

Topical Corticosteroids: Considerations for Appropriate Use

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GOAL

To convey the basic concepts of topical corticosteroid use.

OBJECTIVES

1. Describe the pharmacological actions and adverse effects associated with topical corticosteroids.
2. Identify potential scenarios when percutaneous absorption of topical corticosteroids may be enhanced.
3. Describe specific parameters that steer corticosteroid selection and application.
4. Identify potential dermatological indications for use of topical corticosteroids.

Managed care organizations are a continuously growing source of payment for office visits for common skin complaints.¹ Nearly 2000 different skin disorders are seen by healthcare practitioners daily, with skin rash being the most frequent diagnosis.² As of 1995, preferred provider organizations, health maintenance organizations, or other plans financed nearly 20% of office visits for skin complaints.³ Topical corticosteroids (glucocorticoids) are the most frequently prescribed medication for common skin disorders. Pharmacists share the responsibility of screening patients in order to identify dermatologic disorders, identify drug-induced causes of dermatosis, initiate drug therapy and monitor patient compliance, efficacy, and adverse effects.

Since the 1950s, topical corticosteroids have been used as the mainstay of dermatologic therapy with few reports of adverse effects.⁴ In the last 15 years, new topical corticosteroid preparations have entered the marketplace. New products are characterized by increases in potency, new methods of application, and improvements in vehicles and bases. As a result of continued research, clinical efficacy and utilization have increased.

Despite the growing number of topical corticosteroids available in the marketplace, it is relatively easy to predict their actions, uses, and side effects. The major difference between topical corticosteroids is their degree of potency and adverse effects.⁵

Pharmacology

Topical corticosteroids are compounds combined with a suitable vehicle for application to the skin and mucous membranes. All corticosteroids consist of a hydrocortisone molecule or synthetic analog of hydrocortisone. This analog can be modified by halogenation, methylation, acetylation, esterification, and/or double-band induction to increase the



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therapeutic effect and reduce side effects.⁴ The glucocorticoid effect is primarily due to a cyclopentanophenanthrene nucleus and a 17,21-dihydroxy-20-keto side chain, a structural feature common to all corticosteroids.⁶ Simply stated, topical corticosteroids act as anti-inflammatory agents, just as systemic corticosteroids. Higher tissue concentrations, however, are achieved locally with topical agents without the unwanted side effects seen with systemic corticosteroids.

Most of the pharmacologic actions of the corticosteroids are mediated by nuclear receptors for hydrocortisone to which other steroids bind. The stronger the affinity of the compound for the receptor, the more potent the compound.

Topically applied corticosteroids interact with receptors in dermal and intradermal cells. This interaction induces peptides known as lipocortins. Lipocortins antagonize the action of phospholipase A₂, which in turn depresses the formation, release, and actions of the endogenous chemical mediators of inflammation. These mediators include kinins, histamine, liposomal enzymes, prostaglandins, and the complement system.⁵

Other effects that contribute to the anti-inflammatory activity include lysosomal and cellular membrane stabilization, reduction in the number of Langerhans cells, the inhibition of the movement of inflammatory cells, vasoconstriction, and an antimitotic effect for many cell types, including epidermal cells.⁷

Adverse Effects

Although topical corticosteroids are considered relatively safe, a potential remains for various types of drug-induced side effects. All topical corticosteroids can produce systemic side effects, the most severe being hypothalamic-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome. These types of adverse events usually occur after chronic use with a potent agent over a large area in normal healthy adults. However, small children and patients with liver failure may develop significant HPA axis suppression with the use of less potent corticosteroids.⁸

Localized adverse effects are probably the most frequent adverse events associated with topical corticosteroids. Some common localized side effects that can occur are tissue atrophy, degeneration, and striae which usually involve the epidermal layer. These adverse events primarily are due to the mineralocorticoid, antiproliferative activity of topical corticosteroids on keratinocytes and

fibroblasts. Atrophy may be seen especially in the elderly, whose skin is already thinning due to the aging process.⁸ This thinning can expose the dermal vasculature and result in aggravation of rosacea as well as bruising and telangiectasia. If detected early, these adverse events are reversible upon discontinuation of the corticosteroid. In some cases where potent agents have been used for a long period of time, however, the damage may be permanent. This is especially true with halogenated agents.⁸

Selection Considerations

An attractive advantage of topical therapy, in general, is the ability to deliver an optimal dose of a desired medication directly to the site of need. However, the basic principles of topical therapy should be followed in order to assure selection of appropriate topical agents, specifically corticosteroids.⁴ Several parameters must be evaluated when treating dermatoses with topical corticosteroids. In an effort to ensure appropriate, safe, and successful therapy with these agents, numerous factors must be considered. Potency, safety, and formulation of the drug, disease type, site and severity of the lesion, and patient age must be assessed.⁹

The most relevant factor to consider when planning treatment of skin diseases with a topical corticosteroid is potency. For most practitioners, it is useful to divide the topical steroids into 4 categories: low, medium, high, and very high potency. Selected topical corticosteroid preparations are listed according to their estimated relative potency in Table 1. Drug characteristics and concentration and the vehicle used will influence relative potency of a product. Beyond the inherent characteristics of a particular agent, the vehicle in which the agent is delivered directly affects the potency. For example, clinical efficacy varies between ointments and creams, even those containing the same concentration of the same corticosteroid.⁵ Selection of the appropriate steroid may be irrelevant if an inappropriate vehicle is chosen to deliver the medication. If such a mistake is made, treatment failure is likely.

Ointment formulations are generally very effective for dermatoses associated with extremely dry, thick, fissured, or lichenified skin lesions. Corticosteroid penetration is also enhanced due to the ability of ointments to form an occlusive layer, thus increasing hydration of the stratum corneum (outermost layer of the epidermis) and increasing penetration of the particular corticosteroid. These water insoluble occlusive mixtures of animal, vegetable, or mineral fats have the potential to cause

adverse effects related to excessive occlusion of hair follicles. Conditions such as miliaria, acne, and folliculitis may result. Lanolin and white petrolatum are 2 ointment bases commonly used in topical preparations. White petrolatum is odorless, colorless, and rarely sensitizing; however, lanolin can potentially cause allergic contact dermatitis in individuals with chronic dermatoses. Further consideration should also be given to the fact that patients may consider ointments aesthetically unpleasing.^{4,11}

Creams have a high degree of patient acceptance and are a popular choice for treatment of acute and subacute dermatoses. Moist skin and intertriginous areas (eg, groin, axilla, perineum, and inframammary areas) are especially appropriate sites for the use of corticosteroid creams. These vehicles may potentiate a drying effect; therefore, intermittent application of a moisturizer may prove beneficial in some patients. Possible disadvantages regarding use of creams include matting of hairy areas, poor retention in oozing conditions, and less efficacy than ointments for lubrication or facilitation of percutaneous drug absorption.^{4,11}

Gels, lotions, and sprays are the most aesthetically pleasing preparations for use on hairy areas such as the scalp. Gels are also especially useful to treat intraoral disorders, whereas lotions offer ease of application when treating large cutaneous areas. These vehicles frequently contain alcohol and propylene glycol. They produce cooling and astringent effects, but have the potential to cause irritation and burning when applied to acute dermatoses such as excoriated skin, erosions, or fissures.^{7,11}

Absorption Characteristics

It should be apparent that these agents would remain ineffective unless absorbed into the skin. Assuming the agent of choice is released from its

Table 1. Relative Potency of Topical Corticosteroids*

Corticosteroid	Vehicle	Dosing Strength
Very high potency		
Augmented betamethasone dipropionate	ointment	0.05%
Clobetasol propionate	cream, ointment	0.05%
Diflorasone diacetate	ointment	0.05%
Halobetasol propionate	cream, ointment	0.05%
High potency		
Amcinonide	cream, lotion, ointment	0.1%
Augmented betamethasone dipropionate	cream	0.05%
Betamethasone dipropionate	cream, ointment	0.05%
Betamethasone valerate	ointment	0.1%
Desoximetasone	cream, ointment, gel	0.25% 0.05%
Diflorasone diacetate	cream, ointment	0.05%
Fluocinonide acetone	cream	0.2%
Fluocinonide	cream, ointment, gel	0.05%
Halcinonide	cream, ointment	0.1%
Triamcinolone acetone	ointment	0.1%
Medium potency		
Betamethasone benzoate	cream, gel, lotion	0.025%
Betamethasone dipropionate	lotion	0.05%
Betamethasone valerate	cream	0.1%
Clocortolone pivalate	cream	0.1%
Desoximetasone	cream	0.05%
Fluocinolone acetone	cream, ointment	0.025%
Flurandrenolide	cream, ointment, lotion	0.025% 0.05%
Fluticasone propionate	cream	0.05% 0.005%
Hydrocortisone butyrate	ointment, solution	0.1%
Hydrocortisone valerate	cream, ointment	0.2%
Mometasone furoate	cream, ointment, lotion	0.1%
Triamcinolone acetone	cream, ointment, lotion	0.025% 0.1% 0.5%
Low potency		
Aclometasone dipropionate	cream, ointment	0.05%
Desonide	cream	0.05%
Dexamethasone	aerosol	0.01% 0.04%
Dexamethasone sodium phosphate	cream	0.1%
Fluocinolone acetone	cream, solution	0.01%
Hydrocortisone	lotion	0.25% 0.5% 1% 2.5%
Hydrocortisone acetate	cream, ointment, lotion	0.5% 1% 2.5% 0.5% 1%

*Adapted from reference 10.

vehicle and therapeutic amounts reach the skin, the rate-limiting step is skin transport, which appears to be achieved via passive diffusion.⁷ Aside from the intrinsic properties of the substance itself, several factors can influence topical corticosteroid penetration through the stratum corneum. The degree of hydration at the stratum corneum can directly affect the level of absorption. Enhanced association of water molecules to hydrophilic lipids between cells of the stratum corneum (corneocytes) is seen when hydration of the skin occurs. As a result, water-soluble medications are allowed to permeate the epidermis and into the dermis.

Percutaneous absorption is augmented by any factor that increases skin hydration at the site of application. For example, occlusive dressings and materials are utilized frequently to decrease or prevent evaporative water loss. Polyvinyl chloride sheeting (eg, HandiWrap, SaranWrap), semioclusive polyurethane dressing (eg, Tegaderm), oils and ointments themselves improve hydration.¹¹ A 4- or 5-fold increase in absorption is procured with skin hydration. Consequently, topical corticosteroids yield their best effect when used after a bath.¹² Furthermore, heat and any condition that compromises epidermal integrity (ie, dermatitis), will result in greater percutaneous absorption.

It is generally agreed that the stratum corneum is the primary barrier to percutaneous absorption. As a result, topical steroids applied to areas with thinner skin, with enhanced hydration, or with compromised integrity (ie, diseased skin) tend to exhibit increased absorption.

Dermatoses Responsive to Treatment

Inflammation, hyperproliferation, and aberrant immunologic phenomena characterize the dermatoses that are responsive to the effects of topical corticosteroids.⁸ Not only are topical corticosteroids the first choice of treatment for atopic eczema, but they are also the drug of choice for virtually all inflammatory and pruritic eruptions. Their utility is also exhibited in the treatment of hyperplastic and infiltrative disorders.¹³ Table 2 lists dermatologic conditions with inflammatory and pruritic manifestations commonly amenable to topical steroids.

Beyond the prescription use of these agents, non-prescription hydrocortisone preparations may be used for temporary relief of itching caused by minor skin irritations, inflammation, and rashes due to the following causes: poison ivy, poison oak, poison sumac, eczema, insect bites, soaps, cosmetics, detergents, jewelry, seborrheic dermatitis, psoriasis, and external genital and anal itching. The use of topical corticosteroids is contraindicated in the following conditions: acne vulgaris, ulcers, scabies, warts, molluscum contagiosum, fungal infections, and balanitis.¹³

Treatment Considerations

In choosing a topical corticosteroid, the anatomical site to which it will be applied must be taken into account. Absorption of corticosteroids varies markedly between anatomical sites.⁷ Reduction of corticosteroid penetration can result from the lack of hair follicles and presence of a thick stratum corneum; therefore, the level of potency should be chosen appropriately when treating dermatoses of the soles, palms, knees, and elbows. Areas where the skin is thin, such as the intertriginous areas, flexures, or face display a higher degree of penetration that increases the likelihood of local side effects. The comparative standard absorption of the forearm is 1% whereas the scalp absorbs nearly 4%, the forehead 6-7%, and the scrotum 36-42%.^{7,12}

Moisture, heat, and self-occlusion in intertriginous areas also predispose the patient to local side effects and the possibility of systemic side effects. For obvious reasons, low-potency corticosteroids should be used in these areas of high penetration. Use of more potent agents is occasionally required, but should be limited to brief periods of 2 weeks or less.

Table 2. Dermatoses Responsive to Topical Corticosteroids

Allergic contact dermatitis	Lichen simplex chronicus
Alopecia areata	Lichen striatus
Atopic dermatitis	Necrobiosis lipoidica
Discoid lupus erythematosus	Pretibial myxedema
First and second degree localized burns	Primary irritant dermatitis
Granuloma annulare	Psoriasis
Hypertrophic scars and keloids	Sarcoidosis
Insect and arthropod bite reactions	Seborrheic dermatitis
Intertrigo	Stasis dermatitis
Later phase of allergic contact dermatitis	Varicose eczema
Lichen planus	Various nail disorders

As previously stated, selection of the appropriate potency is a significant factor in choosing a topical steroid. The nature of the skin lesion and its location will steer the level of potency chosen for treatment. Low- to medium-strength topical corticosteroid preparations often yield the desired response when treating thin, acute, inflammatory lesions of the skin. However, dry, thick, hyperkeratotic, lichenified lesions or lesions of the soles, palms, elbows and knees frequently require high- or very high-potency steroids to elicit a response.⁴

When treating large areas of the body, the lowest effective strength should be used in an effort to lessen the risk of systemic absorption. The application of moderate to high potency agents should be reserved for areas resistant to milder preparations.⁷

Age is also a consideration in potency selection as skin characteristics often vary depending on the patient's age. Infants and small children have an increased skin surface area to body weight ratio compared to adults. Due to this characteristic, the possibility of clinically significant systemic absorption of topical medications is more likely to be seen in children and infants. Fragility of an infant's skin caused by prematurity, disorders of keratinization (eg, ichthyosis) or generalized eczema may also predispose a child to systemic effects. Overexposure to topical corticosteroids through chronic application or use of high-potency agents can potentially lead to HPA axis suppression or growth retardation.^{4,11} Due to this fact, the use of topical corticosteroids under diapers should be done with caution because absorption may be increased severalfold due to the occlusive nature of diapers. Skin fragility and thinness is inherent in the elderly, but may be accentuated in cases of congenital abnormalities of keratinization such as ichthyosis. Particular care should be taken to use the lowest effective potency in treating dermatoses of the elderly.⁴

There are many opinions on duration of treatment and frequency of application, but the common concept is to use topical steroids as seldomly as possible while controlling the dermatoses in question. The daily use of very high-potency topical steroids should not exceed 2 consecutive weeks and the total weekly dose should not exceed 50 g due to the potential of HPA axis suppression.¹³ Recalcitrant lesions of the face or intertriginous areas covering small body surface areas may be treated longer. Side effects are rarely seen when medium and high-potency topical steroids are used for 3 months or less; however, this is not true when used on the face or intertriginous areas for such a length of time.

Low-strength topical steroids rarely cause side effects.

Continuous use of topical corticosteroids beyond the resolution of a skin condition is not recommended. Should chronic therapy with these agents be required to manage a chronic condition, the patient should be monitored for development of adverse effects and tachyphylaxis (loss of clinical effect over time).⁴ Although little data exists relating clinical effect to frequency of application, intermittent therapy may prove beneficial in controlling chronic dermatoses and reducing the chance of tachyphylaxis. Some sources even suggest that short courses of therapy with brief resting periods may be more effective than continuous treatment.

In regard to frequency of application, most clinicians concur that twice-daily application is appropriate until clinical response is achieved. Once the response occurs, the method to provide continuous management of the condition depends upon the exact scenario. If the patient is using a low- or medium-potency topical corticosteroid, the patient can continue to use the prescribed topical steroid as frequently as necessary to control the condition. Following long-term use or the use of a very high-potency agent, treatment should not be abruptly discontinued in order to prevent a rebound effect. The patient should switch to a less potent agent or alternate the use of topical corticosteroids and emollient products.¹³ Chronic conditions may also be controlled with low- to high-potency topical steroids using regimens such as every-other-day or weekend-only application. Although twice-daily applications work for most cases, more frequent application may be necessary when skin with a thick stratum corneum is affected. For instance, medication applied to the soles and palms is easily removed during normal activity and may require more frequent application.⁴

The appropriate use of combination topical preparations to treat secondary infected dermatoses such as impetiginized atopic and contact dermatitis is controversial.^{7,12} The rationale for their use is to cover a wide spectrum of potential infecting organisms. Some evidence suggests that antibiotic-corticosteroid combinations do work better to treat such conditions than either agent alone.¹³ The topical corticosteroids are thought to convey their benefits in this condition by allowing the normal skin barrier to reform. Normal immunologic defense mechanisms then ward off infection.⁷ Combinations of corticosteroids and antibacterials or antifungals have produced better responses than corticosteroids

alone to conditions such as diaper rash, otitis externa, intertriginous eruptions, nummular eczema, atopic dermatitis, and possibly seborrheic eczema.¹³ Consequently, antimicrobial-corticosteroid combinations are prescribed in cases where significant secondary infection is likely to be present. Combination therapy should be limited to the initial days of treatment then followed by topical corticosteroids alone unless bacteriology results suggest otherwise.¹²

Antifungal-corticosteroid combinations are often used in intertriginous areas to treat dermatoses involving *Candida albicans*. The corticosteroid in such a combination may prove useful to reduce inflammation more quickly in some dermatologic conditions. Once again, combination therapy should only be used in the initial days of treatment. The two most commonly prescribed antifungal-corticosteroid combination products are triamcinolone and nystatin (Mycolog II®) and clotrimazole and betamethasone (Lotrisone®). Both preparations contain medium-potency and high-potency steroids that are perhaps too potent for their most commonly prescribed uses in intertriginous areas.

General Guidelines

The following is a list of general principles for the proper use of topical corticosteroids.

- Short-term or intermittent use of high- and very high-potency corticosteroids will reduce the risk of local and systemic side effects that are possible with these agents. Once the dermatosis being treated is under control, switch the patient to a less potent agent or alternate the use of corticosteroids and topical moisturizers until complete resolution occurs.
- After long-term treatment with potent corticosteroids, avoid abrupt discontinuation of treatment because a rebound phenomenon can occur that manifests itself as intense redness, crusting, scaling, and sometimes pustulation.
- When large surface areas of the body are affected, a less potent corticosteroid should be utilized.
- Local side effects are more likely to develop in certain anatomical sites such as the face, flexures, and intertriginous areas. Low- to medium potency topical corticosteroids should be used in these areas. Great care should be exercised when more potent corticosteroids are used in these areas.
- The selection of a vehicle depends upon the site and type of lesion to be treated. Ointments are most appropriate for dry and chronic dermatoses

and exposed areas whereas lotions and creams are preferable for acute, moist dermatoses and occluded areas. Gels, solutions, and sprays are especially useful on hair-bearing areas, but due to their high alcohol content, a high potential exists for burning and stinging.

- In general, the least potent topical corticosteroid that is effective should be applied twice daily. Once the dermatoses are controlled, applications can be reduced to once daily or as frequently as necessary to control the condition.
- Special care should be used when using topical corticosteroids in infants and young children due to a greater surface area to body weight ratio. Absorption may also be further enhanced if the agent is applied underneath plastic diapers. Local and systemic effects are more likely to occur and this group should be treated with the lowest-potency topical corticosteroid that is effective.

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Instructions

After reading the article "Topical Corticosteroids: Considerations for Appropriate Use," select the one best answer to each of the following questions.

1. **The glucocorticoid effect of corticosteroids is due to:**
 - a) methylation
 - b) hydrocortisone molecule
 - c) a cyclopentanophenanthrene nucleus
 - d) phospholipase A₂

2. **When used topically, corticosteroids cannot produce systemic side effects such as Cushing's syndrome.**
 - a) true
 - b) false

3. **Common localized side effects due to corticosteroids are usually reversible; however, some damage may be permanent if the corticosteroid is:**
 - a) methylated
 - b) halogenated
 - c) acetylated
 - d) double-banded

4. **When considering a topical corticosteroid for the treatment of a particular skin disease the most relevant factor to consider is:**

- a) age of the patient
- b) condition of the skin
- c) potency of topical steroid
- d) vehicle in which the preparation is suspended

5. **The primary barrier of percutaneous absorption is the outermost layer of the epidermis. This layer is also known as the stratum**

- a) granulosm
- b) lucidum
- c) germinativum
- d) corneum

6. **Possible side effects of topical steroids include:**

- a) tissue atrophy
- b) tissue Degeneration
- c) keratinization
- d) b & c
- e) a & b

7. **The use of topical corticosteroids is contraindicated in all of the following conditions EXCEPT:**

- a) acne vulgaris
- b) ulcers
- c) molluscum contagiosum
- d) pruritic eruptions

(CPE QUESTIONS CONTINUED ON FOLLOWING PAGE)

Topical Corticosteroids: Considerations for Appropriate Use

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... CPE QUIZ ...

(CPE questions continued from previous page)

8. The comparative standard of absorption of the forehead is:

- a) 15%
- b) 1%
- c) 36%
- d) none of the above

9. When using high potency topical corticosteroids, the total daily dose should not exceed 50g.

- a) true
- b) false

10. The most widely accepted frequency of application of a topical corticosteroid is:

- a) QID
- b) TID
- c) BID
- d) QD

11. Once a particular skin disease resolves after use of a medium potency topical corticosteroid the pharmacist should recommend therapy to be:

- a) tapered off
- b) discontinued
- c) continued for 1 more week
- d) none of the above

12. When treating large areas of skin, a low potency corticosteroid should be used initially.

- a) true
- b) false

13. A 87-year-old male would like a recommendation for his "itchy arms," stating he "got into poison ivy while working in his garden." You recommend

- a) clobetasol propionate
- b) amcinonide
- c) hydrocortisone
- d) halcinonide

14. Topical preparations can be divided into 4 categories based on:

- a) potency
- b) vehicle
- c) active ingredient
- d) safety

15. Occlusive dressings (ie, Handiwrap) can produce a 8- to 10-fold increase in absorption.

- a) true
- b) false

16. When using a combination antifungal-corticosteroid, a pharmacist should remind the patient to:

- a) use only during the initial days of therapy
- b) apply heavily to the intertriginous areas
- c) apply until the product is gone
- d) none of the above

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(CPE questions continued from previous page)

17. Other effects that can contribute to the anti-inflammatory activity of corticosteroids include all of the following except:

- a) vasoconstriction
- b) reduction of Langerhans cells
- c) histamine release
- d) cellular membrane stabilization

18. Adverse events associated with topical corticosteroids are due to:

- a) the complement system
- b) mitotic activity
- c) mineralocorticoid activity
- d) antiproliferative activity
- e) b & c
- f) c & d

19. For dermatoses associated with dry thick, fissured, or lichenified skin lesion the preferred vehicle is

- a) lotion
- b) cream
- c) ointment
- d) gel

20. Tachyphylaxis can occur after:

- a) abrupt discontinuation of a topical corticosteroid
- b) chronic use of a topical corticosteroid