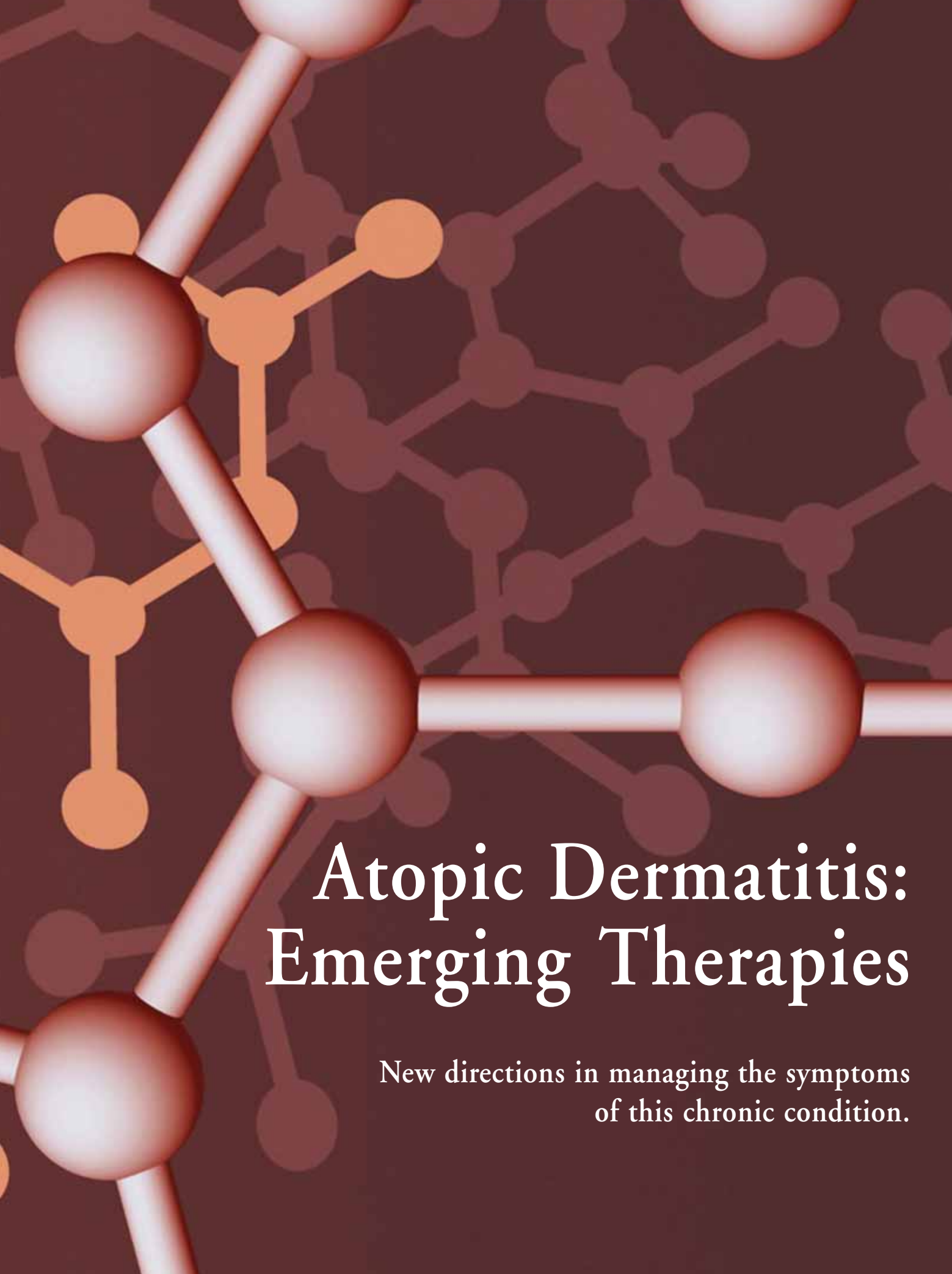

Atopic Dermatitis: Emerging Therapies

New directions in managing the symptoms of this chronic condition.

Introduction

Mark Lebwohl, M.D.

As many as 15 million Americans, primarily children, suffer from the burning and itching of atopic dermatitis (AD). Children who suffer from this disease are tormented by restless nights and recurrent rashes that can result in infections from scratching and rubbing. Adults who have AD may be sentenced to a lifetime of itching, scars from scratching, limitations in their occupations and even lifestyle choices, punctuated with overwhelming flare-ups that can leave them in the depths of despair.

Fortunately, dermatologists can turn to an array of different treatment therapies to help in the fight against this chronic and frustrating condition. Both topical corticosteroids and topical calcineurin inhibitors (TCIs) can be used to control sudden flare-ups in the disease and can also be used as part of an effective, long-term maintenance program. Unfortunately, we have to consider the potential side effects that have been associated with these medications.

Recently, the FDA issued a boxed warning against the possible health risk associated with TCIs, including a theoretical risk of lymphoma with prolonged use. That warning was based on speculation, not on facts. Although TCIs continue to play an important role in our regimen for patients who have AD, there is always room for additional nonsteroidal topical medications. Physicians are searching for new treatment modalities that are both effective in the treatment of this disease and considered safe for extended use. These considerations are imperative, considering the fact that so many patients are young children and consequently face a lengthy treatment exposure commonly measured in years.

As there is no single treatment that is effective in every case, most dermatologists treat AD with combination therapy. Any new medication aimed at the condition must therefore work in conjunction with other treatments. An effective, long-term solution that both directly improves the condition while also reducing the need for medications with potential side effects would be a welcome addition to the arsenal against AD.

At our roundtable meeting, we reviewed and discussed current treatment options and examined the role of Atopiclair, a topical, nonsteroidal therapy indicated for the management of AD.

Mark Lebwohl, M.D.
Professor and Chairman
Department of Dermatology
Mount Sinai School of Medicine
New York City, NY

This supplement is based on a roundtable discussion on atopic dermatitis that Dr. Lebwohl chaired last fall in Scottsdale, AZ. Participants are paid consultants of Chester Valley Pharmaceuticals, Inc. This educational activity may contain discussion of drug uses not approved by the FDA.

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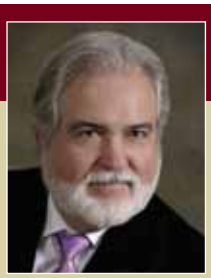

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Living With Atopic Dermatitis

Never life-threatening, but often life-altering, atopic dermatitis compels sufferers to search for fresh approaches to treatment.

Atopic dermatitis (AD) is one of the most common dermatologic complaints affecting approximately 20% of school-aged children and about 3% of adults. As many as 15 million Americans suffer from the symptoms of this disease. Today, a number of effective therapies for managing AD are available, including topical corticosteroids and topical calcineurin inhibitors (TCIs). However, these treatments may be associated with potential side effects. As we do not have a perfect treatment, we are constantly seeking new approaches to managing this condition.

An Unknown Etiology

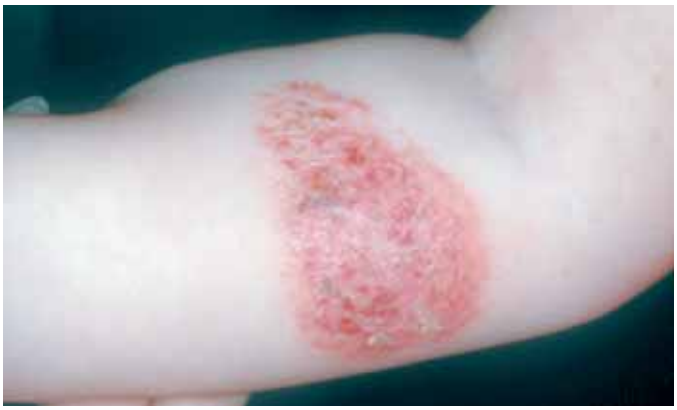
The exact cause or causes of AD remain unknown, but the disease seems to have both environmental and genetic components. Children are more likely to develop AD if at least one parent has had it or has also had allergic conditions such as asthma or hay fever. While some outgrow skin symptoms, approximately three-fourths of children who have AD develop asthma or hay fever. Environmental factors can trigger symptoms at any time in individuals who have a genetic predisposition to the disease. While stress can exacerbate the condition, it is not a direct cause of the disease.

AD may also result from a malfunction of the immune system that guards part of the system against bacteria and viruses. Patients who have AD create excessive cytokines, which lead to clinical evidence of inflammation and may stimulate both increased levels of immunoglobulin E and eosinophilia.

What's in the Arsenal?

Current topical treatment options range from skin care with moisturizers in mild cases, to TCIs and corticosteroids for mild, moderate or severe cases. Practitioners can use phototherapy or systemic medications, such as corticosteroids, cyclosporine or mycophenolate mofetil (CellCept), to treat more severe cases.

Physicians can also administer antihistamines to help sedate the pruritic patient and to allow sleep and antibiotics to combat infections. Practitioners should make sure that all patients who suffer from AD are diligent in their skin care, using non-irritating cleansers, moisturizing daily and avoiding known irritants and allergens. □



Severe atopic dermatitis on the arm of a 14-month-old female. *Photo courtesy of Douglas C. DiRuggiero, P.A.-C., M.H.S., and Jason Smith, M.D.*

Current Treatment Options

An expert panel evaluates how the available treatment options stack up.

Treatment of atopic dermatitis (AD) depends largely on the severity of the condition, the location on the body, the age of the patient and several other factors. Certain treatment options are not appropriate for particular body locations, while others may not be appropriate for young children. The type and course of treatment for a specific patient depends on whether a flare-up has occurred or ongoing maintenance therapy is being established.

> "The body locations most affected and the age of the patient are important considerations when selecting a treatment approach."
>
> — W. Philip Werschler, M.D.

Amy S. Paller, M.D.: I most commonly "hit hard" with a moderate-strength corticosteroid for uncomfortable flares and then taper to a lower-strength steroid, topical calcineurin inhibitor (TCI) or Atopiclair. If the flare is mild, the early introduction of Atopiclair, a nonfluorinated steroid or a TCI will often quell the flare and eliminate the need to apply a stronger, more risky preparation.

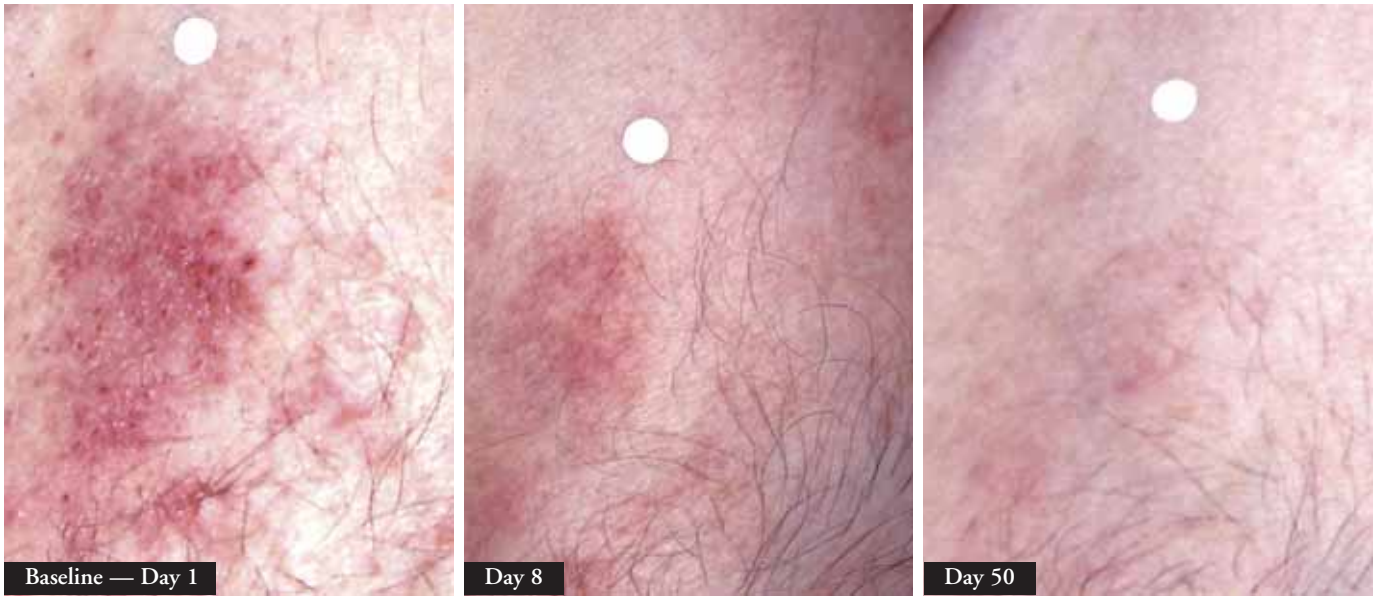
William Abramovits, M.D.: I try to classify each patient into a severity level to determine the best approach to treatment. In general, for very mild cases, I choose a moisturizer and probably Atopiclair. For moderate eczema, I would likely use a combination including Atopiclair, a TCI such as tacrolimus ointment (Protopic) or pimecrolimus cream (Elidel) and, if deemed necessary, a low- to mid-potency steroid, usually to be used briefly and intermittently for more severe eczemas that still would not require phototherapy and systemic interventions.

I'd replace the low- to mid-potency steroid with a high-potency product, but this should not imply that I shy away from starting quite a number of patients on high-potency steroids at our initial encounter. Permutational use of these three categories of topicals is often required, keeping in mind how likely the patient is to comply with a treatment plan if we make it too confusing or burdensome with regard to time and/or cost.

Taking a Tapering Approach

Some physicians prefer to start with a stronger approach and then back off from there, feeling that the patient is better off getting immediate improvement and then dialing down the level of treatment until they find the right level.

W. Philip Werschler, M.D.: If a patient comes in with a flare-up, I always start with the combination of a nonsedating antihistamine and a steroid (sometimes a rather powerful steroid appropriate to the body location). They almost always get better quickly, and when they do, you can start adjusting the treatment. If a patient doesn't get immediate results, which might happen with a less aggressive approach,



Improvement versus baseline with Atopiclair.™*
**Data on file. Chester Valley Pharmaceuticals, Inc., Malvern, PA.*

they're on the phone within a couple of days. The body locations most affected and the age of the patient are important considerations when selecting a treatment approach.

Recognizing the Role of TCIs

TCIs help control inflammation and have reduced the need for long-term use of corticosteroids. When treating mild to moderate cases of AD, most physicians have relied on the use of TCIs for long-term maintenance. Clouding the picture with these medications, however, is the recent FDA issuance of a boxed warning on the prescription patterns for pimecrolimus and tacrolimus. While physicians will continue to prescribe these medications, it's clear that many doctors will want to look for alternatives to treat their patients.

Adelaide A. Hebert, M.D.: We have had success with these drugs in treating patients over the long term. With some patients, we recommend daily application of the medication, or for milder cases, even less frequently. Some patients may even go to an as-needed type program, using the medication when they sense the onset of a flare-up.

Edward F. Ryan Jr., D.O.: I think the boxed warnings for TCIs have impacted pediatrics and primary care more than dermatologists. We tend to use medications off-label, but we should heed some recommendations (e.g., they shouldn't be used in children under 2 years of age, they should be second-line therapy and you should minimize the duration of use).

Keep in mind that these medications are not necessarily automatic home runs. They don't absolutely make whatever inflammatory skin condition you're dealing with go away.

> "We tend to use medications off-label, but we should heed some recommendations (e.g., [TCIs] shouldn't be used in children under 2 years of age)."
>
> — Edward F. Ryan Jr., D.O.

They were initially a steroid-sparing agent. I used to prescribe tacrolimus and pimecrolimus in place of steroids, but I don't anymore. So having an alternative such as Atopiclair, which adds a new layer of treatment, is welcome.

Mark Lebwohl, M.D.: The challenge with steroids is to know which one to use with which patient, and you have to

consider the severity and the part of the body that's affected. You're not going to use a product such as clobetasol on the eyelids most of the time. Non-medical considerations exist as well. For example, if you have a Medicaid patient, then your prescription has to be on the formulary. And if the patient doesn't have insurance, then a generic might be what we would prescribe because it's less expensive.

Dr. Paller: I write 10 different steroids in the course of half a day in the clinic. Given the multiplicity of steroid potencies and possible vehicle bases, I often have to give prescriptions for more than one steroid to the same patient. I would never give a patient a potent steroid to treat the body and then tell them to use it on the face. So you're forced to write prescriptions for two steroids. I traditionally use TCIs as steroid-sparing agents, but have also found Atopiclair helpful for patients who have milder AD. Even if using a single steroid, I might quickly switch the patient to another agent, which allows me to use a stronger steroid initially because I know I'm going to do it for a short period of time.

> "I traditionally use TCIs as steroid-sparing agents, but have also found Atopiclair helpful for patients who have milder AD."
>
> — Amy S. Paller, M.D.

I have so many patients who switch to a generic version when it becomes available and it is not as effective. For example, the generic fluticasone often has not maintained the control that the brand name version did.

Ingredients in the vehicle base of some brands of corticosteroid creams and ointments can irritate the skin or cause allergic contact reactions. Side effects of repeated or long-term use of topical corticosteroids can include thinning of the skin, infections, growth suppression (in children, if potent agents are used chronically) and stretch marks. If topical corticosteroids prove ineffective, then patients may use systemic corticosteroids or other systemically administered immunosuppressants for short periods of time.

I virtually never use systemic corticosteroids to treat AD, even in severe cases. My first choice if topical agents are not helpful is to initiate cyclosporine (Neoral, Sandimmune) therapy. If I do not see improvement after 4 to 6 weeks, I check the trough cyclosporine level, but I will not continue cyclosporine for more than 3 months without seeing a good effect. After that, I taper the medication. I use mycophenolate (CellCept) as my second choice for treating severe disease that's unresponsive to topical agents. I will rarely use systemic corticosteroids if I need to quickly turn someone around who is miserable, so that I can restart topical agents. I make sure, however, that I taper slowly over the course of at least 3 to 4 weeks. A burst of steroid that is discontinued abruptly will almost always lead to rebound, which is often worse than your starting point. The risk in children who use the medication for beyond a month is adrenal suppression and growth reduction. Of the brands of prednisolone, Orapred is the best tasting in that group of horrible-tasting medications.

Dr. Hebert: We've had success with antibiotics, but we have seen so many antibiotic-resistant infections that we have a protocol for diluted bleach baths, which cut down on AD flares tremendously, as well as on our need for antibiotics. The regimen is simple: just put one-eighth of a cup of bleach in a tub of water and soak for 5 to 10 minutes, using a paper cup to dowse the areas that are not immersed. Prevention is helpful for these patients. And if the family ricochets infection off each other, using diluted bleach baths reduces that phenomenon.

Dr. Paller: I agree. We have been using bleach baths for years and they have been tremendous help in not only minimizing the frequency of infections, but also in improving the course of the AD. This observation makes sense, given the known role of *Staphylococcus aureus* in exacerbating AD.

Adding an Antihistamine to the Mix

Although they do not address the disease itself, antihistamines can reduce nighttime scratching by diminishing the level of itching and by inducing drowsiness in patients whose condition is worsened by the scratching. Caution should be

the watchword when administering antihistamines to children because some require a low dose.

Dr. Abramovits: I believe that discriminate use of sedating antihistamines helps to dial down the chronic itch. I often attempt to break the itch-scratch-itch cycle with diphenhydramine (Benadryl), hydroxyzine (Atarax, Vistaril), doxepin (Sinequan) or mirtazapine (Remeron) at bedtime and cetirizine (Zyrtec), if not too sedating, during the day.

Dr. Werschler: While I will use sedating antihistamines to induce drowsiness, if I'm doing long-term antihistamine therapy, I prefer non-sedating histamines such as cetirizine, loratadine (Claritin, Alavert) or fexofenadine (Allegra). Daytime sleep latency studies show that non-sedating histamines don't affect school performance, flying, driving or other related activities, so I'm a big believer in the use of these types of antihistamines.

Dr. Hebert: Because we are a medical center and generally see the worst cases, I've become more of a cyclosporin user. I prescribe oral cyclosporin for 2 weeks, taking care to control skin infections and skin hydration. We then maintain patients with as much cyclosporin as they need, which varies depending on their responsiveness. We've had tremendous success with this regimen.

One real problem is that it can be difficult to get them off of the cyclosporin. Most people respond to cyclosporin, but it may be impossible to stop the drug if the AD is severe. Eventually, you have these patients on a cycle of light therapy, something such as mycophenolate, then cyclosporin. For these patients, the topicals just will not successfully control their degree of dermatitis.

Pearls for Maintaining Healthy Skin

Healing the skin and keeping it healthy are important in preventing further damage and enhancing every patient's quality of life. Developing and adhering to a daily skincare routine is critical to preventing flares.

Dr. Lebwohl: I tell patients that within 1 minute of them getting out of the tub, they need to put on a moisturizer and the medication. But skin care goes beyond what we put on. Patients need to look at things such as humidifiers in the winter and air conditioners in summer to help the skin stay moist and to avoid irritation.

Patients often ask about food as a trigger to the disease. In patients for whom food allergy is a consideration, what they eat should be monitored and their incidence of flares correlated with food intake. If food allergy is suggested by the evidence, patients should simply avoid the foods that seem to cause problems. Unfortunately, with kids this can prove difficult, but parents have to take a role in this.

> "Long-term maintenance is what you need to focus on to keep symptoms under control."
>
> — W. Philip Werschler, M.D.

Dr. Hebert: In my practice, I empower the families to become artists with their treatments, and every single patient is different. There's not one way to manage AD. I think educating your patients and their parents is really key to successful management. You present their options, you say how to use them as guidelines, tell them about the potencies and just explain all you can. My patients have a wide range of disease severity, so for the most part, I administer aggressive treatment initially with tapering levels of medical care. In terms of how long people use certain medications or at what level, that depends on what the patient needs. Fortunately, we now have lots of effective options that we can turn to.

Dr. Werschler: Atopy as a disease state has many different manifestations. Chronic atopics never really get better. They're just bad or worse. And some patients are cyclical. They may be somewhat seasonal, if you get into four-season climates such as those in the Northern tier of the country. So long-term maintenance is what you need to focus on to keep symptoms under control. Empower the family or empower the patient. Having long-term care products such as Atopiclair is an important aspect of that approach. □

Shifting the Landscape

New thinking on the treatment of atopic dermatitis may bring relief to a lifetime of chronic itching and burning.

Atopiclair Nonsteroidal Cream is a new therapeutic approach to safely managing the symptoms of atopic dermatitis (AD). It is safe for patients of all ages, may be used with other topical therapies, and may be used on the face and folds of the skin. Atopiclair is fragrance-free and contains no added dyes. For those who have severe AD, regular use of Atopiclair may reduce the number and severity of acute flare-ups and may significantly reduce the level of topical steroids and/or topical calcineurin inhibitors (TCIs) required to control the acute symptoms. Atopiclair is available by prescription only.

> "You can view Atopiclair as almost a base therapy for AD — something you ought to apply every day to the affected areas."
> — Mark Lebwohl, M.D.

Part of a Regular Regimen

Clinical studies show that Atopiclair's unique combination of ingredients can reduce the itching, burning and pain associated with AD, while helping to restore the normal barrier function of the skin as well as providing essential moisturizers that are critical to the long-term care of this disease. By applying Atopiclair on a regular basis, patients may be able to reduce the level of their disease. For example, moderate dermatitis may become mild or mild dermatitis can become virtually symptom-free. By reducing the severity of the disease and the number of flare-ups, Atopiclair may reduce the dependency on other medications such as a topical steroid or a TCI.

Says Mark Lebwohl, M.D., "You can view Atopiclair as a base therapy for AD — something you ought to apply every day to the affected areas. I think that it has the potential to shift entire dermatitis populations to a lower level of the disease; mild AD sufferers won't get the disease if they use Atopiclair and those who have moderate AD but are also using Atopiclair will now have milder symptoms." He adds, "It's not a replacement for corticosteroids and other therapies, but I think you'll have a portion of patients a little better off with Atopiclair and it should be a part of the regular regimen."

Ideal for Maintenance

Many patients who have mild dermatitis may find that Atopiclair is all that they need as part of their treatment regimen. Most often, patients seek treatment when they're in the middle of a flare. In this case, a common approach would be to establish a course of therapy that addresses the flare while also targeting the root of the problem (a disrupted skin barrier). This may include a topical steroid or a TCI often along with Atopiclair. Once the flares and symptoms are under control, practitioners can often wean the patient off of these agents and, when appropriate, have them continue to use Atopiclair.

"This appears to be an ideal long-term maintenance therapy, not only because it has proven efficacy, but also because there's no age restriction and there's no restriction on the duration of use," comments William Abramovits, M.D. "This may prove to be exactly what you need for a long-term maintenance type of therapy. And the goal is to hopefully prevent these patients from getting into flare-up situations in the future."

Atopiclair should allow patients to reduce the amount of the other medications that they use, which can be important in long-term care. Patients may also benefit from a cost savings if they find that they are using significantly less of a more expensive medication. "If you're really cutting back on your use of steroids or TCIs, then there can be a cost savings for patients," says Adelaide A. Hebert, M.D. "But it is the improvement that the agent brings that is the real benefit. I do think it reduces the need for both the TCIs and the topical steroids. And I think better barrier function of the skin can be achieved. Getting that barrier to work effectively is critical to the success you're going to have in managing AD."

Adding Atopiclair to the Treatment Mix

When using Atopiclair with other topical medications, the order of application may prove important, as it can change the efficacy of either of the medications. Because patients and medications vary, the most effective way to determine the best order of application for two medications is to have the patient apply one medication on one arm and another medication on the other arm. Then have the patient apply the first medication over the second arm, and vice versa. You and the patient can then determine which order works best.

Even though Atopiclair is a steroid-free cream, it should not be viewed as a replacement for steroids because steroids remain the mainstay of therapy. Patients can use Atopiclair in conjunction with steroids, but it should not necessarily replace them.

Says Dr. Lebwohl, "The idea of a product that calms, restores and protects the skin is exciting. The fact that a product has clinical data to support the fact that it calms inflamed skin, itching and erythema, but at the same time addresses the underlying issue of a disrupted skin barrier by replacing key lipids that are missing to protect the patient against future flare-ups, is also exciting." He continues, "Topical steroids, for example, are great at addressing the symptoms and for getting the itch and the inflammation under control, but they don't contribute directly to restoring barrier function. Moisturizers, on the other hand, or your typical barrier repair cream, can replace key lipids and triglycerides and so on, but they often are not proven to provide significant symptom relief. One product that does all of these things at some level is terrific news for our patients."

> "This may prove to be exactly what you need for a long-term maintenance type of therapy."
>
> — William Abramovits, M.D.

"Atopiclair provides a safe and effective addition to TCIs and even to steroids in the treatment of AD," remarks Dr. Lebwohl. □

Pearls for Treating Pediatric Atopic Dermatitis

- **Bathe child in lukewarm water**
- **Apply medications and moisturizers immediately after baths**
- **Limit contact with suspected irritants and allergens**
- **Consider the short-term use of sedating antihistamines to promote sleep and reduce nighttime scratching**
- **Consider the use of non-sedating antihistamines for chronic therapy**
- **File fingernails to reduce injury caused by scratching**
- **Choose clothing made from cotton fabrics**
- **Keep the child cool, minimize activities and environments that induce excessive sweating**
- **Treat skin infections promptly**

A Closer Look at an Up-and-Coming Therapy

Atopiclair provides symptom relief and helps to restore skin barrier function.

When asked to describe their treatment goals for atopic dermatitis (AD), nearly all dermatologists would respond that their primary goals would be to attain patient comfort, stop the itch and prevent future flare-ups. Topical steroids are the mainstay of therapy and are likely to continue in this role. Topical calcineurin inhibitors provide effective relief by reducing irritation and hopefully forestalling the onset of flare-ups. Each of these therapies is effective in some way to treat the symptoms, but many carry a heavy burden of side effects.

Atopiclair Nonsteroidal Cream represents a new level of treatment and care by allowing physicians and patients to more effectively manage the symptoms of AD while also assisting to restore normal skin barrier function. Unlike most topical treatments, Atopiclair relies on a number of ingredients to provide the actions that are effective in relieving the symptoms of AD. Among them is glycyrrhetinic acid (GRA), which provides both anti-inflammatory and anti-pruritic properties. When selecting a topical treatment, physicians need to balance effectiveness and safety. Clinical studies have demonstrated Atopiclair's efficacy and the FDA has granted the product marketing clearance, also endorsing its safety profile.

Proposed Mechanism

In normal skin, cortisol converts to inactive cortisone at a fairly regular rate. In eczematous skin, cortisol converts to inactive cortisone at a significantly higher rate. One enzyme responsible for this conversion is 11ß-hydroxysteroid dehydrogenase. Atopic patients have been shown to have a higher level of this enzyme, which overwhelms their endogenous steroids. If this enzyme can be inhibited, more endogenous steroids can accumulate and activate.

The exact mechanism of action of GRA is unknown. However, the published data that are available support the belief that GRA inhibits the 11ß-hydroxysteroid dehydrogenase enzyme. For example, tests of urine samples from patients who have been treated with 2% topical GRA show a reduction in cortisone byproducts, which demonstrates that the product blocks the production of cortisone.

"By blocking the conversion of cortisol to cortisone, you are increasing the bioavailability of cortisol," explains Edward F. Ryan Jr., D.O. "And that's where the activity of the product comes from. So it's essentially a cortisol metabolism inhibitor. Atopiclair is the first and only entry into this new category." Topical treatments of 2% GRA have been available for years outside of the United States as prescription, nonsteroidal medications, and few incidents of serious side effects have been reported.

Atopiclair's formulation includes two additional key components that target the disrupted skin barrier element of this condition: hyaluronic acid, which offers significant hydrating and moisturizing properties; and essential skin lipids, such as triglycerides and polyunsaturated fatty acids (in the form of shea butter*), which help restore skin barrier function. □

* ***Atopiclair Labeling Caution:*** *Shea butter is a derivative of shea nut oil (not peanut oil). Patients with a known allergy to nuts or nut oils should consult their physician before using this product.*

Results of Clinical Studies

Significant patient improvement demonstrates the effectiveness of Atopiclair.

Two recent, double-blind, vehicle-controlled studies examined the efficacy of Atopiclair; one in the treatment of mild to moderate atopic dermatitis (AD),[1] the other in the treatment of sodium lauryl sulphate-induced irritant contact dermatitis (ICD).[2] Both concluded that Atopiclair may benefit patients suffering from each condition. We'll review the details of these studies.

Atopiclair vs. Vehicle Control Against AD

In this 5-week study, 30 adults patients (in two groups of 15) with mild to moderate AD were enrolled from December 2002 to February 2003. Eligible participants (16 men, 14 women, all Caucasian) included those who had fair or light skin without recent suntan, were 16 years of age or older, had mild to moderate eczema and grading according to Rajka and Langeland's criteria of 3.0 to 7.5 with less than 20% cutaneous involvement. Patients had experienced AD for an average of 13 years and their current episode lasted between 3 and 6 months. Patients receiving topical medications (e.g., antihistamines, corticosteroids, non-steroidal anti-inflammatory drugs) were taken off these medications in a washout period of 7 days before the start of the study, such that no patients were using these medications 7 days before the study or during it.

Patients had an exam at visit 1 (baseline), and completed a demographics questionnaire. They were then randomized to receive Atopiclair or vehicle-only control, according to their order of entry into the study. (Patients, observers and all trial personnel were blinded to which treatment the patients received.) Study participants applied either the vehicle control or Atopiclair for the first time following visit 1 and three times daily thereafter for 21 days. The study investigators examined the patients once again at 8 days (visit 2), 15 days (visit 3) and 22 days (visit 4). They recorded the patients' responses to therapy at each visit. All patients stopped using the cream at visit 4 and were re-examined 2 weeks later at visit 5.

> Patient opinion of Atopiclair on pain and itch was significantly better than the control group and investigators neither observed nor reported adverse events in either patient group.

A Clear Preference

Outcomes for this study included individual measurements of clinical symptoms (e.g., itch score, hours of sleep, the patient's view on how much the cream helped the pain and itch, and whether the patient would choose to use the cream again) and signs: severity of AD (graded according to the Rajka and Langeland criteria), percentage of body area affected and the Eczema Area and Severity Index (EASI) score.

Within the Atopiclair group, investigators saw a general trend of improvement in all clinical outcomes (except for

sleep) from baseline through visits 2, 3 and 4. They noted statistically significant improvements for several of the outcomes (itch score, affected area and the EASI score) between visits 1 and 4. Patients recorded their opinions of their experience at the end of the study.

Of the patients involved in the study, 93% stated that they were likely to use Atopiclair again. In comparison, 67% of the patients from the vehicle control group replied that they would likely use the cream again and 33% said that they "would not" use it again.

Patient opinion of Atopiclair on pain and itch was significantly better than the control group and investigators neither observed nor reported adverse events in either patient group.

Atopiclair vs. Vehicle Control Against ICD

Researchers at the University of California at San Francisco Medical Center assessed the efficacy of Atopiclair versus a vehicle-only control on ICD induced by sodium lauryl sulphate by using visual scores and objective bioengineering techniques.

> In [the ICD] study, Atopiclair demonstrated statistically significant benefit over the vehicle on three clinically meaningful outcomes of irritant contact dermatitis.

Twenty healthy subjects (11 female, 9 male, aged 18 to 65 years) with no obvious skin disease or known history of AD were recruited. Subjects had not used any immunosuppressive medications in the previous 30 days and were willing to refrain from using other topical products on test areas during the study. (Subjects were excluded if pregnant or nursing, had any skin condition that may interfere with evaluation, if allergic or sensitive to any of the ingredients of Atopiclair or if they had used any dermatological drug therapy on the forearm within 7 days.)

Better Effect Shown with Atopiclair

At 48 and 72 hours after starting treatment, the results for Atopiclair were significantly lower, and therefore better, than those for the vehicle control ($p = 0.02, 0.04$) in regard to transepidermal water loss. As for blood flow volume, the mean absolute reduction at 72 hours was 16.4 for Atopiclair, compared with 7.0 for vehicle, representing an improvement of 50% and 25%, respectively. The mean absolute reduction in skin color at 72 hours was 1.7 for Atopiclair, compared with 0.8 for vehicle, representing an improvement of 17.3% and 8.3%, respectively. The values of the visual scores for severity of ICD showed a tendency to be lower for Atopiclair and fell just short of a significant difference 48 and 72 hours after first treatment ($p = 0.057, 0.055$). Few itch magnitude scores were nonzero and no significant treatment difference was found.

In this study, Atopiclair demonstrated statistically significant benefit over the vehicle on three clinically meaningful outcomes of ICD. The study researchers conclude that additional observations with other irritants will clarify the generalizability of these results.

A Definite Role in the Future

The positive results of the two studies reviewed in this article indicate that Atopiclair can play a significant role in managing the symptoms of AD and ICD. In addition, a third study has recently been completed. It further measured the efficacy and safety of Atopiclair Nonsteroidal Cream versus a vehicle cream in 218 adult patients.[3] This U.S. multi-center study has been accepted and is awaiting publication. □

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