

# Skin Therapy Letter<sup>©</sup>

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Clinical Evidence. Practical Advice.

Editor-in-Chief: Dr Stuart Maddin

**Dr. Stuart Maddin, MD, FRCPC**

## EDITOR-IN-CHIEF

Dr. Stuart Maddin, Chairman of SkinCareGuide, is one of North America's leading dermatologists, and is the author of numerous dermatologic journal articles, monographs and textbooks. In addition to providing consultative input to a number of pharmaceutical and biotech companies, he is the director of the clinical trials unit at the Department of Dermatology and Skin Science, University of British Columbia. Dr. Maddin has also acted in an advisory capacity to a number of drug regulatory agencies, such as the Health Protection Branch (Ottawa), the AAD-FDA Liaison Committee, and WHO (Geneva). He is the founder of the Dermatology Update symposia, now in its 24<sup>th</sup> year. As well, he is Past President of the Canadian Dermatology Association and served as Secretary-General of the International Committee of Dermatology — International League of Dermatological Societies.

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## PHARMACIST ADVISOR

Annie Dufour is the pharmacist and manager of the Skin Care Centre Pharmacy located in the Skin Care Centre in Vancouver BC. The Skin Care Centre Pharmacy dispenses all medications, with a specialty in dermatological medications including compounded preparations.



Ms. Dufour holds a degree in biochemistry, as well as a pharmacy degree from the University of Toronto. She has been practicing as a pharmacist since 1998, and has experience in many settings including a hospital pharmacy, community pharmacy and the pharmaceutical industry. She has authored and presented various continuing education programs for pharmacists on the subject of dermatological conditions and their treatments.

## Skin Care as an Adjunct Treatment for Skin Disease

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### Introduction

A good skin care regimen including both prescription and non-prescription treatments for multiple dermatological conditions is very important. Many skin disorders can be caused by a primary dermatological condition but one should remember systemic diseases and drugs prescribed for other conditions can also cause skin problems. Daily skin care is a key component of management for many skin diseases. It is important to educate patients about behavioral changes they can make on a daily basis, in addition to prescribed therapy.

### Dry Skin

#### *Dermatological Causes*

- Atopic dermatitis
- Asteatotic dermatitis
- Ichthyoses
- Irritant contact dermatitis
- Acne vulgaris
- Rosacea
- Retinoid-induced irritant dermatitis
- Psoriasis
- Cosmetic therapies & procedures

#### *Systemic Causes*

- Renal failure
- Diabetes
- Hypothyroidism
- Malnutrition

#### *Therapeutic Causes*

- Systemic retinoids (e.g., isotretinoin [Accutane<sup>®</sup>])
- Epidermal growth factor receptor inhibitors (e.g., cetuximab [Erbix<sup>®</sup>])
- Radiation therapy, chemotherapy

#### *Adjunctive Treatment*

##### Patient education

- Learn how to recognize flares and treat early.

#### Bathing

- Baths are recommended more than showers, lukewarm water, 5-10 minutes, once or twice daily.
- Use a mild cleansing product (e.g., Cetaphil<sup>®</sup> Cleanser, Toleriane<sup>®</sup> Cleanser).
- Add emulsifying oil (e.g., Keri<sup>®</sup> Bath Oil).

#### Laundry

- Mild detergents with no fragrance
- No bleach or fabric softener

#### Skin care

- Use mild cleansing agents.
- Apply moisturizer 3-5 minutes after bathing.
- Avoid light lotions; use products rich in essential fatty acids, and those formulated with appropriate combination of humectants, emollients, and occlusives.

#### Environmental avoidance

- Avoid rough fabrics, chlorine, solvents, and stress.

## Itchy Skin

### *Dermatological Causes*

#### Localized

- Atopic dermatitis
- Urticaria
- Insect bites
- Lichen planus
- Lichen simplex chronicus
- Psoriasis

#### Generalized

- Winter itch
- Infestations (e.g., lice, scabies)
- Pruritus of senescent skin

### *Systemic Causes*

- Renal failure
- Hepatic disease (obstructive biliary disease)
- Endocrine/metabolic (hyper/hypothyroidism, diabetes, gout)
- Neurologic (multiple sclerosis, post-herpes zoster, depression, peripheral nerve injuries)
- Neoplastic (leukemia, lymphoma, multiple myeloma, internal malignant tumors)
- Hematologic (hemochromatosis, iron deficiency anemia)
- Infectious (HIV, hepatitis C)

### *Therapeutic Causes*

- Opiates
- ASA

- Drug reactions (exanthematous eruptions, fixed drug eruptions, urticaria/ angioedema) to antibiotics, antihypertensives, cholesterol lowering agents, etc.
- Radiation therapy, chemotherapy

### *Adjunctive Treatment*

- See management for Dry Skin above.
- Consider allergy testing to determine sensitivity.

### *Lifestyle Measures*

- Decrease alcohol intake.
- Reduce stress.
- Avoid irritants, e.g., no harsh fabrics, harsh soaps, solvents, chlorine.
- Rinse detergents from clothing.
- Use bath oil or baking soda.
- Apply moisturizer regularly after washing.
- Refresh with cool water compresses or cooled moisturizers.

### *Topical Agents*

- Menthol 1% and/or camphor 1/4%-1/2% in aqueous cream (keep refrigerated)
- Combination products with menthol, colloidal oatmeal and shea butter (compounding not necessary).

### *Systemic Agents*

- Antihistamine

## Photosensitivity

### *Dermatological Causes*

- Polymorphous light eruption
- Actinic prurigo
- Solar urticaria
- Brachioradial pruritus

### *Systemic Causes*

- Systemic Lupus Erythematosus
- Porphyrias
- HIV

### *Therapeutic Causes*

- Doxycycline, minocycline, tetracycline
- NSAIDs
- Trimethoprim-sulfamethoxazole
- Thiazide diuretics

- ACE inhibitors
- Antimalarials
- Coal tar and its derivatives
- Chlorpromazine
- Procainamide
- Vitamin A acid derivatives (e.g., isotretinoin [Accutane<sup>®</sup>], topical retinoic acid [Retin-A<sup>®</sup>])
- Skin depigmenting agents (e.g., hydroquinone, kojic acid)

### *Adjunctive Treatment*

- Sun avoidance
- Protective clothing
- Barrier protection with minimum SPF 30 broad spectrum sunscreens
- Antihistamines q.h.s.

## Psoriasis

### *Systemic Causes*

- Post streptococcal infection

### *Therapeutic Causes*

- Beta blockers
- Lithium
- Corticosteroid rebound phenomenon
- Antimalarials

- Interferon
- NSAIDs

### *Adjunctive Treatment*

- Moisturizers
- Antihistamines
- Sunburn avoidance
- Avoidance of drugs that exacerbate the condition

## Scaly Scalp

### *Dermatological Causes*

- Psoriasis
- Seborrheic dermatitis
- Dandruff

### *Adjunctive Treatment*

- Salicylic acid 1%-4% +/- olive oil (never use if patient has

seborrheic dermatitis as it promotes growth of causative yeast), mineral oil

- Shampoos containing selenium sulphide, zinc pyrithione, tar
- Tar (e.g., 10%-20% coal tar solution; liquor carbonis detergent in a topical steroid ointment)

## Pimples/Acne

### *Dermatological Causes*

- Acne vulgaris

### *Systemic Causes*

- Hyperandrogen states (e.g., polycystic ovarian syndrome)
- Menstruation hormonal factors
- NB: foods are not an aggravating factor

### *Therapeutic Causes*

- Cosmetic products containing lipids and cocoa butter
- Heavy oils, greases, and tars
- Topical drugs containing tars, ointments, and corticosteroids
- Corticosteroids
- Androgens
- Halogens (e.g., systemic dioxin poisoning causing chloracne)

- Lithium
- Antituberculosis drugs (e.g., isoniazid)
- Antiepileptics (e.g., carbamazepine, phenytoin)
- Some formulations of oral contraceptives

### *Adjunctive Treatment*

- Daily facial washes and cleansers specially formulated for oily skin
  - Low dose benzoyl peroxide washes
  - Non-comedogenic moisturizing lotion
- For patients taking systemic retinoids (e.g., isotretinoin):
- Eyes: saline drops  
Nose: petroleum jelly ointment  
Lips: lip balm  
Dry skin: daily moisturizers

## Rosacea

### *Therapeutic Causes*

- Niacin

### *Adjunctive Treatment*

- Avoid aggravating factors that induce flushing/telangiectasia development: spicy food, alcohol, hot drinks, and heat-inducing activities.
- Warn patients not to apply potent topical corticosteroids to the face.

- Medical therapies help to resolve pustulation, papulation, and erythema, but have a minimal effect on the suppression of flushing and established telangiectasia.
- Some laser therapies can be effective.
- Cosmetic camouflage (e.g., Cover FX<sup>®</sup>) may be especially helpful for females.
- Methylsulfonylmethane + silymarin (Rosacure<sup>®</sup>) helps minimize appearance of erythema.

## Clinical Pearls

### *Patient Education*

Providing patient education along with adjunctive therapies can help reduce frustration and improve patient compliance.

- Use simple skin care regimen, e.g., mild washes and daily facial moisturizer.

### *Sunscreen*

- Apply broad spectrum, photostable formulation with SPF  $\geq 30$  before going out in the sun.
- Reapply frequently.
- A fairly thick application is needed for effectiveness.

### *Tar and its derivatives*

- Stains fabrics yellow.
  - Apply at night along the grain of hair growth to avoid folliculitis.

- Use old sheets to reduce concern about staining.
- Turns white hair a straw color.
- Patients with white hair should be warned to use on scalp with caution.

### *Benzoyl peroxide*

- Bleaches fabrics. To minimize:
  - Use a white towel to dry face after use.
  - Avoid contact with fabrics until skin is dry.
  - Use at night to avoid bleaching good clothing.

### *Antihistamines*

- Caution patient regarding drowsiness and consider recommending non-drowsy antihistamine (e.g., cetirizine [Reactine<sup>®</sup>], desloratadine [Aerius<sup>®</sup>] during the day).

## Conclusion

Pharmacists can play a key role in helping patients with skin concerns by recognizing causes of common skin symptoms and recommending therapy to patients. They can counsel patients on behavioral strategies to help reduce disease severity and recurrence, and help patients choose products well-matched for a given skin condition. When counseling patients, a reactive approach to their concerns is appropriate, but a proactive approach is superior as this provides the best possible care.

# A Review of Corticosteroids for the Treatment of Psoriasis

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## The Different Potencies

One of the most influential developments in the treatment of psoriasis and other inflammatory skin diseases occurred in the 1950s with the introduction of topical hydrocortisone.

- The further addition of side chains and halogenation increased the potency of topical corticosteroids.
- This in turn further increased the treatment options for psoriasis.

These compounds can be classified in different groups depending on their potency. See Table 1.

Class	Potency	Corticosteroids
I	Super-high potency	Clobetasol propionate
II	Super potent	Betamethasone dipropionate (optimized vehicle) Halobetasol propionate
III	Very potent	Amcinonide Desoximetasone Fluocinonide Halcinonide Mometasone furoate
IV	Potent	Betamethasone dipropionate (regular vehicle)
V	Medium potency	Betamethasone valerate Diflucortolone valerate Fluocinolone acetonide Hydrocortisone valerate Triamcinolone acetonide
VI	Mild potency	Desonide Prednicarbate
VII	Mildest potency	Dexamethasone Flumethasone Hydrocortisone Methylprednisolone Prednisolone Fluticasone propionate

Table 1: Some commonly used topical corticosteroids ranked by potency into 7 different classes.

## The Importance of the Vehicle

Prior to the mid-1970s, the vehicle of a topical medication was not believed to have any impact on the potency and effectiveness of a given formulation.

- When a new molecule was tested, different concentrations were randomly mixed with various preparations and then applied in a variety of quantities in order to observe the effect on diseased skin.
- More controlled research has allowed researchers to determine that the penetration of a given corticosteroid could be greatly improved with the addition of:
  - propylene glycol
  - salicylic acid
  - ethanol.
- Since then, many more compounds have been formulated with different bases in order to increase their efficacy.
- The vehicle is not only what brings a drug in contact with the skin, but is the link between drug potency and therapeutic effectiveness.
- It is a highly engineered balance of numerous chemicals. Each serves a separate or overlapping purpose in order to achieve the characteristics of an effective vehicle:
  - Chemically and physically stable
  - Does not inactivate the drug
  - Nonirritating, hypoallergenic
  - Cosmetically acceptable
  - Easy to use
  - Allow the proper release of the drug.

## The Importance of the Vehicle (continued)

- The same corticosteroid molecule may rank in different classes when formulated in different vehicles, e.g., betamethasone dipropionate prescribed as diprolene ointment .05% and diprosone ointment .05% are categorized in class II and IV, respectively.
- In general, compounds that contain a higher amount of propylene glycol are more potent.
- As a general rule of thumb, ointments tend to be more potent than creams and lotions.
- It is important to remember that creams, gels, solutions, lotions can also be specifically formulated to be almost equipotent to ointments in some cases.
- The vehicle often has beneficial nonspecific effects by possessing cooling, protective, emollient, occlusive, or astringent properties.
  - These effects should not be overlooked. In the end, it is the general acceptability and efficacy of a preparation that will result in patient's compliance.

## Generic vs. Brand-name Products

- No comparative labeling exists to ensure equal efficacy between generic and brand name products.
- The potency of generic products is not always equivalent to the brand name preparation and vice versa.
- Variability exists between the different generic preparations, emphasizing the effect of vehicle on a preparation's potency.

## Proper Use of Steroids for Various Skin Conditions

Since their introduction, topical corticosteroids have become a mainstay in the treatment of many skin diseases such as psoriasis. But to properly use topical corticosteroids, the physician must first choose the desired potency based on:

- A patient's age:
    - Children have a higher ratio of skin surface area to body weight and are less able to metabolize potent glucocorticoids rapidly.
    - Very mild corticosteroids should be prescribed to young children, especially in the diaper area and in the folds.
    - Elderly patients have thinner skin and thus strong corticosteroids should be used with caution.
  - The disease type:
    - Atopic dermatitis, diaper dermatitis, nummular dermatitis, intertriginous psoriasis and seborrheic dermatitis are all conditions typically very sensitive to topical corticosteroids.
    - Mid to mild potency should be used.
  - The location:
    - Penetration through the eyelids and scrotum is 4 times greater than for the forehead and 36 times greater than for the palms and soles.
    - Occluded areas such as flexures, axillae, and the groin area absorb corticosteroids more rapidly; mild preparations should be used.
    - In general, halogenated corticosteroids (i.e., Class 1–5 except hydrocortisone-17-valerate) should not be used on the face, and in the skin folds.
    - Topical corticosteroids are better absorbed on moist skin.
  - The severity and extent of the lesions
  - Pregnancy (Most corticosteroids are Category C.)
- Topical corticosteroids should be applied sparingly and rubbed into the affected area. A rule of thumb for the quantity of cream or ointment to use is a pea-sized amount for a 5cm x 5cm area of skin.

## Adverse Effects

Adverse effects of topical corticosteroids increase with the potency of the preparation. Physicians and pharmacists must be aware of the most frequent adverse side-effects of topical corticosteroids such as:

- stinging and burning upon application
- epidermal atrophy and dermal atrophy (usually after several weeks of use)
- perioral dermatitis, steroid-induced rosacea, steroid acne
- suppression of the pituitary-adrenal axis (especially with the potent ones)
- purpura/ easy bruising
- Tachyphylaxis (decreased effect of the drug)
  - It can occur as early as after 1 week, but generally takes several weeks to a month to occur.
  - Stopping treatment for 4–7 days, and then reinstating treatment thereafter has been shown to be beneficial in stopping tachyphylaxis.

## Conclusion

It is also important, as with most other prescription drugs, to ensure a patient is under proper medical supervision. A patient's follow-up visit with his physician will optimize benefits and minimize adverse effects of a topical corticosteroid treatment. Physicians and pharmacists alike should be aware of the importance and the difference of various vehicles when prescribing topical corticosteroids.



# Sunscreens

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## Sun and UV Exposure

Ultraviolet (UV) light from the sun is the main environmental cause of photodamage and most skin cancers. Its damaging effects are cumulative, so daily protection throughout life is important.

- 70% of Americans are aware that daily sun exposure causes skin damage.[Fitzpatrick TB. *Arch Derm* 124:869-871 (1998).]
- Americans get <25% of their lifetime UV dose by 18 years of age. By the age of 60, they have absorbed 80% of their lifetime dose. [Godar DE, et al. *Photochem Photobiol* 77(4):453-7 (2003 Apr).]

## Sunscreens

- Use of sunscreens rose from 35% in 1986 to 53% in 1996.[Robinson JK, et al. *J Am Acad Dermatol* 37:179-86 (1997).]
- In a 2003 survey by the American Academy of Dermatology, only 47% of women and 33% of men reported using sunscreen regularly.[American Academy of Dermatology. 2005 Skin Cancer Survey Fact Sheet. URL: [www.aad.org](http://www.aad.org)]
- More than half of teens are not too careful or not at all careful to protect their skin from sun exposure.[American Academy of Dermatology. 2005 Skin Cancer Survey Fact Sheet. URL: [www.aad.org](http://www.aad.org)]
- Depending on locale and elevation, sunscreens should be considered for daily use throughout the year, not just in the hot summer months or during prolonged exposure.
- Many people are unaware that daily application is important to help prevent skin damage.
- Skipping sun protection on 1 day out of 4 can lower the skin's defense mechanisms and increase photoaging effects.[Philips TJ, et al. *J Am Acad Dermatol* 43(4):610-18 (2000).]
- Two types of sunscreens:
  - Organic or chemical, which protects against UV by absorbing the energy from UV rays.
  - Inorganic or physical, such as metal oxides or particulate UV filters, which are insoluble particles that reflect UVA and UVB.

## Sun Protection Factor (SPF)

- The SPF number indicates how much longer one can stay out in the sun before burning compared with having no protection.
- SPF relates to UVB protection only and does not indicate whether a product provides adequate protection from UVA rays. However, increasing SPF does generally correlate with increased UVA protection to some degree.
- There is general consensus among experts that daily, year-round, broad-spectrum photoprotection of at least SPF 15 is a key component of a sun-safe strategy to reduce cumulative lifetime exposure to solar UV.
- SPF is a lab assessment that does not generally reflect what's used in the real world.
  - SPF 15 is the minimum recommended level.
  - It means that theoretically one can stay out without burning, 15 times longer than with no protection. However, this should not be used to encourage prolonged sun exposure.
  - The level of UV filtration is not proportional to the SPF. The amount of UV transmission is 1/SPF so with an SPF of 2, 50% of UV light is transmitted. e.g., if you have an SPF of 30, you have blocked out 97% of UV light (1/30 transmitted).
- SPF products in lighter, esthetically pleasing formulations tend to be used more regularly and in sufficient quantity to deliver the intended UV protection.

## UVA Protection

- At present, there is no standardized test for UVA protection in North America.
- Different filters have different absorption profiles in the UVA range and they're not all comparable. These filters must be carefully combined to provide photo-stable protection across the UVA spectrum.
- Some UV filters are degraded by sunlight and unless they're chemically stabilized, they lose their effectiveness in a relatively short time.

## UVA Protection (continued)

### Sunscreen Application

- It is recommended to be applied 15-20 minutes before going outdoors and reapplied every 2 hours or after swimming/ heavy exertion.
- People typically use only half the amount they need for full protection.
- The recommended dose is 2mg/cm<sup>2</sup> of skin, or 30ml (2 tablespoons) for the whole body, or 2.5ml (½ teaspoon) for 1 arm.
  - Published studies indicate that the actual dose being used is much lower:
  - 0.5mg/cm<sup>2</sup>[Bech-Thomsen N, et al. *Photodermatol Photoimmunol Photomed* 9(6):242-4 (1992-1993 Dec).]
  - 1.0mg/cm<sup>2</sup>. [Stenberg C, et al. *Arch Dermatol* 121(11):1400-2 (1985 Nov).]
- In a week-long, double-blinded sunscreen usage test comparing consumer application habits when using SPF 30 vs. SPF 15:
  - Heavy feeling products with a higher SPF were applied much more sparingly.
  - Cosmetically formulated products with a lower SPF were used more consistently and in sufficient quantities to provide the intended protection. [Grosick TL, Tanner PR. Efficacy as used, not as tested, is true measure of sunscreen performance. Proceedings of the 62nd American Academy of Dermatology Annual Meeting; Feb. 6-11, 2004; Washington, DC, USA.]
  - Most dermatologists recommend SPF 30. Those with higher SPF may have better UVA protection.

## Sunscreens and Cancer

- Sunscreens are effective in protecting skin from actinic keratoses and squamous cell carcinomas.
- They have not been shown to reduce the incidence of a first basal cell carcinoma, but they may prolong the time to develop a second lesion.
- In a quantitative review of studies looking at sunscreen use and the risk for melanomas, Dennis et al. reported there was no association between these two factors. [Dennis LK, et al. *Ann Intern Med* 139(12):966-78 (2003 Dec).]

## The Vitamin D Controversy

The UV action spectra for DNA damage leading to skin cancer and for vitamin D photosynthesis are virtually identical. Consequently, the harmful and beneficial effects of UV irradiation are inseparable giving rise to the argument that sun avoidance (in order to prevent skin cancer) could compromise vitamin D sufficiency. [Wolpowitz D, et al. *J Am Acad Dermatol* 54(2):301-17 (2006 Feb).]

In order to analyze the risks/ benefits of sunscreens on vitamin D, Nash, et al. estimated the production of vitamin D based on measures of sunlight exposure and determined the impact of an SPF 15 sunscreen on vitamin D levels in humans. The study included 92 adult women located in 5 different geographic areas and found that the combination of diet and sunlight, even with daily use of an SPF 15 sunscreen provides adequate intake for vitamin D. [Nash JF, et al. *J Am Acad Dermatol* 52(3):161 (2005).]

## Tanning Alternatives

### Tanning Beds

- Avoid them.
- UV from the sun and from tanning beds can cause skin cancer and wrinkling.
- Consider using a self-tanning product instead.

### Self Tanners

- The main ingredient is dihydroxyacetone, hygroscopic white crystalline powder.
- Self tanning lotions and sprays offer a safe alternative to tanning.

- They develop color on the skin's surface via a chemical reaction.
- They are not highly protective – most have an SPF of 3 to 4. [Draelos Z. *Am J Clin Dermatol* 3(5):317-8 (2002).]
- A sunscreen with an SPF of at least 15 (e.g., Olay<sup>®</sup> Complete, Anthelios<sup>®</sup> L or S, Neutrogena<sup>®</sup> Sensitive Skin Sunblock Lotion, Umbrelle<sup>®</sup>) should be used in association with self tanning agents.

## Conclusion

Sunscreens serve an important role in overall sun protection. However, they should be used in conjunction with other sun protection measures such as clothing, hats and sunglasses.

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Pharmacist Edition

Editor-in-Chief: Dr Stuart Maddin

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