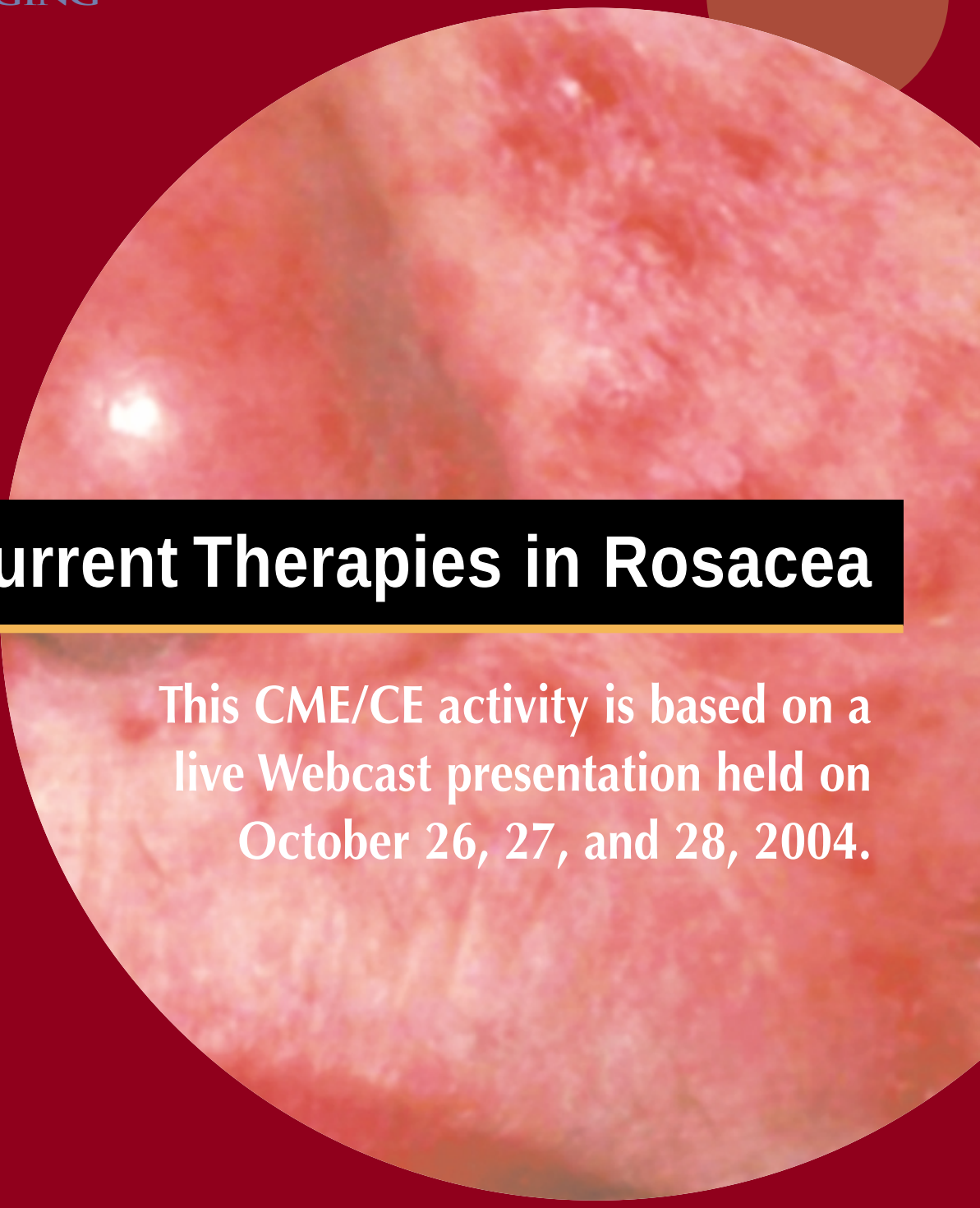
Supplement to the January 2005

skin & AGING



Current Therapies in Rosacea

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CONTINUING EDUCATION

Principal faculty: Joseph Bikowski, M.D., Zoe Draelos, M.D.

Target audience: Dermatologists, internists and family practitioners

Estimated time to completion: 1 hour

Method of participation: Physicians may receive 1 category 1 credit by reading the entire supplement and successfully answering the questions found at the end of the booklet. A score of 70% is required for passing. Fill out the evaluation and answer form (end of booklet), and fax or mail the evaluation and answer form to:
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Faculty disclosures: Dr. Bikowski has disclosed that he is a member of the speakers' bureau and a consultant for Galderma Laboratories, Healthpoint Laboratories, Stiefel, Medicis, and CollaGenex. He is a member of the speakers' bureau for Aventis, Allergan/Proctor & Gamble, Connetics Corporation, Warner Chilcott Laboratories, Biogen-Idec, Fujisawa, Novartis and Glaxo-SmithKline. He is a member of the advisory board for Galderma Laboratories, Healthpoint Laboratories and Intendis, Inc., and he is a stock holder in CollaGenex.

Dr. Draelos has disclosed that she has received research grants from Intendis, Inc., and Galderma.

Learning objectives: At the conclusion of this educational activity, the participants should be able to:
- describe the relationship between maintenance of the biofilm and rosacea treatment.
- discuss the important considerations for cleanser, moisturizer, and sunscreen selection as part of the maintenance skin care routine for patients with rosacea.
- discuss the limitations of systemic antimicrobials and the clinical value of new topical and oral treatments for rosacea
- implement a tiered approach of topical therapy for rosacea

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Diagnosis and Management of Rosacea

An overview.

By Joseph Bikowski, M.D.

Rosacea is a chronic skin disorder of vascular origin that primarily affects the skin of the central face — the cheek, nose, forehead and chin. The condition shows vascular signs of flushing and erythema, telangiectasia, and the inflammatory signs of papules and pustules. It also causes rhinophymas and swelling of other areas besides the nose. There can be ocular involvement, such as conjunctivitis and scleral injection. Women are affected more frequently than men, but the phymas — the swelling of the nose, the ears and the face — occur almost exclusively in men.

DIAGNOSIS

While diagnosing rosacea often calls for a simple visual examination, an article in the April 2002 *Journal of the American Academy of Dermatology (JAAD)* outlined a standard classification of rosacea created by a panel of world renowned dermatologists. The guideline states that primary features include flushing, non-transient erythema, papules, pustules and telangiectasias. Secondary features include burning, stinging, plaque formation, dry appearance, scaling, swelling, ocular manifestations and phymatous changes.

The guidelines divide rosacea into subtypes. Erythematotelangiectatic rosacea refers to redness and dilated blood vessels. Papulopustular rosacea refers to red bumps and pus. Phymatous rosacea refers to swollen enlarged areas of the nose, the ears and the chin. There is also ocular rosacea, and one variant, granulomatous rosacea.

Two articles in the September and October 2004 issues of *JAAD* presented criteria to diagnose and distinguish different types of rosacea. The articles suggested that the sole requisite or criteria (primary feature) for the diagnosis of rosacea is persistent erythema of the central portion of the face lasting for at least 3 months, with a marked sparing in the peri-ocular area. Secondary features include burning, stinging, swelling, plaque formation, dry scaling appearance, ocular manifestations, peripheral locations (other than the face), and phymatous changes.

Identifying these criteria is important because once rosacea is subtyped, you can begin to choose the best therapy. While papulopustular rosacea is not generally known as a hematologic disorder with inflammatory cytokines, there are inflammatory cells in the dermis that release degradated enzymes that produce inflammation and damage to the dermal elastic fibers. Regardless of the etiology of rosacea, there is still a clinical presentation we have to treat.

We have to address the erythema, telangiectasias, papules, pustules, and nodules, as well as the phymas and the ocular changes.

MANAGEMENT

Exactly how we manage rosacea depends on several factors, including the type of rosacea; the extent, severity and duration of the condition; previous treatment; and the patient's desires and expectations.

For example, a 45-year-old woman with no previous treatment presented to my office with erythematous papules and pustules on her forehead, nose, cheeks and chin. Her daughter was to be married in 6 weeks, so she requested clearing of her face in that time-frame.

In a patient like this, the primary signs and symptoms that we can manage are:

Flushing/blushing. Flushing, blushing and subsequent erythema, are the major challenges we face in treating rosacea.

If you ask patients how much flush or blush they have, it can be difficult to get an objective answer. That's why we give all of our rosacea patients a calendar diary and ask them to record their flushing, how often it occurs, how long it lasts and the intensity for all of these on a one to 10 scale. In addition, we ask patients to note any possible trip wires or trigger factors.

The calendar approach helps us to quantitate the disease and the effects of the medication. Once patients are started on a medication, you hope to see a decrease in the frequency, duration and intensity of the flushing at the 1-month follow-up. One of major benefits of this approach is that the patient also can see "objective" evidence of improvement.

Erythema. Treating erythema is the ***real*** challenge. There's an increased incidence of rosacea in association with patients that have migraine headaches.

For years, neurologists have used baby aspirin daily as prophylaxis for migraine headaches. For the last 2 to 3 years, we have been giving a enteric-coated baby aspirin 81 mg each night to rosacea patients. We've seen a decrease in the flush and blush as recorded in patient calendar diaries. The aspirin may inhibit the prostaglandins or the bradykinins, so we're basically talking about anti-inflammatory effects.

Pharmacologic Therapy for Rosacea

A review of the most common therapies.

By Joseph Bikowski, M.D.

When we talk about rosacea therapy, we should be thinking about combination therapy, tiered topical agents in combination with each other or with an oral agent. In general, expect topical medications to show effects in 3 to 12 weeks. Systemic antibiotics or sub-antimicrobial dose doxycycline should be showing effects at 2 to 4 weeks.

Our goal is to produce clearing in 3 to 6 months, and then taper patients off systemic antibiotics. We can then maintain remission with either the topical medication alone or, when necessary, in combination with a systemic antibiotic.

Here's an overview of the most common therapies to treat rosacea.

TOPICAL AGENTS

Metronidazole. Metronidazole gel (MetroGel) has been used since 1988 and was the first drug specifically indicated to treat rosacea. Metronidazole as a therapy for rosacea was discovered serendipitously when physicians noticed that rosacea cleared in a number of women who received the drug orally for trichomonal vaginitis. Topical formulations were later found to produce the same positive effect for treating rosacea.

Metronidazole is available in a variety of formulations (gel, cream and lotion) and two strengths (0.75% to 1%). One study, published by Mark Dahl in the *Archives of Dermatology,* showed that the drug may be the topical drug of choice for maintaining remission. It is a category B drug.

When we talk about rosacea therapy, we should be thinking about combination therapy with topical and oral agents.

The 0.75% formulations appear to be equal to 1% in efficacy. However, that may change as new formulations appear.

I've had success using metronidazole 0.75% (MetroGel) in combination with sodium sulfacetamide 10%/sulfur 5%, specifically Rosanil Cleanser, twice a day. This combination can produce a decrease in erythema, papules and pustules, frequently within 4 weeks.

Azelaic acid. Another first-tier treatment for rosacea is azelaic acid gel 15% (Finacea). While we have found that azelaic acid gel treats acne to a certain extent, many of us have found that it works better for rosacea.

Azelaic acid gel 15% is the first new product to be approved by the FDA for rosacea in the last 10 years. It is a category B drug.

Two large phase III trials have shown effectiveness in reducing inflammatory lesions, papules, pustules and erythema. According to a study published in the June 2003 issue of the *Journal of the American Academy of Dermatology (JAAD),* while there is a relatively high incidence of dermatitis-associated adverse events, 90% of patients have given the gel an excellent rating with good tolerability.

DESI drugs. Another agent is sodium sulfacetamide 10%/sulfur 5%, DESI drugs. This group of drugs takes its name from the Drug Efficacy Implementation Study program, in which the National Academy of Sciences conducted a study to see what drugs could be prescribed without an NDA from the FDA. The result was a category known as DESI drugs, which includes agents like Avar, Clenia, Plexion, Rosac, Rosanil, Rosula, Sulfacet-R, Klaron and Ovace.

While the above drugs have distinctive indications, all can be effective for acne, rosacea and seborrheic dermatitis. Plexion is now available as a cloth for cleansing twice a day. Rosac contains a sunscreen. Klaron is formulated in an elegant vehicle that eliminates dryness. Ovace foam is a cosmetically acceptable product for men who have facial or body hair. The foam vehicle is non-greasy, and is easy to apply over hair-bearing areas.

ORAL AGENTS/ANTIBIOTICS

We are all well aware of the value of oral antibiotics in treating rosacea, but we also know that there are adverse

Patient before (left) and 4 weeks after (right) being treated with azelaic acid gel 15% (Finacea) twice per day.

effects that may be associated with these drugs. A systemic medication that would be effective without the side effects of antibiotics would be ideal.

There is a now such a treatment option: doxycycline hyclate 20 mg twice a day (Periostat), which is also known as sub-antimicrobial dose doxycycline (SDD). It is FDA-approved for adult periodontitis only. I'm talking about strictly off-label use at this time.

Current labeling allows us to prescribe doxycycline hyclate 20 mg twice a day for up to 12 months. No other "antibiotic" has been FDA approved for that length of time.

This dose dramatically decreases the chance of developing doxycycline-resistant microorganisms. At this dose, there is only an anti-inflammatory effect and no anti-microbial effect. That's why this drug has produced a paradigm shift not only in our therapy, but in the entire notion of antibiotic vs. anti-inflammatory. This drug is not used as an antibiotic, but as an anti-inflammatory agent.

How well does SDD therapy work? In a study published in the *Archives of Dermatology* in April 2003 on treating acne, researchers found that a sub-antimicrobial dose of doxycycline reduced inflammatory lesions by 50.1% and reduced comedones by 53.6%. This is the first study to show that systemic antibiotics can reduce comedones. Researchers found no adverse events.

Even more important, there was no change in *Propionibacterium acnes (P. acnes)* counts from baseline to 6 months in this study. *P. acnes* was not affected because this dose of doxycycline has only an anti-inflammatory effect.

In my own research, published in the July/August issue of *SkinMed,* on treating rosacea, I gave 50 patients doxycycline 20 mg twice a day over the course of 4 to 8 weeks. I saw 80% to 100% clearing of inflammatory lesions, a 50% reduction in erythema, and possibly a reduction in the size and diameter of telangiectasias.

Other researchers have focused on combination therapies for rosacea that include doxycycline hyclate 20 mg twice a day. One study, not yet published, looked at the combination of doxycycline hyclate 20 mg (Periostat) and metronidazole lotion 0.75% (MetroLotion). Over 12 weeks, researchers saw a dramatic reduction in inflammatory

FOUR TIERS OF DRUGS TO TREAT ROSACEA

1. Metronidazole gel 0.75% (MetroGel) and azelaic acid gel 15% (Finacea).

2. Sodium sulfacetamide 10% lotion/sulfur 5% (Avar, Clenia, Plexion, Rosac, Rosanil, Rosula, Sulfacet-R, Klaron and Ovace). These agents may work well for rosacea, acne and seborrheic dermatitis.

3. Metronidazole cream 1% (Noritate). This therapy may work well for patients who have a lot of red, dry, scaly skin, but many patients dislike the thick cream.

4. Topical immune response modifiers, including tacrolimus ointment (Protopic) and pimecrolimus cream (Elidel).

lesions. At the end of 12 weeks, researchers stopped giving subjects the metronidazole lotion 0.75%, but continued giving them doxycycline hyclate 20 mg for maintenance.

Why pair doxycycline hyclate 20 mg with metronidazole lotion 0.75%? For patients who experience burning and stinging from topical medicines, using a systemic medicine with no antibiotic effect, may produce an anti-inflammatory effect that will alleviate the signs and symptoms of rosacea without a cutaneous irritant effect.

There's also a large phase III study that treated moderate rosacea in 134 patients for 16 weeks. This is the largest study of systemic therapy in rosacea to date and the first to show that the anti-inflammatory properties of doxycycline alone are sufficient to control the symptoms of rosacea.

Preliminary data analysis indicates that patients treated with doxycycline hyclate 20 mg showed a continued improvement during the 16-week course of the study compared to patients on placebo. In the study, patients on doxycycline hyclate 20 mg had a significantly greater reduction in the number of inflammatory lesions (papules and pustules) compared to patients on placebo. This improvement was clinically and statistically significant.

The erythema in patients in the doxycycline hyclate 20 mg group showed a trend toward greater improvement compared to patients in the placebo group.

AZELAIC ACID VS. METRONIDAZOLE

A study in the *Archives of Dermatology* in 2003 compared the effect of metronidazole gel 0.75% (MetroGel) and azelaic acid gel 15% (Finacea) in treating inflammatory lesions. Researchers found a statistically significant difference between the two therapies after 15 weeks, with azelaic acid gel outperforming metronidazole gel 51% vs. 45% in reducing inflammatory lesions.

Other studies have found similar results. The results of one study found that azelaic acid gel 15% reduced mean inflammatory lesions by 12.9%, compared to a 10.7% reduction with metronidazole gel 0.75%. Erythema reduction was also significantly better, with a 56% reduction from azelaic acid gel 15% compared to a 46% reduction with metronidazole gel 0.75%.

In this study, 75% of patients said azelaic acid gel 15% was cosmetically acceptable and 82% of patients said the same about metronidazole gel 0.75%.

Also, 26% of azelaic acid gel 15% patients complained of adverse events like stinging and burning, compared to 7% of the metronidazole gel 0.75% group. However, it's important to know how long the burning and stinging lasted, how often it occurred, and how intense the sensations were. In this author's experience, adverse effects from the drugs are essentially equal — one or two patients a month may complain about azelaic acid gel 15% gel.

Also, consider the possibility of combination therapy using both agents. We're not sure of the mechanism of action of either, so there may be an advantage to using both therapies in combination.

If a patient is started on metronidazole gel 0.75% twice a day and at the end of 3 months wasn't entirely satisfied, it would be reasonable to add azelaic acid 15% gel to the treatment.

PROBLEMS WITH LONG-TERM ANTIBIOTIC USE

While the long-term use of antibiotics may long be associated with side effects, dermatologists need to be aware of some recent developments in adverse events.

Here's a review of some well-known side effects, and some more recent developments.

PHOTOSENSITIVITY. Doxycycline hyclate and mono hydrate in a dosage of 50 mg to 200 mg a day can produce a photosensitivity in 1% to 3% of patients. This typically presents as erythema of the cheeks, the nose or the dorsum of the hands. If a patient on doxycycline starts to experience erythema, it's time to take them off.

VERTIGO. Minocycline has been associated with vertigo ("the room spins"), especially in patients taking high dosages.

"NEW" ADVERSE EVENTS. You also need to look for what are called the "new" adverse events with minocycline, which include lupus-like syndrome, hypersensitivity reaction and serum sickness. These are all rare, but do occur.

HYPERPIGMENTATION. The biggest difficulty with minocycline is hyperpigmentation, which is why I'm decreasing my use of minocycline. Hyperpigmentation can affect the skin, the sclera, the nails, the mucus membranes and/or the teeth.

TOXIC EPIDERMAL NECROLYSIS (TEN). Trimethoprin and sulfamethoxazole can cause TEN. It's rare, but it occurs. If a patient experiences TEN from a drug, it will occur in 7 to 28 days of the onset of the first administration of the drug.

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA). The newest adverse effect is acquired antibiotic resistance — community-acquired MRSA. In the last year, I've seen more than 40 patients with community-acquired MRSA.

Two to 3 years ago I did not see it at all. As I travel the country, I've found this has been the experience of most clinical dermatologists. We have to ask ourselves if it's possible we, as dermatologists, are in some way contributing to this MRSA? Think of all the tetracycline, doxycycline and minocycline we put into society every day when we treat acne and when we treat rosacea.

Maintaining the Barrier While Altering the Biofilm

Treating the skin surface.

By Zoe Draelos, M.D.

When we treat rosacea, we evaluate what is beneath the skin and treat what is on top of the skin. But, have you ever thought about what lies on top of the skin that might influence the treatment of rosacea?

TREATING THE SKIN'S SURFACE

A new rosacea treatment paradigm encourages treating beyond what we see histologically, thus treating beyond the disease. This means addressing not only histologic components, but also thinking about the skin surface, including sensory concerns, which are so important in rosacea patients.

Rosacea is profoundly impacted by the skin surface. Topical agents are placed on the skin, thus influencing a thin layer that covers the skin known as the biofilm. Whatever is put on the skin surface — whether it's topical metronidazole (MetroGel, Noritate) or azelaic acid gel 15% (Finacea) — it interacts with the biofilm to normalize the skin and improve the appearance of rosacea.

The concept of the biofilm is very important in the skin-care industry because the biofilm interacts with color cosmetics, moisturizers, sunscreens, and all products that are applied to the skin surface.

The ability of sunscreen to function, for example, has a great deal to do with the biofilm. The biofilm influences how long the sunscreen stays on and how well it stays in place. It also determines how greasy or tacky the sunscreen will feel.

Think of the biofilm as the film on the skin surface with which all topical products and medications interact. When we measure the pH of the skin surface, we're actually measuring the pH of the biofilm. When we talk about acne and rosacea possibly being influenced by the overgrowth of *Propionibacterium acnes (P. acnes)*, we are talking about the existence of bacterial organisms in the biofilm.

NORMALIZING THE BIOFILM

When treating rosacea, how can we normalize the biofilm? The rosacea biofilm includes sebum, *P. acnes*, *Demodex*, rosacea medications, skin care products, sunscreens and color cosmetics.

First, consider how rosacea is mediated by the biofilm. We know that *Demodex* may be part of the rosacea equation. Some people believe that the *Demodex* might be important to the granulomatous form of rosacea. We know that *P. acnes* is also responsible for the inflammatory component, especially seen in acne rosacea.

When we try to control rosacea, what are we doing with agents like topical metronidazole and topical azelaic acid, and with oral low-dose antibiotics? We are trying to normalize the biofilm by cutting down on the overgrowth of *Demodex*. We're also trying to cut down on the colonization of *P. acnes*.

Also, the medication must be placed in a well-formulated vehicle, because any medication that is applied to the skin surface that induces irritation and initiates the inflammatory cascade will, indeed, worsen rosacea. It is important to prevent activation of the inflammatory cascade since low-grade chronic inflammation is problematic in rosacea.

THE BARRIER

The biofilm sits on top of the barrier, and the barrier is what prevents our skin from experiencing irritation. We need to keep the barrier intact to help rosacea patients begin healing.

The skin barrier is something that we think about frequently when we're treating eczematous dermatoses, but we tend to not think about it as frequently when we're treating rosacea. The barrier, however, is just as important when treating rosacea. Any medication that is applied to the skin surface that degrades the barrier will ultimately result in initiation of inflammation and worsening of rosacea.

The barrier is basically composed of intercellular lipids that are present between the corneocytes. These lipids are composed of ceramides and cholesterol arranged in a very careful lamellar organization, with the intercellular lipids providing the mortar between the corneocyte that provide the structural integrity of the skin. The barrier is particularly important in rosacea because it provides protection against irritation. Thus, barrier defects are key to initiation of inflammatory cycle resulting in facial erythema.

Activities that damage the barrier can initiate rosacea, such as soaps and cleansers that remove the intercellular lipids. Penetration enhancements present in many topical

rosacea medications are designed to increase the penetration of the active agent through the epidermal, but may also damage the barrier and worsen rosacea.

TREATING THE BIOFILM

There are several ways the biofilm can be normalized in rosacea patients. One of the problems with topical medications is that while they are easily rubbed on the face, they are also easily rubbed off the face. One of the newer concepts in treating rosacea is to use medications that create a follicular reservoir. There are particulate medications that are able to deposit within the follicular ostia, which is the site of *Demodex* and *P. acnes* growth. If we can create a follicular reservoir, we might be able to have longer lasting treatment in the rosacea patient. There are two particulates that are useful in rosacea — azelaic acid and sulfur.

There was an azelaic acid preparation originally introduced onto the marketplace that was a 20% cream (Azelex). Later, a 15% gel (Finacea) was introduced. There was a Franz cell study performed to look at what happened when medication was put on the top of the chamber using hairless mouse skin. With the azelaic acid cream 20%, approximately 68.4% of the medication remained on top of the stratum corneum, with only 3.4% of the medication entering the viable skin. The viable skin in the rosacea patient is actually our target organ.

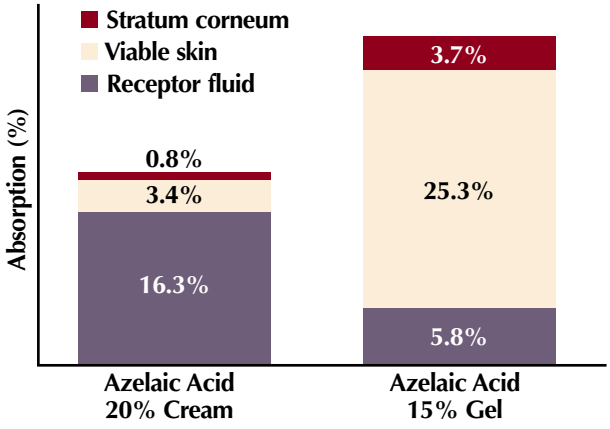
With the azelaic acid gel 15%, 25.3% of the azelaic acid entered the viable skin. This is why the proper vehicle is so important to proper rosacea medication functioning. The amount of medication present in the viable skin is what actually affects the pathology of rosacea. The vehicle is charged not only with being cosmetically elegant, but also with delivering the medication to the proper skin site in a biologically active form. And, this is why lower concentration products can actually have a greater effect than higher concentration products. Concentration does not always translate into efficacy. It's actually the penetration and ability to deliver the active particulate to the proper skin site that determines efficacy.

FACIAL CLEANSING

Face cleansing is also very important to rosacea patients, to restore the barrier and to maintain the biofilm in a healthy state. The trick is to decrease the *Demodex* and *P. acnes* without damaging the barrier.

How do you restore a healthy biofilm without damaging the barrier? One key is to use synthetic detergent cleansers, or non-soap products, such as liquid foaming face washes. Foaming face washes contain synthetic detergents, not soap, to mildly remove lipids from the skin surface without damaging the intercellular lipids.

Rosacea patients can also use open-weave facial cleansing cloths to remove cosmetics, a technique that can help with exfoliation. Facial cleansing cloths that you can't see through — closed-weave cleansing cloths — provide too much irritation.



***In vitro* penetration and absorption of azelaic acid from 15% gel versus 20% cream after 24 hours of topical application to hairless mouse skin (% of applied azelaic acid dose).**

I also suggest that my rosacea patients use lukewarm water on their fingertips to apply cleanser to their face and for rinsing their face. I find that many of my rosacea patients think somehow that they can scrub away their disease, but when the intercellular lipids are removed, the skin can be damaged. The fingertips are recommended for facial cleansing, since they can sense if the skin is being rubbed too hard.

Finally, I tell my rosacea patients to dab their faces with a soft towel when drying. Rubbing or physical manipulation of the skin can result in erythema, which causes rosacea to flare.

CLEANSING AND MOISTURIZING PRODUCTS

When it comes to facial cleansing and moisturizing, rosacea patients are often tempted to use ancillary products sold at cosmetic counters. I believe rosacea patients should keep ancillary products to a minimum. Fewer products yield fewer problems.

Twenty to 30 different botanical ingredients in a skin care product are problematic. The more ingredients that are placed in the formulation, the more difficult it is to determine which ingredient is the source of the problem, and the more likely the patient is to experience irritation.

Rosacea patients should avoid astringents and toners that are sometimes used following cleansing to remove any remaining dirt on the face. These agents induce barrier damage in rosacea patients. Evaporation of the vehicle can provoke a noxious stimuli that results in onset of flushing.

Exfoliants also have no place in the rosacea patient's daily routine. For exfoliation, I prefer open-weave face cloths, which provide physical exfoliation rather than chemical exfoliation.

Rosacea patients should think of their face very much like a silk scarf and handle it carefully and gently to prevent damage.

Using Color Cosmetics

A guide for rosacea patients.

By Zoe Draelos, M.D.

It's important that rosacea patients choose the right cosmetics in order to prevent irritation and flare-ups. Below is an overview of what rosacea patients should look for in foundation, powder,eye makeup and applicators.

FACIAL FOUNDATION AND POWDER

Facial foundations tend to migrate over the skin as they mix with sebum and the other components of the biofilm. When this mixing occurs, the facial foundation moves to the follicular ostia, which may be one of the reasons perifollicular acne lesions are very common, not only in rosacea patients, but in dermatology patients in general. As a result, it's important for rosacea patients to select a facial foundation that produces very little irritation.

The preferred facial foundation should contain silicone, either in the form of dimethicone or cyclomethicone. Silicone is found in oil-free foundations that do not contain mineral oil or vegetable oil. These foundations form a thin film over the skin surface, and silicone is not comedogenic or acnegenic, making it an ideal ingredient for rosacea patients.

Rosacea patients should avoid light reflective particles, so I recommend a matte or a dull finish. I suggest rosacea patients stay away from specialty foundations, because many of these products contain chemical sunscreen ingredients, such as octylmethoxycinnamate, vitamins, salicylic acid and other herbal extracts for anti-aging purposes. Foundations should be selected with a simple formulation and a minimum number of ingredients.

Face powder can be very important to rosacea patients. Facial powder not only camouflages erythema of the face, but when used with facial foundation, it can also camouflage underlying skin abnormalities.

Rosacea patients need to select facial powder very carefully. They should stay away any facial blushes or powders that use light reflective particles. Matte powders and cosmetics are a better choice.

If you look at a frosted powder on the skin surface, you will see light reflective particles adherent to the vellus facial hairs. These small particles actually can lodge in the follicular ostia and act like itching powder on the skin surface. Rough-edged particles can irritate a rosacea patient's face.

It's also important that the tiny particles from which the powders are made are small and even in size. You may want to recommend that rosacea patients purchase quality cosmetics, where the particle size and the powders are a little bit higher quality.

Advise rosacea patients to stay away from deeply pigmented blushers, which can be more irritating to the skin.

EYE COSMETICS

The same recommendations that apply to facial powders apply to powdered eye shadows or colored eye cosmetics.

Rosacea patients should use a pencil eyeliner. They should also apply all eye cosmetics with a brush and use lightly pigmented powdered matte finish.

Eyelash cosmetics should be black. They are available in purples and greens and deep blues, but for the patient with ocular rosacea, these pigmented eye cosmetics may be irritating. Carbon black is the only pigment that is not allergenic.

Avoiding waterproof eyelash cosmetics is important. You have to use a solvent to remove the cosmetic from the eyelids, which possess few small sebaceous glands. It is important not to remove the intercellular lipids and not to remove too many lipids from the skin surface.

I also tell my rosacea patients to purchase new eyelid and eyelash cosmetics every 3 months. Eye cosmetics, particularly mascara, can become contaminated, which should be a particular concern for patients with ocular rosacea.

Sponges can be a source of irritation for rosacea patients, especially if the sponge has sharp edges or if the patient is latex-sensitive.

APPLICATORS

Brush applicators should be composed of soft, pliable fibers. Many sponges are irritating to the face and to the eye area.

Sponges can be a source of irritation for rosacea patients, especially when the sponge has sharp edges or when the patient is latex-sensitive. Rosacea patients should use a brush, which can be cleaned in the dishwasher, when applying any facial cosmetics.

Questions & Answers

Q: Given the safety profile of doxycycline hyclate 20 mg (Periostat), why would you want to use either a high-dose doxycycline or minocycline to treat rosacea?

A: If doxycycline hyclate 20 mg is effective, I would not go to the higher dose of doxycycline or use minocycline. It's most likely that doxycycline hyclate 20 mg will be effective because of its anti-inflammatory effect. *—Dr. Bikowski*

Q: Are the anti-inflammatory effects of doxycycline hyclate 20 mg equivalent to higher dose doxycycline?

A: Yes. There was an interesting study of 72 periodontal patients that examined inflammation in the crevices around the teeth and the amount of matrix metalloproteinase that was present and inhibited by doxycycline hyclate 20 mg.

Researchers discovered that 20mg of doxycycline hyclate twice a day was equal to 40mg of doxycycline hyclate twice a day in terms of producing an anti-inflammatory effect. That research says there is no reason to go above 20 mg twice a day, because it will provide no increase in the anti-inflammatory effect. *—Dr. Bikowski*

Q: How do you communicate the difference of a sub-antimicrobial dose doxycycline hyclate 20 mg versus a low or high dose of doxycycline with your patients?

A: This is an excellent opportunity to reassure patients that you are doing everything you can to make sure that they don't get a systemic antibiotic unless it's absolutely necessary. I tell patients that we're trying to treat inflammation, and that doxycycline hyclate 20 mg gives us a pure anti-inflammatory effect without the antibiotic effect. Most patients are grateful to understand the fact that there are medications out there now that have purely anti-inflammatory effect without the antibiotic effect. *—Dr. Bikowski*

Q: Do patients experience a reduction in side effects over time as they use topical azelaic acid gel 15% (Finacea)?

A: While azelaic acid gel 15% is relatively free of side effects, some patients may experience some stinging and burning when they initiate therapy. It's important to make sure that these patients continue to apply the product, however, because the side effects usually resolve after 2 or 3 days, and certainly after a week, of application.

We did a small study to examine what might be causing this stinging. We found that it was probably related to some high neuro-sensory awareness in rosacea patients that resolves as they acclimate to continued use of the azelaic acid. *—Dr. Draelos*

Q: Why is liquid eyeliner not recommended versus a pencil black based eyeliner?

A: Many of the liquid eyeliner products are designed to be waterproof, and they contain latex. The evaporation of the vehicle that leaves a latex film on the eyelid can actually worsen ocular rosacea. In addition, you need a special solvent to remove this latex liquid eyeliner. This agent not only removes the oil materials in the liquid eyeliner, but it can remove sebum from the eyelids, which are not sebum-rich. This can create more irritation and inflammation.

That's why I suggest using a pencil black-based eyeliner. Because this is basically carbon pigment that's been waxed, there are no ingredients to evaporate. It's easy to sharpen the pencil with each use to prevent contamination. *—Dr. Draelos*

Q: Do you notice a difference between sodium sulfacetamide cleansers with sulfur that wash off compared to the lotions that you leave on?

A: There is definitely is a difference. The longer products stay on the skin, the greater the efficacy. Cleansers that are washed away are not going to be nearly as effective as creams, lotions or other formulations that stay on the skin.

—Dr. Draelos

Q: Is there a role for topical steroids in treating rosacea?

A: I sometimes use topical corticosteroids on patients who present with extremely inflammatory rosacea, but I will never use them for more than 1 week. I do not believe chronic corticosteroid use on the face is worthwhile, especially in patients who have overlap with rosacea and seborrheic dermatitis.

That said, 1 week of corticosteroids is a nice quick way to ameliorate the inflammatory response of both of these dermatoses. For long-term treatment, however, I do not think topical corticosteroids have a place in rosacea therapy.

—Dr. Draelos

Q: Have researchers examined the topical use of niacinamide to prevent the inflammatory reactions of rosacea?

A: We did a fairly large 60-patient study looking at a topical niacinamide preparation that's available in the over-the-counter market that also contains camphor and vitamin E. We found that in addition to prescription medication, topical niacinamide was able to improve erythema.

I do not believe that niacinamide replaces topical or oral prescription medications, but I do think topical niacinamide in the form a moisturizer might help rosacea patients.

—Dr. Draelos

Test Questions

1. The biofilm on the skin surface in rosacea patients is composed of:
- a. sweat
- b. sebum
- c. *P. acnes*
- d. environmental dirt
- e. all of the above

2. The skin of subjects with rosacea is:
- a. resistant to irritants due to the presence of chronic inflammation
- b. an important subtype of sensitive skin
- c. thinner than normal due to the prominent telangiectasias
- d. all of the above
- e. none of the above

3. Patients afflicted with rosacea typically have:
- a. dry skin
- b. combination skin
- c. oily skin
- d. all of the above
- e. none of the above

4. The erythema associated with rosacea may be worsened by:
- a. astringents with rapidly evaporating vehicles
- b. moisturizers with low grade irritants such as propylene glycol
- c. high concentration glycolic acid exfoliants
- d. abrasive scrubs with ground fruit pits
- e. all of the above

5. Rosacea is related to:
- a. the effects of chronic photodamage
- b. exposure to eggs at an early age
- c. a family history of pernicious anemia
- d. increased incidence of myocardial infarction
- e. none of the above

6. Rosacea is most prevalent in:
- a. Caucasians with fair skin
- b. Caucasians with darkly complected skin
- c. Asians
- d. Latinos
- e. African-Americans

7. Which of the following is not a subtype of rosacea?
- a. Erythematotelangiectatic
- b. Papulopustular
- c. Phymatous
- d. Ocular
- e. Granulomatous

8. The first drug specifically designed for rosacea is:
- a. Sodium sulfacetamide
- b. Sodium sulfacetamide and sulfur
- c. Metronidazole
- d. Azelaic acid
- e. None of the above

9. Azelaic acid gel's pregnancy category is:
- a. A
- b. B
- c. C
- d. D
- e. X

10. Subantimicrobial dose doxycycline (SDD):
- a. Is doxycycline hyclate 20 mg bid
- b. Inhibits MMPs and is therefore anti-inflammatory
- c. Has not been shown to be phototoxic
- d. Is FDA approved for up to 12 months of continual administration
- e. All of the above

Current Therapies in Rosacea

Answer and Evaluation Form

(see page 2 for instructions)

Please print clearly:

Name | Degree | Position/Title

Organization/Institute | Department

Mailing Address for Certificate (H or W):

City | State | Zip Code | Email Address

Social Security Number | Phone (area code) | Fax (area code)

Answers (Refer to questions on other side of page) Circle one letter for each answer:

1.	A B C D E	6.	A B C D E
2.	A B C D E	7.	A B C D E
3.	A B C D E	8.	A B C D E
4.	A B C D E	9.	A B C D E
5.	A B C D E	10.	A B C D E

Evaluation (circle one)
Excellent (4) Good (3) Satisfactory (2) Poor (1)

Accuracy and timeliness of content:	4	3	2	1
Relevance to your daily practice:	4	3	2	1
Impact on your professional effectiveness:	4	3	2	1
Relevance of the content to the learning objectives:	4	3	2	1
Effectiveness of the teaching/learning methods:	4	3	2	1
This activity avoided commercial bias or influence	YES	NO		

Upon completion of this activity, I am able to:

1. Describe the relationship between maintenance of the biofilm and rosacea treatment.	YES	NO
2. Discuss the important considerations for cleanser, moisturizer, and sunscreen selection as part of the maintenance skin care routine for patients with rosacea.	YES	NO
3. Discuss the limitations of systemic antimicrobials and the clinical value of new topical and oral treatments for rosacea.	YES	NO
4. Implement a tiered approach of topical therapy for rosacea.	YES	NO

What questions do you still have? _____

_____

How will you use what you have learned from this activity? _____

_____

All tests must be received by 1/15/06.