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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 24th 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.



Dr. Chris S Sladden MBBCH, DRCOG, MRCGP, CCFP

FAMILY PRACTICE
ADVISOR

Dr. Sladden has more than 14 years' experience working as a physician in the UK, Australia and Canada, as well as being the medical officer on a number of climbing and kayaking expeditions. Prior to moving to Kamloops, where he practices as a GP, he worked for 6 years in the beautiful rural community of Clearwater, British Columbia. He is Canadian and British certified in family practice and has examined for the Canadian College of Family Practice. His diverse experience includes seeing patients with the bubonic plague and carrying out a survey of the ear diseases of Mongolian Nomads, but his special interest continues to be in Dermatology. He will be pursuing this in greater depth in the near future.



Hair Care

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Background

Each part of the body requires specific care, and without exception, hair has its own unique needs that demand special attention. The most noticeable and densest hair on the human body is on the head, where, on average, there are approximately 100,000 hairs that typically grow at a rate of 12mm/month. The self-perceived state of an individual's hair, especially in women, can contribute to heightened social distress, self-consciousness, and lower self-esteem. Consequently, for many people, the management of head hair can cause ongoing frustration and the drive to achieve the perfect head of hair often becomes an elusive pursuit; for some this can evolve into a disruptive preoccupation. A simple common sense approach is recommended for promoting and maintaining healthy hair. Apart from getting a cut or re-style, basic modifications in hair care can be easily implemented to achieve desirable effects.

Hair Structure

Hair is mostly made up of keratin, which is also found in the skin and nails. Each strand of hair is comprised of three distinct layers:

- Cuticle – the outermost protective layer of the hair shaft.
- Cortex – mainly composed of keratin, this layer gives the hair its strength, color, shape, elasticity, and texture.
- Medulla – the innermost or core layer is usually only present in coarse hair, and absent in fine strands.

Ethnic Hair

Although there are no biochemical differences in the hair of people from different backgrounds, there are structural variations. For example:

- Asians tend to have straight hair with the largest mean cross-sectional areas and hair follicles that are round.
- Caucasians have intermediate mean cross-sectional areas and oval shaped hair follicles.
- People of African descent have hair that is spiraled with the smallest cross-sectional areas and follicles that are elliptical.
 - Hair tends to be kinky and usually does not need to be shampooed as often as straight hair.
 - The removal of natural oils can leave the hair dull and difficult to style.
 - In general, their hair is more fragile; its spiral structure makes it more difficult for the sebum to easily coat the hair shaft, producing drier and less manageable hair.

Hair Growth Cycle

Hair follicles grow in repetitive cycles, which include three phases:

- Anagen - growth phase, which typically continues for 150 weeks on the scalp.
- Catagen - transitional phase, during which time, the bulbar portion of the follicle is almost completely degraded through apoptosis. Catagen lasts for 1 week.
- Telogen - resting phase, lasts for 12 weeks on the scalp. Approximately 50-100 telogen hairs are shed daily, mostly because of normal washing and combing.

Shampooing

- Shampooing regularly is the first step in maintaining healthy hair and scalp.
- Sebum lubricates and protects hair, but particles of dirt become embedded in the oil.
- Shampooing too frequently can cause extensive sebum removal, which results in dull looking, static-prone hair that is difficult to comb.
- Shampoos consist primarily of:
 - surfactants
 - contain both hydrophobic ingredients, those attracted to oil, and hydrophilic ingredients, those attracted to water.
 - allow shampoo to bind to and emulsify dirt, sebum and styling products in the hair, and then remove them when rinsing.
 - silicones
 - responsible for lubricating the hair, allowing for easier brushing and a smoother look and feel to the hair when dried.
 - cationic polymers
 - provide unique wet-conditioning and delivery benefits.
- allow many consumers to forego a separate conditioner if their hair is already in good condition.
- contains preservatives, perfumes, and sometimes dyes and anti-dandruff ingredients.
- Added ingredients such as vitamins B and E, jojoba and aloe vera claim to strengthen hair, but there is no scientific validation.
- An endless array of formulations are available, and selecting an appropriate product can be confusing. A good place to start is to determine suitability by hair type, e.g., normal or dry.
- Other types of shampoo include:
 - products designed for chemically treated or damaged hair.
 - mild infant formulations that do not irritate the eyes and exclude perfumes
 - those with added medical ingredients
 - conditioning shampoos that contain hydrolyzed proteins designed to penetrate the hair shaft
 - professional-grade cationic acidic shampoos that neutralize the residual alkalinity of chemical treatments.

Hair Conditioners

- Conditioners efficiently restore moisture that has been removed through washing.
 - They contain many of the same ingredients that are found in shampoos, but in different concentrations.
 - They effectively flatten the cuticle on the hair shaft and detangle the hair, which:
 - makes brushing easier.
 - creates smoother texture.
 - improves overall manageability.
 - reduces static electricity by
 - adding positively-charged ions on the hair shafts.
 - neutralizing the negative electric charges on the shaft that are generated following brushing.
 - They are particularly useful for dry or damaged hair.
 - Overuse of conditioners can result in a flattened, limp or oily appearance.
 - Apply only to the hair and not the scalp.
 - The cationic polymers found in conditioners are attracted to the damaged cuticle in the hair shaft, which results in the protection and repair of these areas by filling in the defects.
- Damage to the hair shaft can be caused by:
- overdrying
 - vigorous towel-drying
 - washing long hair too frequently (e.g., more than once per day)
 - excessive combing and brushing
 - chemical treatments (e.g., permanent waving, bleaching, dyeing, straightening)
 - over-exposure to sun and chlorine.
- Anyone using heat generating devices or chemical-based products for hair curling or straightening should be encouraged to carry out a regular conditioning regimen. Applications that provide lubrication can somewhat reduce the damage and brittle texture that is associated with some of the chemicals that are used.

Drying Hair

Hair frequently sustains damage from the intense heat generated by hairdryers in combination with the pulling and tugging of styling.

- Air-dry or gently towel-dry whenever possible.
- Set hairdryer at a lower temperature.
- Chemically-damaged hair is more susceptible to further damage to the hair shaft.

Brushing

- Wet hair can be more easily damaged.
- Use a wide-tooth comb to gently untangle damp hair.
- When dry, particularly if the hair is fine or brittle, use of a natural bristle brush or comb will assist in spreading the oil (sebum) along the hair shaft.
 - Makes the hair easier to style.
 - Gives it a glossy appearance.

Treating Dandruff

- Dandruff is influenced by the presence of 3 factors: sebum, *Malassezia* yeasts, and one's individual susceptibility to irritation caused by the yeasts metabolic byproducts (free fatty acids).
- Primary ingredients in anti-dandruff shampoos include:
 - Pyrithione zinc, ketoconazole, selenium sulfide, and cyclopyroxolamine
 - believed to address the fungal cause of dandruff
 - Salicylic acid and coal tar
 - treat the symptoms of flakes and skin hyperproliferation.
- Pyrithione zinc-containing anti-dandruff formulations are safe for daily use.
- Patient compliance is improved with the use of a cosmetically appealing and effective product.
- Use of a shampoo and conditioner containing the same active ingredient can improve efficacy.
 - In Canada, an anti-dandruff conditioner will become available in early 2008.
 - Using a regular conditioner can reduce the dandruff shampoo's efficacy.
 - For conditioners containing anti-dandruff active ingredients, massage product into the scalp, then distribute evenly from hair root to tip.
- Avoid scratching the scalp, as this will loosen more flakes and cause further irritation.

Other Factors Influencing the Condition of Hair

- Excessive or incorrect use of chemical hair treatment processes such as dyeing, straightening, bleaching or perming can result in damage, accelerated hair loss and allergic reactions, more specifically, contact dermatitis.
- Exposure to the sun, chlorine in swimming pools, and seawater can inflict additional damage to hair and alter its color. Wearing a hat or applying special sunscreens formulated for the hair can provide some protection.
- Longer hair is particularly susceptible to additional damage due to the cumulative effects of various treatments and environmental elements.
- Drastic dietary changes can cause hair loss and retard growth through protein depletion.
- Tension on the hair shaft from styling can cause frontal shedding; heavy/tight ponytails can promote hair loss.
- During pregnancy, hair is particularly full and vibrant in appearance; however, postpartum hair loss (telogen effluvium) is commonly experienced by women for several months before returning to normal.
- Avoid shampooing prior to applying chemical hair treatments, as this will prevent removal of the natural oils or sebum, which will, to some degree, reduce the harsh effects of the agents used.
- Backcombing or teasing the hair by combing in the reverse direction can create damage to the hair shaft cuticle.

Allergic Contact Dermatitis

Symptoms of cosmetic, allergic, and contact dermatitis include swelling and inflammation on the scalp, face, neck, ears, and hands. Some common examples of chemical allergens in hair products include:

- permanent hair waving agents such as glycerol monothioglycolate
- many additives in shampoos can be irritating to those with eczema
- metallic salts in permanent dyes; semipermanent and temporary variations tend to be less irritating to the scalp and cause less damage to the hair
- paraphenylenediamine, an ingredient in most hair dyes, commonly causes allergic contact dermatitis; owing to the high frequency of these reactions, manufacturers of at-home hair-coloring products encourage patch testing before use.

Conclusion

Implementing basic proper hair care is essential to maintaining healthy hair. Furthermore, minimizing exposure to chemical agents, inadvisable grooming techniques, and prolonged exposure to environmental elements, will promote healthier hair and avoid unnecessary hair loss.

Tips for Maximizing the Effectiveness of Topical Acne Therapy

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Background

Topical medications are the cornerstone of therapy for the vast majority of acne patients. However, use of these products is generally regarded by patients to be time-consuming, inconvenient, irritating, and less effective than oral medications. Adherence to topical agent use is also compromised by the lag time to effect, the potential complexity of treatment regimens, and the desire to incorporate cosmetics such as foundations, moisturizers, and sunscreen. While adherence rates to the use of topical acne medications have previously been reported to be as high as 48%-49% [Flanders PA, et al. *Behav Res Ther* 23:225-7 (1985); Flanders P, et al. *J Psychol* 118:31-6 (1984)], a recent Canadian observational survey of acne patients provided a rate of only 24% (Tan J. unpublished data). In this group of patients, the most common reasons for poor adherence were forgetfulness, side-effects, did not feel the need, and inconvenience. Poor adherence to topical acne therapy contributes to treatment failure, wasted health care resources, and dissatisfaction with physician care. This paper presents tips to maximize adherence and effectiveness of topical acne therapy.

Factors Influencing Patient Compliance

In dermatology patients, the two primary areas identified in poor adherence to treatment include [Renzi C, et al. *Arch Derm* 138:337-42 (2002)]:

- Problems with patient-physician relationship (i.e., miscommunication, lack of dialogue, poor understanding of benefits, and risks of treatment).
- Treatment-related issues (i.e., complexity, effectiveness, tolerability).

Considerations for Treatment Selection

In choosing topical acne products, the following considerations may further enhance adherence:

- accessibility of anatomical site for topical therapy (i.e., face, chest and shoulders are accessible; the back is harder to treat)
- efficacy
- tolerability, e.g., facial erythema, irritation, dryness, redness, and scaling

- cosmetic acceptability
- regimen simplicity
- convenience
- ease of application.

Patients should then be evaluated at 2-4 weeks to encourage adherence and to evaluate for potential side effects; thereafter every 2-3 months to evaluate treatment effectiveness.

Types of Treatment Vehicles

In determining the most appropriate topical treatment regime for each patient, physicians must conduct an individualized assessment that includes disease severity, patient preference, skin type, formulation availability, and delivery vehicle considerations. Active agents are formulated in a variety of vehicles to address the possible combinations. In general, patients with drier skin may favor creams for their moisturizing effect while those with oilier skin may prefer gels or solutions. The use of foams may be particularly well suited for application to larger regions and hair bearing sites.

- Creams
 - are available in oil and water base formulations.

- tend to be less irritating.
- help to retain moisture in the skin.
- are most suitable for patients with dry or sensitive skin.
 - may result in an oily feel due to thicker consistency.
- Lotions
 - can have either water or alcohol base.
 - are the most versatile.
 - can be used for all skin types.
 - can cause skin irritation, e.g., burning and dryness.
 - have a lighter feel, which patients may prefer.
 - preferred for treatment of large or hairy areas.

Types of Treatment Vehicles (continued)

- Solutions
 - usually contain an alcohol base, which can exacerbate dryness and irritation.
- Gels
 - contain high water content.
 - are most suitable for oily skin types.
 - have a cooling effect on the face.
- Foams
 - may leave a surface residue.
 - tend to cause skin irritation, e.g., burning and dryness.
- Foams
 - spread easily, especially helpful if treating larger areas of the body.
 - leave minimal residue on skin surface.

Topical Acne Agents

The spectrum of effective topical acne medications may be grouped into:

Antibiotics

- Clindamycin
- Erythromycin
- Sodium sulfacetamide

Overview of Antibiotics:

- They are directed against *P. acnes*.
- They are formulated in creams, lotions, gels and foam.
- There is one product also available with SPF 15 + antibiotic.
- It may induce irritation.

Combination Products

- Benzoyl peroxide (BPO) + antibiotic
- Topical retinoid + antibiotic

Overview of Combination Products:

- BPO inhibits selection of antibiotic resistant bacteria.
- They may induce irritation and dryness; BPO can fade colored fabrics.
- They treat multiple pathogenic factors.
- They are gel formulations.
- The combined efficacy is typically greater than either agent alone.
- They reduce treatment regimen complexity.

- They have the potential to improve adherence because there are two active ingredients.

Retinoids

- Adapalene
 - It is photostable, can be applied in the morning.
- Tazarotene
 - It photostable, can be applied in the morning.
- Tretinoin
 - It is photolabile, best to apply in evening.
 - Micronized version may be less irritating, but more costly.

Overview of Retinoids:

- They are formulated in creams, gels and solutions.
- Advancements in vehicle delivery for retinoids to reduce irritation:
 - emollient cream
 - microsphere gel
- They are known to be effective against acne vulgaris through comedolysis, which acts to reduce dyskeratosis at the pilosebaceous outlet.
- They are formulated as gels and creams, which may induce irritation and dryness.

Tips for Topical Treatment

- Minimize irritation by using aqueous vehicles rather than those containing alcohol when possible.
- Adjust frequency and duration of application to reduce potential for dryness and irritation; increase duration as tolerated.
- Provide estimates of amounts to apply (e.g., pea-size amount to each of the 4 facial regions: forehead, each cheek, central face).
- Use simple regimens:
 - for patients not using foundation or sunblock, apply topical medications in the morning and evening.
 - for those using foundation and sunblock, apply medication in the evening only or apply combination clindamycin/ SPF 15 product in morning.
- Gentle cleansers should be used to avoid compounding irritation and dryness.

Conclusion

Successful treatment of acne with topical therapy can be achieved with:

- Patient education on acne and the aims of initial and maintenance treatment.
- Patient engagement in treatment selection.
- Counseling on aggravating factors, such as stress, dairy intake, occlusive hair products, hats, sports equipment, damp clothing, make-up, medication use, adverse events, and the importance of adherence.

New Developments in Hormonal Therapy for Acne

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Background

Oral contraceptives (OCs) have been used for many years by dermatologists as a treatment option for women with acne. The onset of acne is triggered by the increased production of androgens. Oral contraceptives inhibit ovulation, thereby resulting in the prevention of androgen production. The lower serum androgen levels reduce sebum secretion, which consequentially exerts an antiacne effect. OCs that are indicated for use in acne are effective across the spectrum of disease severity:

- in mild acne as an adjunct to topical therapy for female patients desiring contraception.
- in moderate acne as a form of systemic therapy.
- in severe acne
 - as a primary form of therapy (e.g., ethinyl estradiol/ cyproterone acetate).
 - as one of two preferred forms of contraception for women treated with systemic isotretinoin.

These preparations have evolved to include less estrogen and incorporate progestins with less intrinsic androgenicity in order to reduce the potential risk of thromboembolic events, hepatic tumors, hypertension, altered glucose metabolism, and rare androgenic side-effects, such as acne, hirsutism, and weight gain.

OCs for the Treatment of Acne

In Canada, 4 hormonal preparations are presently indicated for the treatment of acne.

- They all contain estrogen in the form of ethinyl estradiol (EE) and progestins, either with
 - minimal androgenicity
 - EE/ norgestimate
 - EE/ levonorgestrel
 - or antiandrogenic potential
 - EE/ drospirenone
 - EE/ cyproterone acetate.
- They all have demonstrated efficacy for the treatment of acne and have acceptable long-term safety profiles.
- A reasonable duration of use to determine effectiveness in clinical practice with these products is 6 months
- Typically, topical acne products would also be used in conjunction with OCs to accelerate onset of effect.
- In practice, improvement of acne at other sites, including the torso and shoulders, can also be expected.

EE 0.030mg/ Drospirenone 3mg

Drospirenone (DRSP) is a novel progestogen derived from spironolactone, which is an antiandrogen.

- This formulation is available in Canada and the US.
- Competitively binds to androgen receptors.
- Inhibits 5-reductase activity, which reduces sebum production.
- Reduces androgen biosynthesis.
- For antiminerlocorticoid activity, the dose equivalence for DRSP 3mg is spironolactone 25mg.

EE/ Norgestimate

- EE 0.035mg with norgestimate in increasing doses: 0.180mg/ 0.215mg/ 0.250mg
- Norgestimate has low intrinsic androgenicity with low binding affinity for androgen receptors. It is strongly selective and avidly bound to progesterone receptor sites. This combination estrogen and progestin preparation produces a synergistic effect which enhances regulation of hormonal levels.
- Shown to be efficacious in moderate facial acne in two randomized placebo-controlled trials involving 324 subjects over 6 cycles.[Lucky AW, et al. *J Am Acad Dermatol* 37(5 Pt 1):746-54 (1997 Nov); Redmond GP, et al. *Obstet Gynecol* 89(4): 615-22 (1997 Apr).]
 - Inflammatory lesions were reduced by 56%, noninflammatory lesions by 41%, and 32% achieved excellent improvement using investigator's global assessment scores.[Redmond GP, et al. *Obstet Gynecol* 89(4): 615-22 (1997 Apr).]

EE/ Levonorgestrel

- EE 0.020mg and levonorgestrel 100µg
- Shown to be efficacious for moderate facial acne in two randomized placebo-controlled trials.[Leyden J, et al. *J Am Acad Dermatol* 47(3):399-409 (2002 Sep); Thiboutot D, et al. *Fertil Steril* 76(3):461-8 (2001 Sep).]
- A compilation of both studies (721 women treated for 6 cycles) showed:
 - Reduction in acne lesion counts:
 - 32%–47% inflammatory
 - 13%–25% noninflammatory
 - 23%–40% total lesions
 - Investigator's global assessment scores were rated as clear to almost clear in 48%–58% of subjects.

EE/ Cyproterone Acetate

- The combination of EE 0.035mg and cyproterone acetate 2mg has been available as a hormonal treatment for acne in Canada since 1998.
- Cyproterone acetate is an analogue of hydroxyprogesterone and has progestational activity.
 - It acts as a potent antiandrogen:
 - by competitive inhibition of testosterone and dihydrotestosterone (DHT) binding to the androgen receptor.
 - by inhibiting gonadotropin secretion.
 - Efficacious in mild-to-moderate facial acne based on smaller trials with variable study designs and parameters. [Tan J. *J Cutan Med Surg* 8(Suppl 4):11-5 (2004 Dec).]

Head to Head Studies

- Efficacy for treating acne vulgaris was evaluated in a randomized controlled trial with EE 0.035mg/ cyproterone acetate 2mg as the active comparator.[van Vloten WA, et al. *Cutis* 69(4 Suppl):2-15 (2002 Apr).]
- 125 subjects aged 16-35 years with mild-to-moderate facial acne treated were for 9 cycles
- Median reduction in total facial acne lesions:
 - 62% for EE 0.030mg/ drospirenone 3mg
 - 59% for EE 0.035mg/ cyproterone acetate 2mg
- Both formulations were effective for the treatment of acne and were well tolerated.
 - Adverse events were mild-to-moderate in intensity and typical of those associated with OCs.
- A European multinational, prospective, observational new-user cohort study evaluated the safety of DRSP-containing OCs and other OCs. [Dinger JC, et al. *Contraception* 75(5):344-54 (2007 May).]
- 58,674 women were observed for 142,475 women-years.
- Serious adverse and fatal events were rare.
- Regression analysis of adverse cardiovascular events:
 - Hazard ratios for DRSP-containing OCs vs. levonorgestrel-containing and other OCs:
 - 1.0 vs. 0.8 (upper 95% confidence intervals [CI], 1.8, 1.3) for venous thromboembolism
 - 0.3 vs. 0.3 (upper 95% CI, 1.2,1.5) for arterial thromboembolism.

The risks of adverse cardiovascular and other serious events in users of DRSP-containing OCs were found to be similar to those associated with other OCs.

Conclusion

The proven therapeutic benefits of OCs offer a valuable option to physicians for the treatment of acne. The accumulating evidence on the efficacy and safety of recently available drospirenone-containing hormonal preparations provides dermatologists with a new option for the treatment of acne and other hyperandrogenic disorders.

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