Insights into the pathogenesis and pathology of rosacea have established the condition as having varying subtypes. However, many patients with rosacea have features that overlap more than one subtype, experts say. Tailoring treatment options based on individual patient features is ideal to optimize outcomes, one expert says in context of an updated report on the available management options.
ARTIFICIAL INTELLIGENCE is an assistive tool that could present opportunities for physicians to streamline such activities as collecting patient data, processing and analyzing diagnostic tests, and monitoring patients, among other tasks. While some have had concerns about the use of AI, many experts say incorporating intelligent technology into practice can improve the physician’s efficiency and enhance patient care. However, some experts say, the implementation of AI has been hindered by a lack of standards around imaging. The International Skin Imaging Collaboration (ISIC), which was organized in 2013, is addressing this obstacle in its effort to move the field forward and to bring AI into dermatology practice. Now, a working group is continuing to publish consensus standards pertaining to terminology that relates to diagnosis, dermoscopic features, anatomic site and more. The group is also working on developing an image archive that can be used to train algorithms (p. 33).

This idea for training algorithms has been applied in both skin cancer and acne, where researchers have shown the capability of AI-based recognition of melanoma (p. 1), as well as in identifying acne lesion severity (p. 10). In acne, researchers have examined the use of an algorithm at measuring the severity of acne lesions as well as whether smartphone images offer the appropriate sensitivity for grading acne severity among patients with darker Fitzpatrick skin types (p. 12). According to the investigators of these trials, the implementation of such technology in the long-term management and follow-up of patients with acne appears effective and may help to improve patient treatment outcomes.

Looking ahead, one expert predicts that wide-scale implementation of deep learning algorithms and AI could become a reality within the next five years. However, she emphasizes, AI will not replace the human side of medicine.
I REQUESTED MY EMPLOYEES NOT WEAR MASKS

Will I be cited by OSHA?
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Although several employees wanted to wear masks, ... their state governor and city mayor did not require their use.”

Will OSHA cite me for requesting employees not wear masks?

by DAVID J. GOLDBERG, M.D., J.D.

Dr. Goldberg is director of Skin Laser and Surgery Specialists of New York and New Jersey, past director of Mohs and Laser Research, Icahn School of Medicine at Mt. Sinai; and, adjunct professor of law, Fordham Law School in New York City.

Dr. Covid has a 20-year highly successful dermatology practice, which, like many in the United States, shut its doors in early March. He felt quite fortunate that he lived in a state that “opened” early.

By May, he was back to being as busy as ever. His state guidelines do not require the use of protective masks in his office setting. So he has asked his staff not to scare his patients by wearing masks due to his high-end practice. While several employees wanted to wear masks, Dr. Covid reminded them that their state governor and city mayor did not require their use.

Soon after resuming practice, one of his employees became infected with COVID-19. Contact tracing showed the employee likely became infected from a patient. The employee quit her job and put Dr. Covid on notice that she will sue him over his policies.

The employee sought advice from friends, one of which is a healthcare expert who advised her to file a complaint with the Occupational Safety and Health Administration (OSHA). She let Dr. Covid know that she has done this, and he contacted his medical malpractice carrier to ask about his coverage for such a lawsuit. He found out that his general liability insurance company and is informed that alleged OSHA violations are also not covered under this policy. Dr. Covid hires an attorney. Is OSHA likely to come after him?

The reality is that OSHA, which is the federal agency meant to protect employees has mostly not inserted itself in COVID-19 employee-related issues. As the number of infections continues to climb, OSHA has not provided any clear directions to employers.

The New York Times published an opinion in June, which noted that courts have not offered relief to workers.1 In fact, the article states, “the U.S. Court of Appeals for the District of Columbia [recently] dismissed a lawsuit by the AFL-CIO that would have compelled OSHA to issue emergency rules for worker protection, saying the agency can determine its own standards.” The result of this statement, the article states is that millions of employees are working under a variety of conditions – some more hazardous than others.

Even when OSHA has received credible complaints of unsafe conditions, thus far, OSHA has failed to act, the New York Times states. For example, the article cites an incident in which workers at a Nebraska beef processing plant alleged that they were not able to social distance during lunch-time or in locker rooms “despite a number of positive COVID-19 cases.” OSHA did not inspect the site and did not issue any citations; yet, hundreds of workers became infected with the virus. In fact, according to the New York Times, OSHA has, thus far, received over 5,000 complaints related to the coronavirus since the earliest days of the pandemic. However, the organization has issued only one citation, which was to a Georgia nursing home for failing to file the required report employees hospitalized with COVID-19 within 24 hours.

Of note, “even before the pandemic, OSHA has always been too overwhelmed to meet its mandate,” the New York Times states. There are just not enough inspectors to cover the United States. In fact, it has about 200 fewer than were employed in 1975, the article states.

One may question the wisdom of Dr. Covid’s decision not to have staff wear masks during the pandemic. However, it is not likely that he will be cited by OSHA.

Reference

The claim ‘paraben-free’ may actually mean the product is less safe.

How safe are cosmetics?

by ZOE DIANA DRAELOS, M.D.

Dr. Draelos is a consulting professor of dermatology, Duke University School of Medicine, Durham, NC.

Q. Are preservatives in my cosmetics killing me?

The simple answer is “no.” Preservatives are functioning to protect from infection, which may actually be prolonging your life! Yet, it may be worthwhile to take a deeper dive into the role of preservatives in cosmetics.

The most commonly used preservatives in cosmetics are parabens. The incidence of allergic and irritant contact dermatitis due to parabens is extremely low and they are highly effective at killing bacterial contaminants at low concentration.

Lately, many cosmetics contain labels that state they are paraben-free. I find this to be an interesting and clever marketing ploy. The cosmetics industry thrives on new products, new formulations, and new packaging. If you have nothing new to put into your product, you can make it appear new by eliminating an ingredient and replacing it with something else. This is exactly what is happening in the preservative realm.

Many products are eliminating paraben preservatives and replacing them with Kathon-CG, also known as methychloroisothiazolinone. The Kathons are effective preservatives, but they do not have as clean a safety record as parabens. There is a much higher incidence of allergic contact dermatitis, so much so that this category of preservatives is only allowed in rinse off products in the EU, such as hair shampoos and conditioners. The claim “paraben-free” may actually mean the product is less safe.

If the cosmetic product contains water and is not refrigerated, it must contain a preservative. Preservatives are necessary to prevent bacterial growth in water-containing products. The cosmetic products are not designed for ingestion and should not be placed in open wounds where absorption may be enhanced. In general, preservatives in cosmetics are very safe and should not be a source of concern.

Q. Are my cosmetics saving me from skin pollution damage?

Many cosmetics are now claiming to protect from environmental damage and pollution. Is this possible? The answer is “yes,” but some explanation is required. Air pollution is composed of tiny highly reactive nanoparticles produced during the combustion process. Combustion occurs during burning and may arise from the burning of gasoline in a car engine, the burning of coal to run power plants, the burning of garbage in an incinerator, the burning of trees in a forest fire, etc.

These nanoparticles land on the skin and produce reactive oxygen species that damage the skin by perforating dermal collagen and elastin fibers. If the nanoparticle is not allowed to touch the skin, the reactive oxygen species are not formed and no damage occurs.

Most facial foundations and moisturizers placed a thin layer of an oily occlusive substance over the skin’s surface. This may be a layer of dimethicone, mineral oil, shea butter, etc. The nanoparticles reside on top of the film unable to penetrate and never touch the skin, thus preventing skin damage. So, yes. It is possible to prevent skin damage from pollution, but any film-forming product will accomplish this goal.

Some cosmetic formulations contain additional antioxidants and claim these ingredients provide skin pollution protection. An antioxidant is a substance able to donate an electron to a reactive oxygen species. Such substances include Vitamin C, Vitamin E, Vitamin A, green tea catechins, resveratrol, etc. While these antioxidants could donate an electron to a reactive oxygen species created when a nanoparticle lands on naked skin, there are many other oxidative insults, such as sun exposure, that are occurring simultaneously. Antioxidants are rapidly consumed on the skin when sun exposure occurs. The challenge is to be sure enough antioxidants are present! Physically trapping the nanoparticles seems to be a more viable mechanism for cosmetic skin pollution protection than chemical antioxidants.
WE WILL CHALLENGE THE STATUS QUO.
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”This is the first validated AI algorithm which … provides a fast determination of the severity of acne and identifies the different lesion types, thus supporting the early therapeutic management of acne patients.”

Sophie Seité, Ph.D.
La Roche-Posay Dermatological Laboratories, Levallois-Perret, France

AI algorithm effectively evaluates acne severity

ILYA PETROU, M.D. | Staff Correspondent

A novel artificial intelligence algorithm (AIA) appears effective in accurately assessing acne severity and lesion quantification via smartphone application, a recent study found.1

“This is the first validated AI algorithm which, using smartphones, allows the grading of acne severity based on the GEA scale. It provides a fast determination of the severity of acne and identifies the different lesion types, thus supporting the early therapeutic management of acne patients,” says Sophie Seité, Ph.D., La Roche-Posay Dermatological Laboratories, Levallois-Perret, France, and co-author of the study.

Dr. Seité and fellow colleagues developed the novel AIA for acne severity assessment based on the Global Acne Severity (GEA) scale and for acne lesion identification and compared it to clinical diagnosis by trained dermatologists.

In the five-stage development of the AIA, the researchers collected 5,972 images (face, right and left profiles) from 1,072 acne patients from France (32.7%), South Africa (46.5%), China (14.4%), India (5.1%), and Brazil (1.3%) using one or two types of smartphone for each patient [IOS (n=2,933) and Android (n=3,039) systems]. Three dermatologists assessed GEA for each patient on images. The GEA for each patient as assessed by the majority of dermatologists was used to train the algorithm. Using a tagging tool, dermatologists quantified lesions and identified post-inflammatory hyperpigmentation (PIHP) via images.

The model algorithm was then trained using 4,958 images corresponding to 903 patients as well as images with tagged lesions and PIHP (2,939 tagged patient images). The implementation of artificial intelligence technology may have a positive impact on patient outcomes.

Quick Takes

- An artificial intelligence algorithm was developed to assess acne severity and quantify lesions.
- Results highlight the need for appropriate and timely management to avoid residual hyperpigmentation, scars or a negative impact on quality of life.
- The implementation of artificial intelligence technology may have a positive impact on patient outcomes.
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Inflammatory lesions, 7,603 tagged non-inflammatory lesions and 5,702 tagged PIHP). Researchers then tested the algorithm internally using 1,014 new images from 169 acne patients.

For lesions and PIHP identification, results were submitted to the dermatologist for correction, which led to refinements and improvement of the algorithm in further versions. After improving the algorithm, the GEA grading reached 68%, which the researchers found was similar to the grade provided by the majority of dermatologists.

The correct grading and identification of acne lesions is the first step in the successful treatment of acne and, according to Dr. Seité, the promising results achieved with the AIA could prove to be useful in forging future management strategies for acne patients.

With a decreasing number of dermatologists over the last decades, getting appointments with dermatologists has become more and more difficult for patients, resulting in irregular patient follow-up, poor treatment outcome and a positive correlation between the duration of the disease prior to treatment and the development of scars,” Dr. Seité says.

On a larger scale going forward, Dr. Seité says that the study results essentially highlight the need for an appropriate and timely management of acne patients to avoid the development of residual hyperpigmentation and scars or a negative impact on the patient’s quality of life. As such, the introduction and implementation of AIA technology can have a positive impact on patient outcomes.

“Non-adherence to acne treatment is a common problem worldwide and this application can help practitioners evaluate their patients’ improvement between consultations. Such an approach can help for early management and serve as an educative tool to help the parents and adolescents to follow prescribed acne treatments,” Dr. Seité says. "

Disclosure:
Dr. Seité, D. Moyal, and G. La Dantec are employees of La Roche-Posay, France.

Reference:

Acne is a very common polymorphic skin condition that can be characterized by a mosaic of signs and symptoms including comedones, papules, pustules, and nodules, which can in some cases lead to scarring. There are a number of different measures and techniques currently employed to grade the severity of acne such as simple grading techniques based on clinical examination, and lesion counting, as well as various types of photography, video microscopy, and measurement of sebum production. The GEA scale has been validated on photographs of acne patients and has been found to be very useful in helping clinicians to grade acne severity in their patients.

"Acne affects more than 85% of adolescents and often continues into adulthood regardless of skin color. The GEA scale largely used particularly by European health practitioners but has only been validated for face-to-face and photo evaluations for regardless of skin color. This tool can help them make easier and quicker assessments of acne severity.

Compared with the Caucasian population, acne patients of Black African and, to a lesser degree, Asian (Chinese) origins may have issues with post-inflammatory hyperpigmentation (PIHP) as well as keloid formation. According to Dr. Seité, a regular patient follow-up, as well as poor treatment outcomes associated with a positive correlation between the duration of the disease prior to treatment and the development of scars and post-inflammatory hyperpigmentation are the main challenges for clinicians and their patients.

"It is sometimes difficult to quantify inflammatory and comedonal lesions as well as post-inflammatory hyperpigmentation in non-Caucasian patients. As such, this technology can be useful for those health practitioners with a low number of consultations with non-Caucasian patients for the evaluation of acne severity, which could assist them in choosing the best therapeutic option for their patients," Dr. Seité says.

According to Dr. Seité, health agencies recommend both the inflammatory and non-inflammatory acne lesion count, so a computational method, including the automatic counting of lesions, may help in regard to the short time of the consultation.

"This is a useful approach to help dermatologists and especially other healthcare practitioners in providing the best care and early management of acne patients regardless of skin color. Nevertheless, post-inflammatory hyperpigmentation evaluation is key in non-Caucasian acne patients and for dermatologists with few consultations with patients of skin color, this tool can help them make easier and quicker assessments of acne severity," Dr. Seité says.

Disclosures:
Dr. Seité, D. Moyal, and G. La Dantec are employees of La Roche-Posay, France.

References:

SMARTPHONES AID GEA SCALE ASSESSMENT
IN PATIENTS WITH DARKER SKIN

By ILAYA PETROU, M.D.

SMARTPHONES CAN BE USED to assess acne severity using the Global Evaluation Acne (GEA) scale in darker Fitzpatrick skin types, according to a poster presented during the AAD VMX Virtual Meeting Experience 2020 July 12-14.

Acne is a very common polymorphic skin condition that can be characterized by a mosaic of signs and symptoms including comedones, papules, pustules, and nodules, which can in some cases lead to scarring. There are a number of different measures and techniques currently employed to grade the severity of acne such as simple grading techniques based on clinical examination, and lesion counting, as well as various types of photography, video microscopy, and measurement of sebum production. The GEA scale has been validated on photographs of acne patients and has been found to be very useful in helping clinicians to grade acne severity in their patients.

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Disclosures:
Dr. Seité, D. Moyal, and G. La Dantec are employees of La Roche-Posay, France.

References:
Combination therapies improve keloid treatment

ILYA PETROU, M.D. | Staff Correspondent

Although there is no wide consensus as to which combination therapies work best for keloid lesions, many specialists around the world are independently using and experimenting with combinations of older and newer treatment modalities, many of which are proving to be very effective, an expert says.

“Keloids are challenging to treat and as such, many clinicians will typically combine a number of different treatments and delivery modalities in order to help achieve optimal clinical outcomes. However, currently, there is no agreement as to which are the most effective combination treatments for keloids and which combination therapy might work better for keloids of a different anatomical location,” says David M. Ozog, M.D., FAAD, chair, department of dermatology, C.S. Livingston Chair in Dermatology, director of cosmetic dermatology, division of Mohs and dermatological surgery, Henry Ford Hospital, Detroit.

The treatment of keloids has always been complex and includes a wide spectrum of therapies ranging from more traditional surgical procedures to intralesional or topical agents, radiation, botulinum toxin and energy-based devices. Though many of these therapies can work well in keloid treatment as stand-alone therapies, it is the clever combinations of these treatment approaches and how they are optimally delivered that has been somewhat revolutionary in keloid therapy of late, Dr. Ozog says.

In his keloid patients, Dr. Ozog usually treats the lesion with either a combination of pulsed dye laser (injection) or fractional ablative laser (topical) prior to the application corticosteroids or 5-FU drugs due to the tissue edema created.

For painful keloids and particularly those located on the trunk, Dr. Ozog found that pretreating these lesions with pulsed dye or CO2 laser enables a quicker and more efficient delivery of steroid or 5-FU drugs due to the tissue edema created.

“The positive response to these new and experimental keloid therapies independently performed by specialists around the world is testament to their efficacy and reinforces their place in keloid therapy.”

David M. Ozog, M.D., FAAD
Henry Ford Hospital, Detroit

Other leading specialists around the world are also currently using similar combination treatments, Dr. Ozog says, and achieving similar positive clinical outcomes. Matteo Clementoni, M.D., Milan, Italy, has achieved remarkable clinical results using a CO2 laser followed by a combination of botulinum toxin, steroids, and 5-FU applied topically on the skin, Dr. Ozog says. The delivery of the topical drugs to the keloid is far more effective and quicker through the micro-channels created by the CO2 laser, he says.

“The positive response to these new and experimental keloid therapies independently performed by specialists around the world is testament to their efficacy and reinforces their place in keloid therapy,” Dr. Ozog says.

Another interesting treatment approach pioneered by Somesh Gupta, M.D., New Delhi, India, combines RF energy with the delivery of steroids and 5-FU at the same time. According to Dr. Ozog, the novel treatment using insulated probes protects the outer keloidal skin from the heat produced by the RF device, helping to prevent any unwanted pigmenary changes, and allows the clinician to deliver the RF waves to the core of the lesion while simultaneously incrementally delivering the drugs chosen for treatment.

“For ear keloids, surgery followed by some other treatment such as steroids or 5-FU is still commonly employed. However, for truncal lesions where recurrence rates are high, there is a definite trend towards combination approaches that incorporate energy-based modalities such as laser and RF,” Dr. Ozog says.

One of the newer developments in keloid research revealed in a recent study by Ardesher Bayat, M.D., from the University of Manchester, UK, was that hypertrophic scars and keloidal scars are very different and that there are specific biomarkers that can help clinicians differentiate between them.

According to Dr. Ozog, there are distinct molecular differences between keloids of different anatomical locations and these lesions behave differently in the same patient depending on the location they occur.

“Many specialists from all around the world are currently using combinations of energy-based devices and medications whether they are cytotoxic, steroids, or even botulinum toxin. New and exciting combinations of treatments combined with clever drug delivery modalities is what is making the difference and allowing us to achieve exceptional clinical outcomes,” Dr. Ozog says.

Disclosure:
Dr. Ozog reports no relevant disclosures.

Reference:
Pathophysiologic pathways provide treatment insights

CHERYL GUTTMAN KRADER, B.S. PHARM | Staff Correspondent

A recent review examines the complex inflammatory processes of rosacea and the spectrum of topical and systemic agents used as anti-inflammatory treatments with a focus on the potential mechanisms of each therapy.1

“From our review, we concluded that there are no regimens available that confer long-term relief of erythema, remission of papules and pustules in large proportions of those affected, or reduced risk of progression to phymatous changes,” says Jerry Tan, M.D., adjunct professor of internal medicine and dermatology, Western University, London, Ontario, Canada, who conducted the review with colleague J. Mark Jackson, M.D., clinical professor of dermatology, University of Louisville, Ky. “These limitations indicate an unmet need for more efficacious treatments that can address the inflammation that gives rise to most signs and symptoms of rosacea and that will offer patients the possibility of complete clearance.”

MULTIFACTORIAL PATHOGENESIS

Drs. Tan and Jackson note that prior research has identified four converging inflammatory pathways: 1) activation of innate immunity via toll-like receptor 2 (TLR2); 2) protein activated receptor 2 (PAR2); 3) inflammasome activation; and 4) transient receptor potential (TRP) channels. These pathways are described in more detail in the body of the article and outlined graphically. The researchers illustrate the common exogenous and endogenous triggers for each of the contributory inflammatory pathways. In addition, they summarize their signal transduction pathways, including the cellular and molecular participants, and illustrate how they translate into various pathological features (ie., vasodilation, angiogenesis, inflammation/neurogenic inflammation, fibrosis), as well as show the downstream phenotypic signs and symptoms (ie., erythema/persistent erythema, flushing, telangiectasia, papules/pustules, phyma, heat sensation, edema) that are associated with the various pathologies. In addition, the article identifies therapies that have mechanisms of action specific to each pathway.

Dr. Tan points out that erythema developing as a consequence of vasodilation or angiogenesis is a feature of rosacea that is common to the activation of all four pathways. However, specific pathway activation may lead to specific presentations, suggesting the possibility of personalizing treatment selection if clinical features or biomarkers can be identified that indicate which pathways are dominant in the individual.

“As an example, activation of the TRP channels leads to transient and fixed erythema, but it does not lead to the development of papules/pustules. Presence of the latter inflammatory lesions may be more representative of activation of the TLR2, PAR2 and inflammasome pathways,” he explains.

There may also be crosstalk between the four pathways that can perpetuate a loop of inflammatory responses and progression of the phenotypic features of rosacea in some patients, they note.

TREATMENT REVIEW

The authors summarize information for products that have regulatory agency approval for use in rosacea and for commercially available modalities that are used off-label. Included in their discussion are efficacy results from clinical trials, available data from preclinical and clinical studies relating to effects on inflammatory mediators, and efficacy results from clinical trials investigating combination regimens using oral subantimicrobial doxycycline and various topical agents.

In addition, emerging treatments such as topical minocycline foam, which was recently approved by the FDA, is covered, as well as several therapies in clinical trials, including encapsulated 5% benzoyl peroxide cream; topical antimicrobial peptide gel (Omiganan); the proteasome inhibitor ACCU-D1; extended release, low-dose oral minocycline (DFD-29); rifaximin; a topical formulation of beneficial ammonia oxidizing bacteria (B244); and the human interleukin-17A antagonist secukinumab (Cosentyx, Novartis).

FUTURE NEEDS

Drs. Tan and Jackson identify the importance of long-term studies that can provide insights on predictive factors for risk of developing inflammatory lesions and/or phyma and whether early intervention for erythema mitigates progression. They also highlight the limitations of existing treatments and describe some features of “ideal” therapies that address the underlying inflammatory pathways of rosacea while avoiding unwanted side effects.

Disclosure: Dr. Tan and Dr. Jackson have been an advisor, consultant, investigator, and/or speaker for companies that market treatments for rosacea.

Reference:
For clinicians who treat patients with atopic dermatitis

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Specialized skincare improves symptoms

Cheryl Guttmann Kradar, B.S. Pharm | Staff Correspondent

Patients with rosacea using a set of skincare products formulated for sensitive and redness-prone skin benefited with improvements in disease-related signs and symptoms as well as quality of life, reported researchers in a study published online in the Journal of Cosmetic Dermatology.1

The skincare regimen comprised of three commercially available products (LETENR sensitive and red skin), including micellar water for cleansing in the morning and evening, a broad-spectrum (UVA/UVB) SPF20 cream, and night serum.

At the end of the eight-week, prospective, randomized study, patients using the specialized skincare products experienced greater relief of rosacea symptoms, reduction of objectively measured erythema, and improvement in the Dermatology Life Quality Index (DLQI) score compared with controls who continued to use their previous skincare products.

The investigators observed that the findings are strengthened by the prospective controlled design of their study and its use of an objective method to quantitate facial erythema. Commenting further, they state, “With countless available skincare products, in vivo studies with objective evaluation methods are necessary in order to prove their efficacy.”

The study was conducted by members of the Department of Dermatology and Allergy, University Hospital Munich, Germany, and enrolled 60 Caucasian patients (44 women, 16 men) with rosacea who had persistent centrofacial erythema. Eligible patients were required to have persistent or recurrent facial redness, burning, and dryness.

Of the 60 enrolled patients, 44 (73%) completed the eight-week study. Thirteen of the 16 patients who did not complete the study were lost to follow-up and all were in the intervention group. Two patients in the intervention group withdrew early due to mild worsening of facial redness and pustules accompanied by a burning sensation. Treatment adherence in the intervention group had a statistically significant improvement in disease-related signs and symptoms compared with controls who continued to use their previous skincare products.

The analyses of facial erythema showed a statistically significant improvement after just four weeks in both study groups. However, only the intervention group had a statistically significant further improvement over the next four weeks. At study completion, facial erythema was reduced from baseline by 10% in the intervention group and 8% in the control group. The investigators commented that the continuous improvement observed in the intervention group might indicate the superior efficacy of the study products.

Overall, the patients participating in the study had mild symptoms at baseline. The mean total symptom score in the intervention group improved by 28.6% after four weeks and by 57.1% after eight weeks. Both changes were statistically significant. At eight weeks, symptoms in the intervention group were nearly fully diminished. There was no change from baseline in mean total symptom score in the control group at either follow-up visit.

The intervention was associated with improvements in objectively measured erythema, rosacea symptoms, and health-related quality of life.

The investigators observed that the findings are strengthened by the prospective controlled design of their study and its use of an objective method to quantitate facial erythema.

57.1%

The improvement in mean total symptom score for the intervention group after eight weeks. (28.6% after four weeks). Changes were statistically significant and symptoms were nearly fully diminished.

Mean baseline DLQI scores were 3.3 in the intervention group and 2.1 in the control group, indicating that the patients in the study had a relatively high overall quality of life. Nevertheless, statistically significant reductions in DLQI score (indicating improvement) were achieved in the intervention group at both 4 weeks (-51.5%) and 8 weeks (-54.5%), and the change was attributed to improvement in clinical appearance. Relative to baseline, the mean DLQI score in the control group decreased by 4.8% at 4 weeks and by 23.8% at 8 weeks, but neither change was statistically significant.

The two patients in the intervention group who withdrew from the study because of side effects experienced slight aggravation of erythema and pustules along with burning. The patients declined patch testing to investigate the cause, and so the investigators stated that an association with use of the skincare products could not be established.

Disclosure:

The study was funded by the manufacturer of the skincare products used in the intervention group. One of the authors disclosed receiving fees as a speaker and advisor to LETI Pharma and other companies that market pharmaceutical and cosmeceuticals for rosacea.

Reference:
Phenotypes inform management options

An article published in the Journal of the American Academy of Dermatology and developed by members of the National Rosacea Society (NRS) Expert Committee presents a review of treatment options (available at the time of the review), including summary tables that categorize modalities based on features they target. The updated management options represent the companion to the updated standard classification of rosacea, which were published in 2018, the classification is based on phenotype versus strict subtyping of rosacea, according to Diane M. Thiboutot, M.D., professor of dermatology, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, Penn., who served as chair of the NRS Expert Committee.

The NRS Expert Committee was comprised of a multidisciplinary panel of 27 members providing expertise in dermatology, laser therapy, skin care, and ophthalmology. The committee believes that categorizing treatment modalities and presenting them according to the features they target will facilitate treatment selections that address the specific needs of individual patients, Dr. Thiboutot tells Dermatology Times.

“In the interest of considering the broad spectrum of potential therapies for rosacea, we made the best effort to have representation from a variety of dermatology specialists and ophthalmologists recognized for their knowledge in medical, procedural, and aesthetic dermatology and in the care of the ocular symptoms of rosacea,” Dr. Thiboutot says.

The development process began with a review of the relevant literature. The committee then convened to discuss the evidence and the efficacy of the therapies based on the available literature and clinical experience. In creating the report, the committee’s intention was to present the management options as a menu of choices rather than as a tiered protocol or algorithmic approach.

“Because the phenotypes of rosacea are so varied and there are nuances with regard to patient preferences for treatment, the committee members believed that listing treatment options and ratings of their evidence base would best afford clinicians the flexibility to tailor a regimen to an individual patient,” Dr. Thiboutot says.

The narrative portion of the article presents overviews of medications, light devices, and treatments for ocular rosacea as well as for lifestyle management and skincare. Three separate tables list treatment options for diagnostic features (i.e., persistent erythema and phymas), major features (i.e., papules/pustules, telangiectasia, and flushing), and ocular rosacea. Relative efficacy ratings for the various management options are reported graphically using a system of circles, which can range in number from one (least effective) to four (most effective). Filled versus open circles are used to indicate whether the strength of the evidence base for rating relative efficacy was considered strong versus weak.

The report also points out that prior to selecting treatment, it is important that clinicians understand which features of rosacea are the most bothersome to the patient because the information may be important for deciding on the level of therapy. It is noted that although patients’ perceptions of their facial appearance and its impact on their lives can vary, survey findings indicate that regardless of rosacea severity, patients may suffer substantial negative psychosocial sequelae.

“As mentioned in the management recommendations, clearing of inflammatory lesions may be appropriate and is often feasible. However, patients with concerns about erythema may need to be advised that complete elimination of facial coloration can result in an undesirable sallow appearance,” Dr. Thiboutot says.

ANTICIPATING REVISION

The NRS Expert Committee notes that the recommended management options are considered provisional and may need to be updated pending new information and the emergence of new therapies.

“Since this project was completed, additional therapies have been approved for use in rosacea that were not available for evaluation at the time,” Dr. Thiboutot says.

References:
What we know today about cellular and molecular wound healing mechanisms

Physicians can harness the knowledge for achieving improved post-procedure outcomes.

Doctors and aesthetic medicine physicians generally have a global understanding of the microbiome and its importance as a secondary immune system. What hasn’t been clear until recently and plays a vital role in skin health is the connection between the microbiome and wound repair.

“We understood that inflammation occupied both necessary and possibly deleterious roles in wound repair. The connection to the microbiome finally allows us to understand how to tilt the balance towards ‘healthy’ inflammation,” according to Ted Lain, M.D., M.B.A., dermatologist and chief medical officer at Sanova Dermatology, with practices throughout Texas and Louisiana.

About 100,000 bacteria reside on each square centimeter of the skin. Commensal, symbiotic and pathogenic organisms share the body’s space. Keeping in check the microorganisms that cause disease and are pathogenic is what’s important. Because once the balance is lost, dysbiosis occurs and pathogenic organisms dominate, leading to inflammation and an unhealthy immune response.

Factors contributing to microbiome variation include the host physiology; environment; immune system, including previous exposures and inflammation; host genotype, including susceptibility genes; pathology, including underlying chronic conditions; lifestyle, including occupation; and hygiene, which in the COVID-19 era is particularly relevant as things like antibacterial soaps can have a negative impact on the microbiome.

Clinicians often encounter patients with dysbiosis-driven skin diseases. Dysbiosis, in particular Staphylococcus aureus colonization drives inflammation in atopic dermatitis. Acne and psoriasis are dysbiotic diseases. And one of the causes of chronic wounds is dysbiosis, according to Dr. Lain.

“The Hygiene Hypothesis teaches us that our environment has a direct impact on the skin’s immune response. Those who are raised in an environment of high microbial diversity tend to have Th-1 biased immunity, while those raised in an environment of low microbial diversity, as is often found in developed countries, have Th-2 biased immunity,” according to Dr. Lain. “Taking this one step further, those raised in low microbial diversity (dysbiosis) tend to have low microbial diversity on their skin surface, which, along with a Th-2 biased immune response, results in an allergic/atopic diathesis. The barrier impairment that ensues, along with an unhealthy microbiome with high Staph aureus load, prevents wound healing.”

Clinicians, therefore, should strive to redirect the immune system response as much as possible to the Th-1 cytokines via a healthy microbiome. Because while the general environment is difficult to change, supporting a diverse and healthy microbiome through skincare and healthy habits lies within the Dermatology and aesthetic practice purview.

Toll-like receptors’ role in skin restoration

Keratinocytes continuously sample the microbiome colonizing the skin surface through a family of pattern recognition receptors, of which toll-like receptors are a member. Pattern recognition receptors/toll-like receptors recognize pathogen-associated molecular patterns and, when activated, initiate the innate immune response. This results in production of antimicrobial peptides, cytokines and chemokines.

“Since flagellin acts as a pathogen-associated molecular pattern, it can be used to activate toll-like receptors, resulting in a healthy immune response,” Dr. Lain said.

Scientists have learned a lot about the microbiome and wound healing by studying the small intestine, according to Dr. Lain. “The small intestine renews its epithelial lining very quickly, which could be due to the diverse microbiome in the gut,” Dr. Lain said. “We see that there’s a very high concentration of flagellin.”

With a skin injury, bacteria that predominantly live in the upper layers of the stratum corneum migrate into the wound and allow for greater release of antimicrobial proteins. That allows the skin to maintain balance unless a dysbiotic state occurs, which results in chronic wounds.

In essence, bacteria play a major role in wound repair. They secrete molecules that can activate cell multiplication and stimulate skin repair. The biofilm helps to protect that wound from invasion and helps to keep that balance.

About 100,000 bacteria reside on each square centimeter of the skin.
The connection to the microbiome finally allows us to understand how to tilt the balance towards ‘healthy’ inflammation.”

Ted Lain, M.D., M.B.A., chief medical officer, Sanova Dermatology, Texas and Louisiana

between symbiotic and pathogenic bacteria, according to Dr. Lain.
By understanding the molecular and immunologic underpinnings of the interplay between the microbiome and keratinocytes, clinicians can hasten wound repair by taking advantage of certain pathways to direct a healthy and supportive microbiome, as well as a reparative immune response, he said.

PUTTING THE INFORMATION TO PRACTICE
Dr. Lain recommends patients use a topical cosmetic product by Eau Thermale Avène, Cicalfate+ Restorative Protective Cream.
"Cicalfate+ Restorative Protective Cream is a recovery cream that helps support the skin microbiome. These properties make it an excellent choice for post-procedure (medical and aesthetic) and skin requiring recovery due to common irritants," he said.
Key ingredients in Cicalfate+ Restorative Protective Cream have properties that aid in skin recovery and influence keratinocyte migration.
"Dermatologists understand how important it is to activate these pattern recognition receptors during skin recovery because they will establish the skin recovery response to remove debris and cause keratinocyte migration," he said. "Now, it’s clear how the microbiome is so incredibly important in the skin recovery response."
Meta-analysis compares systemic treatments

JOHN JESITUS | Staff Correspondent

A recent systematic review and meta-analysis shows that dupilumab (Dupixent, Sanofi Genzyme and Regeneron) and cyclosporine may outperform methotrexate and azathioprine in adults with atopic dermatitis (AD) treated for up to 16 weeks.¹

“We know from many well-done trials that dupilumab is better than placebo,” says co-author Aaron Drucker, M.D., Sc.M. He is a clinician scientist, division of dermatology, at Women’s College Hospital and Women’s College Research Institute and assistant professor, department of medicine, University of Toronto.

However, says Dr. Drucker, no randomized trials compare dupilumab with older systemic treatments including methotrexate, cyclosporine and azathioprine, and few trials show how these older treatments compare with each other.

“So while we can estimate from our data that it looks like dupilumab and cyclosporine are roughly equally effective, and better than methotrexate and azathioprine, which should be better than placebo, it’s still hard to make firm conclusions,” he says. The study was published online April 22 in *JAMA Dermatology*.

Because only six studies reported outcomes beyond 16 weeks, investigators limited their analysis to this time frame. With a mean reduction of 11.3 points (95% confidence interval, 9.7-13.1) on the Eczema Area and Severity Index (EASI), dupilumab 300 mg every two weeks was superior to placebo, with high certainty according to Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria. Investigational medications that also demonstrated EASI reductions versus placebo (moderate certainty in all analyses) included baricitinib (Olumiant, Lilly) 2 mg daily (5.6 points) and 4 mg daily (5.2 points) and tralokinumab (Leo Pharma) 150 mg every two weeks (4.3 points) and 300 mg every two weeks (4.9 points).

In standardized mean difference (SMD) calculations, azathioprine, low- and high-dose cyclosporine, methotrexate and dupilumab had moderate or large benefits relative to placebo. Higher-dose cyclosporine (SMD, -1.1, low certainty) and dupilumab (SMD, -0.9, high certainty) appeared similarly effective versus placebo in clearing clinical signs of AD. These medications moreover may be superior to methotrexate (SMD, -0.6, low certainty) and azathioprine (SMD, -0.4, low certainty).

Additionally, dupilumab 300 mg every two weeks was associated with clinically relevant improvements in Patient-Oriented Eczema Measure (POEM, -7.5, high certainty) and Dermatology Life Quality Index (DLQI, -4.8, high certainty) scores.

Investigators analyzed 39 trials that included 6,360 patients total. Most trials (29) were industry-sponsored, and most comparisons were against placebo. Sixteen studies had at least one element at high risk of bias. But even in some newer studies with lower risk of blinding-associated bias, incomplete outcome data introduced potential bias.

Investigators were somewhat disappointed that a relative dearth of reported adverse events prevented valid safety comparisons.

“Fortunately, a lot of that is due to the fact that in randomized, controlled trials for many of these medications, there aren’t many serious adverse events,” Dr. Drucker says.

For clinicians, he says, the study is helpful for putting the above treatments in context because until now, no valid comparisons using randomized, controlled data have existed.

“Even though our estimates aren’t very precise, and there’s a lot of uncertainty, we can at least help physicians with an estimate of how these treatments compare.”

Aaron Drucker, M.D., Sc.M.
Women’s College Hospital and Women’s College Research Institute, University of Toronto

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“Even though our estimates aren’t very precise, and there’s a lot of uncertainty, we can at least help physicians with an estimate of how these treatments compare,” he says.

Perhaps more importantly, Dr. Drucker and colleagues plan to update the meta-analysis every four months with results listed at eczematherapies.com.
In search of a better way to assess itch

Researchers evaluating several available itch assessment tools found that the Itch Severity Scale (ISS) isn’t ideal for practice. It’s too time-consuming for routine clinical use. However, it does demonstrate good retest reliability and high correlation with the pruritus-specific quality of life instrument ItchyQoL.

The researchers conclude that dermatologists and others who assess patients in practice need an easier-to-perform alternative itch measurement scale. The alternative test, possibly a simplified Itch Severity Scale, needs to be highly reproducible and accurate in the way it reflects patients’ quality of life, according to the paper published January 2020 in the Journal of the American Academy of Dermatology (JAAD).1

While there are many tools for evaluating patients’ itch, there is no gold standard pruritus evaluation tool for dermatologists and other providers to use in practice. Optimal tools are also needed in research, according to the authors.

“Studies evaluating pruritus have tended to focus on the pathogenesis and effective treatment and often overlook the measurement of symptoms,” they wrote. “However, the investigation of validated and reliable itch intensity scales may provide a more accurate representation of pruritus and play a useful role as a benchmark for research and clinical practice.”

Studies comparing the validity and reliability of itch measurement scales are lacking, according to the paper.

Researchers studied 419 patients with chronic itch at 11 Korean hospitals. They evaluated use of the Visual Analog Scale (VAS), Numeric Rating Scale (NRS), Verbal Rating Scale (VRS) and the multidimensional Itch Severity Scale questionnaire. They also assessed these tools’ correlations with the ItchyQoL.

The Visual Analog Scale is a horizontal image with “no itch” on the far left and “worst imaginable itch” on the far right. Patients mark a place on the 10-cm scale indicating the severity of their itch. The Numeric Rating Scale allows patients to assign a numeric score to their itch, from 0, or no itch, to 10, which is the worst possible itch. Patients using the Verbal Rating Scale score itch intensities as 0 to 4, with 0 being no itch and 4 indicating very severe itch. The International Forum for the Study of Itch studied these three scales and reported high reliability and validity, according to the paper.

The seven-category Itch Severity Scale addresses itch frequency, itch description, body surface area impacted and itch intensity according to one’s state of itching (best, average or worst). It also addresses how one’s itch affects mood, sexual desire and function, as well as sleep.

Subjects in the JAAD paper recorded itch intensity using the four scales. Researchers then analyzed retest reliability three hours after the first assessment. All subjects answered the ItchyQoL, which includes 22 pruritus-specific questions about symptoms, functional limitations and emotions. Patients score their responses from 1, or never, to 5, or always.

Researchers found a significantly strong correlation among the Visual Analog Scale, Numeric Rating Scale and Verbal Rating Scale. The Itch Severity Scale, a multidimensional scale, showed a low intercorrelation validity with these three scales but demonstrated a notably better retest reliability and stronger ItchyQoL correlation than the three unidimensional tools.

The Itch Severity Scale, while it performed well in the study, isn’t easy to use in a busy practice, according to the paper. What providers need is a less time consuming, reliable itch assessment tool that they can use routinely in practice—one that overcomes the challenge of accurately measuring patients’ complex and subjective feelings of itch.

Patient heterogeneity and recall bias are study limitations.

Disclosures: The authors report no conflicts of interest.

Reference:

“However, the investigation of validated and reliable itch intensity scales may provide a more accurate representation of pruritus and play a useful role as a benchmark for research and clinical practice.”

Jang Yong Hyun, M.D., and colleagues, Kyungpook National University Hospital, Daegu, Republic of Korea
Research advances pediatric eczema treatment

LISETTE HILTON | Staff Correspondent

Research over the past few years has significantly shifted what is known about pediatric atopic dermatitis, according to Jeffrey Sugarman, M.D., Ph.D., immediate past president, Society for Pediatric Dermatology. Scientists are performing controlled studies to answer basic skincare questions and investigating novel molecules that target specific immune abnormalities.

Dermatologists have long debated if a bad skin barrier or abnormal immune response causes atopic dermatitis. Researchers are finding that it’s probably both, according to Dr. Sugarman, clinical professor of dermatology and family medicine at University of California San Francisco and in practice at Redwood Family Dermatology in Santa Rosa, Calif.

“There’s evidence on both sides. It’s an important question because it directs our therapeutic management and the way we research how to best manage atopic dermatitis,” he says.

SKINCARE RECOMMENDATIONS
Basic aspects of eczema skincare, like best bathing practices, haven’t been well studied. But that’s changing, he says.

In one study, researchers compared frequent soaking baths, twice daily for two weeks, followed by the application of an occlusive moisturizer (the soak and seal method) to infrequent bathing, twice weekly for two weeks, for atopic dermatitis management. Subjects in the randomized, controlled trial comparing topical steroid application to wet versus dry skin in children with eczema.

“I turned out that it didn’t make a difference whether you applied the topical corticosteroid to presoaked damp skin or dry skin in terms of the effectiveness,” Dr. Sugarman says.

Bleach baths can play an important role in atopic dermatitis. Their results, published in 2017, suggest using bleach baths were not more effective than just a plain water bath.

“There are some caveats here. It’s a meta-analysis, and some of these trials were done in different ways. But sometimes it’s useful to look at a collection of studies to try to guide us,” Dr. Sugarman says.

Researchers also are studying whether other bathing additives, like vinegar or acetic acid, make a difference for atopic skin. Researchers divided patients into several groups. There was a plain water bathing group. There was water plus dilute vinegar or acetic acid for treatment of atopic dermatitis,” he says. “We don’t have data yet, but it’s a study that’s ongoing and we will have data probably in the next six to 12 months.”

BIOMARKERS WILL BE BIG NEWS
Biomarker research is hot – not just in atopic dermatitis but also in other areas in dermatology, according to Dr. Sugarman.

“Specifically related to atopic dermatitis, the idea is that the immune system worsens the skin barrier in atopic dermatitis and that blood levels...
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We know that there are well-done trials coming for multiple new agents. Once we can incorporate that data into our review on an ongoing basis, clinicians will be able to make comparisons between dupilumab and all these new treatments.”

Aaron Drucker, M.D., Sc.M., Women’s College Hospital and Women’s College Research Institute, University of Toronto

Systematic review to be updated regularly for most current guidance

Disclosure:
Dr. Drucker has served as an investigator and received research funding from Sanofi and Regeneron. He has been a consultant for Sanofi and Pfizer Health Solutions, and his institution has received educational grants from Sanofi and Abbvie.

Reference:

Biomarker studies seek to predict patients at risk for severe AD

There are other JAK inhibitors in clinical trials for atopic dermatitis: the oral agent upadacitinib (Rinvoq, Abbvie) and a cream formulation nelgocitinib (Leo Pharma), baricitinib (Eli Lilly) and the JAK 1 inhibitor PF-04965842 (Pfizer) is in phase 3 trials in adolescents.

MORE ON THE PDE-4 FRONT
The FDA approved phosphodiesterase-4 (PDE-4) inhibitor crisaborole (Eucrisa, Pfizer) for children as young as 2 years.

“Treatment needs to be individualized based on age, severity of disease and the location of skin that’s affected by atopic dermatitis,” he says. “We really need as many tools in the toolbox as possible.”

Disclosure:
Dr. Sugarman is a consultant and speaker for Regeneron, Sanofi and Pfizer.
The BE VIVID and BE READY studies examining bimekizumab (UCB4940, UCB) for the treatment of psoriasis show strong, long-lasting patient responses and no unexpected safety signals, investigators say.

“Dermatologists and patients with psoriasis are looking for a treatment that delivers speed, depth and durability,” says Kenneth Gordon, M.D., professor and chair of dermatology at the Medical College of Wisconsin, Milwaukee, and principal BE READY investigator.

The phase 3 data demonstrate bimekizumab’s strong potential to deliver in these areas, adds principal BE VIVID investigator Kristian Reich, M.D., Ph.D. He is professor for translational research in inflammatory skin diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Germany.

Bimekizumab is a second-generation IL-17 inhibitor, says Dr. Reich. Ixekizumab (Taltz, Eli Lilly) and secukinumab (Cosentyx, Novartis) block IL-17A, and brodalumab (Siliq, Valeant Pharmaceuticals) inhibits the IL-17A receptor.

“We believe IL-17A and F are the main drivers of the psoriatic disease process,” Dr. Reich says.

The proportion of patients randomized to bimekizumab who achieved PASI 90 at week 16. And the proportion who achieved PASI 100 was 58.6%.

Bimekizumab phase 3 data reflect rapid, durable response

JOHN JESITUS  |  Staff Correspondent

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“We believe IL-17A and F are the main drivers of the psoriatic disease process,” Dr. Reich says.
New Insights on Diagnosing and Treating Generalized Pustular Psoriasis

LEARNING OBJECTIVES

Upon successful completion of this activity, you should be better prepared to:

• Discuss recent pathophysiological findings in pustular psoriasis to differentiate from plaque psoriasis
• Demonstrate increased knowledge of clinical data on emerging biologic therapies targeting the inflammatory pathway for treatment of pustular psoriasis

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Commonly regarded as the most severe form of psoriasis, generalized pustular psoriasis (GPP) causes the loss of protective skin functions and can lead to life-threatening complications such as sepsis, acute respiratory distress, and cardiac failure.1,2 Although cases are often idiopathic, medications and infections may trigger the disease, which can take a relapsing course with symptoms lasting for months.1

A lack of approved therapies in the United States creates challenges for managing GPP. However, recent developments offer potential for new opportunities in diagnosis and treatment.

RECENT INTERNATIONAL STATEMENTS PROVIDE DIAGNOSIS AND SCORING SYSTEMS

The 2018 guidelines from the Japanese Dermatological Association (JDA) for treating GPP provide a set of 4 diagnostic criteria:

1. Systemic symptoms (such as fever or fatigue)
2. Systemic or extensive flushing with sterile pustules that may merge to form “lakes” of pus
3. Neutrophilic subcorneal pustules characterized by Kogoj spongiform pustules
4. Features 1 through 3 are recurring

The presence of all 4 criteria supports a definitive diagnosis of GPP, and clinicians should suspect the disease in patients who have the second and third features. This definition is intended to rule out acute generalized exanthemeous pustulosis (AGEP), which can be difficult to differentiate from GPP.3,4

The European Rare and Severe Psoriasis Expert Network defines GPP as primary, sterile, macro-
scopically visible pustules on nonacral skin (excluding cases where pustulation is restricted to psoriatic plaques); GPP may be accompanied by systemic inflammation or psoriasis vulgaris, and is either relapsing or persistent.¹

The JDA guidelines also provide a scoring system for GPP severity, which includes a scale from 0 to 3 for each of the following skin symptoms: percentage of body surface area of erythema, erythema with pustules, and edema.¹ Additional points are given for severity of fever, white blood cell count, C-reactive protein (CRP) level, and serum albumin level. Total scores range from 0 to 6 (mild) to 11 to 17 (severe).

### INTERLEUKIN-36 (IL-36) PRESENTS A GPP TREATMENT TARGET

A number of cell types, including keratinocytes, express the cytokines IL-36α, IL-36β, and IL-36γ, as well as IL-36 receptor antagonist (IL-36Ra).² When these cytokines bind to IL-36Ra, the process triggers inflammatory responses that lead to activation and recruitment of neutrophils, macrophages, dendritic cells, and T cells. The binding of IL-36Ra to this receptor, conversely, hinders those inflammatory responses.

Loss-of-function mutations in the gene IL36RN, which encodes IL-36Ra, drive increased inflammatory responses that involve a substantial release of inflammatory mediators.²,³ These mutations have been identified in cases of familial and sporadic GPP worldwide, and they are more common in patients with GPP who do not have plaque psoriasis.²,⁴

Although a 2019 study found that only 23.7% of 190 patients with GPP had IL36RN mutations, they were associated with earlier age of onset.⁴ The authors suggested that IL36RN mutation screening in patients with symptoms before the age of 30 may become more important in an era with available biologics that target this pathway.

### CLINICAL TRIAL TESTING IS UNDERWAY FOR THERAPIES TARGETING IL-36R

A phase 1 trial of patients (n = 7) with or without IL36RN mutations investigated spesolimab, a monoclonal antibody against IL-36Ra.³ By 2 weeks following infusion, 6 patients had complete pustule clearance, and at 4 weeks the study group had a 79.8% mean percent improvement in Generalized Pustular Psoriasis Area and Severity Index score. In addition, mean CRP levels fell from 69.4 mg/dL at baseline to 4.5 mg/dL at week 2. All patients had mild or moderate adverse events (AEs) following infusion, and no reported serious AEs. The therapy is now in phase 2 testing.³

Investigators are studying the monoclonal antibody ANB019 in the phase 2 GALLOP trial (NCT03619902) in adults with GPP.¹,³,⁴ Patients receive an intravenous loading dose upon enrollment, with additional subcutaneous monthly doses for up to 16 weeks. A release of interim data on 2 patients showed an average of 58% improvement in GPP at day 8 and 63% improvement at day 113 using modified JDA scoring. Skin pustules were cleared by day 8 through day 113, and CRP levels were reduced by an average of 75% at day 113, nearly normalizing. The therapy was generally well-tolerated, and no serious or severe adverse events were reported; however, another patient dropped out due to bacteremia that was possibly drug-related.

Other interest in the IL-36 pathway comes from the therapeutics arm of a consumer genetics company, which is partnering with a pharmaceutical company to develop an anti–IL-36 antibody.¹,⁵

### TO LEARN MORE about this topic, including information on the pathophysiology, diagnosis, and emerging treatments for pustular psoriasis, go to gotoper.com/online-cme-activities/medical-crossfire/mxf-pp20

To learn more about this topic, including information on the pathophysiology, diagnosis, and emerging treatments for pustular psoriasis, go to gotoper.com/online-cme-activities/medical-crossfire/mxf-pp20
Data from both BE READY and BE VIVID suggest that bimekizumab may allow patients to have a very high likelihood of robust responses in their psoriasis and even clearance of their disease.

Kenneth Gordon, M.D., Medical College of Wisconsin, Milwaukee

Data demonstrate bimekizumab's potential

Dr. Gordon adds that the IL-17F protein is considerably more present in psoriatic plaques than IL-17A.

“So, while IL-17A might have a little more physiological activity, both of these molecules are considered significant for the treatment of psoriasis,” he says.

“Theoretically,” says Dr. Reich, “if you block F in addition to A, hopefully you should see even higher levels of response.”

Indeed, the 567-patient BE VIVID trial produced some of the highest response levels ever recorded. At week 16, the proportions of patients randomized to bimekizumab who achieved Psoriasis Area and Severity Index (PASI) 90 were 85% and 58.6%, respectively. The corresponding figures for ustekinumab were 47.7% and 20.9%. Also at week 16, 84.1% and 53.4% of patients on bimekizumab and ustekinumab reached investigator global assessment (IGA) scores of zero or one with at least a two-point improvement over baseline.

Additionally, 76.9% of bimekizumab-treated patients reached PASI 75 by week four, versus 15.3% of ustekinumab-treated patients. At week 52, an approximately 25-point improvement over baseline.

The BE VIVID study spotlights bimekizumab's speed and durability of response, says Dr. Reich. “There is no longer a trade-off when it comes to onset and maintenance of response with this IL-17 inhibitor. You’re getting the best of both worlds by blocking IL-17F in addition to A.”

In BE READY, investigators randomized 435 patients with moderate-to-severe plaque psoriasis to bimekizumab every four weeks or placebo. At week 16, investigators re-randomized PASI 90 responders to bimekizumab every eight weeks, every four weeks or placebo through week 56.

Week 16 PASI 90, PASI 100 and IGA 0/1 rates among bimekizumab-treated patients were 90.8%, 68.2% and 92.6%, respectively, versus 76%, 45% and 19%.

Week 56 PASI 90 rates for four- and eight-week dosing were 86.8% and 91%, respectively; the corresponding figures for IGA 0/1 were 86.5% and 90%. Conversely, 16.2% of patients re-randomized to placebo maintained PASI 90 by week 56. “But this is not a rapid return of disease with bimekizumab therapy,” says Dr. Gordon. Median time to relapse (defined as PASI 75) was 28 weeks.

In both studies, bimekizumab was well tolerated. The most common bimekizumab-related adverse events included nasopharyngitis and oral candidiasis, the latter of which was generally mild-to-moderate and an expected effect of IL-17 inhibitors. No BE READY patients stopped therapy due to candidiasis, while five did so in BE VIVID.

Dr. Gordon says, “Data from both BE READY and BE VIVID suggest that bimekizumab may allow patients to have a very high likelihood of robust responses in their psoriasis and even clearance of their disease. This happens quickly and can be maintained effectively while having very good tolerability.”

Disclosures:
Dr. Reich has served as advisor and/or participated in and/or participated in clinical trials sponsored by AbbVie, Amgen, Celltrion, Galapagos, Janssen, Merck, Novartis, Pfizer, Regeneron, Sanoft, Sanofi, UCB and Valeant and has served as advisor and/or participated in and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Astellas, Boehringer Ingelheim, Braftl-Myers Squibb, Celgene, Centocor, Covagen, Dermira, Eli Lilly, ForsythPharma, Fresenius Medical Care, Galapagos, GSK, Janssen-Cilag, Kendreion, LEO Pharma, Medac, Merck Sharp & Dohme, Miltenyi Biotec, Novartis, CozoPharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Sun Pharma, Takeda, UCB Pharma, Valeant and/or Sanofi.

Dr. Gordon has received honoraria and/or research support from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Braftl-Myers Squibb, Celgene, Dermira, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma and/or UCB Pharma.

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Data show foam safe, effective maintenance Tx

JOHN JESITUS | Staff Correspondent

Twice-weekly Enstilar Foam (calcipotriene-betamethasone dipropionate, LEO Pharma) provides safe and effective maintenance treatment for plaque psoriasis, according to results of the PSO-LONG phase 3 trial.

To address psoriasis, says Mark Lebwohl, M.D., strong topical steroids are approved by the U.S. Food and Drug Administration (FDA) — some for limited periods such as two to four weeks.

“Then the question becomes, what do you do for a disease that is long-term? How do you avoid steroid side effects such as stretch marks, telangiectasia, cutaneous atrophy and adrenal suppression? We know that long-term steroid use will create those side effects.”

He is Waldman Professor and Chairman, Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, and principal PSO-LONG investigator.

Combining calcipotriene with betamethasone dipropionate (a class II steroid) creates the efficacy of a superpotent steroid while avoiding the associated risks, he says. In PSO-LONG, investigators randomized patients who achieved investigator global assessment scores of zero or one (clear or almost clear) after four weeks’ daily open-label use of calcipotriene-betamethasone foam to twice-weekly foam or vehicle for 52 weeks.

After the initial month of treatment, 521 of 650 patients achieved treatment success; 545 entered the double-blinded maintenance phase, which include monthly follow-up visits. Patients who experienced breakthrough flares during this period were put on daily active treatment until clearance before returning to twice-weekly calcipotriene-betamethasone foam or placebo.

Regarding median time to relapse, says Dr. Lebwohl, calcipotriene-betamethasone foam showed a clear advantage — 56 (95% confidence interval/CI 34-59) days versus 30 (95% CI 29-31) days for vehicle. The corresponding times until 75% of patients experienced a first relapse were 169 (95% CI 140-197) days and 57 (95% CI 55-61) days.

Over the course of a year, the investigational foam furthermore provided an average of 34.5 more remission days versus placebo (256.5 versus 222 days, respectively). Mean percentage of days in remission was 70% for calcipotriene-betamethasone foam versus 61% for placebo. Average number of relapses per year was three for active treatment versus 4.7 for placebo.

“Keep in mind that people in the vehicle group were allowed to use rescue treatment,” he says. This fact boosted remission numbers in the vehicle cohort. Additionally, active treatment reduced the relapse rate 46% (95% CI 37%-54%) versus vehicle.

“And there were more rebounds, meaning the disease came back worse, in the vehicle group,” says Dr. Lebwohl.

As a drawback of the study’s design, he says that with a year-long topical medication trial, PSO-LONG investigators expected a fairly significant number of dropouts — 251 patients (46.1%) completed the study.

“In terms of safety, there were no steroid-related side effects with this prolonged regimen. The number of adverse events was similar between the two arms,” Dr. Lebwohl says.

In the actively treated cohort, one patient each experienced chorioretinopathy and skin pain, which investigators adjudicated to be possibly related and unrelated to treatment, respectively. No patients experienced calcium-related side effects.

“Across the board,” he says, “the results are excellent.”

Until now, says Dr. Lebwohl, guidelines in package inserts of topical steroids indicated for psoriasis allowed medication use for a limited time.

“Once that period of time is over, what do you do with a patient with a chronic disease? Can you keep treating them? Use the medication twice a week or go to a weekend-only regimen?” he asks.

No one really knew what to do, he says. “This is the first time we have a large, multicenter, double-blinded study in which we proved that using twice-weekly calcipotriene-betamethasone dipropionate foam for a year does not result in more side effects but does result in better outcomes. It gives everyone a sensible, practical regimen to follow,” Dr. Lebwohl says.

Disclosures: Dr. Lebwohl is a consultant and investigator for LEO and works with many other companies that market psoriasis treatments. All payments to research go to his employer, the Icahn School of Medicine at Mount Sinai; and he receives personal direct compensation from the manufacturers of psoriasis therapies.


“"This is the first time we have a large, multicenter, double-blinded study in which we proved that using twice-weekly calcipotriene-betamethasone dipropionate foam for a year does not result in more side effects, but does result in better outcomes.”

Mark Lebwohl, M.D., Icahn School of Medicine, Mount Sinai, New York
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Study IDs potential psoriasis predictive marker

JOHN JESITUS | Staff Correspondent

Using a novel autoantigen array, researchers have shown that the immunoglobulin G4 (IgG4) anti-gliadin autoantibody might provide useful information for diagnosis and prognosis of psoriasis. The study appeared in the March issue of Proteomics Clinical Applications.

“We are looking at markers that would predict who gets psoriasis versus who doesn’t, and who can be at risk for developing comorbidities,” says study co-author Stephen K. Tyring, M.D., Ph.D., M.B.A. He is clinical professor of dermatology, microbiology/molecular genetics and internal medicine at the University of Texas Health Science Center, and medical director of the Center for Clinical Studies in Houston.

Identifying the IgG4 anti-gliadin autoantibody and its potential role in psoriasis required constructing a novel 75-antigen autoantigen array in a project spearheaded by senior author Tianfu Wu, Ph.D. He is associate professor of biomedicine engineering at the University of Houston.

Because there are no commercially available autoantigen arrays for psoriasis, Dr. Wu designed the first psoriasis-specific autoantigen array.

“We have quite a bit of experience in developing autoantibody arrays. After a lot of research into disease mechanisms, we selected potential autoantigens that could be useful for disease-related screening,” he says. Researchers printed these autoantigens on a chip and obtained serum obtained from Dr. Tyring’s clinic.

“And then we could use the detection reagents with fluorescent labels to detect the signals,” says Dr. Wu.

Using serum is more practical than cultures or biopsies, which may or may not have predictive value, says Dr. Tyring. Unlike skin biopsies, he adds, patients don’t mind having serum taken because starting biologic therapy requires an initial blood draw.

“A little extra tube for serum can predict reproducibly — and maybe in the future, in a commercially available manner — who would respond to which medicine and who would get comorbidities,” Dr. Tyring says.

Researchers first performed protein array screening with samples from 12 patients with psoriasis and 12 healthy controls. To validate these findings, the team used ELISA-based methods to confirm that IgG4 anti-gliadin autoantibody levels not only distinguished psoriasis from healthy controls, but also that levels of this antibody correlated with Psoriasis Area and Severity Index (PASI) scores. Specifically, 42% of patients with psoriasis who had IgG4 anti-gliadin autoantibody levels greater than 0.4 on ELISA had the PASI correlation, coefficient r = 0.65 (P<0.001).

Along with PsA, researchers plan to use the autoantigen array to explore other psoriasis comorbidities such as metabolic syndrome.

Dr. Tyring says, “We’ve recognized for decades that psoriatic arthritis develops in one-third of patients with psoriasis.”

One day, the antigen microarray may allow physicians to intervene in at-risk patients with medication to prevent PsA.

“If we can also predict other comorbidities,” says Dr. Tyring “then we can hopefully work with primary doctors and help patients avoid the cardiovascular and diabetic comorbidities that are also associated with severe psoriasis.”

Meanwhile, Drs. Wu and Tyring are exploring some of the same questions in atopic dermatitis, where they have garnered preliminary data. Disclosure: Drs. Tyring and Wu report no relevant financial interests.

References:
A lack of standards for dermatologic imaging has been a major reason why the development of AI for dermatology has lagged behind the progress occurring in other medical specialties.

The International Skin Imaging Collaboration (ISIC), which was organized in 2013, is addressing this obstacle in its effort to move the field forward and bring AI into dermatology practice. At the same time, practicing dermatologists can play a valuable role in the process by becoming active participants in AI design and implementation, says Allan C. Halpern, M.D., chief, dermatology service, Memorial Sloan-Kettering Cancer Center, New York, NY, and founder, ISIC.

“ISIC is an academic and industry partnership being led by Memorial Sloan-Kettering Cancer Center that is designed to facilitate the clinical application of digital skin imaging,” Dr. Halpern explains. “It is exciting that in a short time, the work being done by ISIC has led to the development of AI algorithms for image-based diagnosis that are able to outperform most dermatologists. But there is still a lot that needs to be done, and dermatologists can be important contributors to the ongoing evolution as we aim to promote the application of AI and make it as clinically useful as possible.”

STANDARDIZING IMAGING

Although imaging of skin lesions would seem to be a “no brainer,” for a variety of reasons it is not something that has been routinely done in clinical practice. The situation has been changing, however, driven in part by patient demand for access to services and being particularly accelerated by the wider adoption of telemedicine as a means for delivering care during the COVID-19 pandemic.

ISIC was created based on recognition that in order to provide reliable information, AI algorithms need to be trained with good data. In terms of algorithms for image-based diagnosis, that means having a large set of quality images that are representative of the entire population and accurately annotated. To address the existing gap in this area, ISIC set out to lay the groundwork for applying the Digital Imaging and Communication in Medicine (DICOM) metadata model to dermatology imaging.

“Without standards, images in dermatology will continue to find their way into electronic medical records without any quality assurance or systematic way for sharing,” Dr. Halpern says. “DICOM standards provide both a quality check and interoperability.”

Thus far, a dermatology DICOM Working Group has developed consensus standards around techniques, technology, and terminology used for dermatologic imaging. The group has published multiple consensus standards pertaining to terminology that relates to clinical diagnosis, dermoscopic features, anatomic site, and more.

ALGORITHM DEVELOPMENT

ISIC is also building a public archive of clinical and dermoscopic images that can be used to train AI algorithms, and it has engaged the computer science community in algorithm development by holding annual lesion analysis challenges. Over the years, the challenges have become more and more complex as they have featured a growing number of images that are associated with more data and representing an increasing number of diagnoses. The challenges have also garnered the participation of a growing number of machine-learning lab teams, Dr. Halpern says.

Each challenge is hosted in partnership with a different imaging organization. The 2020 event, which took place in May 2020, was held in conjunction with the Society for Imaging Informatics in Medicine (SIIM), which is the premier professional organization for medical imaging. The challenge represented the first large scale interaction of dermatology AI with the rest of the medical computer imaging world, and for the first time, it used images with a DICOM wrapper, Dr. Halpern says.

“To date, there have been hundreds of technical papers published from the annual challenges, and they are having a significant impact on developing new approaches to AI algorithms,” he adds.

As it works towards optimizing the benefits of AI algorithms to support clinicians, ISIC is also investigating how the utility of the output is affected by the way it is presented. This question was explored in a recent study reported in Nature Medicine.

The path forward

As Dr. Halpern and his ISIC colleagues continue working towards achieving their goals, they are looking to engage clinician cooperation.

“I invite anyone who has a large collection of images with accurate associated information to contribute the dataset to ISIC and participate as part of our organizing committee. In addition, there are increasing opportunities through ISIC for dermatologists to participate in studies that can help us understand the best ways to share AI insights with practicing clinicians,” he says.

In seeking to enlist help from the dermatology community in contributing toward AI design, testing, and implementation, Dr. Halpern emphasized that the benefits of AI in medicine are the product of a human-computer collaboration.

“AI has the potential to augment clinicians’ diagnostic capability and can bring multiple additional benefits. Dermatologists should not feel threatened by AI because it is not going to replace physicians,” he says.

Reference:
Emerging options for high-risk melanoma

Immunotherapy trial explores neoadjuvant approach

JOHN JESITUS | Staff Correspondent

A n ongoing study is attempting to build on what researchers have learned in recent years regarding neoadjuvant approaches to immunotherapy for high-risk melanoma.

With the increasing number of approved immunotherapies and targeted therapies for patients with stage 3 melanoma, accurate pathologic microstaging assumes increasing importance, says Giorgos Karakousis, M.D., associate professor of surgery at the Hospital of the University of Pennsylvania, Philadelphia.

“There have been ongoing discussions about the role and utility of sentinel lymph node (SLN) biopsy in patients with melanoma. But more so now than before, where a large part of the procedure’s value was prognostic, there is value in terms of helping guide decisions about effective adjuvant therapies,” he says.

Interest in neoadjuvant therapy — treatment before surgical excision — is growing. “We’ve initiated studies here at Penn looking at that approach in patients with lymph node involvement, treating with immune checkpoint inhibitor therapy prior to surgical removal of the disease,” he says. “In an appreciable portion of those patients, we see a very good pathologic response of the tumor.”

In a study published in the March 2019 Nature Medicine, nearly 30% of patients with stage 3 or 4 melanoma achieved complete pathologic response after a single dose of pembrolizumab.1 This response correlates with durable disease-free control and provides a valuable biomarker to indicate if the therapy is working in a particular patient, he says.

To identify viable biomarkers of response, investigators also will investigate several additional immune-related factors through gene expression analyses and characterization of the cellular changes within the SLN. The study is expected to complete accrual within two years. ▲

Disclosure: The ongoing study is supported by Merck, but Dr. Karakousis receives no personal funds from the company.

References:

“Quick Takes”

Recruiting is ongoing for an investigator-initiated clinical trial of pembrolizumab in clinical stage 2B/C melanoma.

The study will test whether treatment with pembrolizumab before surgery to remove melanoma reduces the rate of positive sentinel lymph nodes in patients with stage IIB/C melanoma.

Researchers will also investigate several immune-related factors through gene expression analyses and characterize cellular changes within the SLN.

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Researchers will also investigate several immune-related factors through gene expression analyses and characterize cellular changes within the SLN.

“This will give us an opportunity to learn a lot more about what’s happening at the level of the sentinel lymph node, ... which may give us important clues about which patients may benefit most from this approach.”

Giorgos Karakousis, M.D., Hospital of the University of Pennsylvania, Philadelphia
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Artificial intelligence may improve melanoma detection [FROM PAGE 1]

Susan M. Swetter, M.D., Stanford University Medical Center and Cancer Institute, Stanford, Calif.

and director, pigmented lesion & melanoma program, Stanford University Medical Center and Cancer Institute, Stanford, Calif.

“In these ways, it could bring a more standardized level of diagnostic accuracy and provide more reliable triage and patient care. By expanding access to dermatologists’ expertise, AI could democratize care and could lead to melanoma detection at an earlier, more curable stage. By reducing time spent on more mundane tasks, physicians would have more time to devote to the physician-patient relationship.”

Echoing the American Academy of Dermatology’s (AAD) position statement on the assistive role of AII, Dr. Swetter explains that, considering the limitations of AI, there is little fear that it will replace clinicians. Conventional neural networks (CNNs) far exceed human brain capability in terms of pattern recognition, but they cannot reproduce human decision-making skills. Computers lack the ability to “blink, think and compare” when evaluating melanocytic neoplasms or incorporate context other than the visual and dermoscopic features they’re been trained to assess.

“Furthermore, computers perform poorly in the ‘gray zone’ of diagnostic uncertainty, which is critical because diagnoses and clinical management are not always clear cut,” Dr. Swetter says. “Likewise, computers don’t work to manage the patient following diagnosis or exhibit empathy or compassion, and so they can never replace human interactions in medicine.”

What CNNs can do is to take over some of the routine aspects of classifying skin lesions.

Dr. Swetter also notes the initial evaluation of the AI algorithm was done as a retrospective study and used an artificial in silico construct. Results from the next step in which the CNN performance was evaluated in a prospective clinical setting were “humbling” in terms of highlighting the impact of issues encountered in the real-world on its diagnostic accuracy. Through further testing, it became clear that the output of any deep learning algorithm is constrained by the nature of the dataset used for training.2

In this case, one of those constraints was the fact that example images in the training set were from a relatively homogenous population, which did not contain many individuals with skin of color. Future datasets will need to include lesions from people of all Fitzpatrick skin types, Dr. Swetter says.

“Otherwise we risk that the application of AI will worsen health inequities that are prevalent already,” she points out.4

Dr. Swetter and her colleagues are continuing to evaluate the performance of their AI system in the clinical setting and have enlisted the collaboration of other centers for prospective, external validation testing.

“The process we are following reflects the AI development pathway outlined in the AAD position statement, and it does not stop after clinical deployment. With collection of new data, the model can and should continue to be refined and improved,” Dr. Swetter says.

Outside of Dr. Swetter’s group, independent researchers have published papers describing CNNs for diagnosis of melanomas, nonmelanoma skin cancers, and onychomycosis using pathology, dermoscopy, and/or clinical images. Overall, the algorithms were found to perform similarly to or better than dermatologists. But, again, most were conducted in the artificial construct, and rigorous prospective clinical validation is needed before any can be incorporated into best practices.

Looking ahead, Dr. Swetter suggests that wide-scale implementation of deep learning algorithms and AI could become reality within the next five years.

“That is exciting because AI can help us move the bar towards addressing inequities in access to specialty care and improving health outcomes for all. But there is still a lot of work to be done, and we have to remember that AI will not replace the human side of medicine,” she says. “Clinicians still need to apply their judgment to decide if the AI output is correct and then decide how to apply the information for delivering the best possible patient care. Using technology to accomplish mundane tasks gives physicians more time to devote to the physician-patient relationship.”

Disclosure: Dr. Swetter reports no relevant disclosures.

Reference:

Quick TAKES

Artificial intelligence can improve melanoma diagnosis, but should not pose a threat to the dermatologist’s role.

Computers lack the ability to “blink, think and compare” when evaluating melanocytic neoplasms or incorporate context.

What technology can do is to take over some of the routine aspects of classifying skin lesions.

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COVID-19 safety protocols to protect staff, patients

CHERYL GUTTMAN KRADER, B.S. PHARM | Staff Correspondent

Although non-surgical aesthetic facial procedures are elective and non-essential medical services, they can have a significant impact on quality of life. Yet, as patients and practices return to these procedures during the pandemic, the potential for acquiring and transmitting COVID-19 is real and a cause of concern for patients and physicians.

Safety guidelines for non-surgical facial procedures developed by the 12 influential members of the European Academy of Facial Plastic Surgery (EAFPS) Aesthetic Medicine Focus Group address this issue. The guidelines outline protocols for protecting clinic staff and patients from SARS-CoV-2 infection. While they were developed in a short time frame, experts anticipate that the COVID-19 pandemic will persist for an extended time. The guidelines appear in a paper published in the August issue of the Journal of Cosmetic Dermatology.¹

“As COVID-19 is with us to stay, and whilst our esteemed researchers are working tirelessly to develop vaccines to combat this highly infective and often lethal disease, the group felt it was our utmost responsibility to set out guidelines to help our patients and practitioners,” Dario Bertossi, M.D., tells Dermatology Times. He is associate professor in maxillofacial surgery, University of Verona, Italy; professor of practice, Centre for Integrated Medical and Translational Research, University of London, UK; and chairman of the Aesthetic Medicine Focus Group.

“As each member of the group has immense experience in non-surgical interventions and its safety aspects, it was my obligation to crystalize this knowledge and experience for the benefit of all concerned. This is exactly what this publication sets out at present with the caveat that this guidance will evolve with time, and we are absolutely committed to update the guidance as the COVID-19 situation progresses,” Dr. Bertossi says.

SYNTHESIZING THE GUIDELINES

The EAFPS Aesthetic Medicine Focus Group members include highly experienced facial plastic surgeons, general plastic surgeons and dermatologists practicing across Europe, Asia and Africa. The process of developing the safety guidelines included an initial virtual meeting in which the task force members offered their suggestions for resuming elective non-surgical facial aesthetic services safely taking into consideration experiences from individual countries. Dr. Bertossi led the discussion using a road map that he developed based on a comprehensive review of the literature, existing guidelines developed by other specialty groups, and his personal experience including personal communication with leaders within the group.

“This was possibly the most important part of the process, yet hugely rewarding,” he says. The information from the meeting was systematically analyzed by a multidisciplinary research team using a thematic and iterative approach. Specific data were verified as needed.

GUIDELINE CONTENT

The safety recommendations developed from the group’s input are divided into three sections that provide guidance on measures to be taken before, during, and after the clinic visit. Each of the three sections is further divided into subsections of guidelines for patients and for healthcare professionals and staff.

The written recommendations are supplemented by images and figures. These illustrative materials include a flowchart showing the route followed by patients between their arrival to and exit from the clinic. A second flowchart details protective processes to be used by providers. In addition, the paper provides a sample form that can be distributed to and returned by patients by encrypted means prior to their visit. The form is designed to identify individuals who may have COVID-19 or have been exposed. The form also asks for the patient’s signature documenting acknowledgment of potential risk and absolving the practice of any criminal or medico-legal liability.

A second sample form intended for distribution to patients includes general information...
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Quick TAKES

- Eating significant amounts of sugars and foods cooked at high temperatures can lead to formation of advanced glycation end products, which may impact skin aging.
- The Mediterranean diet has the most evidence with regard to impact on skin aging and health.
- Supplements should be used only in cases of nutritional deficiencies as they are not regulated by the FDA, and it is difficult to measure dose and effectiveness in any study.

What we know (and don’t) about diet and skin aging

JOHN JESITUS | Staff Correspondent

To minimize the impact of diet on skin aging, an expert suggests changing cooking techniques, embracing the Mediterranean diet and avoiding nutritional supplements except in situations involving specific deficiencies.

“We need more evidence to know for certain how diet impacts skin aging. Some studies suggest ways in which we may alter our diets that might help, but we need more large-scale studies before we can know the true impact of dietary patterns on aging,” says Emmy Graber, M.D., MBA. She is president and founder of The Dermatology Institute of Boston, PC, Boston.

Emerging evidence including a 2010 Clinics in Dermatology report supports the importance of avoiding glycation wherever possible.

“The glycation process of sugars attaching to collagen in the skin can have an impact on how we and the skin age,” Dr. Graber says.

More specifically, she says, cross-linked collagen created by this process is unable to repair itself as it normally would, resulting in stiffer, older-looking skin. Avoiding glycation also helps other organs age more gracefully.

Eating significant amounts of sugars can lead to the formation of advanced glycation end products (AGEs).

“We can also ingest already formed advanced glycation end products,” she says. “These exogenously formed advanced glycation end products often result from high-temperature cooking techniques such as grilling, frying and roasting.”

When foods cooked in these ways are eaten, AGEs are deposited in the skin.

“Some small studies suggest that avoiding these methods of cooking may be preferential to prevent aging skin,” she says.

Instead, poaching, boiling or steaming foods may be safer.

Similarly, small studies suggest that the Mediterranean diet may help slow down skin aging.

“Mediterranean diets are rich in fruits, vegetables, fish and olive oil, low in sugars and lower meats and refined carbohydrates,” she says.

Dr. Graber advises caution regarding nutritional supplements.

“People always ask, ‘if I can’t change my diet, could I take a vitamin or supplement?’”

Because supplements are not regulated by the FDA, she says, it is very difficult to measure both the dose and the effectiveness in any study.

“As dermatologists, we should not be recommending supplements at this time unless a patient is deficient in a certain vitamin,” she says.

The take-home message, says Dr. Graber, is that if patients want to alter their diet for antiaging advantages, she recommends the Mediterranean diet because it has the most evidence in this regard.

“I also recommend lowering their sugar intake and changing their cooking methods to avoid high-temperature cooking methods, looking more towards steaming or boiling foods,” she says.

Disclosure: Dr. Graber reports no relevant financial interests.

Reference:

COVID-19 safety protocols inform practice operations FROM PAGE 38

For patients undergoing a nasal or intranasal procedure, 0.23% povidone-iodine solution is recommended for use as a virucide in a nasal spray or oral rinse. This added measure is important given the potential for aerosolization of respiratory droplets with these procedures.

The post-visit recommendations identify the value of minimizing follow-up visits. As an alternative to having patients return to the clinic, the guidelines suggest asking patients to submit a photograph and participate in a video consultation to communicate relevant details about their condition.

In their conclusion, the members of the EAFPS Aesthetic Medicine Focus Group note that crafting an optimal set of safety recommendations in a short period of time represents a challenge.

Nevertheless, they state their belief that the product they released could offer a foundation for COVID-19 safety guidelines in aesthetic practices worldwide.
JOIN US IN 2021
CSF Live is on hold for 2020.

2020 has certainly ushered in wholly unthinkable challenges! Like all of you, the Cosmetic Surgery Forum team has been facing them head-on and doing all we can to care for those around us and make a better community for us all.

CSF has always been committed to providing a meaningful experience for all of our participants - which includes doing our part to keep everyone safe. While we will certainly miss the camaraderie and energy of a face-to-face meeting, we truly feel this is the right decision.

In lieu of a live event in 2020, Cosmetic Surgery Forum will host sessions throughout the next 12 months offering you the same type of in-depth learning and collegial discussion you have come to expect from us. Check out our website (CosmeticSurgeryForum.com), Facebook and LinkedIn over the next few weeks for updates! We will see all of you again Wednesday, December 1 – Saturday, December 4, 2021 at the JW Marriott in Nashville, TN. Please save the date!

For more information, please contact: Natasha Mohr or Meg Housholder - info@CosmeticSurgeryForum.com - 402-697-6564
Quick Takes

Anatomical variation in the vascular network in the glabellar region increases the risk for necrosis when performing filler correction of glabellar rhytids.

Pre-treatment punch guides safe injection

CHERYL GUTTMAN KRADER, B.S. PHARM | Staff Correspondent

Soft tissue augmentation with a hyaluronic acid filler can be effective for improving the appearance of deep vertical glabellar rhytids. However, filler injections into the glabellar region carry a higher risk of necrosis from inadvertent vascular compression, obstruction or direct injury.

In a recently published article, Pınar Özdemir Çetinkaya, M.D., and colleagues described their technique for maximizing safety using a filler to correct glabellar rhytids and reported outcomes with its use in a retrospective study including 50 patients.

To guide the filler injections, their approach utilizes a needle punching technique that assesses for the presence of the supratrochlear artery and/or its branches. Deep placement of the filler onto the periosteum further minimizes risk and makes the procedure ideal for correcting moderate to deep glabellar wrinkles, said Dr. Özdemir Çetinkaya, department of dermatology and venereology, Nazilli State Hospital, Aydin, Turkey.

“There can be anatomical variations in the vascular network in the glabellar region. A three-point puncture technique allows the practitioner to estimate the course of the underlying vessels and deliver the filler accordingly,” she explains.

“Although the size of our study population may be too small to determine the true prevalence of a rare severe complication, we encountered no cases of skin necrosis or visual impairment among our patients, and we achieved a very high rate of patient satisfaction.”

The punctures are made at three equidistantly spaced sites along the glabellar line(s) using a 23-gauge punching needle that is inserted perpendicularly through the skin, advanced until it meets the periosteum of the frontal bone, and then withdrawn. Then, the amount of bleeding is assessed.

“If the bleeding is excessive, fast, and hard to stop, it is assumed that the needle entered into the lumen of the supratrochlear artery or one of its branches. Once the bleeding is controlled through pressure application, an alternate site located 1-2 mm above or below is tested for safety using the puncture technique.”

Standard recommendations for safe filler injection are also followed. Filler delivery for moderate-to-deep glabellar rhytids is performed using a 25-gauge, 50-mm cannula that is inserted perpendicularly to the periosteum of the bone. Aspiration is performed prior to injecting the filler to verify that the instrument has not entered into any vessel. Then, the hyaluronic acid is delivered using small droplets (0.05 to 0.2 mL) and with a slow flow rate while patients are questioned about the presence of any pain.

In the retrospective study reported by Dr. Özdemir Çetinkaya and colleagues, cross-linked hyaluronic acid 20 mg/mL with 0.3% lidocaine (Juvéderm VOLUMA XC) was used as the filler material. Other hyaluronic acid products fillers are also suitable, Dr. Özdemir Çetinkaya says.

The 50 patients included in the review had moderate-to-severe glabellar rhytids (grade 3 or higher on the Rao-Goldman 5-point wrinkle scale) – 28 patients (56%) had moderately deep wrinkles (Rao-Goldman score of 3), 17 patients (34%) had deep wrinkles with well-defined edges (Rao-Goldman score of 4), and two patients (10%) had very deep wrinkles with redundant folds (Rao-Goldman score of 5). The cohort included 39 females and 11 males with a mean age of approximately 40 years (range 25 to 50 years).

All patients underwent neurotoxin injection in the glabellar complex two weeks prior to the filler procedure. At two weeks after the filler injection, patients’ outcomes were assessed and, if needed, they received touch-ups with filler injection into the subdermal plane from a single distant entry point. Eight patients (16%) underwent a touch-up.

Outcomes were evaluated at two weeks after the first injection. The results showed that all patients achieved a one- to two-grade improvement from baseline in the Rao-Goldman score. Forty-one patients (82%) achieved complete effacement of their glabellar wrinkles, eight patients (16%) had shallow wrinkles, and one patient (2%) had moderately deep wrinkles.

“The latter patient had a Rao-Goldman score of five at baseline, improved to grade three, and received a touch-up,” Dr. Özdemir Çetinkaya tells Dermatology Times.

Patient satisfaction was good. No patients were dissatisfied, and 45 patients (90%) said they were satisfied or extremely satisfied with their treatment.

Eight patients developed procedure-related complications, including bruising (4%), erythema and edema (10%) and a local infection (2%). Each event was mild, managed with minor interventions, and resolved within three to seven days.

Disclosure:
Dr Özdemir Çetinkaya has no relevant financial interests to disclose.

References:
Beauty & the Bacteria
An Exploration into the World of the Skin Microbiome

In this upcoming new educational docuseries, hosted by geneticist Thomas M. Hitchcock, PhD, we will take you on a journey inside the world of the skin microbiome.

Through this journey you will appreciate the entangled relationship between our skin and the microbes living on and in it—and how that affects our lives. Featuring special appearances by a number of leading U.S. dermatologists, the series will guide the audience through the basics of what the skin microbiome actually is and why it is critical to the health of our skin.

Watch here:
crownlaboratories.com/microbiome
Research lacks effective microbial-based therapies

JOHN JESITUS | Staff Correspondent

Manipulating the microbiome has been shown to impact conditions like acne, atopic dermatitis (AD), autoimmune diseases and melanoma; however, there aren’t yet effective treatment strategies that target the microbiome for any of these conditions, one expert says.

“Hopefully,” says Teri Greiling, M.D., Ph.D., “research in these areas will provide us with therapeutic options in the future, but we’re not there yet.” She is assistant professor of dermatology and associate program director of dermatology research at Oregon Health & Science University, Portland.

ACNE

Dermatologists target *Cutibacterium acnes* with antimicrobial strategies because this entity has the most evidence showing that it plays a key role in acne, she says.

“However, it’s unclear whether a single culprit strain of *C. acnes* causes acne, or if a patient’s individual immune response to *C. acnes* is to blame,” she says.

Emerging strategies to target *C. acnes* involve colonization with probiotic “good” bacteria, and killing *C. acnes* specifically while sparing beneficial bacteria.

AUTOIMMUNE CONDITIONS

“There’s been some emerging evidence that interactions between specific bacterial species and the immune system can trigger and sustain autoimmunity in multiple different autoimmune diseases,” she explains.

For example, certain skin and gut bacteria may initiate lupus in genetically susceptible individuals.

“The immune system is attacking the bacteria, but those bacteria have conserved proteins that cross-react with human cells, turning a healthy immune response into autoimmunity,” she says.

In ulcerative colitis, the first clinical trials of fecal transplants have shown the ability to allow patients to achieve remission without immunosuppressive therapy.

ATOPIC DERMATITIS

“We know that flares of atopic dermatitis are associated with overgrowth of *Staphylococcus aureus* and loss of most other healthy microbes on the skin,” she says.

In early clinical trials, topical replacement of *Roseomonas mucosa* reduced AD flares, she says.

“Interestingly, without treating the bacteria itself, just treating the immune response with steroids or dupilumab can also restore the healthy microbiota. It’s counterintuitive that immune suppression allows restoration of the normal healthy microbiota,” she says.

MELANOMA

Well-done studies have shown that when using PD-1 inhibitors or CTLA4 inhibitors for metastatic melanoma, investigators can predict who will survive based on the balance of patients’ gut bacteria, Dr. Greiling says. But because three recent publications highlight helpful or harmful impacts of different bacteria, she adds, the key players remain unclear.

“However, a meta-analysis has shown that if you’re treated with antibiotics within six weeks before starting immune therapy, you have a much poorer likelihood of responding to immune therapy,” she says.

Regarding probiotics in general, Dr. Greiling says that the dozen or so FDA-approved strains earned approval due to their safety.

“But these strains are probably not that useful in terms of most of these diseases. There are finally clinical trials in progress of microbiota-based therapies, but the safety and efficacy in big trials aren’t proven,” she says.

Disclosures:

Dr. Greiling reports no relevant financial interests.

Reference:

One hypothesis that we will be testing is that biologic agents that target some immune axes may be protective.

Emma Guttman-Yassky, M.D., Ph.D., Mount Sinai Medical Center, New York

Systemic therapies may protect patients from becoming severely or critically ill with COVID-19. In fact, it appears that some medications may even have protective effects.

Through research she is leading at Mount Sinai Medical Center in New York, Emma Guttman-Yassky, M.D., Ph.D., hopes to provide more definitive insight on this topic.

Early in the pandemic, Dr. Guttman-Yassky and colleagues created a registry to collect data on COVID-19 in patients with eczema and psoriasis who have moderate to severe disease and are candidates for systemic treatments with anticipated funding from Regeneron and Sanofi.

In July, she received a grant from the National Institutes of Health (NIH) on behalf of the National Institute of Allergy and Infectious Disease to support some laboratory analyses of immune responses in blood of patients with eczema who had developed COVID-19. Dr. Guttman-Yassky is the Sol and Clara Kest Professor of Dermatology and Vice Chair of the department of dermatology, Icahn School of Medicine at Mount Sinai. She tells Dermatology Times that with access to a large population of patients with inflammatory skin diseases on immunomodulatory treatment who became infected with COVID-19, her group is particularly well-positioned to investigate interactions between immunomodulatory treatment and the viral disease.

“The dermatology practices within the Mount Sinai Health System treat a huge number of patients with systemic medications for psoriasis and eczema. For example, we have more than 1,200 patients receiving dupilumab for moderate-to-severe eczema. Because New York City was an epicenter of the COVID-19 pandemic for some time, many of our patients were also affected by the coronavirus infection,” Dr. Guttman-Yassky explains.

“Considering our patient volume, we think our research will have sufficient power to identify associations if they exist and allow us to provide information that will be valuable for the entire dermatology community and our patients. Not only will it provide a foundation for developing a better treatment scheme for our patients with inflammatory skin diseases, but perhaps it may also suggest new approaches for treating COVID-19.”

The two-year grant from the NIH is in addition to a seven-year grant Dr. Guttman-Yassky was awarded previously to study mechanisms underlying variations in eczema phenotypes. The new grant supports determination of immune responses in blood collected from patients on systemic immunomodulatory treatment for eczema who developed COVID-19 and to detect potential treatment-related differences in mounting immune responses.

“The idea that systemic immunomodulatory treatments -- and some biologic medications in particular -- may protect patients from becoming severely or critically ill with COVID-19 is based on information that a hyperinflammatory response that is characterized by elevated levels of various cytokines drives severity of the viral infection.

“One hypothesis that we will be testing is that biologic agents that target some immune axes may be protective,” Dr. Guttman-Yassky says.

“Patients in the Mount Sinai dermatology registry are being asked to complete a questionnaire that identifies whether or not they developed COVID-19 or had exposure to anyone known to have the viral infection. Information on symptoms is gathered from patients with a confirmed diagnosis of COVID-19 so they can be categorized based on severity. Data are also being collected on comorbidities that are considered risk factors for COVID-19, including asthma, age, hypertension, diabetes, and ethnicity.

“Asthma is common in many patients with eczema, and hypertension and diabetes are both common among adults who have eczema or psoriasis. In addition, ethnic populations, including African Americans and Latinos, are more affected by severe eczema and have a higher prevalence of asthma, diabetes, and hypertension,” Dr. Guttman-Yassky says. “Stratification of patients by COVID-19 risk factors will be important for investigating the effects of immunomodulatory treatments and differences in immunological responses to COVID-19.”
Atopic Dermatitis
Treatment Strategies for Children

When talking to families of babies and young children with atopic dermatitis, how can you best outline treatment goals? What initial regimen should you consider? What is the earliest appropriate patient age for treatment with a monoclonal antibody? What kind of overall safety concerns will parents typically voice?

In this *Dermatology Times*® podcast, Amy Paller, MS, MD, shares her strategic approach to reducing the discomfort experienced by babies or young children with atopic dermatitis.

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ARAZLO™ (tazarotene) Lotion, 0.045% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

Important Safety Information
ARAZLO Lotion is for topical use only. Not for oral, ophthalmic, or intravaginal use.

Contraindication
ARAZLO Lotion is contraindicated in pregnancy due to the potential harm to the fetus.

Warnings and Precautions
Embryofetal Risk Females of childbearing potential should be warned of the potential risk and should use adequate birth-control measures when ARAZLO Lotion is used. A negative result for pregnancy should be obtained within 2 weeks prior to ARAZLO Lotion therapy, and therapy begun during a menstrual period. If the patient becomes pregnant while using ARAZLO Lotion, treatment should be discontinued.

Skin Irritation Patients using ARAZLO Lotion may experience application site pain, dryness, exfoliation, erythema, and pruritus. Depending upon severity, adjust or interrupt dosing as needed, increasing or resuming treatment as tolerated. Avoid application of ARAZLO Lotion to eczematous or sunburned skin.

Photosensitivity and Risk for Sunburn
Minimize unprotected exposure to ultraviolet light, including sunlight, sunlamps and tanning beds, during the use of ARAZLO Lotion. Warn patients with high levels of sun exposure and those with inherent sensitivity to sun to exercise caution. Instruct patients to use sunscreen products and protective clothing over treated areas when sun exposure cannot be avoided.

ARAZLO Lotion should be administered with caution if the patient is taking drugs known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the increased possibility of augmented photosensitivity.

Weather extremes, such as wind or cold, may be more irritating to patients using ARAZLO Lotion.

Adverse Reactions
The most common adverse reactions (in ≥1% of patients and greater than vehicle) were: application site pain, dryness, exfoliation, erythema, and pruritus.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch Health US, LLC at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Brief Summary of full Prescribing Information on following page.


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