AARS HOT TOPICS MEMBER NEWSLETTER

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Industry News

BioPharmX Announces Preliminary Data from Rosacea Feasibility Study – Data Suggest Feasability of BPX-01 1% and 2% in patients with rosacea. BioPharmX. Sep 12, 2017. http://biopharmx.investorroom.com/2017-09-12-BioPharmX-Announces-Preliminary-Data-from-Rosacea-Feasibility-Study

BioPharmX Corporation (NYSE MKT: BPMX), a specialty pharmaceutical company focusing on dermatology, is announcing preliminary data from a feasibility study of BPX-01 to assess the safety and efficacy of topical minocycline gel at both the 1% and 2% doses for the treatment of rosacea. The preliminary data from the ongoing study suggest good tolerability and promising efficacy of BPX-01 in this indication and highlight the value of BioPharmX's dermatology delivery system. This ongoing 12-week, open-label feasibility study to assess the safety and efficacy of BPX-01 topical minocycline gel in rosacea patients enrolled 20 subjects with moderate-to-severe papulopustular rosacea, who applied BPX-01 once daily. Safety was assessed by reviewing treatment emergent adverse events, shifts from baseline in hematology and chemistry laboratory tests as well as cutaneous tolerance scores as assessed both by study subjects and investigators. The preliminary data show that BPX-01 was well tolerated in all subjects treated to date. No adverse events were determined to be treatment related and there were no clinically significant shifts from baseline in hematology and chemistry laboratory tests. The primary efficacy endpoint from this study is change in Investigator's Global Assessment (IGA) of rosacea at 12 weeks. The secondary efficacy endpoint is change in facial lesion count from baseline at 12 weeks. The preliminary data obtained to date suggest a positive effect on rosacea lesions. Of the 15 subjects that have completed 12 weeks of treatment in the study, 100% have IGA scores of clear (0) or almost clear (1), compared to their baseline scores of moderate (3) or severe (4). Investigators also observed a 93% reduction in total inflammatory lesions from baseline to week 12 in the same subjects who have completed the 12-week study. "BPX-01 has been well tolerated by the study subjects," said Dr. Neal Bhatia, a board-certified dermatologist at Therapeutics Clinical Research who is the study's principal investigator. "We are pleased with the initial data on efficacy. We look forward to the final results of the study and determining next steps." Company executives said they expect to pursue additional research to evaluate the efficacy of BPX-01 in rosacea. "These preliminary results are encouraging and give us guidance as we evaluate our clinical development plan for rosacea. They also reinforce the potential value of our unique drug delivery platform across various dermatology indications," said Anja Krammer, president of BioPharmX. "Additionally, we are excited by the prospect that it may offer rosacea patients a long-overdue therapeutic innovation.

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Generic Acne Treatment Launches in US. Julie Gould. The Dermatologist, July 28, 2017 http://www.the-dermatologist.com/content/generic-acne-treatment-launches-us

The generic acne treatment adapalene and benzoyl peroxide (Epiduo) gel, 0.1%/2.5%, has launched in the United States, according to drug maker Teva Pharmaceutical Industries Ltd. Teva is the first company that filed a generic application for the branded treatment. Created with a combination of adapalene, a retinoid, and benzoyl peroxide, adapalene and benzoyl peroxide gel 0.1%/2.5%, is currently indicated for the topical treatment of acne vulgaris in patients 9 years of age and older. Currently, Teva markets approximately 600 generic medicines, and has more than 100 pending first-to-files in the US. It is estimated that 1 in 6 generic prescriptions dispensed in the US is filled with a Teva-branded product.

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New Medical Research

Treatment of erythemato-telangiectatic rosacea with brimonidine alone or combined with vascular laser based on preliminary instrumental evaluation of the vascular component. Micali G, Dall'Oglio F, Verzì AE, Luppino I, Bhatt K, Lacarrubba F. Lasers Med Sci. 2017 Sep 9. doi: 10.1007/s10103-017-2318-3. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28889348

The purpose of this study is to evaluate the outcome of a series of patients with erythematotelangiectatic rosacea (ETR) affected by persistent erythema and varying degree of telangiectasias being treated with brimonidine alone or combined with a vascular laser based on the type of vascular components preliminarily evaluated by clinical and instrumental observation. Ten patients affected by ETR were enrolled in a pilot, open study. Instrumental evaluation included erythema-directed digital photography by VISIA-CR™ system and X10 dermoscopy. Those patients showing marked background erythema and minimal telangiectasias (group A) were treated with a single application of brimonidine 0.33% gel, while patients showing both marked background erythema and marked telangiectasias (group B) were treated with a session of Nd:YAG laser and reevaluated 1 month later after a single application of brimonidine. An Investigator Global Assessment (IGA) of treatment outcome was performed at the end of treatment in both groups. In group A, 6 h after brimonidine application, a marked reduction of the background erythema was observed in all patients, and IGA was rated as excellent. In group B, 6 h following the application of brimonidine, a marked reduction of the background erythema was observed in all cases, while telangiectasias remained unchanged. A further treatment with brimonidine 1 month after the Nd:YAG laser session determined complete clearing of facial erythema, and IGA was rated as excellent. In conclusion, a preliminary evaluation of the vascular component by erythema-directed digital photography and dermoscopy in ETR may be helpful to select the most appropriate therapeutic strategy.

Comparative Effects of Schisandrin A, B, and C on Acne-Related Inflammation. Guo M, An F, Wei X, Hong M, Lu Y. Inflammation. 2017 Sep 5. doi: 0.1007/s10753-017-0656-8. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28875271

Inflammatory responses induced by Propionibacterium acnes are a major etiological factor in the pathogenesis of acne vulgaris. Schisandrin A, schisandrin B, and schisandrin C are the representative lignans of Schisandra chinensis (Turcz.) Baill. extract. Although anti-inflammatory effects of the lignans have been shown, their effects on acne-related inflammation caused by P. acnes have not been investigated and compared. We pretreated THP-1 human monocytic cells with 5, 10, and 20 μM schisandrin A, B, and C, and stimulated the cells with P. acnes. Schisandrin B and C inhibited the release of inflammatory cytokines at a concentration of 5 μM, while schisandrin A required a concentration of 10 μM to exert the effects. All of the schisandrins decreased the levels of toll-like receptor 2, and schisandrin B and C reduced the intracellular mRNA expression of the receptor gene. We also studied the influence of schisandrins on the MAPK signaling pathway. Schisandrin A suppressed the P. acnes-induced activation of JNK, while exerting only a weak effect on ERK and p38. Schisandrin B exerted a strong effect on p38, a lesser effect on ERK, and almost no effect on JNK. Schisandrin C inhibited the phosphorylation of all three proteins, especially ERK. Furthermore, the three lignans also prevented the nuclear translocation of NF-κB. These results contribute to our understanding of the mechanisms underlying the effects of the three lignans on P. acnes-induced inflammation and suggest that schisandrins might be developed as pharmacological agents for acne therapy.

Immune discrepancies during in vitro granuloma formation in response to Cutibacterium (formerly Propionibacterium) acnes infection. Aubin GG, Ada Da Silva G, Eishi Y, Jacqueline C, Altare F, Corvec S, Asehnoune K. Anaerobe. 2017 Aug 30;48:172-176. doi: 10.1016/j.anaerobe.2017.08.014. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28859990

Cutibacterium (formerly Propionibacterium) acnes is involved in chronic/low-grade pathologies such as sarcoidosis or prosthetic joint infection (PJI). In these diseases, granulomatous structures are frequently observed. In this study, we induced a physiological granulomatous reaction in response to different well-characterized clinical C. acnes isolates in order to investigate the cellular process during granuloma formation. Three C. acnes isolates selected according to their origin (PJI, sarcoidosis and acne) were typed by MLST. All C. acnes isolates generated granulomatous structures in our experimental conditions. The bacterial burden was better controlled by granulomas induced by the sarcoidosis C. acnes isolate. The PJI C. acnes isolate, belonging to CC36, promoted the recruitment of CD8+ lymphocytes inside the granuloma. In contrast, the acne and sarcoidosis C. acnes isolates, belonging to phylotypes IA1/CC18 and IA2/CC28, respectively, generated a higher number of granulomas and promoted the recruitment of CD4+ lymphocytes inside the granuloma. Our results provide new evidence supporting the role of C. acnes in the development of sarcoidosis and new explanations concerning the mechanisms underlying PJI due to C. acnes.

Evaluation of autologous platelet rich plasma plus ablative carbon dioxide fractional laser in the treatment of acne scars. Abdel Aal AM1, Ibrahim IM, Sami NA, Abdel Kareem IM. J Cosmet Laser Ther. 2017 Aug 30. doi: 10.1080/14764172.2017.1368667. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28853968

INTRODUCTION: Acne scar is a common distressing complication of acne vulgaris. CO2 laser resurfacing proved effective for treatment of such problem but the associated complications may limit its use. Platelet rich plasma (PRP) may increase the chance of favorable outcome. AIM OF THE WORK: To evaluate the synergistic effects of autologous PRP with fractional CO2 laser resurfacing in treatment of acne scars among Egyptian patients. PATIENTS AND METHOD: This study included 30 patients suffering from post-acne scars. CO2 laser treatment was applied to both sides of the face followed by PRP injection for the right side. Evaluation was carried out through operating physicians, two blinded physicians as well as patient`s satisfaction. RESULT: The right side of the face (PRP treated side) achieved excellent improvement in 13.3% of patients while there was no excellent improvement on the left side. CONCLUSION: combination of fractional CO2 laser resurfacing and intradermal PRP was superior to CO2 laser alone for acne scar treatment.

Safety of non-ablative fractional laser for acne scars within 1 month after treatment with oral isotretinoin: A randomized split-face controlled trial. Saluja SS, Walker ML, Summers EM, Tristani-Firouzi P, Smart DR. Lasers Surg Med. 2017 Aug 29. doi: 10.1002/lsm.22711. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28853175

BACKGROUND AND OBJECTIVE: Based on reports of poor wound healing and scarring, it is currently recommended that patients wait 6 months after completion of oral isotretinoin therapy before the safe initiation of laser treatment. Our aim was to evaluate the safety of non-ablative fractional laser (NAFL) treatment for acne scars within 1 month after isotretinoin therapy. STUDY DESIGN/METHODS: This was a randomized split-face controlled trial involving 10 patients with acne scars who had completed isotretinoin treatment. All patients received three treatments each spaced 4 weeks apart with an erbium-doped 1550 nm NAFL on one side of the face within 1 month

after isotretinoin therapy. The untreated side acted as a control. Wound healing and adverse effects as well as acnescar improvement were evaluated by two blinded dermatologists. RESULTS: All patients demonstrated normal wound healing post NAFL treatments, and neither hypertrophic scars nor keloids were observed. Acne scar improvement was satisfactory. CONCLUSION: NAFL treatment for acne scarring appears to be well tolerated within 1 month of completing isotretinoin treatment. Dermatologists should reevaluate the current recommendation to wait 6 months after isotretinoin treatment for acne scar revision with lasers. Other larger studies are necessary to further challenge this dogma.

Clinical Reviews

SAPHO syndrome associated with hidradenitis suppurativa and pyoderma gangrenosum successfully treated with adalimumab and methotrexate: a case report and review of the literature. Vekic DA, Woods J, Lin P, Cains GD. Int J Dermatol. 2017 Sep 7. doi: 10.1111/ijd.13740. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28884797

SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome is a rare inflammatory condition describing the combination of skin, bone, and joint manifestations that has a heterogeneous presentation. We report a case of severe SAPHO syndrome in association with hidradenitis suppurativa and pyoderma gangrenosum in a 27-year-old male. The patient had an initial migratory arthritis affecting the knees, ankles, metacarpophalangeal joints, proximal interphalangeal joints, wrists, shoulder, and lower back, which progressed to a persistent arthritis and swelling at the sternum, shoulders, wrists, hands, feet, and lower back. Radiographic changes were consistent with the diagnosis of SAPHO syndrome. Serum proinflammatory cytokine levels were significantly elevated and improved substantially after 3 months of therapy. Rationale for therapy in this patient was the observation that tumor necrosis alpha antagonists have been successfully used in SAPHO syndrome, and since arthropathy was so prominent in our patient, we elected to use adalimumab combined with methotrexate.

The microbiota matters: In acne, it's not us versus them. By: Kari Oakes. Dermatology News. August 23, 2017

http://www.mdedge.com/edermatologynews/article/145195/acne/microbiota-matters-acne-its-not-us-versus-them?channel=171&utm_source=News_DERM_acne_082517_F&utm_medium=email&utm_content=The%20microbiota%20matters:%20In%20acne,%20it%27s%20not%20us%20versus%20them

EXPERT ANALYSIS FROM THE 2017 AAD SUMMER MEETING. Just as an imbalance in the intestinal microbiota can disrupt gut function, dysbiosis of the facial skin can allow acne-causing bacteria to flourish. In acne, said Adam Friedman, MD, "we've always been talking about bacteria," but now the thinking has shifted from just controlling Propionibacterium acnes to a subtler understanding of what's happening on the skin of individuals with acne. Individuals may have their own unique skin microbiota – the community of organisms resident on the skin – but dysbiosis characterized by a lack of diversity is increasingly understood as a common theme in many skin disorders, and acne is no exception. As in many other areas of medicine, dermatology's understanding has been informed by genetic work that moves beyond the human genome. "Using newer technology, we were able to identify that our genome really was overshadowed by the microbial genome that makes up the populations in our skin, in our gut, and what have you," said Dr. Friedman, speaking at the summer meeting of the American Academy of Dermatology. There are more than 500 bacterial species that live on healthy skin, and together, these bacteria express more than 2 million genes. There are about 20,000 human genes. "We are actually more bacteria than we

are human. So the question is – is it us versus them? Bad guy versus good guy? No. The answer is that together, we make a superorganism. We work together. There is symbiosis and harmony between these countless organisms and ourselves," he said. The human body is like a planet to the bacteria that live on the human skin, and like a planet, the skin provides multiple "climates" for many bacterial ecosystems, said Dr. Friedman, director of translational research and dermatology residency program director, at George Washington University, Washington, DC. Some areas are dry, some are moist; some are more oily, and some areas of the skin produce little sebum; while some are mostly dark and some are more likely to be exposed to light. Considering skin from this perspective, it makes sense that bacterial microbiota for these disparate areas varies widely, with a different mix of bacteria found in the groin than on the forearm, he noted. Further, "each individual has his or her own microbiota fingerprint," said Dr. Friedman, citing a 2012 study showing that in four healthy volunteers, the microbiota from swabs at four sites (antecubital fossa, back, nare, and plantar heel) varied widely both in diversity and composition (Genome Res. 2012 May;22[5]:850-9). Multiple factors can contribute to this variability, which can include endogenous factors, such as host genotype, sex, age, immune system, and pathobiology. Exogenous factors, such as climate, geographic location, and occupational exposures, also play a part. Increasingly, said Dr. Friedman, lack of bacterial diversity in skin microbiota is recognized as an important factor in many disease states, including atopic dermatitis and psoriasis. And bacterial diversity has recently been shown to be reduced on the facial skin of patients with acne, even on areas of clear skin. When acne treatments work, a healthy facial microbiota is restored. And perhaps counterintuitively, patients with acne who receive isotretinoin and antibiotics have much greater diversity in the microbiota of their facial skin after treatment than before, according to a study recently published online (Exp Dermatol. 2017 Jun 21. doi: 10.1111/exd.13397). For now, this is still a chicken-and-egg situation, Dr. Friedman said. "Does the disease cause the lack of diversity, or does the lack of diversity cause the disease to develop? We don't know yet." (Nat Rev Microbiol. 2011 Apr;9[4]:244-53). However, it's logical to try to maintain a healthy skin barrier by avoiding abrasive products, minimizing use of antibiotics and steroids, and facilitating barrier repair with quality moisturizers. "If we're going to think about the surface of our skin as a barrier, we must consider the microbiota as part of that barrier." P. acnes "is a clear instigator in eliciting a host inflammatory response," through its recognition by toll-like receptors and the inflammasome to induce inflammation, Dr. Friedman said. However, it can also help prevent the colonization of opportunistic pathogens, including methicillin-resistant Staphylococcus aureus and Streptococcus pyogenes by helping maintain an acidic skin pH. "When and how does a commensal [organism] become a pathogen?" he asked. The fact that P. acnes is a commensal bacterium on healthy skin seems to muddy the picture, until one also recognizes that there are different strains of P. acnes. Only some of these phylotypes cause acne, with an exaggerated host inflammatory response being one possible causative factor, noted Dr. Friedman. A clue to how this occurs comes from a recent study that found that some types of P. acnes actually convert sebum to short-chain fatty acids that "interfere with how our bodies regulate toll-like receptors, uncoupling them and then laying them loose to create inflammation," said Dr. Friedman (Sci Immunol. 2016 Oct 28;1[4]. pii: eaah4609). When considering what to do with the available information, something for dermatologists to consider is the effect moisturizers have on the skin of patients with acne, Dr. Friedman said. A moisturizer contains water; it may also contain a carbon source in the form of a sugar like mannose, nitrogen in the form of amino acids, and some oligoelements such as calcium, magnesium, manganese, strontium, and selenium. All of these ingredients really serve as prebiotics for the skin microbiota, Dr. Friedman noted, adding that products that create a prebiotic environment where acnegenic P. acnes are suppressed and a healthy microbiota can flourish are being developed. "What does all this mean? We do not know yet," said Dr. Friedman. But, he added, "clearly, what we're using is having an effect, and we need to figure it out." Dr. Friedman reported financial relationships with several pharmaceutical and skin care companies. He serves on the editorial board of Dermatology News.

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Rosacea and Helicobacter pylori: links and risks. Elizabeth Lazaridou, Chrysovalantis Korfitis, Christina Kemanetzi, Elena Sotiriou, Zoe Apalla, Efstratios Vakirlis, Christina Fotiadou, Aimilios Lallas, and Demetrios Ioannides. Clin Cosmet Investig Dermatol. 2017; 10: 305–310. Published online 2017 Aug 10. doi: 10.2147/CCID.S121117 PMCID: PMC5556181 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5556181/

Rosacea is a chronic skin disease characterized by facial erythema and telangiectasia. Despite the fact that many hypotheses have been proposed, its etiology remains unknown. In the present review, the possible link and clinical significance of Helicobacter pylori in the pathogenesis of rosacea are being sought. A PubMed and Google Scholar search was performed using the terms “rosacea”, “H.pylori”, “gastrointestinal disorders and H.pylori”, “microorganisms and rosacea”, “pathogenesis and treatment of rosacea”, and “risk factors of rosacea”, and selected publications were studied and referenced in text. Although a possible pathogenetic link between H. pylori and rosacea is advocated by many authors, evidence is still interpreted differently by others. We conclude that further studies are needed in order to fully elucidate the pathogenesis of rosacea.

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Adalimumab for Hidradenitis Suppurativa. Daniel J. No, BA Mina Amin, BS Jashin J. Wu, MD. Cutis. 2017 August;100(2):100. http://www.mdedge.com/cutis/article/143780/rare-diseases/adalimumab-hidradenitis-suppurativa?utm_source=Clin_CUT_weekly_090117_F&utm_medium=email&utm_content=Athlete%27s%20foot%20products%20|%20Adalimumab%20for%20hidradenitis%20suppurativa.

We applaud Kimball et al on their report that adalimumab demonstrated clinical improvement in patients with hidradenitis suppurativa (HS) versus placebo in 2 phase 3 trials. Hidradenitis suppurativa is a chronic relapsing condition with painful subcutaneous abscesses, malodorous drainage, sinus tract formation, and scarring that typically occurs in the axillae and anogenital region. It impairs the quality of life for these patients, as evidenced by higher Dermatology Life Quality Index scores compared to psoriasis, pimples, hand rash, atopic eczema, or control. The exact pathogenesis of HS is unknown but likely involves a complex interaction of genetic, hormonal, immunologic, and environmental factors. The levels of inflammatory cytokines are elevated in HS lesions, specifically IL-1β, tumor necrosis factor α, IL-10, and CXCL9, as well as monokines from IFN-γ, IL-11, and IL-17A. Additionally, the dermis of affected regions contains IL-12– and IL-23–containing macrophages along with IL-17–producing T cells. These findings reveal many potential therapeutic targets for the treatment of HS. PIONEER I and PIONEER II are similarly designed 36-week phase 3 trials of 633 patients with HS who were unresponsive to oral antibiotic treatment. By week 12, a significantly greater proportion of patients receiving adalimumab demonstrated clinical improvement (≥50% reduction in total abscess and nodule count) compared to placebo in both trials (PIONEER I: 41.8% vs 26.0%, P=.003; PIONEER II: 58.9% vs 27.6%, P<.001). Secondary end points (inflammatory-nodule count, pain score, and disease severity) were only achieved in PIONEER II. The difference in clinical improvement between the trials is likely due to higher baseline disease severity in the HS patients in PIONEER I versus PIONEER II. No new safety risks were reported and were in accordance with prior adalimumab trials for other diseases. Notably, 10 paradoxical psoriasis-like eruptions were reported. Adalimumab is the first and only US Food and Drug Administration–approved therapy for HS. Further understanding of the pathogenesis of HS may result in additional biologic treatments for HS. We encourage the manufacturers of other biologic therapies, such as infliximab, ustekinumab, anakinra, secukinumab, ixekizumab, and brodalumab, to consider conducting further clinical trials in HS to enhance the therapeutic options available for this debilitating disease.

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Adult female acne treated with spironolactone: a retrospective data review of 70 cases. Isvy-Joubert A, Nguyen JM, Gaultier A, Saint-Jean M, Le Moigne M, Boisrobert E, Khammari A, Dreno B. Eur J Dermatol. 2017 Aug 1;27(4):393-398. doi: 10.1684/ejd.2017.3062. https://www.ncbi.nlm.nih.gov/pubmed/28862134

The prevalence of acne in the adult population is increasing, particularly in women. Spironolactone regulates sebaceous gland activity by blocking androgen receptor. To evaluate retrospectively the efficacy of spironolactone in women with acne. Data from 70 women of at least 20 years, treated for their acne between 2010 and 2015 with low-dose spironolactone (≤150 mg/day), were analysed. Remission was defined by the number of retentional lesions inferior or equal to five and inflammatory lesions inferior or equal to two on the face. Variables influencing the response were studied using the Cox model. The mean age was 31.3 years; 39 (56%) women had prior courses of isotretinoin and 53 (76%) had an oral contraception prior to treatment. Remission data from a median treatment period of six months (95% CI: 4-9) were obtained from 47 (71%) women. Markers for a positive response to spironolactone were a high number of inflammatory lesions at inclusion (OR: 1.08; 95% CI: 1.03-1.13; p = 0.001) and relapse with previous isotretinoin (OR: 2.46; 95% CI: 1.09-5.54; p = 0.03). The marker for a negative response was an association with oral contraceptives containing first or second-generation progestin (OR: 2.77; 95% CI: 1.35-5.71; p = 0.005). This retrospective data analysis confirms that the use of low doses of spironolactone is a valuable alternative in women with acnein whom oral isotretinoin has failed. Moreover, the analysis shows that first and second-generation oral contraceptives decrease the efficacy of spironolactone, confirming the interest of using two third or fourth-generation oral contraceptives.

Study finds family history, chocolate intake increases acne risk. Bianca Nogrady. Dermatology News. July 21, 2017. http://www.mdedge.com/edermatologynews/article/143016/acne/study-finds-family-history-chocolate-intake-increases-acne-risk?channel=171&utm_source=News_DERM_acne_082517_F&utm_medium=email&utm_content=The%20microbiota%20matters:%20In%20acne,%20it%27s%20not%20us%20versus%20them

FROM THE JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY. Having two parents with a history of acne was associated with an eightfold higher risk of acne during adolescence and young adulthood, in a European study that surveyed people aged 15-24 years in seven European countries. Researchers conducted an online population-based survey of 10,521 individuals aged 15-24 years in Belgium, Czech and Slovak republics, France, Italy, Poland, and Spain, with questions about the presence or absence of acne, sociodemographic characteristics, and lifestyle factors (such as diet, tobacco, cannabis or alcohol use, and family history). The results were published online on July 14. The overall prevalence of self-reported acne was 57.8%, with the highest prevalence – 65.8% – found in the 15- to 17-years age group, and the lowest being 52.6% in the 21- to 24-years age group. Individuals who reported having one parent with a history of acne had a threefold greater incidence of acne compared to those without a history of paternal or maternal acne (P less than .0001 for both). Individuals whose parents both had acne had a nearly eightfold higher risk, which the authors noted was consistent with other studies showing a strong hereditary component of acne (J Eur Acad Dermatol Venereol. 2017 Jul 14. doi: 10.1111/jdv.14475). Chocolate consumption was associated with a nearly 30% higher probability of having acne, depending on the level of consumption. However, there were no significant effects seen with consumption of other foods such as dairy products, pasta, ice cream, and fruit juice. Smoking tobacco was associated with about a 30% lower incidence of acne. “Previous studies have demonstrated an association between high glycemic index foods and acne, although in our study, only chocolate, and not pasta or sweets, was independently associated in multivariate analysis,” wrote Pierre Wolkenstein, MD, of the department of dermatology, Hôpital Henri Mondor, Créteil, France, and his coauthors. “The relationship between smoking and acne is not clear. Some observational

studies have found that smoking increases the prevalence of acne, others have found a negative association, and some have found no relationship," they added. The study also showed significant variation in the incidence of acne across different countries. Using Spain, which had a median prevalence of acne, as a reference point, the researchers found that respondents in the Czech and Slovak republics had a 96% higher incidence of acne, while those in Poland had a 55% lower incidence. The authors cautioned that their results were based on self-report, rather than a physician diagnosis, but they noted that since acne is so common, false positive or false negative reports were unlikely. "An association between self-reported acne and chocolate consumption, and an apparent inverse relationship with smoking, need to be confirmed by additional studies," they noted. The survey was funded and supported by Pierre Fabre Dermatologie. Five authors declared fees as members of the European Severe Acne Board, supported by Pierre Fabre Dermatologie, and one author is an employee of the company.

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Dietary carbohydrate and glycemic load linked to acne. Dan Watson. Dermatology News. June 22, 2017. http://www.mdedge.com/edermatologynews/article/141036/acne/dietary-carbohydrate-and-glycemic-load-linked-acne?channel=171&utm_source=News_DERM_acne_082517_F&utm_medium=email&utm_content=The%20microbiota%20matters:%20In%20acne,%20it%27s%20not%20us%20versus%20them

FROM THE JOURNAL OF THE ACADEMY OF NUTRITION AND DIETETICS. A cross-sectional study of 64 adults in New York City with and without moderate/severe acne found a significant association between dietary

carbohydrate consumption and acne, which the authors said merited further study. "Epidemiologic studies typically report a low incidence of acne in non-developed nations, suggesting that environmental factors, such as diet, can play a role in acne pathogenesis," wrote Jennifer Burris, PhD, of the department of nutrition and food studies, at Steinhardt School of Culture, Education, and Human Development, New York University, and her coauthors. The study participants either had no acne (32) or had moderate or severe acne (32); those with mild or shorter-term acne (less than 6 months) were excluded. They made a 5-day food record and took a questionnaire, and had blood drawn and anthropometric measurements taken during two visits. Moderate and severe acne was associated with significantly greater total carbohydrate consumption (P = .003), available carbohydrate (total carbohydrate minus dietary fiber), percent energy from carbohydrate, and glycemic load (all Pless than .001), compared with those who did not have acne. The patients with moderate or severe acne also had greater insulin and insulin growth factor–1 concentrations, and lower sex hormone–binding globulin concentrations, (P = .002, .009, and .015, respectively); and greater insulin resistance (P= .001), compared with those who did not have acne. "Although the results from our study cannot determine causation, these preliminary results suggest a relationship between dietary [glycemic load] and acne," Dr. Burris and her coauthors wrote. "In addition to replicating our findings, future research is necessary to elucidate the mechanisms linking diet and acne and to evaluate the effectiveness of [medical nutrition therapy] on biological factors associated with acne and conceivably acne-specific quality of life," they added (J Acad Nutr Diet. 2017 Jun 9. doi: 10.1016/j.jand.2017.03.024).

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Patient Counseling/Communication

Birth Control Pills for Acne: Tips From Julie Harper at the Summer AAD Publish date: August 14, 2017 http://www.mdedge.com/cutis/article/144550/acne/birth-control-pills-acne-tips-julie-harper-summer-aad?channel=171

Acne treatment options now extend beyond antibiotics, and hormonal therapy, particularly birth control pills (BCPs), may provide clearance of acne in women who may not respond to other therapies. "Challenge [yourselves] to learn how to safely use BCPs," said Dr. Julie Harper, Clinical Associate Professor of Dermatology at the University of Alabama in Birmingham, in the presentation, "Use of Hormonal Therapy for Acne," at the Summer Meeting of the American Academy of Dermatology. The use of BCPs for acne has a strength-of-recommendation grade of A (consistent, good-quality patient-oriented evidence). According to Dr. Harper, all combination BCPs should work for acne, except progestin-only BCPs, which will make acne worse. Currently, there are 4 BCPs approved by the US Food and Drug Administration for acne: norgestimate-ethinyl estradiol (Ortho Tri-Cyclen); norethindrone acetate-ethinyl estradiol (Estrostep Fe); drospirenone-ethinyl estradiol (Yaz); and drospirenone-ethinyl estradiol-levomefolate calcium (Beyaz). Birth control pills are known to carry risks for venous thromboembolism (VTE), stroke, hypertension, and myocardial infarction; however, they are generally well tolerated in acne patients. "The risk of venous thromboembolism in women who take BCPs is doubled or tripled compared to women who do not take these pills. This sounds scary until you put it into context," said Dr. Harper. She explains the risks to patients using the following 3-6-9-12 model: A woman's baseline risk of having a VTE if she is not on a BCP is approximately 3 in 10,000 women in one year. When she takes a BCP, her risk doubles to 6 per 10,000 women in one year. If she takes a BCP that contains drospirenone, her risk is 9 per 10,000 women in one year. If she gets pregnant, her risk is 12 per 10,000 women in one year. Dermatologists may be apprehensive to prescribe BCPs, but Dr. Harper provided several important tips on managing patient expectations and monitoring patients.

Dr. Harper emphasized that BCPs should be used patiently for acne. "It frequently takes at least 3 cycles of BCPs to see a meaningful change in acne reduction," she advised. She recommended obtaining a thorough medical history and blood pressure measurement prior to prescribing BCPs. However, a Papanicolaou test and bimanual pelvic examination are no longer deemed mandatory prior to initiating a BCP, according to the World Health Organization and the American Congress of Obstetricians and Gynecologists. "While these exams may help to detect cervical cancer and other pelvic diseases, BCPs help to prevent unwanted pregnancies and the risks that accompany those pregnancies," said Dr. Harper. "Remember that BCPs reduce the risk of ovarian, uterine and colorectal cancer and also lessen ovarian cysts and pelvic inflammatory disease." Dermatologists also should inform patients that rifampin and griseofulvin, both anti-infectives, will interact with BCPs, lessening their effectiveness. A March 2017 study published in Cutis (2017;99:195-201) of US dermatologists' knowledge, comfort, and prescribing practices (N=116) revealed that most dermatologists (95.4%) believe BCPs effectively treat acne; however, only 54% reported prescribing them. The American Academy of Dermatology's guidelines of care for the management of acne vulgaris published in February 2016 (J Am Acad Dermatol. 2016;74:945-973) stated that "estrogen-containing combined oral contraceptives are effective and recommended in the treatment of inflammatory acne in females." Overall, Dr. Harper's take-home message was that dermatologists should not be afraid to prescribe BCPs, even in teenaged girls (following the onset of menarche). "Birth control pills can be used in younger patients but it is not my first line of treatment," said Dr. Harper. "It is recommended that BCPs not be prescribed for acne until 2 years after the young woman has achieved menarche. When considering whether or not to use a BCP in the early teenage years, keep in mind that these are not short-term treatments. If a BCP does help acne, it will

likely need to be maintained for many years." When discussing this treatment in front of parents/guardians, consider referring to it as hormonal therapy and use the term birth control pills only initially.

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Cosmeceuticals and Alternative Therapies for Rosacea. Maritza I. Perez, MD. Cutis. 2017 July;100(1):36 http://www.mdedge.com/cutis/article/141862/rosacea/cosmeceuticals-and-alternative-therapies-rosacea?utm_source=Clin_CUT_eNL_090717_F&utm_medium=email&utm_content=Pearls:%20Cosmeceuticals%20for%20rosacea%20|%20Isotretinoin%20|%20Wound%20care.

Rosacea is a skin condition mediated by a proinflammatory predisposition on the skin. A cosmeceutical approach supports the stable microbiome of the skin to maintain the health of the skin barrier. Herein, a regimen including cleansers, barrier repair creams, supplements, and antioxidants is provided, as well as alternative therapies. What do your patients need to know? Vascular instability associated with rosacea is exacerbated by triggers such as sunlight, hot drinks, spicy foods, stress, and rapid changing weather, which make patients flush and blush, increase the appearance of telangiectasia, and disrupt the normal skin barrier. Because the patients feel on fire, an anti-inflammatory approach is indicated. The regimen I recommend includes mild cleansers, barrier repair creams and supplements, antioxidants (topical and oral), and sun protection, all without parabens and harsh chemicals. I always recommend a product that I dispense at the office and another one of similar effectiveness that can be found over-the-counter. What are your go-to treatments? Cleansing is indispensable to maintain the normal flow in and out of the skin. I recommend mild cleansers without potentially sensitizing agents such as propylene glycol or parabens. It also should have calming agents (eg, fruit extracts) that remove the contaminants from the skin surface without stripping the important layers of lipids that constitute the barrier of the skin as well as ingredients (eg, prebiotics) that promote the healthy skin biome. Selenium in thermal spring water has free radical scavenging and anti-inflammatory properties as well as protection against heavy metals. After cleansing, I recommend a product to repair, maintain, and improve the barrier of the skin. A healthy skin barrier has an equal ratio of cholesterol, ceramides, and free fatty acids, the building blocks of the skin. In a barrier repair cream I look for ingredients that stop and prevent damaging inflammation, improve the skin's natural ability to repair and heal (eg, niacinamide), and protect against environmental insults. It should contain petrolatum and/or dimethicone to form a protective barrier on the skin to seal in moisture. Oral niacinamide should be taken as a photoprotective agent. Oral supplementation (500 mg twice daily) is effective in reducing skin cancer. Because UV light is a trigger factor, oral photoprotection is recommended. Topical antioxidants also are important. Free radical formation has been documented even in photoprotected skin. These free radicals have been implicated in skin cancer development and metalloproteinase production and are triggers of rosacea. As a result, I advise my patients to apply topical encapsulated vitamin C every night. The encapsulated form prevents oxidation of the product before application. In addition, I recommend oral vitamin C (1 g daily) and vitamin E (400 U daily). For sun protection I recommend sunblocks with titanium dioxide and zinc oxide for total UVA and UVB protection. If the patient has a darker skin type, sun protection should contain iron oxide. Chemical agents can cause irritation, photocontact dermatitis, and exacerbation of rosacea symptoms. Daily application of sun protection with reapplication every 2 hours is reinforced. What holistic therapies do you recommend? Stress reduction activities, including yoga, relaxation, massages, and meditation, can help. Oral consumption of trigger factors is discouraged. Antioxidant green tea is recommended instead of caffeinated beverages.

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Isotretinoin for Acne: Tips for Prescribing and Managing Patient Concerns. Stephen P. Stone, MD. Cutis. 2017 June;99(6):378, 388 http://www.mdedge.com/cutis/article/139719/acne/isotretinoin-acne-tips-prescribing-and-managing-patient-concerns?utm_source=Clin_CUT_eNL_090717_F&utm_medium=email&utm_content=Pearls:%20Cosmeceuticals%20for%20rosacea%20|%20Isotretinoin%20|%20Wound%20care

Isotretinoin may be a useful treatment for patients with severe acne. The physician, the pharmacy, and the patient must be registered with the iPLEDGE program (https://www.ipledgeprogram.com). These pearls provide guidance on managing acne with isotretinoin, discussing side effects and false information with patients and/or parents/guardians, and providing reliable resources to them. What does your patient need to know at the first visit? Most important is what you need to know before the first visit. As the prescribing physician, you must be familiar with the iPLEDGE program. Because of the complexity of the program, consider identifying a physician in your area to refer patients if you are not going to be a regular prescriber of the medication. If you are enrolled in iPLEDGE, let your patients (and/or their parents/guardians) know that there is a great deal of misinformation on the Internet. Reiterate that you and your staff are available to discuss their concerns. Also, give them reliable sources of information, such as the American Academy of Dermatology's patient information sheet as well as the Mayo Clinic's acne information. Drugs.com is another resource. All patients—males, females who cannot become pregnant, and females of childbearing potential (FCBPs)—must be aware that this medication can cause birth defects if taken during pregnancy. They must be informed that the medication is not to be shared with anyone and that they should not give blood while taking this medication. What treatment course do you recommend? My evidence-based approach is a course of isotretinoin totaling a minimum of 150 mg per kilogram body weight. Do not give a more abbreviated course unless the patient has cleared early; even then I tend to complete 150 mg when possible. There is published evidence that pushing the course to a total of 220 mg per kilogram body weight results in a longer remission. Generally, I do few laboratory tests other than pretreatment lipid panels as well as 1 or 2 follow-up lipid panels at monthly intervals. To comply with the iPLEDGE program, FCBP patients must have a monthly pregnancy test, which is reported on the iPLEDGE website before the patient can be prescribed the drug and receive the drug from a pharmacist who is participating in the iPLEDGE program. One of the defects of the iPLEDGE system is that although only a 30-day supply of pills can be prescribed, it is difficult to always bring a patient back in exactly 30 days; for example, we work on a 4-week cycle and 30 days brings us into the next week or uncommonly the weekend when we do not see patients. Our male patients or females not of childbearing potential are not affected, but for our FCBP patients, it means usually scheduling visits at 35-day intervals because the pregnancy tests must be performed at minimum 28-day intervals and the prescription cannot be written and the pregnancy test recorded until after at least 30 days. What are the side effects? The common side effects are what you would expect from a medicine that is supposed to dry up the oil on your skin: dryness of the lips, mouth, and skin, as well as rashes due to the dryness. There also can be minor swelling of the eyelids or lips, nosebleeds, upset stomach, and thinning of the hair; dryness of the scalp may occur. I recommend using a little petroleum jelly inside the nostrils at night to counteract the dryness that leads to nosebleeds, and saline drops or gel for the eyes, especially for contact lens wearers. Joint aches and pains have been reported, though I rarely see those effects in patients who are physically active such as those participating in competitive sports. Mood changes have been reported, including suicidal ideation. What do you do if patients refuse treatment? There is so much false information on the Internet about the dangers of isotretinoin, leaving some patients (and parents/guardians) too afraid to use it. I sympathize with this anxiety, but I do endeavor to point out that the birth defects occur only in women taking the drug while pregnant and have not been reported to occur after the drug is out of the patient's system. Similarly, I point out that almost all of the evidence-based studies failed to confirm any association between the use of isotretinoin and depression, teenage suicide, and subsequent inflammatory bowel disease. Nonetheless, I mention these issues and recommend that the parents/guardians observe the teenager; in the case of adult patients, they themselves must be sensitive to symptoms.

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