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Corticosteroids for Skin Conditions: What every clinician needs to Know

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Disclosure

- ▶ Lilly
- ▶ AbbVie
- ▶ Sun



Objectives

1. Describe the pharmacodynamics of corticosteroids.
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 corticosteroid therapies.



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 planks
- ▶ 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



TCS: Percutaneous absorption

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

TCS: Choice of Vehicle

**Most
alcohol**



**Least
alcohol**

Foams

Gels

Lotions

Creams

Ointment

**Most
irritating**



**Least
irritating**





TCS: Selection of potency

- ▶ Vasoconstriction 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



TCS: Alternatives

- ▶ Calcineurin inhibitors
 - Pimecrolimus 1% (Elidel)
 - Tacrolimus 0.1 and 0.03% (Protopic)
- ▶ PDE4 inhibitors
 - Crisaborole 2% (Eucrisa)

Pearls for prescribing TCS

- ▶ Control/monitor QUANTITY and REFILLS
- ▶ Written instructions: how, when, and when to stop
- ▶ Advise patients 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

PEARL:
Remember a
couple from
each category

Category	Potency	Examples
Class 1	Super Potency	
Class 2	High Potency	Clobetasol 0.05%
Class 3	Upper Mid-Potency	
Class 4	Moderate Mid-Potency	Fluocinonide 0.05%
Class 5	Lower Mid-Potency	Triamcinalone 0.1%
Class 6	Mild Potency	Desonide 0.05%
Class 7	Least Potency	Hydrocortisone 2.5%

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

Dispensing for BID dosing for 2 weeks

Location	Adult Dosage		Child tube size (gm)	Infant Tube size (gm)
	gms	FTUs		
Entire face & neck	35	2.5	15	15
One entire hand	14	1	15	15
Entire foot (not both)	28	2	15	15
One entire arm	42	3	30	15
One leg	84	6	30	30
Entire body	30gm for one application		n/a	n/a



1 Finger tip unit (FTU) = 0.5 gm

Rule of thumb: Children = $\frac{1}{2}$ adult amount; Infants (6-12 months) = $\frac{1}{4}$ adult amount

Rule of hands: Area equal to 2 adult hands (palm & fingers) = 1 FTU

FDA approved TCS in children

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

Corticosteroids in pregnancy & lactation

- ▶ 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
- ▶ Lactating women tx >20mg/d can discard breast milk for 4 hrs following dose

Chi, C., Wang, S., Mayon-White, R., & Wojnarowska, F. (2013, September 4, 2013). Pregnancy Outcomes After Maternal Exposure to Topical Corticosteroids; A UK Population-Based Cohort Study. *Journal of the American Medical Association*, E 1-7.

Gupta, R., High, W.A, Butler, D., & Murase, J.E. (2013) Medicolegal aspects of prescribing dermatologic medications during pregnancy. *Seminars in Cutaneous Medical Surgery*, 32(4), 209-216.

Cutaneous/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
- ▶ Reduce to less potent
- ▶ Taper instead of abrupt cessation
- ▶ Reduce frequency (alternate days, weekend, etc.)
- ▶ Can use other non-steroid topicals to reduce dependency
- ▶ Use caution on flexural surfaces, face, genitals and intertriginous
- ▶ Avoid occlusion
- ▶ Use of 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

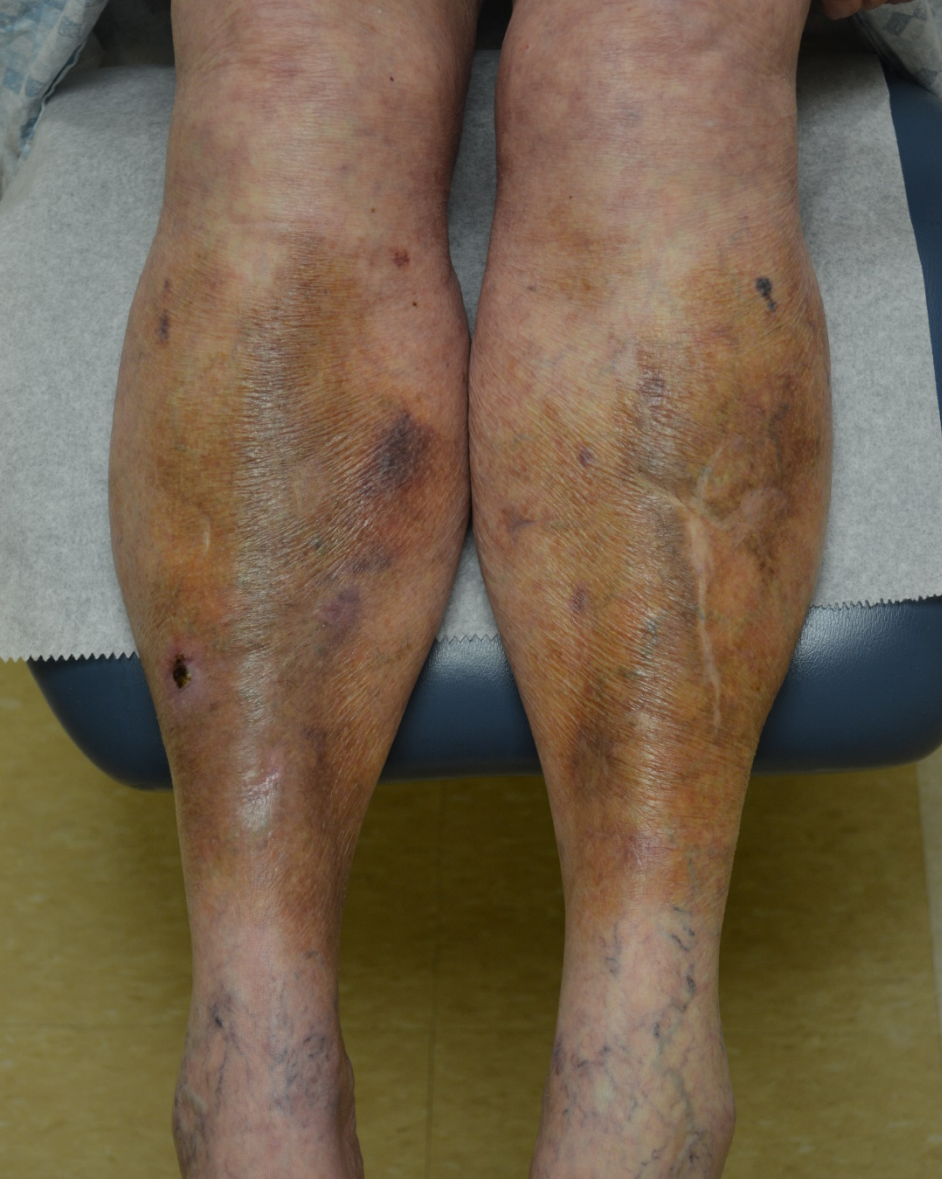


Therapeutic approach

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



Topical corticosteroids or antimicrobials ?



Stasis dermatitis

Frequently in presence of venous insufficiency

- ▶ Pruritus
- ▶ Eczema
- ▶ Hemosiderin staining
- ▶ Ankle (medial) involvement
- ▶ Varicosities
- ▶ Edema

Can develop into:

Secondary infection, cellulitis, ulcers,

Most frequent cause for patients admitted unnecessarily w/misdiagnosis of cellulitis

Stasis Dermatitis

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





Beyond topical steroids

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

Comparison of Oral and Intramuscular Corticosteroids

	ORAL	INTRAMUSCULAR
ABSORPTION	Predictable	Variable
COMPLIANCE	Relies on patient	Total dose administered
DURATION	Any time period	Select short, intermediate or long-acting
PATIENT HEALTH	Req. functional GI tract	Not affected by N/V
PATEINT'S ROLE	Active control/participation	No role or control
CLINICIAN'S ROLE	Prescribe and monitor	Assured of delivery from IM
DIURNAL VARIATION	Some with AM dosing	No diurnal variation
Tapering	Precise	Based on metabolism



Intramuscular CCS

- ▶ Systemic side effects including effect on HPA axis
- ▶ Suppression noted up to 3-4 wks after injection triamcinalone
- ▶ Can cause anovulatory menstrual cycles
- ▶ KEY: not the dose but the interval BETWEEN doses that has the greatest effect on HPA axis
- ▶ Lower dose q2-4 wk interval had greater suppression than higher dose q 6 week intervals

Carson, T.E. et al. (1977) Effect of intramuscular triamcinalone acetate on the human ovulatory cycle. *Cutis* 19: 633-637.

Mikhail, G.R Sweet, L.C., & Mellinger, R.C (1973). Parenteral long-acting corticosteroids: effect on HPA function. *Ann Allergy*. 31: 337-342.



Intramuscular CCS

Summary (Wolverton, 2012)

- ▶ There are rare SEs with a single IM of CCS.
- ▶ Focus should be on disease triggers and use of topicals to avoid additional oral or systemic
- ▶ When more than one injection is needed:
 - ▶ Short- to intermediate-acting CCS (Celstone or Aristocort) for repeated IMs
 - ▶ Long-acting CCS limited to 3-4 times a year

Complications: abscess, SQ atrophy, crystal deposition

Side effects: menstrual irregularities, purpura



Intralesional corticosteroids(CCS) for skin conditions

Indications based on standard for your specialty (literature)....vague

- Alopecia areata
- Keloids
- Plaques of recalcitrant dermatoses
- Cystic lesions



Side effects intralesional CCS

- Painful
- Hypo- or depigmentation
- Atrophy
- Increased risk of infection
- Fat necrosis

It takes a lot of practice to achieve effective outcomes and minimal side effects.



Oral prednisone

- ▶ Corticosteroid of choice for outpatient
- ▶ Inactive form, is converted in the liver
- ▶ Patients with liver disease should tx with prednisolone
- ▶ Little data comparing or recommending
- ▶ Daily dosing vs divided doses reserve for severe cases
- ▶ Consistent dosing vs Medrol dose pack (incr. risk rebound of disease)
- ▶ Tapering is VARIABLE!!!

EXAMPLE: Contact dermatitis 40-60mg for 2wk (no taper) or 60mg x 1wk then TAPER taper over 10-14 days



Considerations for systemic corticosteroids

- ▶ Dermatology: rare need to long term tx
- ▶ Age and weight
- ▶ Comorbidities (DM, HTN, PUD, osteoporosis)
- ▶ Discontinue NSAIDs
- ▶ Systemic infections
- ▶ Short term (2-3 wks) vs long term (months)
- ▶ Need for Vit D and calcium supplementation
- ▶ Biphosphonates if longer than 1 month
- ▶ Know hypersensitivities
- ▶ Drug interactions
- ▶ Frequency of dosing: BID more potent than QD

SPECIAL ARTICLE

2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis

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Case Study





To treat..... or not to treat?

Seborrheic dermatitis (seb derm)

- ▶ 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

Seb Derm



Treatment

Alternating therapies: anti-yeast shampoos, antifungal topicals, TCS, and calcineurin inhibitors (CIs)

Cochran Review (2014)

- ▶ TCS and CI's comparable **short-term** efficacy & outcomes but fewer SEs with TCS
- ▶ Mild vs "strong" TCS comparable outcomes but **BETTER** total clearance with mild TCS
- ▶ TCS has similar outcomes to azoles in the short term

Summary: only minor differences in treatment outcomes and no clear differences between the agents



Combination TCS and antifungals

- ▶ Not all dermatitis requires corticosteroids
 - ▶ Some antifungals have anti-inflammatory effects
- 

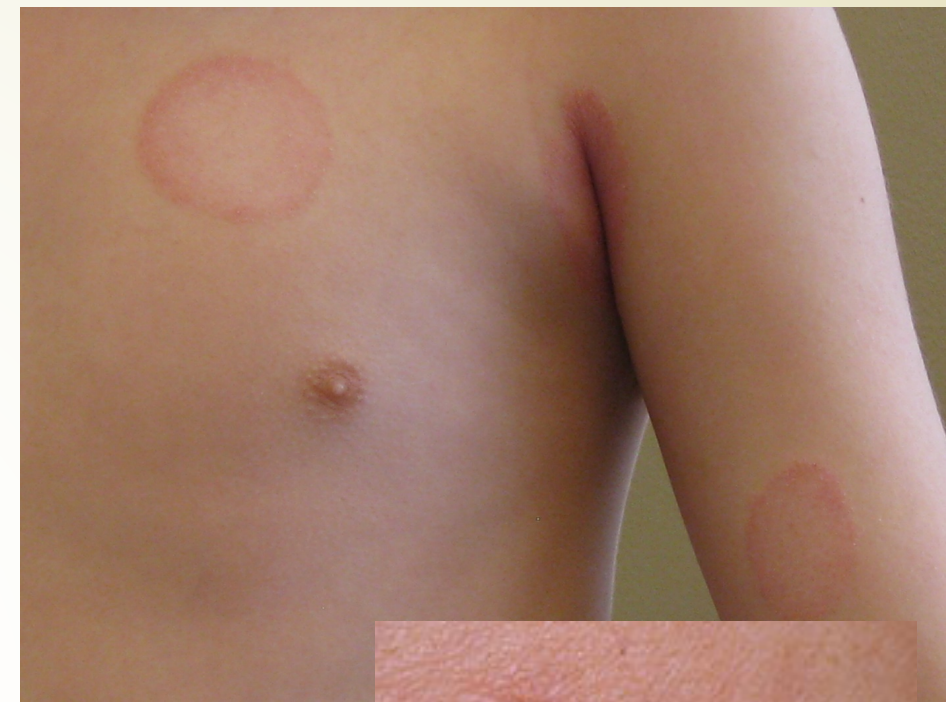


Topical agents: superficial fungal infections

- ▶ 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

Tinea Corporis

- “Ringworm”
- Very contagious
- *T. rubrum*
- Tx topically or systemically



Tinea cruris

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

DDX: intertrigo, contact dermatitis, candidiasis, erythema, bacterial infection



DDX Tinea cruris

- Unilateral, half-moon
- Spreads peripherally (thigh & perianal)
- Not usually scrotum





“Diaper” candidiasis

- ▶ *C. albicans* 80%
- ▶ Marginal scaling
- ▶ Beefy 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 & breasts/nipples
- ▶ Adult incontinence garments

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

Class & Indications	Generic name	Dermatophyte	Yeast	Gram +	Gram -	Anti-inflammatory
Polyenes (fungistatic)						
Candidiasis	Nystatin	0	++++			
Azoles (fungistatic)						
Tinea	Miconazole	+	+++			
Pityriasis/tinea versicolor	Clotrimazole	+	+++			
Candidiasis	Ketoconazole	+	+++	++		++
Seborrheic dermatitis	Oxiconazole	+	+++			
	Econazole	+	+++	+	+	+
	Sertaconazole	+	+++	++		
Allylamines/ Benzylamine (fungicidal)						
Tinea	Naftifine	+	+			+++
Pityriasis/tinea versicolor	Terbinafine	+++	+			+++
	Butenafine	++++	++			+++
Other Agents						
Tinea; Onychomycosis; Candidiasis Pityriasis/tinea versicolor; Seborrheic dermatitis	Ciclopirox	++	++++ C. Albicans	+++	+++	+++
Pityriasis/tinea versicolor	Selenium sulfide		+++			



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**

Clinical pearls treating superficial fungal

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



Case study



Psoriasis

- ▶ Chronic, immune-mediated skin disease
 - Most common autoimmune disease
 - Correlation between skin and systemic inflammation
- ▶ High comorbidity burden
- ▶ Affects almost 8 million Americans

Psoriasis Types

Nail psoriasis

Scalp

Plaque

Plaque

Genital/Inverse



Disease burden of psoriasis

Types

- ▶ Plaque
- ▶ Scalp
- ▶ Nail
- ▶ Genitals
- ▶ Arthritis/joints

Severity

- How is it measured?
- Quality of life measures
- Comparison of severity patient vs health care provider



Comorbidities Established in Psoriasis and PsA

- Cardiovascular disease (CVD)
- Metabolic syndrome
- Obesity
- Dyslipidemia
- Diabetes
- Mood disorders
- Inflammatory bowel disease
- Malignancy
- Uveitis
- Alcohol and addictive behaviors

Abuaara K, et al. *Br J Dermatol*. 2010;163(3):586-592; Armstrong AW, et al. *J Hypertens*. 2013;31:433-442; discussion 442-443; Azfar RS, et al. *Arch Dermatol*. 2012;148(9):995-1000; Gelfand JM, et al. *JAMA*. 2006;296(14):17351-741; Gelfand JM, et al. *J Invest Dermatol*. 2006;126(10):2194-2201; Kurd SK, et al. *Arch Derm*. 2010;146:891-895; Langan SM, et al. *J Invest Derm*. 2012;132(3 Pt 1):556-562; Li W, et al. *Am J Epidemiol*. 2012;175(5):402-413; Ma C, et al. *Br J Dermatol*. 2013;168(3):486-495; Mehta NN, et al. *Eur Heart J*. 2010;31(8):1000-1006; Najarian DJ, et al. *J Am Acad Dermatol*. 2003;48(6):805-821; Yeung H, et al. *JAMA Derm*. 2013;149(10):1173-1179.

Risk of Cardiometabolic Disease in Severe Psoriasis Patients

Clinical significance:

- ▶ Increased risk of MI, stroke, CV death, and DM
- ▶ 5 years shorter life expectancy
- ▶ 10-year risk of major CV event attributable to psoriasis = 6%
- ▶ Risk of CV disease similar patient with diabetes
- ▶ Patients with severe psoriasis are 30x more likely to experience MACE (attributable to psoriasis) than to develop a melanoma skin cancer

MI = myocardial infarction, MACE = major adverse cardiac events, RR = relative risk.

1. Abuaara K, et al. *Br. J. Dermatol.* 2010;163(3):586-592;
2. Gelfand JM, et al. *JAMA.* 2006;296(14):1735-1741.
3. Gelfand JM, et al. *J Invest Derm.* 2009;129(10):2411-2418;
4. Mehta NN, et al. *Eur Heart J.* 2010;31(8):1000-1006.
5. Mehta NN, et al. *Am J Med.* 2011;124(8):775.e1-6.
6. Azfar R, et al. *Arch Derm.* 2012;148(9):995-1000.

Treatment of Psoriasis

Type of treatment	Recommended for	Comments
Topical Therapy (emollients, corticosteroids, vitamin D analogues, calcipotriene, tazarotene, calcineurin inhibitors, anthralin)	Mild disease	Limited by poor adherence rates
Ultraviolet (UV) Light (UVB radiation, narrow-band UVB, photochemotherapy [PUVA])	Moderate-to-severe disease	Associated with accelerated photodamage and increased risk of malignancy; will not treat PsA
Methotrexate	Moderate-to-severe disease	Most widely used systemic treatment; inexpensive; pregnancy category X
Cyclosporine	Psoriasis flares	Used as a bridging agent during induction of other maintenance agents or for flares
Acitretin	Moderate-to-severe disease	Low toxicity and no immunosuppression; can be used in patients with infection, malignancy, or HIV; need to monitor LFTs and triglycerides; contraindicated if considering pregnancy
Biologic Agents	Moderate-to-severe disease	May be used as first-line systemic agent depending on comorbidities and other considerations; highly efficacious; expensive

Treatment of Mild-to-Moderate Psoriasis

Up to 80% of psoriasis patients receive no treatment or only topical therapy

Topical therapy

- ▶ Corticosteroids, vitamin D derivatives, tazarotene, anthralin, tacrolimus, pimecrolimus, newer tar formulations
- ▶ Must be prescribed appropriately and used consistently for weeks to months for clinical improvement
- ▶ Potential AEs
 - Cutaneous atrophy
 - Telangiectasias
 - Hypothalamic-pituitary axis suppression

Treatment of Mild-to-Moderate Psoriasis

Topical therapy (cont'd)

- ▶ Primary limitation is medication adherence
- ▶ Strategies to optimize adherence:
 - Consider dosage/schedule, choice of vehicle
Fixed-combination gels, foams
 - Address patient preference about treatment
 - Address concerns about treatment-related toxicities
 - Manage patient expectations
- ▶ Assess patient response and know when to refer!

Psoriasis management & monitoring

- Refer to dermatology if not controlled
- Refer to dermatology or rheumatology for PsA
- National Psoriasis Foundation (NPF) treatment targets for plaque psoriasis
 - **Acceptable:** Either BSA $\leq 3\%$ or BSA improvement $\geq 75\%$ from baseline at 3 months after treatment initiation
 - **Target:** BSA $\leq 1\%$ at 3 months after treatment initiation
- Monitor at least every 3 to 6 months during maintenance therapy
- Reassess if skin symptoms or arthritis not under control



REMEMBER:

- ▶ Successful use of TCS depends on the **correct diagnosis**.
- ▶ Indications vague
- ▶ All brands vs generics are NOT equal
- ▶ Monitor for secondary infections
- ▶ Control risk for side effects and dispensing
- ▶ Contraindicated in skin with infection, patients with perioral dermatitis, acne or rosacea



Take home message

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



Objectives

1. Describe the pharmacodynamics of corticosteroids- **MOAs**
2. Discuss important concepts in selecting appropriate agents to optimize patient outcomes and minimize risks, side effects and complications- **indications, duration, variables & routes of administration.**
3. Review three case studies of dermatologic conditions and selection of corticosteroid therapies- **atopic dermatitis, stasis dermatitis, seborrheic dermatitis and psoriasis.**



"The eyes see only what the
mind knows"

Resources

Berth-Jones, J. (Ed.). (2010). Chapter 73 Topical therapy. *Rook's Textbook of Dermatology* (8th ed., pp. 73.1-73.52). Chichester, West Sussex UK: Wiley-Blackwell.

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Wolverton, S. (2013). *Comprehensive Dermatologic Drug Therapy*, 3rd Ed. London: Elsevier.