The Role of Skin Care as an Integral Component in the Management of Acne Vulgaris

Part 1: The Importance of Cleanser and Moisturizer Ingredients, Design, and Product Selection

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ABSTRACT

Acne vulgaris is a very common facial skin disorder accounting for approximately 10 percent of all visits to ambulatory dermatology practices across the United States annually. Over time, greater attention has been directed to the roles of multiple epidermal barrier functions in various dermatological disorders, especially the stratum corneum permeability barrier and antimicrobial barrier. As a result, it has become readily apparent that professional direction of skin care is very important in the overall management of acne vulgaris. This article discusses several reasons that support the importance of incorporating specified skin care recommendations and instructions into the overall management plan for acne vulgaris. In addition, the article reviews formulation characteristics and some of the scientific data on two commercially available products that are recommended for use as a skin care regimen in patients with acne-prone and acne-affected skin, a foam wash and a moisturizer with a sun protection factor 30 broad spectrum photoprotection rating. The rationale for inclusion of specific ingredients are discussed along with an overview of research results including use in patients with acne vulgaris. (*J Clin Aesthet Dermatol.* 2013;6(12):19–27.)

Acne vulgaris (AV) has long been considered the most common skin disorder overall, and has been reported to affect nearly 70 percent of adolescents.[1] Although well known as a common disorder affecting the facial and truncal skin of many teenagers, AV also commonly affects pre-teens and post-teens, with the latter group inclusive of women with persistent AV and late-onset AV.[2–4] Many clinicians including pediatric dermatologists have observed that pediatric acne is starting earlier in many patients, primarily due to earlier onset of adrenarche. Preadolescent AV, currently defined as between 7 and 11 years of age, is not often associated with an underlying endocrinopathy.[5] Many preadolescent girls present with multiple facial comedonal lesions, often with forehead predominance, and in many cases also exhibit some superficial papules/pustules (Figure 1). In a five-year longitudinal study of preadolescent-premenstrual girls with AV as just described (N=871), higher serum levels of dihydroepiandrosterone sulfate (DHEA-S) and testosterone (free and total) were noted, which correlated with persistence of severe comedonal AV and also increased severity of inflammatory AV over time.[6] The "extra androgen drive" present in this subset of young girls serves as a good predictor that a greater severity of AV will emerge over time and is associated with pilosebaceous enlargement and

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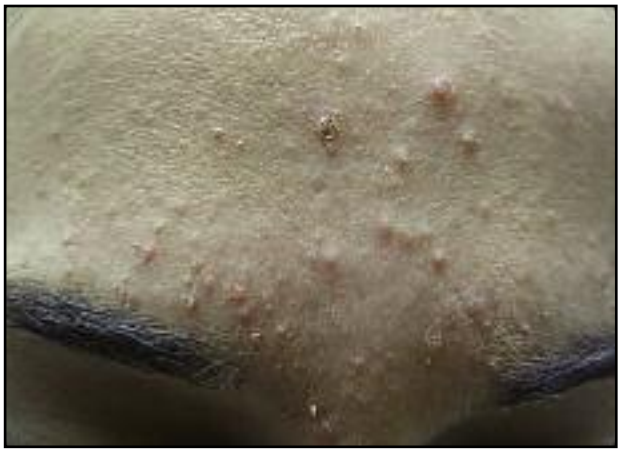

Figure 1. Pre-adolescent acne vulgaris. An 11-year-old girl presented with multiple closed comedones and scattered superficial inflammatory papules/pustules with a marked predominance of forehead involvement.
Photograph courtesy of James Q. Del Rosso, DO, FAOCD

increased sebum production ("oily skin").[6,7] Ultimately, the age range of patients who commonly present with AV has broadened to include more pre-teen and post-teen patients. This change requires that dermatologists address the specific questions, concerns, and clinical challenges that commonly affect these subsets of AV patients, with obvious emphasis on efficacy and safety considerations, but also the potential psychosocial impact on different patient subsets.[8] Additionally, education about fundamental skin care recommendations for patients with AV is appreciated by patients and has been shown to reduce signs and symptoms of cutaneous irritation.[9–13] AV is an equal opportunity disease, affecting individuals of all ethnicities and skin colors.

Based on representative data from the National Ambulatory Medical Care Survey (NAMCS) that assesses leading diagnoses in patient visits to dermatologists from 1993 to 2009, AV ranks among the top five dermatological diagnoses most commonly encountered in dermatology practices in the United States.[14,15] In 2009, AV accounted for 10.2 percent of all visits to US dermatologists in outpatient practices.[16]

In the review of NAMCS data from 1993 to 2009, AV was found to be the leading diagnosis in African American, Asian Pacific Islander, and Hispanic patients and was second only to actinic keratosis in the Caucasian patient population.[14] Another study aimed to define the prevalence and clinical presentations of AV in 2,895 female patients of different races. It was found among the entire group of female patients included in the study that African Americans had the highest prevalence of AV (37%), followed by Hispanics (32%), Asians (30%), Caucasians (24%), and Continental Indians (23%).[15]

AV is a common, chronic, inflammatory, facial skin disorder that can affect individuals from any race, ethnicity, or cultural background. The onset of AV is usually shortly before or during early adolescence; however, some cases start in latter childhood with the subset of preadolescent acne defined within the ages of 7 and 11 years.[17] In addition, many adult women with post-teen acne are encountered in clinical practice, with some presenting in their mid-to-late 20s or in their 30s with AV similar to what they experienced as teens (persistent AV), or AV that they are first experiencing with little to no prior history of AV (late-onset AV).[3,4] As AV involves the face in 97 percent of cases with or without truncal involvement, the visibility of AV is psychologically problematic for many affected individuals.[18] Scarring and dyschromia are unfortunate physical sequelae after resolution of AV lesions that prolong the adverse psychosocial effects of AV for many people. However, what is not always fully appreciated during the limitations of an office visit is that many patients are affected from a psychosocial perspective, with adverse consequences reported that alter both overall quality of life and mental health status.[8,19] Ultimately, AV is overall the most common dermatological disorder seen in office-based dermatology practices, affecting many teenagers, preadolescents, and post-teenage adults, and almost always affects facial skin with or without truncal involvement. As acne is not curable, it has a protracted course over several years in most affected individuals even with treatment, and can be late in onset, especially in adult women. Prolonged dyschromias are a common sequelae of acne, which also causes various forms of scarring in some cases. Acne can be managed effectively; however, this requires consistent adherence with long-term therapy and timely adjustments in the treatment regimen when the character and severity change over time. It is also common for acne to impart adverse psychosocial effects that can significantly impair quality of life and in some cases cause profound anxiety and/or depression. Therefore, it is important for dermatology practices to incorporate a well-organized and comprehensive approach to the evaluation and management of patients with AV.

EXPANDED INFORMATION SOURCES AND ACCESSIBLE CARE FOR ACNE OUTSIDE OF DERMATOLOGY PRACTICES

There is an extensive network of communications that promote care for AV outside of seeing a dermatologist. These include television-based and web-based infomercials on specific products, retail stores dedicated only to skin care, classic "department stores" with designated skin care sections, skin care/spa centers directed by nondermatologists, printed electronic or "hard copy" advertisements on the internet or in countless magazines and other publications, and the plethora of OTC products for AV available at pharmacies that are marketed by many cosmetic and pharmaceutical companies. As a result, patient expectations are set at a high bar when encountering a dermatologist for management of AV, as they expect a level of service and the quality of the outcome to be far superior to what they can obtain by just going to a search engine on their computer or from an aesthetician at a spa or skin care center that is not dermatologist-supervised. Therefore, it is important for the dermatology practice to efficiently provide an office visit experience that is highly educational and includes the integration of proper skin care

and product selection along with medication selection and proper use. Ultimately, the dermatologist and his or her staff are encouraged to understand the scientific rationale for proper skin care in AV management, why specific products are selected, and how they are to be utilized and integrated with topical medications for AV.

Professional treatment. In addition to the large volume of patients with AV who seek care from dermatologists across the United States, many more undergo professional treatment, both medical and procedural, via their primary care physician. AV accounted for 0.4 percent of all outpatient visits to all US physicians in 2009, reflecting a large number of visits for AV to primary care physicians including pediatricians.[16] The recent publication, *Evidence-Based Recommendations for the Diagnosis and Treatment of Pediatric Acne*, developed through the combined efforts of the American Academy of Pediatrics and the American Acne and Rosacea Society, and accepted by the AAP as its policy, should assist practitioners with the management of AV in pediatric patients.[20]

Over-the-counter and nonphysician-directed options. In addition, many individuals seek advice and/or elect to self-treat by purchasing products that are marketed for AV and sold over-the-counter (OTC) at pharmacies, via the internet, or at retail stores and skin care/cosmetic centers, which have large sections designed to attract individuals with skin-related needs, including OTC treatments for AV. Many cosmetic companies and pharmaceutical companies have divisions dedicated to the development and marketing of OTC products and treatment systems, which include many for AV. In addition to OTC products applied to skin, many patients undergo a variety of physical procedures (i.e., nonablative devices, photodynamic therapy [PDT], peels, extraction procedures) offered at spas and cosmetic centers that fall outside of the realm of dermatologist-supervised care for AV. The level of knowledge and education about AV by providers of services who are not under the direction of a dermatologist or physician well-versed in dermatology are unknown and likely to be highly variable in quality.

THE IMPORTANCE OF DERMATOLOGISTS MAINTAINING THEIR FOCUS ON COMMON DISORDERS SUCH AS ACNE

Simply stated, people with AV have many options in seeking information and accessing therapies outside of the care provided by the dermatologist, thus creating an important challenge to the dermatologist and his or her staff during encounters with patients presenting with AV. It is important for the dermatologist and his or her entire staff to provide a high level of well-coordinated service and comprehensive care to patients with AV as they can easily seek treatment elsewhere, including via the internet or other nondermatologist-directed options. Patient education focused on AV itself, treatment selection, proper medication use, the importance of adherence with the full regimen, possible adverse effects, time course of response, reasonable expectations, and follow-up instructions are all vital to the overall success of AV management. What is often forgotten, however, is the importance of proper skin care and product selection in the treatment of AV, especially as AV itself and many of the therapies used to treat AV (i.e., benzoyl peroxide, topical retinoids, oral isotretinoin) can induce impairment of the stratum coneum (SC) permeability barrier, resulting in increased transepidermal water loss (TEWL), xerotic and inflammatory skin changes, and increased skin sensitivity. If there is any question regarding the public interest level about AV, one can see the enormous magnitude of interest by going to one of the major internet search engines such as Google, separately searching "acne" and "acne treatment," and seeing the plethora of options and the number of "results" directed at these two subject areas. On May 21, 2013, the author found 25,100,000 results when searching "acne" and 9,390,000 when searching "acne treatment" on Google. When Ask Jeeves was searched for "What are the best treatments for acne?" the first response was a proprietary page entitled Acne Treatment Reviews. This page stated, "See which acne treatment products are best for your skin and discover which acne ingredients are actually better than a prescription." This page tabulated five brand OTC and/or internet-based "scientific actives" products/product systems containing ingredients, such as benzoyl peroxide, salicyclic acid, and sulfur, and five brand OTC and/or internet-based "natural extracts" products/product systems "proven to heal skin" containing ingredients, such as green tea, passion flower, and sage extract. Under the tables that outlined the top five lists, there was a by-line that stated, "The acne treatments listed in this site were carefully selected by our staff and recommended by acne sufferers around the world." Interestingly, this leading page that Ask Jeeves provided did not indicate who comprises "our staff"—the people who are making specific product recommendations—and did not include any type of disclaimer suggesting that the individual consult with a dermatologist or their physician if their acne was not responsive to any treatments or was worsening. Dermatologists need to be keenly aware that the internet and many other sources of information that do not evaluate the patient with AV and other conditions are commonly consulted and trusted by the public. These products would disappear from websites and retail locations if people, many of whom are or have been our patients, were not buying and using them.

EPIDERMAL BARRIER DYSFUNCTIONS IN ACNE VULGARIS

Management of AV obviously requires the rational selection of therapeutic agents and modalities commensurate with the severity of AV and other patient-related factors, adherence with the therapeutic regimen, and appropriate follow up. However, proper skin care provides adjunctive value to the medical regimen and can reduce local tolerability reactions associated with topical medications.[9,11–13]

Epidermal barrier impairments innate to acne. Although much more research is needed on the structural and functional integrity of the SC and epidermal barrier functions inherent to acne-prone and acne-affected skin, there is some evidence of SC permeability impairment

innate to AV.[9,10,21,22] Sebum secretion, SC lipids, TEWL, and skin conductance (corneometry) were determined in 36 male patients between the ages of 14 and 26 years who presented with mild-to-moderate AV as compared to a control group comprised of 29 age-matched male subjects.[21] The patients with AV demonstrated higher levels of both sebum secretion and TEWL along with decreased SC conductance. The increase in TEWL and decrease in SC hydration (determined through corneometry) demonstrates the presence of SC permeability barrier impairment innate to AV. The patients with AV also exhibited markedly diminished SC levels of free sphingosine and total ceramides.[21] These latter findings support a deficiency of the intercellular lipid membrane, which provides at least a partial explanation for decreased TEWL, and correlate directly with SC permeability barrier dysfunction.[10,21] In addition, the increase in TEWL and the decrease in SC hydration were of greater magnitude in subjects with moderate AV severity as compared to subjects with mild AV severity and in normal controls, suggesting that the magnitude of SC permeability barrier impairment correlates directly with the severity of AV.[21] It is not known whether the qualitative or quantitative changes in SC structure and/or function noted with AV occur only in association with the inflammation present in active AV or if they are also present in the epidermis of unaffected facial skin of AV patients where AV lesions are not present at the time of SC testing. Nevertheless, untreated skin in individuals with AV exhibit impairment of the SC permeability barrier that is important to correct as part of the management of AV in order to reduce signs and symptoms of facial irritation, dryness (i.e., peeling due to faulty desquamation), and skin sensitivity.[9,10,21]

Medication-induced epidermal changes. Some topical medications and/or vehicle formulations and oral medications used to treat AV can induce changes within the epidermis that alter barrier functions, especially the SC permeability barrier. [9,10,23–28]

Benzoyl peroxide. Benzoyl peroxide (BP) has been shown to increase TEWL by 1.8-fold in a study evaluating a 10% formulation and has also been shown to reduce cutaneous levels of vitamin E (tocopherol).[23] Concomitant use of topical tocotrienol, an isomer of vitamin E, along with application of BP did not offset an increase in TEWL, but did reduce BP-induced SC lipid peroxidation, likely through the antioxidant replenishment from the applied vitamin E isomer (tocotrienol).[23] It appears based on these data that BP can adversely modify two epidermal barrier functions by producing impairment of both the antioxidant barrier and the SC permeability barrier.[10,23]

Topical retinoids. Topical retinoids have been shown to modulate epidermal keratinization and differentiation, downregulate expression of toll-like receptor-2 (TLR2), decrease dermal matrix degradation through inhibition of the activator protein-1 (AP-1) pathway and matrix metalloproteinases (MMPs), and alter various transcription factors involved in cascades of skin inflammation.[24,26,27,29–31]

These multiple effects of topical retinoids on skin, which account for their therapeutic benefit, also create an initial adjustment phase over the first few weeks of use that correlates with "dermatitis changes" that may be visible clinically in some patients with variable interpatient severity.[10,26] Many patients develop some magnitude of "retinoid dermatitis" characterized by erythema, fine scaling, and desquamation, within the initial 1 to 3 weeks after starting application of a topical retinoid; these changes are often mild with the availability of improved vehicles, and are characteristically transient with continued application of the topical retinoid over the first 2 to 4 weeks of use.[10,29,30] Most patients treated with a topical retinoid exhibit initial signs and symptoms of skin irritation that are clinically absent or negligible and that resolve after a few weeks, especially with improved vehicle formulations. In cases where the initial retinoid dermatitis is mildly visible but tolerable, proper skin care assists in mitigating signs, such as fine redness and scaling. In occasional cases, the magnitude of cutaneous irritation is severe enough to warrant discontinuation of use. However, dermatologists commonly adjust the regimen by incorporating approaches to topical retinoid therapy that are often successful in getting past the hurdle of skin irritation that some patients experience when first starting a topical retinoid for acne. These approaches include temporary discontinuation coupled with proper adjunctive skin care, use of a vehicle shown to be well tolerated, stopping the retinoid for 5 to 7 days then restarting with a reduced frequency of application (i.e., every other night instead of every night) for the first few weeks, and using a topical retinoid with a track record of low irritation potential and comparable efficacy. Interestingly, patients initiate some of these approaches on their own when using topical acne therapies (i.e., temporarily stopping use, cutting back on frequency of use, moisturizer use).[31]

In both animals and human skin research models, topical retinoid application has been shown to induce acanthosis, hypergranulosis, and a relative decrease in SC thickness, and in murine skin, application of a topical retinoid increased epidermal labeling index, with a plateau effect noted after approximately one week as acanthosis peaked.[26] Interestingly, acanthosis reverted partially toward baseline after approximately two weeks followed by a steady-state equilibrium, which persisted thereafter, correlating with the typical time course of retinoid dermatitis.[10] It is believed that the visible retinoid dermatitis commonly observed after starting topical retinoid therapy reflects at least partially the modes of action that a topical retinoid induces within the epidermis.[10,26] Concurrent moisturizer use to pre-emptively reduce the SC permeability barrier impairment and increase in TEWL that can be induced by topical retinoid application has been reported, and is a common technique that is self-initiated by patients to reduce signs and symptoms of skin irritation and dryness.[31] In a study of 50 women between the ages of 35 and 55 years treated with tretinoin cream 0.025% for facial photoaging, application of a moisturizer for two weeks before and during tretinoin treatment prevented an increase in TEWL.[24] Retinoid-induced desmosomal shedding within the stratum spinosum, a reduction in tonofilaments, and deposition on non-mucin glycoconjugates results in

greater skin fragility due to loosening (dyscohesion) within the upper SC, and has been shown to occur with oral and topical retinoids.[26] The SC dyscohesion associated with topical retinoid use explains why patients report superficial denudation of skin after undergoing tape strip-type techniques to remove unwanted hair usually on the upper lip or eyebrow region.[10]

Oral isotretinoin. Oral isotretinoin predictably induces xerotic and desquamative cutaneous changes, also related to SC dyscohesion, which is of a greater magnitude than with topical retinoid therapy.[10,26,28] The marked sebosuppressive effect of oral isotretinoin also induces a change in the cutaneous microflora, with greater tendency for staphylococcal colonization.[28] The alterations in the SC permeability barrier associated with both topical and oral retinoid therapy do not appear to be related to reductions or alterations in SC lipids that comprise the intercellular lipid membrane of the SC.[26,28] The changes in epidermal surface lipids that are due to the sebosuppressive effects and altered sebum lipid content induced by oral isotretinoin are not believed to significantly influence SC permeability barrier function.[26,28]

Table 1. Major Ingredients in Foam Wash Designed for Acne-Prone and Acne-Affected Skin*

Ingredient	Rationale For Inclusion in Formulation
Zinc coceth sulfate (ZnCS)[32-34]	Mild surfactant; provides balance between detergent power, foaming ability and low irritation potential; is able to maintain function at lower pH range; minimal preservative need
Zinc gluconate[35,36]	May be linked to anti-inflammatory effects; properties related to acne in topical formulations not as well substantiated as compared to oral administration
Dipotassium glycyrrhizate[38-39]	Derived from licorice root (*Glycyrrhiza inflate* and *Glycyrrhiza glabra*); potential anti-inflammatory properties may include inhibition of superoxide formation, cyclo-oxygenase activity, and cortisol breakdown in skin
Glycerin[13]	Humectant, promotes retention of water in stratum corneum to help maintain optimal enzyme function

*Cetaphil® DermaControl™ Foam Wash

Table 2. Major Ingredients in Moisturizer with SPF 30 Designed for Acne-Prone and Acne-Affected Skin*

Ingredient	Rationale for Inclusion
Oleosome Technology[39-40,41]	Patented delivery system; utilizes plant-derived lipid-based organelles; partition the sunscreen ingredient allowing for broad spectrum SPF 30 protection with lower sunscreen concentration (15%) as compared to several other daily moisturizer SPF 30 products (18.5% - 29.5%) Contains 3 photostabilized UV organic sunscreens (avobenzone [UVA], octisalate [UVB], and octocrylene [UVB]); lipid based emulsion and lower sunscreen concentrations improves tolerability; well tolerated in patients with sensitive skin
Glycyrrhetinic acid[38-39]	Same as Table 1
PMMA spherical powder (Micropearl Technology[TM])[42]	A matte-effect powder (softening effect) imparts a smooth-appearing and non-shiny appearance to skin
Pseudo-Ceramide-5[43] (5 N-2-hydroxyhexadecanoyl sphinganine)	Appears to be incorporated (likely through conversion to endogenous ceramides) as physiologic lipid into the stratum corneum to support permeability barrier integrity and function; pseudoceramides well established for use in moisturizer/barrier repair products
Silica microbeads and corn starch[43]	Absorbs sebum on skin surface to reduce facial shininess; established use in skin care products for "oil control"

*Cetaphil® DermaControl™ Moisturizer SPF 30

DEVELOPMENT OF SKIN CARE FORMULATIONS DESIGNATED FOR USE IN ACNE-PRONE AND ACNE-AFFECTED SKIN

There is good practical and scientific rationale for the routine use of proper skin care in patients with AV, especially those undergoing professionally recommended therapy. Use of proper skin care for facial skin is helpful when AV is actively present (acne-affected skin) and also during periods of quiescence when facial acne is essentially clear and well controlled (acne-prone skin). To add, both groups (acne-affected skin and acne-prone skin) are commonly using over-the-counter or prescription therapies for acne that can cause SC permeability barrier damage, which can be subclinical or visibly apparent with signs of dermatitis. In both cases, proper skin care is beneficial for these patients.

Importantly, dermatologist-directed skin care, selected by the dermatologist and his or her designated staff (i.e., physician assistant, nurse practitioner, nurse, medical assistant) provides recommendations and instructions on proper use, thus demonstrating to the patient (and parents/guardian when applicable) a strong professional interest in the overall management of AV selected for that individual patient. This approach focuses on the individual patient beyond the obvious selection of prescription therapies and possibly physical modalities, and obviates questions that patients have while at the office, but often do not ask. As a result, the patient with AV may remain confused regarding the proper general care of their skin including what products they should use and how to integrate them with topical medication use. To add, dermatologist-directed skin care reduces the likelihood that the patient will self-select skin care or nonprescription acne treatment products that are advertised and promoted for use in people with AV, often with spurious and unsubstantiated claims. Many of these products can induce skin irritation that actually sabotages the acne therapy prescribed by the dermatology office. It is important that the patient be informed of the rationale for both the recommended skin care products and the medications selected along with specific information on how

Table 3. Foam Wash and Moisturizer with SPF 30
Designed For Acne-Prone and Acne-Affected Skin*
Collection of Studies on Individual Products and Regimen Use (N=723)

FORMULATION(S) / Study Type(s)	COMPLETED STUDY (N/n)	OUTCOMES
Foam Wash	**N=282**	• Hypoallergenic • (-) sensitization testing • Diminished skin shininess/oiliness • Non-comedogenic • Non-acnegenic (no worsening) • Well tolerated
Human Repeat Epicutaneous Patch Testing for Sensitizing Potential	n=215	
A Kinetic Study to Evaluate the Effect on Skin Sebum	n=27	
Comedogenicity and Tolerability	n=40	
Moisturizer with SPF 30	**N=350**	• (-) allergic reactions noted • (-) sensitization testing • Favorable skin tolerability • Prolonged hydration • Hydration vs competitive brand products • Decreased transepidermal water loss (TEWL) • Increase in corneometry (hydration) • High cosmetic acceptability • Non-comedogenic • Non-acnegenic (including in vivo use) • Broad spectrum photoprotection • SPF 30 (UV-A + UV-B)
Human Repeat Epicutaneous Patch Testing for Sensitizing Potential	n=108	
Dermatological Use Test for Sensitive Skin	n=32	
24 Hour Moisturization	n=29	
Tolerance and Performance in Acne Subjects Under Acne Treatment[44] / Use with topical tretinoin[45]	n=116	
Tolerability / Acnegenicity / Comedogenicity / Acceptability	n=55	
SPF Testing (current SPF and Broad Spectrum criteria)	n=10	
Foam Wash + Moisturizer SPF 30 (Regimen)	**N=91**	• Well tolerated in patients undergoing treatment for acne • Decrease in TEWL • Increase in corneometry (epidermal hydration)
Tolerability and Performance in Acne Subjects Under Treatment[45]	N=91	

*Cetaphil® DermaControl™ Foam Wash and Cetaphil® DermaControl™ Moisturizer SPF 30, Galderma Laboratories LLC, Fort Worth, TX; [a]publication in progress

and when to use them.

Several options are available for selection of a gentle cleanser and moisturizer as well as photoprotectant formulations. Unfortunately, there is a conspicuous absence of many studies evaluating specific skin care products (specifically cleansers, moisturizers, and photoprotectants) in patients with AV both with and without concomitant treatments, especially well-designed studies that compare the advantages and disadvantages of specific formulations and ingredients. The following summarizes a skin care system that includes a gentle foam wash primarily for facial cleansing (Cetaphil® DermaControl™ Foam Wash, Galderma Laboratories, L.P., Fort Worth, Texas), hereafter referred to as foam wash, and a moisturizer with sun protection factor 30 (SPF 30) (Cetaphil® DermaControl™ Moisturizer SPF 30, Galderma), hereafter referred to as moisturizer SPF 30. Both formulations were specifically designed for use on acne-prone skin and acne-affected skin with rationale for inclusion of specific ingredients and are supported by studies evaluating characteristics such as cutaneous irritation, comedogenicity, acnegenicity, photoprotection, and data related to clinical use.

There are three tables that assist the reader in understanding many of the major ingredients incorporated into the foam wash and/or into the moisturizer SPF 30. Table 1 depicts major ingredients in the foam wash and a basic outline of rationale for their inclusion.[13,32–39] Table 2 depicts major ingredients in the moisturizer SPF 30 and also lists basic features that explain the rationale for their inclusion.[36–42] Table 3 outlines many of the studies completed with the individual products that demonstrate little-to-no irritation potential, absence of comedogenicity, no worsening of AV, diminished facial shine and skin oiliness due to sebum absorption, decrease in TEWL, increase in skin hydration, broad spectrum photoprotection (SPF 30), and little-to-no elicitation of sensitization or irritancy potential based on preclinical and clinical testing.[43–45]

A complete review of the formulations of the foam wash and moisturizer with SPF 30 designed for use in patients with AV and acne-prone skin is beyond the scope of this paper; however, a few general comments will assist the reader in understanding what the included ingredients are designed to provide, especially for patients with acne-prone skin and acne-affected skin, and what potential advantages may be offered for many of the patients with AV. The moisturizer SPF 30 also incorporates sebum absorbant ingredients that are helpful for "oily skin" that is diffuse on facial skin or affects certain focal areas, such as the forehead and central face, but are not problematic for non-oily skin (i.e., do not cause dryness), and has been studied in patients using topical medications for AV with favorable results reported.[43–45] It is important to recognize that all topical products may be associated with skin tolerability reactions or lack of preference with some users. The foam wash and moisturizer were well tolerated with high ratings for patient satisfaction and cosmetic acceptability by most patients who participated in studies with these products. More than 85 percent of 91 study patients reported their impression that the moisturizer SPF 30 helped them better tolerate their acne

treatment.[43,44] The following discusses information from a "top line" perspective on both the foam wash and moisturizer SPF 30, with additional information on formulation and study data available through direct contact with the manufacturer or in the literature.

Foam Wash

- *Surfactant.* The foam wash utilizes a novel surfactant (zinc coceth sulfate), which helps to balance tolerability, improves the ability to lather, effectively cleans skin and removes surface debris (i.e., dirt, sebum), and retains its effectiveness at a low pH.[34]
- *Skin type.* The foam wash can be used in patients with oily skin, normal skin, dry skin, or combination skin ("T-zone").
- *Clinical use*. The foam wash was utilized as a component of the skin care regimen (along with moisturizer SPF 30) in patients undergoing treatment for AV with a variety of topical medications, such as retinoids and BP-containing formulations (N=91).[43,44] The majority of study subjects were pleased with the cosmetic acceptability and lack of irritation associated with use of the foam wash.

Moisturizer SPF 30

- *Barrier protection/repair.* The moisturizer with SPF 30 has been shown to reduce TEWL and increase skin hydration, including when used in patients who are under active treatment with a variety of topical medications for AV, such as topical retinoids and BP-containing formulations.[43–45]
  - The formulation contains pseudoceramide-5 (5 N-2-hydroxyhexadecanoyl sphinganine), which has been shown in a reconstructed human skin model and *in vivo* (in patients with atopic skin) to increase (epidermal) cutaneous levels of endogenous ceramides likely via intracutaneous conversion.[42,43,46,47] The use of pseudoceramides as a means of delivering ceramides in topical products is well established in the skin care industry, primarily due to the high cost of endogenous ceramides and the demonstration of endogenous ceramide delivery within the SC after application of some pseudoceramides (i.e., pseudoceramide 5).[46–48]
  - As the level of cutaneous ceramides has been shown in one study to be decreased in AV, and directly correlated with the severity of AV, and ceramides are the predominant component of the intercellular lipid membrane of the SC which functions to modulate TEWL, the incorporation of pseudoceramide 5 (a ceramide precursor), along with other ingredients designed to diminish cutaneous irritation and inflammation, (ie. allantoin, glycyrrhetinic acid) is scientifically rational.[21]
- *Photoprotection.* The moisturizer SPF 30 is broad spectrum with three sunscreens included in a lower total concentration (15%) as compared to several other brand moisturizers with a SPF 30 designation.[43] The SPF 30 designation of the moisturizer SPF 30 was established in accordance with new testing guidelines from the 2011 United States Food and Drug Administration (FDA) Final Rule.[43]
  - The ability to use a lower concentration of sunscreen filtering agents is due to use of oleosomes (oil-bodies), which are lipid-based plant-derived organelles with a small central oil droplet core surrounded by an outer lamellar layer.[41,43,49] The individual sunscreen ingredients are housed within individual oleosomes, which serves to partition the sunscreens and reduces their degradation by not allowing physiochemical interaction between the sunscreen ingredients prior to application.[41,43] The lipid-based emulsion of small olesome spheres and the reduced sunscreen concentration provided by oleosome partitioning of sunscreen ingredients enhances the favorable tolerability and lack of irritancy of the moisturizer formulation and allows for even dispersion of sunscreen upon application to skin.
  - The moisturizer SPF 30 inherently provides photoprotection as is commonly desired in a daily moisturizer product that is also designed to protect against incidental UV exposure. This is advantageous in patients with AV as they are commonly on medications where photoprotection is specifically recommended in product monographs, FDA-approved package inserts, and other publications (i.e., topical retinoids, oral tetracyclines, BP-containing products).[50–55]
  - The inclusion of SPF 30 obviates the need to purchase an additional sunscreen product that may not get utilized regularly, adds an additional topical application step that my reduce compliance, can independently cause skin irritation that confounds clinical assessment, and stacks on an additional cost to the management program.
- *Skin type.* The moisturizer SPF 30 can be used in patients with oily skin, normal skin, dry skin, or combination skin ("T-zone").[43] The moisturizer with SPF 30 specifically includes ingredients adaptable for use in oily skin (silica microbeads and corn starch) that are sebum-absorbant and do not directly induce dryness so they are not problematic if applied to dry skin.
  - "Facial shine" refers to the shiny appearance of facial skin, often most pronounced on the forehead, cheeks, and chin, that is created by the accumulation of sebum on the skin surface. This is often accentuated in flash-lighted photographs where these shiny areas are magnified in intensity by light reflectance. Facial shine is bothersome to many patients with acne as part of their concerns about having "oily skin" and can be temporarily reduced in magnitude to some degree by the application of nonirritating agents that absorb sebum. Ingredients that can absorb sebum are commonly incorporated into cosmetic products

promoted to reduce "oily skin" (i.e., kaolin, talc, bentonite). Application of the moisturizer SPF 30 reduced "facial skin" over a time period of at least a few hours and up to eight hours in some patients; skin shininess and surface sebum levels were reduced on both the forehead and cheeks after application using Sebumeter (Courage+Khazaka electronic GmbH, Cologne, Germany) and Sebutape (CuDerm, Dallas, Texas) measurements, respectively.[43] Incorporating ingredients that can reduce skin oiliness and facial shine into the moisturizer SPF 30 can reduce the need for the patient to apply an additional OTC product used specifically for "oil control". Avoiding the need for the patient to purchase that additional product prevents any associated skin irritation potential and another cost.

- *Clinical use.* The moisturizer SPF 30 was utilized as a component of the skin care regimen (along with the foam wash) in patients treated for AV with various topical medications (N=91), including retinoids and BP-containing formulations, and in a 4-week randomized, investigator/evaluator-blinded, split-face comparison study (N=31), where tretinoin 0.05% cream was applied to both sides of the face at bedtime 30 minutes after facial cleansing, and the moisturizer SPF 30 was randomized to be applied regularly to one side of the face each morning.[43–45]
  - In the split-face study with topical tretinoin, 91.2 percent of study subjects observed that the moisturizer SPF 30 was not irritating to their facial skin. Also, 88.2 percent reported no facial skin stinging or burning and also that their facial skin appeared less greasy or less oily on the side where the moisturizer SPF 30 was applied.[45]

SUMMARY

AV is a very common inflammatory facial skin disorder that predominantly affects teenagers, but is also frequently seen in preteens, and post-teens, including adult women with either persistent AV or late-onset AV. There is some evidence that impairment of the SC permeability barrier is inherent to AV and/or to the inflammation that occurs in association with AV. In addition, many of the topical medications used to treat AV, and some of the vehicles used, may induce impairment of the SC permeability barrier either via an innate mode of action and/or by inducing cutaneous irritation. The resultant increase in TEWL and decrease in epidermal water content (hydration) that occurs when the SC permeability barrier is compromised leads to skin inflammation, scaling, peeling, and symptoms of sensitive skin, all of which create greater difficulty with further application of topical therapy for AV. Oral isotretinoin also impairs the SC permeability barrier by causing corneocyte dyscohesion and also induces marked sebosuppression and alteration in the cutaneous microflora.

This article reviews the significance of incorporating dermatologist-selected skin care into the overall management plan for AV for both the patient and the clinician. It also discusses much of the "top line" information on formulation characteristics and ingredients and the available data on both a brand foam wash and a brand moisturizer SPF 30. These two products were designed to be used together as a skin care regimen, or may be used separately with other skin care products if preferred by the clinician, in patients with acne-prone skin and acne-affected skin. The available data supports both the foam wash and moisturizer SPF 30 as options that are likely to be favorable from both scientific and patient preference perspectives in many patients affected by AV, especially those who are undergoing treatment with topical medications for AV.

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