular Corticosteroids

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<thead>
<tr>
<th></th>
<th>ORAL</th>
<th>INTRAMUSCULAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption</td>
<td>Predictable</td>
<td>Variable</td>
</tr>
<tr>
<td>Compliance</td>
<td>Relies on patient</td>
<td>Total dose administered</td>
</tr>
<tr>
<td>Duration</td>
<td>Any time period</td>
<td>Select short, intermediate, or long-acting</td>
</tr>
<tr>
<td>Parent Health</td>
<td>Reg. functional GI tract</td>
<td>Not affected by N/V</td>
</tr>
<tr>
<td>Parent's Role</td>
<td>Active control/participation</td>
<td>No role or control</td>
</tr>
<tr>
<td>Clinician's Role</td>
<td>Prescribe and monitor</td>
<td>Assured of delivery from IM</td>
</tr>
<tr>
<td>Diurnal Vary</td>
<td>Same with AM dosing</td>
<td>No diurnal variation</td>
</tr>
<tr>
<td>Tapering</td>
<td>Precise</td>
<td>Based on metabolism</td>
</tr>
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Beyond topical steroids

- Large body surface areas
- Underlying systemic disease
- Recalcitrant or severe disease
- Thick lesions
- Significant impact on QOL
- Consider comorbidities
- Oral, intramuscular, intralobesal intravenous
- Steroid sparing agents & therapies

No clear superior efficacy comparing IM to oral
Advantages vs disadvantages
Clinical preference on individual basis
Case Study

To treat.......... or not to treat?
- Aka: cradle cap, dandruff (misdiagnosis of acne in adolescence)
- Unknown etiology but suspect *Pityrosporum* (M. furfur)
- Inflammation and scale
- Clinical presentation varies with age
- Distribution of sebaceous glands
- Flares

Seborrheic dermatitis (Seb derm)
Seb Derm

Treatment
Alternating therapies: anti-yeast shampoos, antifungal topicals, TCS, and calcineurin inhibitors

Cochran Review (2014)
Only minor differences in treatment outcomes and no clear differences between the agents


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Antifungals
(superficial fungal infections)

Topical agents for superficial fungal infections
- Yeast vs dermatophytes
- Selection based on organism
- Location (skin, hair and nails)
- Vehicle
- Fungistatic vs fungicidal
- Other properties: antimicrobial and anti-inflammatory
- Recurrence
- Prevention
- Systemics

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Tinea

"Ringworm"
Very contagious
T. rubrum
Topical or systemic

Tinea Corporis

Differential Diagnosis
**Tinea Pedis**
- T. Rubrum, T. mentagrophytes
- Several types
- Check other body sites

**Tinea cruris**
- +/- mixed candida & dermatophytes
- Not common in kids
- Tx with topical azoles 2-4 wks
- Oral griseofulvin, if severe
- Always check feet

**DDX: intertrigo, contact derm, candidiasis, erythasma, bacterial infection**

**DDX Tinea cruris**
- Unilateral, half-moon
- Spreads peripherally
- Not usually scrotum
Diaper candidiasis

- C. albicans 80%
- Marginal scaling
- Beely red confluent plaques & erosions
- Satellite papules/pustules (hallmark)
- Includes skin folds, concave surfaces
- No improvement with barrier creams (zinc oxide, A&D, petrolatum, triple paste)
- KOH preparation or fungal culture ???
- Check oral mucosa and mother breasts/nipples if breast feeding

Dx of yeast is not always a SLAM DUNK!

Diaper candidiasis therapies

- Nystatin cream is DOC
- Imidazoles: not as effective, irritating
- Allylamines: not as effective
- If severe inflammation, okay to use hydrocortisone 1% ointment for a couple days (LIMITED TIME)
- May need tx oral nystatin for oral thrush (mother’s nipples)
- Refer if severe and not responsive to tx. Reconsider Dx
- Never use combination products
- Clotrimazole/betamethasone dipropionate (Lotrisone)
- Nystatin/triamcinolone acetonide (Mycolog)

Indications and Effectiveness of Topical Antifungals

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<th>Class &amp; Indications</th>
<th>Generic name</th>
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</table>
Betamethasone dipropionate/clotrimazole (Lotrisone)

**High potency topical corticosteroid**

**Indications:**
- Tinea cruris or corporis - twice daily for 1 week
- Tinea pedis - twice daily for 2 weeks.

*Not recommended for children under 17 years old or diaper dermatitis*

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**Case Study**

**Tinea Capitis**

- T. tonsurans 90 to 95%
- School children and adolescents
- Alopecia, papules, pustules, inflammation, scale
- May have: boggy scalp, secondary infections, and lymphadenopathy.
- “Kerion”
- **TOC: systemics**
  - Griseofulvin 5-10 mg/kg/day (higher off-label)

Prevent further transmission!
Clinical pearls treating superficial fungal

- Remember high rate of reinfection
- Maybe secondary infections
- Systemics for extensive involvement & comorbidities
- Examine entire body (esp. hands, feet, & groin)
- Hair and nails require longer treatment - 6 to 12 wks
- Fungistatic and fungicidal
- Social history is very important for dx and tx
- Environmental control is essential
- If not responsive, RETHINK diagnosis

Tinea Versicolor

- Pityrosporum
- More often in adolescents and young adults
- Hypopigmented, oval, sometimes scaly lesions
- Involving mostly trunk, neck, upper extremities
- Selenium sulfide or ketoconazole shampoos
- NO LONGER use oral antifungal (ketoconazole)
  BLACK BOX WARNING!

Clinical presentations of tinea versicolor
Antibacterials
for superficial wounds

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Antibacterial agents

- High local concentrations of drug
- Minimal systemic absorption>> reduced risk and side effects
- Minor or superficial wounds
- Usually NOT for burns and deep wounds

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Factors influencing route of administration

- Size and location
- Depth and underlying structure
- Mechanism of injury or etiology
- Comorbidities
- Suspected organism
- Allergies and sensitivities of causative organism
- Circulation
- Socioeconomic
- Time

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### Topical antibacterial agents - OTC

<table>
<thead>
<tr>
<th>Name</th>
<th>Bactericidal against</th>
<th>MOA</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacitracin</td>
<td>Gram + and Neisseria sp.</td>
<td>Interferes bacterial wall synthesis</td>
<td>Common sensitizer; rare but serious anaphylaxis w/application to ulcer bed</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>Gram – and P. aeruginosa</td>
<td>Increases permeability bacterial cell membrane</td>
<td>Usually combined with bacitracin or neomycin for broad spectrum</td>
</tr>
</tbody>
</table>

### Topical antibacterial agents - Prescribed

<table>
<thead>
<tr>
<th>Name</th>
<th>Bactericidal against</th>
<th>MOA</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neomycin</td>
<td>Gram + and – S. aureus</td>
<td>Aminoglycoside; inhibits protein synthesis</td>
<td>Common sensitizer; Optimum coverage combined w/bacitracin &amp; polymyxin B (Neosporin); risk of ototoxicity and nephrotoxicity if systemic absorption</td>
</tr>
<tr>
<td>Mupirocin</td>
<td>MSSA, +/- MDMRSA, Staphylococci</td>
<td>Inhibits RNA and protein synthesis</td>
<td>Rare sensitization; Less effective in serum or exudate or weeping wounds (Highly protein bound); used for eradicating nasal staph carriage</td>
</tr>
<tr>
<td>Retapamulin</td>
<td>Gram +/MRSA</td>
<td>Inhibits protein synthesis</td>
<td>Shorter tx time BID for 5days; Broader spectrum than mupirocin</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>Gram + and – esp P. aeruginosa; not good against strains of Strep or Neisserias.</td>
<td>Aminoglycoside; inhibits protein synthesis</td>
<td>Stingy common SE; uncommon sensitization but common cross-reactivity with neomycin sensitivity patients; risk of ototoxicity and nephrotoxicity if systemic absorption</td>
</tr>
</tbody>
</table>

### Impetigo Treatment

- **Bacitracin**: Effective against Gram-positive bacteria.
- **Polymyxin B**: Effective against Gram-negative bacteria.
- **Neomycin**: Effective against Gram-positive and Gram-negative bacteria.
- **Retapamulin**: Effective against antibiotics-resistant bacteria.
- **Gentamycin**: Effective against Gram-negative bacteria, particularly Pseudomonas aeruginosa.
Topical Antivirals

Most are FDA approved for ≥ 12 year
Usually in combination with systemic
Suppression vs episodic
Newer agents/formulations
Most not FDA indicated for genital HSV
Combination products
Consider comorbidities

Acyclovir 5% (Zovirax)

Herpes Labialis (cream)
Adults (≥ 12 years) – For “cold sores” apply 5 times daily for 4 days. Cover lesions and symptomatic area (tingling). Start at the earliest sign or symptom (prodrome).

Genital Herpes (Ointment)
Apply ointment to all of the affected areas/lesions, 6 times daily for 7 days.

Pregnancy Category B; Lactation- unknown
**Acyclovir**
- Combination acyclovir 5%/hydrocortisone 1% (Xerese) for herpes labialis
- Buccal mucosa tablets acyclovir (Sitavig) for herpes labialis

**Penciclovir 1% (Denavir)**
- Inhibits replication within the cell d/t inhibits viral DNA polymerase
- Maintains higher cellular concentration for longer time within cell (compared to acyclovir)
- Indication Recurrent herpes labialis (≥12 years old)
- Dosage- every 2 hours for 4 days

**Docosanol (Abreva)**
- Prevents replication by inhibiting fusion of virus and host
- Shortens healing time and reduces symptoms
- Pediatrics- ≥12 years old
- Indications- herpes labialis; not genital herpes
- Dosage- 5 times daily till gone (max 10 days)
- SE- minimal
Take home message

- Consider topical therapy for inflammatory conditions and infections
- Treatment must be individualized
- Compare topicals vs systemics
- Cultures are an important diagnostic tool
- Rethink diagnosis if not responsive in 2 weeks
- Consider differential diagnoses

“The eyes see only what the mind knows”

Resources


