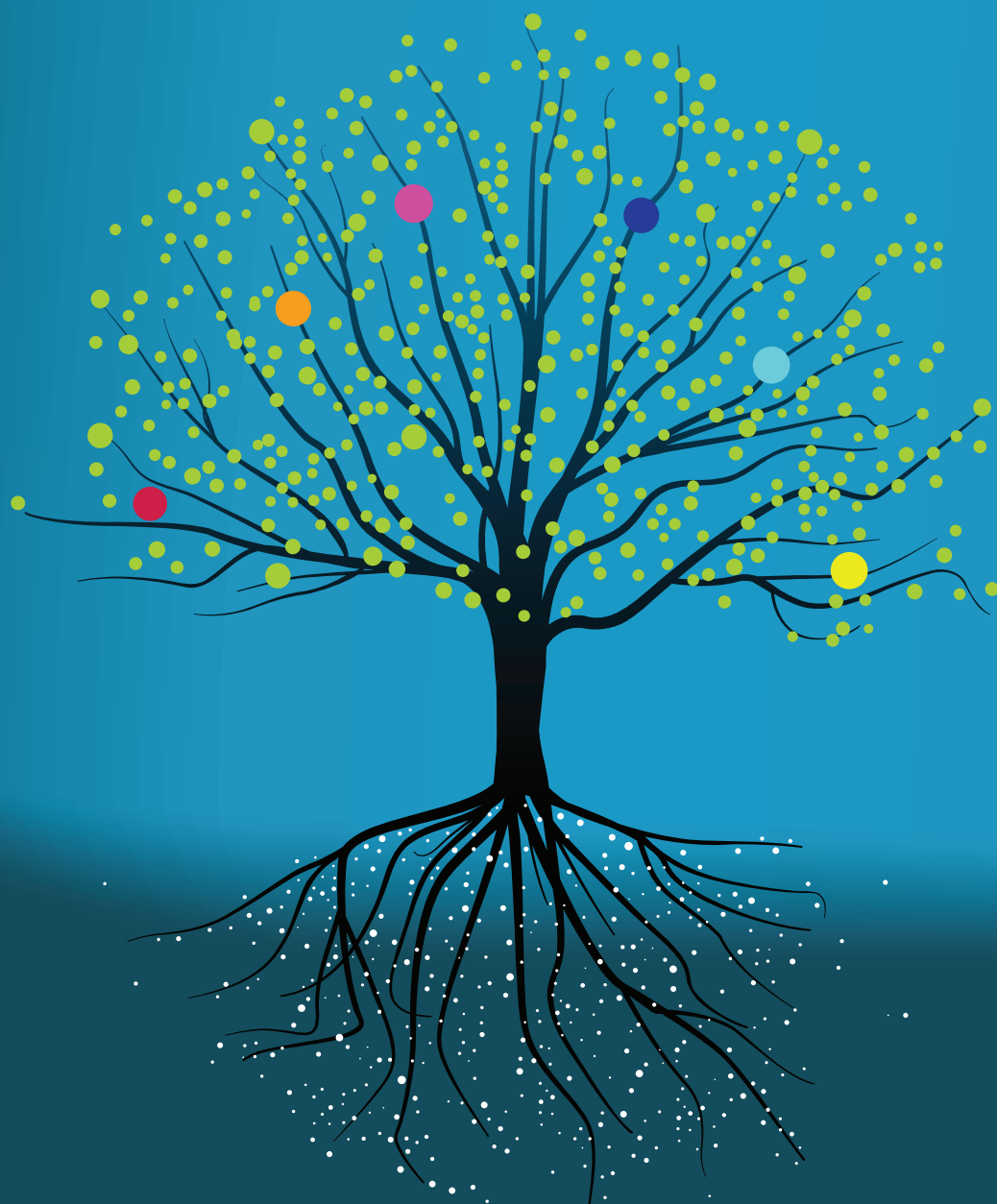


# RIPE FOR THE PICKING

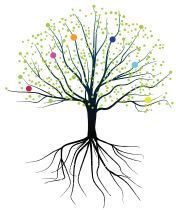
Experts profile the future of biologic treatments



BY **VICTORIA HOUGHTON**, ASSISTANT MANAGING EDITOR

John Harris, MD, PhD, assistant professor of medicine at the University of Massachusetts in the division of dermatology — like many dermatologists — has watched the impressive evolution of treatments for psoriasis over the last decade with anticipation. “We initially had very broad immunosuppressants that were somewhat effective in some patients, but they also had significant side effects,” Dr. Harris said. However, “The onset of biologics and other targeted therapies has been incredible. They’ve revolutionized treatment for psoriasis.” However, while physicians are enthusiastic about the progress of these treatments for psoriasis, there is also hope that interest in developing these innovative therapies is increasingly shifting to other skin conditions. “Pharmaceutical companies have to start looking elsewhere, given how good current psoriasis therapies are,” Dr. Harris said. “The real room for growth is in other diseases.” As psoriasis has paved the way for an interest in developing biologic and other targeted treatments in skin conditions, physicians are anticipating a promising future for these treatments in the following conditions:

- **Atopic dermatitis**
- **Hidradenitis suppurativa**
- **Chronic urticaria**
- **Vitiligo**
- **Dermatomyositis**
- **Alopecia areata** >>



# RIPE FOR THE PICKING

## Atopic dermatitis

According to Lawrence Eichenfield, MD, professor of dermatology and pediatrics at the University of California, San Diego and chief of pediatric and adolescent dermatology at Rady Children's Hospital, we are on the cusp of a new biologic age for the treatment of atopic dermatitis (AD). "The situation for atopic dermatitis today parallels where psoriasis was 10 to 15 years ago. There is an explosion of new studies, medications, and biologics, and increasing knowledge of the immunologic basis of the disease and how the immunology can be mediated," Dr. Eichenfield said. "In a way, we are just getting going with atopic dermatitis, as the early psoriasis-focused biologics had minimal efficacy on AD, and we are just now getting agents designed to work for AD. Also, it is now recognized that a subset of patients with AD have severe disease, and that the impact of the AD, including comorbidities and quality of life impact, is tremendous." Roughly 10 to 20 percent of children and 1 to 3 percent of adults throughout the world have AD.

Treatment for AD often consists of systemic immunosuppressive therapies, such as cyclosporine (CsA), when topical anti-inflammatories and phototherapy aren't enough. "The therapeutic schema is quite poor right now — phototherapy, cyclosporine and other immunosuppressants, and topical and oral steroids — this is what was available for psoriasis 15 years ago, only in psoriasis there was an impressive therapeutic development in the last decade, while in AD it only started," said Emma Guttman-Yassky, MD, PhD, director of the center for excellence in eczema and laboratory for inflammatory skin diseases at Mount Sinai Hospital in New York. "Most moderate-to-severe patients are not well controlled long term with currently available treatments." In fact, a study published in the *Acta Dermato-Venereologica* journal has shown that while CsA is effective in treating severe cases of AD, long-term use of the immunosuppressive therapy is a cause for concern with several adverse effects such as hypertension, kidney disease or damage, and skin and other cancers (*Acta Derm Venereol* 2007; 87:100-11).

Researchers are intrigued, however, by what they are learning from the use of immunosuppressants as a treatment for the condition. In 2014, Dr. Guttman-Yassky and her colleagues published a study that looked at how well CsA controlled the immunologic changes that could affect the disease's pathogenic characteristics (*JACI* 2014;

133; 6:1626-34). The study showed that by blocking the immune pathways with CsA, the molecular abnormalities with AD skin barrier genes, such as filaggrin and loricrin, normalized. "It became clear through research that atopic dermatitis has immune abnormalities and these can be normalized with broad immune-targeting treatment such as CsA," Dr. Guttman-Yassky said. "That pointed toward a primary immune hypothesis for atopic dermatitis and that immune hypothesis was cemented with the first biologic treatment for atopic dermatitis, which is dupilumab."

Dupilumab — developed by Regeneron Pharmaceuticals and Sanofi — is a monoclonal antibody that blocks the signaling from interleukin (IL)-4 and IL-13 — cytokines that are responsible for the Th2 immune response to inflammation which, according to Dr. Guttman-Yassky, is a likely pathogenic pathway for AD. "It's very clear that Th2 and this IL-4 receptor are important." A study published by Dr. Guttman-Yassky's group in the *Journal of Allergy and Clinical Immunology* found that AD was reversed after only four weeks of dupilumab treatment, showing a dose effect molecular and histologic response, with associate clinical responses (*JACI* 2014; 134; 6:1293-1300). But while it appears that the IL-4/IL-13 pathway is pathogenic, Dr. Guttman-Yassky says that there are other pathways that could play a role in the condition. "In atopic dermatitis, we are still deciphering the pathways — Th22 and maybe even IL-23 and IL-17. Clinical trials that we are now conducting and others are required to determine the role of these cytokine pathways to AD. There are no good mouse models for atopic dermatitis and the only way you learn is through these targeted treatments to see if it works and which pathways it shuts off in tissues."

Dupilumab is now in the third phase of clinical trials and continues to prove a likely candidate for the treatment of AD. "Dupilumab is the agent that is the most far along in its development and progress. This has been studied in adults and has shown excellent efficacy so far with a good safety record," Dr. Eichenfield said. However, dupilumab has only been tested in adults and according to Dr. Eichenfield, pediatric trials in the United States will hopefully begin within the next year. "It's really an exciting time," Dr. Guttman-Yassky said. "I feel that we are actually living history and I feel very fortunate to be a part of this therapeutic development in atopic dermatitis."

### Hidradenitis suppurativa

Hidradenitis suppurativa (HS) has been a mystery ailment for many years. “The disease has been hidden in many ways,” said Alexa B. Kimball, MD, MPH, professor of dermatology at Harvard Medical School and medical director for the Massachusetts General Physicians Organization. “Patients experience a delay in diagnosis and may not have been promptly referred to physicians with appropriate expertise.”

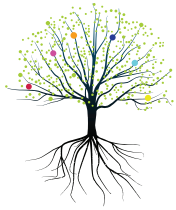
Treatments for this condition vary from antibiotics, to bleach baths, to corticosteroid injections. However, the results of these off-label treatments are inconsistent and often not effective enough. “It’s a tough disease to treat. Even our best therapies have limitations and often have to be combined,” Dr. Kimball said. The disease may affect as much as 1 to 4 percent of the population — mostly women between the ages of 11 and 55— and has been gaining attention because it often leaves patients embarrassed, depressed, and in some cases with suicidal ideation. The painful boils that develop in sensitive areas of the body such as the underarm and genital areas can rupture, leaving foul-smelling pus and sometimes blood on the patient’s clothing. As such, Dr. Kimball is encouraged by the increased focus the disease has garnered. “There certainly has been a surge of interest in HS, with substantial increases in the number of publications around the epidemiology, comorbidities, and therapeutic approaches. It makes me optimistic about the future for these patients.”

While researchers are still unsure of the disease’s pathogenesis, they are starting to hone in on the imbalances that play a role in the prevalence of HS. Researchers discovered that tumor necrosis factor (TNF-alpha) cytokines that regulate pro-inflammatory responses could be the likely culprit. In a study published in the *British Journal of Dermatology* in 2011 (*BJD*; 2011; 164; 6:1292-8), both lesional and normal skin in HS patients were tested against healthy skin samples. The tests found significantly elevated levels of TNF-alpha cytokines in the HS sample cultures. Additionally, the study showed a positive correlation between the TNF-alpha levels and the disease severity.

Thus, these studies indicate that blocking the elevated levels of TNF-alpha in HS patients could suppress the condition by easing the inflammatory response.

A TNF-alpha inhibitor that has undergone extensive testing for HS treatment is adalimumab (Humira®) — a biologic antibody. Subsequently, with this discovery, questions remained: how much and how often? “There was preliminary information about the use of TNF-alpha agents in the literature, but the key was to figure out the right dose and duration of therapy and develop the right scoring systems to be able to detect the effectiveness of therapies.” Dr. Kimball and her colleagues set out to test the dosage and duration of treatment with this biologic. As a result, according to recent data from two phase 3 trials of the drug, 43 percent of patients saw at least a 50 percent decrease in the number of HS abscesses and nodules when treated with 40 mg of adalimumab a week. “We were delighted to present the results from phase 3 studies testing adalimumab in HS — which showed a statistically significant improvement in the weekly treated group over placebo. It also improved pain and treated patients had fewer flares,” Dr. Kimball said.

And in terms of adverse side effects, “The safety profile of adalimumab has been well characterized over the development of the several indications for which it is FDA approved, including psoriasis and psoriatic arthritis. We didn’t note any new safety signals in the phase 2 or phase 3 studies.” Adalimumab is not approved for use in HS patients in the U.S. yet. However, in June the European Medicines Agency recommended that the EU authorize the drug as approved for use in adults who suffer from moderate to severe HS and have not responded to first-line systemic treatments. Clearly, the progress of adalimumab appears promising for HS patients, but Dr. Kimball believes there is more work to be done. “We are still working on the pathogenesis of the disease,” Dr. Kimball said. However, “As all of these avenues of inquiry mature, I am confident we will see real progress.”



# RIPE FOR THE PICKING

## Chronic urticaria

Gil Yosipovitch, MD, remembers a patient who was willing to try anything to relieve her chronic urticaria symptoms. “She was taking all the immunosuppressants that you could think of — sulfasalazine, cyclosporine, cellcept, and IVIg — and she was miserable. But, nothing we gave her helped.” Dr. Yosipovitch is chair of the department of dermatology and directs the Temple Itch Center at Temple University Hospital, and has seen no shortage of chronic urticaria patients seeking relief from the itchy hives that last six weeks or more and often reoccur several times a year. “This is a horrible disease,” Dr. Yosipovitch said. “People might say, ‘okay, big deal, you have a rash,’ but it is not so fun at all to have these rashes that are unpredictable.”

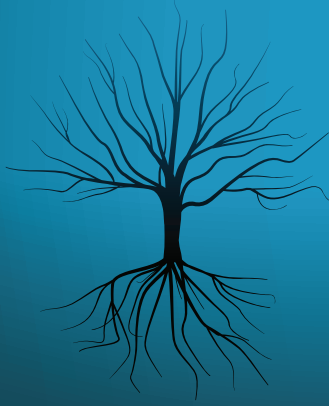
In addition to treatment through immunosuppressants, historically, treatments for chronic urticaria have included high doses of antihistamines as well as small injections of leukotriene receptor antagonists — often used for the treatment of asthma — but these yield inconsistent results. “The literature says that you give patients an antihistamine and it works well as long as the patients take it. This is not correct,” Dr. Yosipovitch said. “Many patients use antihistamines as directed and it just doesn’t work anymore. I’m not saying antihistamines do not work for urticaria, but in many chronic urticaria cases it just doesn’t yield results.” Consequently, the development of an effective biologic treatment for chronic urticaria has been a welcome change for the almost 2 percent of the adult population and up to 0.3 percent of children who are suffering from this condition (*World Allergy Organization Journal*; 2014; 7:31).

Given that these treatments and the symptoms associated with chronic urticaria fell in the allergen department, researchers have focused on the antibodies responsible for the release of histamines with chronic urticaria patients. A 2010 study published in the *International Archives of Allergy and Immunology* (*Int Arch Allergy Immunol*; 2010; 153; 3: 288-93) showed

that patients with chronic urticaria have elevated immunoglobulin E (IgE) levels — the level of which increased with the severity of the disease. “It’s clear that IgE antibodies were involved and IgE itself was a factor in inducing urticaria,” Dr. Yosipovitch said. The IgE antibody is responsible for the release of histamines when an allergen appears — and consequently, the symptoms associated with allergic reactions.

Thus, researchers turned to a biologic agent commonly used for the treatment of asthma to see if it would work in chronic urticaria patients: omalizumab (Xolair). “It has been an asthma treatment for quite a while and has been on the market quite a long time,” Dr. Yosipovitch said. “The idea was, let’s see if we can target with an antibody and reduce the IgE levels. In fact, it worked well. I think that this is the most exciting drug for urticaria that we’ve seen in the last decade.” In 2013, treatment for chronic urticaria hit a milestone when results from clinical trials showed that chronic urticaria patients who were injected with 150 mg and 300 mg of omalizumab every four weeks experienced a reduction in itching by 57 and 71 percent respectively, while a placebo group experienced a 37 percent reduction in itching (*N Engl J Med* 2013; 368:924-935).

Shortly thereafter, the FDA approved the use of omalizumab for patients with chronic urticaria. “This has really changed the landscape for many patients who have retractable chronic hives. Clearly, those patients who do not respond to conventional first-line treatments of high-dose antihistamines should not waste time and should get the treatment that works for them,” Dr. Yosipovitch said. However, “It’s important that we don’t give it to patients who don’t need treatment. It’s not a first line and it’s very costly.” Going forward, Dr. Yosipovitch remains cautiously optimistic about this biologic treatment for chronic urticaria patients. “I have to admit that with any biologic, my main concern is: Are there potential safety issues for the long term? But, so far so good. We don’t see any problems in terms of adverse effects. We’ve always respected the biologics — long-term use may cause adverse effects like any new drug in the field, but I feel comfortable at this stage.”



# Biologic barriers

The development of biologic treatments for various skin-related diseases has made promising strides over the last several years. However, dermatologists can cite several roadblocks related to the speed at which they're developed, as well as the availability of the treatments once they are approved for use.



**Awareness:** Dermatologists who work closely with patients suffering from vitiligo and atopic dermatitis will argue that while the conditions are not life-threatening, the side effects that these patients experience are debilitating enough to warrant an increased focus on the development of treatments. "Vitiligo patients have 10 percent or more of their body surface area covered," said John Harris, MD, PhD, assistant professor of medicine at the University of Massachusetts in the division of dermatology. "These patients are walking around with these big white spots. If their quality of life is impaired, there's no reason why they shouldn't be treated and given relief." Additionally, Gil Yosipovitch, MD, who leads the Temple Itch Center at Temple University Hospital, reasons that for many conditions, there are no foundations lobbying on those patients' behalf. "There is no society for hives patients," Dr. Yosipovitch said. Yet, "These groups are extremely important in the development of drugs. They go to legislators. They put on the front page of their newspapers that patients want better treatment. There's importance in that type of approach." (To learn more about how patient advocates are having an impact on drug development, read DW's recent feature on them at [www.aad.org/dw/monthly/2015/june/a-powerful-voice](http://www.aad.org/dw/monthly/2015/june/a-powerful-voice).)

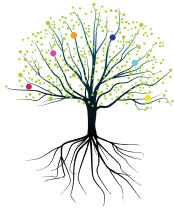


**Lack of specialty focus:** Some diseases do not have a logical home in terms of specialty care because they include multiple symptoms that can involve various systems, and therefore, various specialties. Dermatomyositis, a condition marked by skin rashes and muscle weakness, includes a subset of predominantly cutaneous patients who are often left out of clinical trials and studies. "A lot of the patients who have been targeted for studies have been more muscle-predominant patients," said Victoria Werth, MD, chief of dermatology at the Philadelphia Veteran's Administration Hospital. Additionally, when the cause of certain symptoms is unknown, dermatologic care might get overlooked. "I see quite a lot of chronic urticaria," Dr. Yosipovitch said. However, "A lot of dermatologists don't see it so much because a lot of it goes to allergists."



**Cost of treatments:** Regardless of whether or not new biologic treatments are developed and approved for use for dermatologic conditions, the exorbitant price tag for these therapies often leaves many patients without access. As such, dermatologists often find themselves battling with insurance companies on their patients' behalf. In some cases, insurance companies have instituted step therapy, or drug tiering, systems that require patients to fail less-expensive drugs before moving to a more expensive biologic. "Medications and biologics are costly and no one is arguing that," Dr. Yosipovitch said. "However, to prevent doctors — who are well-trained and have a lot of experience in the field — from giving medications to patients who do require it, it's very saddening."





# RIPE FOR THE PICKING

## Vitiligo

John Harris, MD, PhD, director of the Vitiligo Clinic and Research Center at the University of Massachusetts, frequently travels throughout the world speaking to physicians and scientists about the progress of targeted treatments for vitiligo. “Everywhere I go people approach me and say, ‘I hope you’re successful soon because I really need something to offer my patients.’” These patients are among the millions of people worldwide who have vitiligo — a condition that causes depigmentation of the skin, hair, and mucous membranes. Almost half of these patients develop the condition before the age of 20, and will likely live with the condition for the rest of their lives. “Patients are devastated by this,” Dr. Harris said. “If you look at quality-of-life studies in vitiligo patients, they are just as impacted as patients with psoriasis and atopic dermatitis. There’s no reason we shouldn’t be treating them. The big barrier was that we just did not know how. But I think we have that now.”

Dr. Harris had to work backwards to determine the pathway responsible for vitiligo. In 2012, Dr. Harris et al. developed a mouse model, alongside using human tissues, through the transfer of melanocyte-specific CD8+ T cells — the T cells responsible for depigmentation — into mice with black skin and hair. The mice not only developed depigmentation in the skin in four to five weeks after the treatment, but similar to humans, they also had increased production of interferon (IFN) gamma in their skin (*Science Transl Med* 2014; 6:223, *J Invest Dermatol* 2012; 132(7):1869-76). “Our studies show that interferon gamma is the primary cytokine pathway activated in vitiligo, suggesting that targeting just this pathway could be an effective treatment strategy” Dr. Harris said. “So from there, our next question was: what is interferon gamma doing? Can we figure out what’s downstream?”

Using antibodies, the researchers neutralized IFN-gamma in the mouse model and discovered that the T cells couldn’t get into the skin to cause the disease. “So that gave us a hint that it was a skin-homing chemokine that was really what was important.” Those highly induced chemokines — according to Dr. Harris’s research — were CXCL9

and CXCL10. “If we got rid of CXCL10 or used an antibody to shut it off, we could both prevent and reverse established disease in mice,” Dr. Harris said. Ultimately, “If you block interferon gamma, or CXCL10, or the CXCL10 receptor, or if you knock out components of the signaling pathway — the signaling between interferon gamma and CXCL10 — then you can shut off the disease. IFN-G, the IFN-G receptor, JAK 1, JAK 2, Stat 1, CXCL10, and CXCR3 (the CXCL10 receptor) — those are the components of the pathway.”

Fortunately, according to Dr. Harris, biologic and other targeted therapies for vitiligo may already be sitting on the shelves collecting dust. “We’re now talking to a lot of pharmaceutical companies who already have drugs that target the pathway.” According to Dr. Harris, fontolizumab — an IFN-gamma antibody that failed treatment in psoriasis — could be an excellent candidate for vitiligo treatments. “There are also companies that have CXCL10 antibodies that were tested in Crohn’s disease and were not effective, so they gave up on them.” Additionally, dermatologists are starting to look at current therapies that can target one of the signaling components between IFN-gamma and CXCL10. A June 24 case study published in *JAMA Dermatology* showed that treatment with oral tofacitinib citrate (Xeljanz) — an FDA-approved treatment for rheumatoid arthritis — demonstrated partial repigmentation in a vitiligo patient (*JAMA Dermatol* 2015;1520). Tofacitinib is a JAK 1/3 inhibitor — and JAK1 is an important signaling component for the IFN gamma pathway.

Consequently, Dr. Harris is confident that with a little more nudging, pharmaceutical companies will dust these therapies off and start focusing on vitiligo patients. “If we can help the company to realize that there is a very likely possibility that they already have the first effective drugs for these diseases, and that there’s a huge potential for profit there, they may make the effort,” Dr. Harris said. “The benefit is that a lot of these companies have already put up the costs of developing the drug, and all they have to do is pull it back off the shelf and test it. I think it’s all coming together. It’s about to explode and it’s very exciting.”

## Dermatomyositis

Perhaps some of the most complex skin-related conditions to develop biologic treatments for are those that may also involve other organs. Dermatomyositis — a muscle disease that causes muscle weakness and often a skin rash — is one of those conditions. “A lot of the patients who have been targeted for studies have been more muscle-predominant patients,” said Victoria Werth, MD, chief of dermatology at the Corporal Michael J. Crescenz Veteran’s Administration Medical Center (Philadelphia) and professor of dermatology at the Hospital of the University of Pennsylvania and the Veteran’s Administration Medical Center. “Half of dermatomyositis patients in my practice have skin-predominant diseases, but it’s maybe overall 20 percent. That’s a population that really hasn’t been targeted or studied therapeutically.”

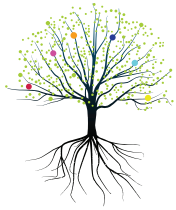
Current treatments for the cutaneous effects of dermatomyositis have typically involved first-line topical treatments such as anti-pruritics or corticosteroids, to more powerful treatments such as antimalarials, immunosuppressants, and sometimes systemic corticosteroids. However, as researchers learn more about the disease, the inflammatory pathways are becoming clearer, paving the way for the development of a biologic treatment for the skin-predominant cases. “There is some work that has shown that interferons are important in dermatomyositis,” Dr. Werth said. “There are companies that have been developing treatments against the inflammatory cytokine because of the fact that there are interferon signatures in the blood and the skin.” As such, according to Dr. Werth, targeting the interferon or the interferon receptor would be an obvious starting point for the development of biologic treatments. “This is very much a T-cell-driven disease. The different dendritic cells — plasmacytoid dendritic cells (pDCs) — produce interferons that then stimulate T cells. There has been work done with an antibody against interferon in dermatomyositis.” However, “That data has not been published.” There is also an ongoing NIH-funded clinical trial of an oral, synthetic, preferential cannabinoid receptor type 2 agonist, JBT-101, that Dr. Werth’s group has shown inhibits both TNF $\alpha$  and IFN $\alpha$  production by stimulated and unstimulated peripheral blood mononuclear cells from patients with

dermatomyositis (*J Invest Dermatol* 135:S10, 2015). This is the first randomized controlled trial in patients with skin-predominant dermatomyositis.

Another roadblock that Dr. Werth and her colleagues are working to overcome is determining disease severity for patients who have cutaneous dermatomyositis and methods for measuring improvements. “The skin is a really visible organ that in some ways can be measured fairly objectively,” Dr. Werth said. However, “There really wasn’t a way to measure the skin disease in dermatomyositis until recently when we developed an outcome disease severity tool called the CDASI (Cutaneous Dermatomyositis Disease Area and Severity Index).” So far, the CDASI has proven valid. “We’ve done a number of validation studies to try to show that there’s good inter-rater and intra-rater reliability (*J Invest Dermatol* 2012; 132(4):1117-724). CDASI has been evaluated for responsiveness and also correlation with quality of life.” Results from Dr. Werth’s studies have been accepted for publication in the *British Journal of Dermatology* (DOI: 10.1111/bjd.13915).

Dr. Werth is fairly confident that the CDASI will become a useful index for determining severity and improvements in skin-dominant dermatomyositis. However, she acknowledges that there is still a long way to go in developing biologic treatments for this disease — particularly if dermatologists are not involved in developing a therapy for the cutaneous side of dermatomyositis. “We need to embrace that this is something that we consider to be a part of our field and that we can contribute to the growing body of evidence for potentially new therapy,” Dr. Werth said. “If we don’t enroll our patients in trials or if trials are designed in a way where our patients are excluded, then our patients who need new treatments may be excluded from using those new treatments.” Additionally, although the condition is not life-threatening, Dr. Werth argues that given the disease’s enormous impact on quality of life, there is an urgent need for effective treatments. “Patients can’t go outside because they have a photosensitivity or because they have social problems associated with having an inflammatory skin disease,” Dr. Werth said. “That can really impact their participation in society so there needs to be awareness that this is really important and we do need better treatment for patients.”





# RIPE FOR THE PICKING

## Alopecia areata

According to Dr. Guttman-Yassky, the availability of comprehensive and specific treatment options for the 147 million people who suffer from alopecia areata worldwide has been nonexistent. The disease — which affects 6.6 million Americans — is marked by hair loss on the scalp (patchy alopecia or alopecia totalis involving the whole scalp), as well as other areas of the body where hair grows (alopecia universalis, when all body hair is lost). “You can imagine that alopecia areata causes tremendous emotional and psychological distress to both patients and families — both men and women,” Dr. Guttman-Yassky said. “They are devastated by the loss of hair.”

Unfortunately, according to Dr. Guttman-Yassky, the treatment options for this condition not only cause significant side effects, but they have limited efficacy because they do not specifically target the pathogenic components of the disease. “Currently, we have a very poor treatment scenario for alopecia areata,” Dr. Guttman-Yassky said. “We use intralesional steroids that are very painful and can cause scalp atrophy, and frankly, they are less efficient. We also have topical sensitizers such as the DPCP [diphencyprone] and they cause allergic reactions and pain, and have limited efficacy.” Patients are also sometimes treated with CsA which is not approved for alopecia areata in the United States and has multiple side effects. Additionally, “There are also few clinical trials with oral JAK inhibitors that are also broad, not specific immunosuppressants. When immune suppressants are stopped, patients often shed their hair, making a safe, long-term solution for patients highly desirable.”

Fortunately, researchers are getting closer to pinpointing the specific components and pathways that cause this disease. In a study published online in the August issue of the *Journal of Allergy and Clinical Immunology*, Dr. Guttman-Yassky and her colleagues conducted molecular profiling of 27 alopecia areata

patients and six controlled subjects. “Our data associated the molecular signature of alopecia areata not only with a high inflammatory profile but also with inflammatory cytokine pathways beyond Th1,” Dr. Guttman-Yassky said. The profiles indicated highly elevated levels of IL-13 and IL-23 cytokines and PDE4 in alopecia areata patients, compared to the non-lesional scalps of alopecia patients as well as the normal scalps. “We started to think that maybe some of the treatments that are now available for treatment of psoriasis or that are being studied for atopic dermatitis can potentially be considered for alopecia areata.” These include treatments targeting Th2 responses which are currently being studied for eczema patients (biologic therapies that block the signaling from the Th2 cytokines), PDE4 antagonists (apremilast), or IL-23 p40 or IL-23 p19 antagonists. The latter are either approved or in late phase clinical trials for psoriasis and/or AD. “Our study suggests that alopecia areata, like the other two diseases, might be targeted by specific treatments.”

However, without clear proof of which pathway is causing the disease, Dr. Guttman-Yassky says it is too soon to make any definitive declarations about which biologic treatment might work for alopecia areata. “Only clinical trials with targeted immune antagonists and small molecules will be able to dissect which one of the cytokine pathways is pathogenic for alopecia areata and it might be more than one. I think the good thing about it is that it opens the door for specific therapeutic targeting for clinical trials for specific targets. Only these will be able to map out the disease to understand which one is pathogenic. I am happy that my group at Mount Sinai will be starting several large trials with biologic therapies and small molecules to test the contribution of these pathways to alopecia areata.” These studies, all coupled with mechanistic studies, will be able to shed light into the disease pathogenesis and hopefully help bring effective treatment with a good safety profile to patients in need. *dw*