



AARS **HOT TOPICS** MEMBER NEWSLETTER

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AARS Updated Rosacea Guidelines

Update on the management of rosacea from the American Acne & Rosacea Society (AARS). Del Rosso JQ, Tanghetti E, Webster G, et al. J Clin Aesthet Dermatol. 2019;12(6):17–24. <http://jcadonline.com/aars-june-2019/>

Importance: Previous consensus articles on rosacea from the American Acne and Rosacea Society (AARS) have focused on pathophysiology, clinical assessment based on phenotypic expressions of rosacea, management guidelines, discussions of individual medical therapies, and reviews of physical modalities. Pathophysiologic mechanisms believed to be operative in rosacea have been covered extensively in the literature. **Objective:** This article updates the previously published consensus recommendations from the AARS on the management of rosacea, including systematic literature and evidence-based reviews of available therapeutic agents and physical modalities. **Observations:** This article includes discussions of available published data on topical ivermectin, topical oxymetazoline, combination therapy approaches, and physical devices for the management of rosacea. Consistent with what many publications on rosacea currently emphasize, clinicians are encouraged to define the clinical manifestations present in the patient and to select therapies that correlate with the optimal treatment of those manifestations. There are less data available on how to optimally integrate therapies; however, it appears that rationally selected medical therapies can be utilized concurrently. **Conclusion:** Due to the multifactorial pathogenesis of rosacea, its clinical presentation is heterogeneous. Rosacea is a chronic and recurrent inflammatory disorder, and clinical manifestations often vary in nature and severity over time, which might necessitate an adjustment in treatment. As new data become available, rosacea management approaches should be updated.

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Industry News

Positive results seen in phase 3 FMX101 acne study. July 9, 2019. DermWire, Practical Dermatology. <https://practicaldermatology.com/news/study-positive-results-see-in-phase-3-fmx101-acne-study?c4src=news-landing:feed>

In patients with moderate to severe acne vulgaris, treatment with FMX101 4% topical minocycline foam is well tolerated and effective for reducing the number of inflammatory lesions, according to results of a randomized trial published in the Journal of the American Academy of Dermatology. The study was conducted by Foamix to support the New Drug Application (NDA) submission of FMX101, which is currently under review by the FDA for the treatment of inflammatory lesions of non-nodular moderate-to-severe acne vulgaris in patients nine years of age and older.

Highlights from the study:

- The study showed high statistically significant superiority of FMX101 compared with vehicle in both primary endpoints of absolute inflammatory lesion reduction and IGA treatment success at week 12.
- FMX101 also met all secondary endpoints, showing statistically significant improvement in absolute reductions in both inflammatory lesions (papules, pustules and nodules) and non-inflammatory lesions (open and closed comedones).
- There was a statistically significant reduction in inflammatory lesions versus vehicle as early as week 3 of treatment, and all subsequently assessed timepoints throughout the entire treatment course of the study.

- Statistically, participants were no more likely to experience treatment-emergent adverse events (TEAEs) from FMX101 than from vehicle treatment. The majority of TEAEs were mild to moderate.
- More than 95% of participants using FMX101 had no or mild skin tolerability scores at the treatment application site at week 12.

“These data show that FMX101 has potential as both a safe and effective option for patients,” said Dr. T. Joseph Raouf of the Encino Research Center in Encino, CA., a clinical investigator on the study. “As a convenient, topical formulation of minocycline for acne, FMX101 has been designed to deliver the drug’s bacteriostatic and anti-inflammatory effects while minimizing systemic absorption and the resulting safety concerns associated with oral minocycline. Given that acne is the most common skin condition in the United States, FMX101 has the potential to positively impact millions of people.” “We are pleased that the prestigious JAAD has chosen to highlight Study 22 in its current edition,” said Dr. Iain Stuart, Chief Scientific Officer of Foamix. “The American Academy of Dermatology is the largest and most influential dermatology group in the United States and JAAD is the ideal platform to share the results from this successful Phase 3 study with the broader clinical dermatology community. As FMX101 is the first topical formulation of minocycline to reach regulatory agency review for the treatment of any disease, publication of this pivotal study in JAAD is befitting of its uniqueness and a testament to the innovation happening at Foamix.”

New Medical Research

Cutibacterium acnes phylotypes diversity loss: a trigger for skin inflammatory process. Dagnelie MA, Corvec S, Saint-Jean M, et al. J Eur Acad Dermatol Venereol. 2019 Jul 12. doi: 10.1111/jdv.15795. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31299116>

Background: Acne has long been understood as a multifactorial chronic inflammatory disease of the pilosebaceous follicle, where *Cutibacterium acnes* (subdivided into six main phylotypes) is a crucial actor. In parallel, the loss of microbial diversity among the skin commensal communities has recently been shown as often accompanied with inflammatory skin disorders. Objective: This study investigated the association of *C. acnes* phylotype diversity loss and the impact on Innate Immune System (IIS) activation. Methods: The IIS response of skin after incubation with phylotypes IA1, II or III individually and with the combination of IA1+II+III phylotypes, was studied in an in vitro skin explant system. The inflammatory response was monitored by immunohistochemistry and ELISA assays, targeting a selection of Innate Immune Markers (IIMs) (IL-6, IL-8, IL-10, IL-17, TGF- β). Results: IIMs were significantly upregulated in skin when being incubated with phylotype IA1 alone compared with the combination IA1+II+III. In parallel, ELISA assays confirmed these results in supernatants for IL-17, IL-8, and IL-10. Conclusion: We identify the loss of *C. acnes* phylotype diversity as a trigger for IIS activation, leading to cutaneous inflammation. These innovative data underline the possibility to set up new approaches to treat acne. Indeed, maintaining the balance between the different phylotypes of *C. acnes* may be an interesting target for the development of drugs.

Evaluation of autologous adipose-derived stem cells vs. fractional carbon dioxide laser in the treatment of post acne scars: a split-face study. Abou Eitta RS, Ismail AA, Abdelmaksoud RA, et al. Int J Dermatol. 2019 Jul 11. doi: 10.1111/ijd.14567. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31297798>

Background: Scarring is a distressing outcome of acne, as it causes cosmetic and psychological problems to the patients. Unfortunately, no single treatment is satisfactory; instead, employing multiple modalities may have better

outcome. Autologous adipose tissue-derived adult stem cells (AT-ASCs) and their secretory factors can stimulate collagen synthesis; angiogenesis and migration of fibroblasts thus regenerate damaged tissues. Also, conventional treatments for acne scarring, such as lasers and topical regimens, induce new collagen synthesis via activation of dermal fibroblasts or growth factors. The aim of the study was to verify the effectiveness of AT-ASCs for the treatment of acne scarring vs. the fractional carbon dioxide laser (FxCr). Subjects and methods: Split face comparative study included 10 adult patients with post-acne scars on both sides of the face. One side received AT-ASCs single injection while the other received three sessions of FxCr. Scars were then assessed using the global scoring system Goodman and Baron, scar area percent using NIH ImageJ software and functional assessment by measuring the transepidermal water loss (TEWL) and skin hydration. Both sides were followed for three months. Results: A significant improvement in the degree of scar severity, scar area percent, skin hydration, and TEWL after 3 months of treatment on both sides of the face with insignificant differences between both treatment modalities, provided that AT-ASCs treatment was employed once vs. three sessions of FxCr. Conclusion: One injection of AT-ASCs is as effective as three sessions of FxCr in the treatment of atrophic acne scars.

Skin microbiome differences relate to the grade of acne vulgaris. Li CX, You ZX, Lin YX, et al. *J Dermatol.* 2019 Jul 10. doi: 10.1111/1346-8138.14952. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31290561>

The skin microbiome plays important roles in the pathogenesis and development of acne. We aimed to investigate the facial skin microbiome of acne and microbiome differences related to different grades of acne. Skin swabs from nine healthy controls and 67 acne patients were collected, and the skin microbiomes were analyzed using 16S rRNA gene sequencing. Compared with healthy controls, acne patients harbored significantly altered skin microbiomes. The skin microbiomes of patients with grade 1-3 acne were similar, but patients with grade 4 acne showed a significantly different skin microbiome compared with grade 1-3 acne, including increased alpha diversity and increased proportions of four Gram-negative bacteria (Faecalibacterium, Klebsiella, Odoribacter and Bacteroides). In conclusion, acne patients harbored an altered skin microbiome, and more significant dysbiosis was found in patients with grade 4 acne (severe acne). Our findings may provide evidence for the pathogenic mechanisms of acne and microbial-based strategies to avoid and treat acne, especially grade 4 acne.

Treatment of acne scarring with a novel dual-wavelength laser. Gold MH, Wilson A, Mordon SR. *J Cosmet Dermatol.* 2019 Jul 10. doi: 10.1111/jocd.13068. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31290591>

Background: Facial acne scarring is a prevalent disease with both physical and psychosocial sequelae. Aims: This study aims to evaluate an innovative solid-state dual wavelength 1,319 and 589 nm laser, which does not require consumable dye, for the treatment of acne scars. Patients/methods: A total of 12 patients (11 female, 1 man - Fitzpatrick skin phototypes II & III) with acne scar for more than one year, were treated with 1319 nm and subsequently by 589 nm, all having four-sessions, one every other week. A full face was covered in approximately 30 minutes. Acne scars were scored by one physician evaluator using the ECCA grading scale before, 2 weeks after each treatment and 1 month and 6 months after the 4th treatment. Safety was measured by recording subject discomfort scores and adverse effects. Results: 12 subjects were enrolled into the study, 10 completed all 4 treatments and 2 were lost to follow up. Fluence used was $28 \text{ J/cm}^2 \pm 2.4 \text{ J/cm}^2$ at 1,319 nm and $16 \pm 2.9 \text{ J/cm}^2$ at 589 nm. At baseline, mean ECCA score was 98 ± 23 . This score was reduced to 88 ± 30 ($p < 0.02$), after one session, to 68 ± 21 ($p < 0.01$) after 2 sessions, to 58 ± 17 ($p < 0.01$) after 3 sessions to reach 58 ± 15 ($p < 0.01$) 1 month after the 4th and finally 66 ± 11 ($p < 0.01$) at 6

month follow up. This observation corresponds respectively to 14%, 33%, 42%, 40% and 30% reduction of the ECCA score. Only one patient (ECCA score: 120) did not improve after 3 sessions. Slight to moderate erythema was sometimes observed without dryness or bruising. No or minimal burning or stinging was reported. No crust was observed. Conclusion: Improvement in scarring was noted in almost all patients with minimal discomfort and minimal downtime. Combining both minimal side effects with effective acne scar reduction, this laser appears to be highly effective. Long-term evaluation remains necessary to confirm the efficacy of this new laser.

Hidradenitis Suppurativa Area and Severity Index (HASI): a pilot study to develop a novel instrument to measure the physical signs of hidradenitis suppurativa. Goldfarb N, Ingram JR, Jemec GBE, et al. *Br J Dermatol*. 2019 Jul 8. doi: 10.1111/bjd.18335. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31286486>

A valid and reliable disease severity assessment instrument for Hidradenitis Suppurativa (HS) is lacking. While validated tools exist, including Hidradenitis Suppurativa Clinical Response (HiSCR)¹, International Hidradenitis Suppurativa Severity Score System (IHS4)², and Severity Assessment of Hidradenitis Suppurativa Score (SAHS)³, each has limitations. These include, inability to measure cross-sectional severity, lack of inter-rater reliability (IHS4 intraclass correlation coefficient 0.47 [0.32-0.65])⁴, and issues inherent to composite physician- and patient-reported outcomes, respectively.

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Homocysteine, folic acid, and vitamin B12 levels in patients on isotretinoin therapy for acne vulgaris: a meta-analysis. Kim HJ, Lee SM, Lee JS, et al. *J Cosmet Dermatol*. 2019 Jul 5. doi: 10.1111/jocd.13059. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31276303>

Background: Oral isotretinoin (Iso) is one of the most commonly used drugs for patients with moderate-to-severe acne; however, its use has been associated with several adverse effects. Some studies have suggested an association between Iso therapy and homocysteine (Hcy), folic acid, and vitamin B12 plasma levels. Objective: To evaluate the changes in plasma Hcy, folic acid, and vitamin B12 levels during Iso therapy for acne using meta-analytic methods. Methods: Five scientific databases (MEDLINE, EMBASE, Cochrane Library, SCOPUS, and Web of Science) were searched according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines up to December 2018. A review of 734 publications identified 10 studies that assessed plasma levels of Hcy, folic acid, and vitamin B12 during Iso therapy in acne patients. Results: A total of 10 studies consisting of 592 patients were included in the meta-analysis. Plasma Hcy levels were significantly increased after Iso therapy (weighted mean difference [WMD]: 2.99, 95% confidence interval [CI]: 1.78-4.20, I² = 86%), whereas folic acid levels were significantly decreased after Iso therapy (WMD: -1.03, 95% CI: -1.90 to -0.17, I² = 89%). Conclusions: This meta-analysis found that Iso therapy was associated with changes in plasma levels of Hcy and folic acid in acne patients. However, further evaluation in controlled studies is needed to verify these results.

Psychiatric adverse events in patients taking isotretinoin as reported in a food and drug administration database from 1997 to 2017. Singer S, Tkachenko E, Sharma P, et al. *JAMA Dermatol*. 2019 Jul 3. doi: 10.1001/jamadermatol.2019.1416. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31268488>

Importance: Isotretinoin is a highly effective medication for severe acne. Although no causal link between isotretinoin

and psychiatric adverse effects has been established, widespread media reporting of depression and suicidality with use of isotretinoin have raised concerns in both patients and clinicians and generated numerous cases of costly litigation. Objective: To evaluate reports of psychiatric adverse events associated with isotretinoin use submitted to the US Food and Drug Administration from January 1, 1997, through December 31, 2017. Design, setting, and participants: This retrospective study evaluated reports of psychiatric adverse events with isotretinoin as the primary suspect drug in the US Food and Drug Administration's Adverse Event Reporting System from 1997 through 2017. Publicly available data on number of patients enrolled in the iPLEDGE program were used to calculate rates of completed suicide per 100 000 patients enrolled in iPLEDGE in 2009 and 2010. All data were analyzed between July 1, 2018, and January 31, 2019. Main outcomes and measures: The main outcomes were frequency and type of psychiatric adverse events in patients taking isotretinoin. Secondary analyses were stratification by age and sex and evaluation of completed suicide rates. Results: Between 1997 and 2017, 17 829 psychiatric adverse events with isotretinoin use were reported to the US Food and Drug Administration, with depressive disorders, emotional lability, and anxiety disorders reported most frequently. Of these events, 8936 (50.1%) were reported among men and 8362 (46.9%) among women; the sex of the individual was not reported for 531 events (3.0%). Of the 13 553 reports that included patient age, the mean (SD) age was 22.1 (8.6) years. More than half (52.5%) of all events occurred in 10- to 19-year-old individuals. Whereas depression and anxiety were reported equally between sexes, eating disorders were more common in females (58 of 85 [68.2%]), while attention-deficit/hyperactivity disorder (55 of 83 events [66.3%]) and completed suicides (290 of 368 [78.8%]) were more common in males. The rates of completed suicide were 8.4 and 5.6 suicides per 100 000 patients enrolled in iPLEDGE in 2009 and 2010, respectively. Conclusions and relevance: Although depressive disorders and suicidality were frequently reported with isotretinoin use, these reports must be considered in the context of elevated rates of depression and suicide among patients with acne at large. These data suggest that the rate of completed suicide in patients taking isotretinoin may be lower than that of the general US population. Many psychiatric adverse events unrelated to depression and suicidality were also reported, but it is unclear if they were a result of isotretinoin therapy. Although no causal link between isotretinoin and psychiatric risk has been established, patients taking the drug appear vulnerable to psychiatric concerns. Mandated monthly iPLEDGE visits may provide an opportunity to screen patients for psychiatric conditions and improve outcomes.

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The combined effect of tranilast 8% liposomal gel on the final cosmesis of acne scarring in patients concomitantly treated by isotretinoin: prospective double-blind split-face study. Weinstein A, Koren A, Sprecher E, et al. Clin Exp Dermatol. 2019 Jul 1. doi: 10.1111/ced.14032. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31260124>

Background: Tranilast, N-(3,4-dimethoxycinnoyl) anthranilic acid has never been investigated for the prevention and treatment of acne scars. Aim: To evaluate the efficacy and safety of tranilast 8% gel in improving the final appearance of patients with acne scarring concomitantly treated by isotretinoin. Methods: One-half of the faces of 40 healthy subjects (aged 18-49 years) with facial acne scars were treated with tranilast 8% liposomal gel and the other half with an aqua-based placebo in this prospective double-blind split-face study. Acne scars were evaluated by two dermatologists and by the patients (Global Aesthetic Improvement Scale [GAIS]), who also rated their satisfaction with the treatment and reported side effects. Results: Thirty-two participants completed the trial. The mean GAIS scores at 5 months post-treatment were significantly lower (better outcome) for the tranilast-treated side than the placebo-treated areas in patients concomitantly treated with isotretinoin ($P < 0.001$). All the isotretinoin-treated patients reported greater satisfaction and better general improvement in the skin's appearance and texture, as well

as greater improvement of pigmentary and redness alteration on the tranilast 8% gel-treated side compared to the control side. Conclusion: Combined topical application of tranilast 8% gel twice daily with oral isotretinoin treatment in the active phase of acne vulgaris may result in fewer scars, finer skin texture, and enhanced appearance.

Long-term remarkable remission of SAPHO syndrome in response to short-term systemic corticosteroids treatment in an immunoglobulin E elevated patient: a case report. Wang L, Li C, Yu M, et al. *Medicine* (Baltimore). 2019 Jul;98(27):e16045. doi: 10.1097/MD.00000000000016045.

<https://www.ncbi.nlm.nih.gov/pubmed/31277098>

Rationale: Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare auto-inflammatory disease with no standardized treatment. Systemic corticosteroids are only transiently effective, but long-term use would bring complications and would not bring long-term remission. Bone scintigraphy is a first-line method for systematic evaluation of osteoarticular lesions but seems to show an "imprinting" pattern. Patient concerns: A 31-year-old female patient presented significant palmoplantar pustulosis and nail lesion as well as typical tracer accumulation feature on bone scintigraphy with normal hypersensitivity C-reactive protein and erythrocyte sedimentation rate, but an elevated serum immunoglobulin E level. Diagnosis: The diagnosis was made by dermatological manifestations and classical sign in bone scintigraphy in accordance with the diagnostic criteria proposed in 1988. Interventions: Methylprednisolone was given with a primary dose of 40mg/day for 1 week followed with a subsequent 20mg/day oral prednisone for another 1 week and then reduced in a rate of 5mg/week until the eventual cessation. Outcomes: Long-term remarkable remission on clinical manifestations, MRI performance, and quantitative analysis of bone scintigraphy was achieved. Lessons: Identification of specific subtype of SAPHO patient according to skin and nail manifestations as well as immunoglobulin E level may guide the selection of short-term systemic corticosteroids strategy, leading to remarkable long-term remission. Besides, the lesions on bone scintigraphy can hardly disappear in SAPHO patients, and instead, the quantitative analysis of bone scintigraphy and MRI performances may better reflect the change of disease condition and serve as indicator for treatment efficiency.

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Analysis of potential genes and pathways involved in the pathogenesis of acne by bioinformatics. Chen B, Zheng Y, Liang Y. *Biomed Res Int*. 2019 Jun 9;2019:3739086. doi: 10.1155/2019/3739086. eCollection 2019.

<https://www.ncbi.nlm.nih.gov/pubmed/31281837>

Acne is the eighth most frequent disease worldwide. Inflammatory response runs through all stages of acne. It is complicated and is involved in innate and adaptive immunity. This study aimed to explore the candidate genes and their relative signaling pathways in inflammatory acne using data mining analysis. Microarray data GSE6475 and GSE53795, including 18 acne lesion tissues and 18 matched normal skin tissues, were obtained. Differentially expressed genes (DEGs) were filtered and subjected to functional and pathway enrichment analyses. Protein-protein interaction (PPI) network and module analyses were also performed based on the DEGs. In this work, 154 common DEGs, including 145 upregulated and 9 downregulated, were obtained from two microarray profiles. Gene Ontology and pathway enrichment of DEGs were clustered using significant enrichment analysis. A PPI network containing 110 nodes/DEGs was constructed, and 31 hub genes were obtained. Four modules in the PPI network, which mainly participated in chemokine signaling pathway, cytokine-cytokine receptor interaction, and Fc gamma R-mediated phagocytosis, were extracted. In conclusion, aberrant DEGs and pathways involved in acne pathogenesis were

identified using bioinformatic analysis. The DEGs included FPR2, ITGB2, CXCL8, C3AR1, CXCL1, FCER1G, LILRB2, PTPRC, SAA1, CCR2, ICAM1, and FPR1, and the pathways included chemokine signaling pathway, cytokine-cytokine receptor interaction, and Fc gamma R-mediated phagocytosis. This study could serve as a basis for further understanding the pathogenesis and potential therapeutic targets of inflammatory acne.

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Clinical Reviews

Radiofrequency microneedling: overview of technology, advantages, differences in devices, studies, and indications. Weiner SF. *Facial Plast Surg Clin North Am.* 2019 Aug;27(3):291-303. doi: 10.1016/j.fsc.2019.03.002. Epub 2019 May 22. <https://www.ncbi.nlm.nih.gov/pubmed/31280844>

Radiofrequency (RF) skin rejuvenation is improved using RF microneedling (RFM) devices. More aggressive treatments are performed safely with minimal downtime than previous RF devices. Optimizing treatment parameters is essential for safety and efficacy. Multiple RFM studies support minimal risks even in dark skin types. RFM has been used to treat acne scarring successfully as well as skin laxity and hyperhidrosis.

Oral antibiotics in acne: a retrospective single center analysis of current prescribing in primary care and it's alignment with the national antibiotic quality premium. Whitehouse H, Solman L, Eady EA, Layton AM. *Br J Dermatol.* 2019 Jul 13. doi: 10.1111/bjd.18339. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31301232>

Oral antibiotics are widely prescribed for acne due to anti-inflammatory and antimicrobial action against *Propionibacterium acnes*. Potential for antibiotic resistance is a global concern. Public Health England (PHE) estimates 10 million deaths/year by 2050 and £66 trillion in loss of productivity globally, due to drug-resistant microbial infections. NHS England recently developed a Quality Premium for antibiotic use, incentivizing Clinical Commissioning Groups (CCGs) to reduce antibiotic prescribing in primary care.

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Acne and rosacea: what's new for treatment? Dursun R, Daye M, Durmaz K. *Dermatol Ther.* 2019 Jul 11:e13020. doi: 10.1111/dth.13020. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31294907>

Acne and rosacea are two well-known chronic skin diseases in dermatology. There are many known therapeutic options of both diseases, but new treatment agents and therapeutic advances come to the agenda day by day. We would like to summarize new treatment advances for acne and rosacea diseases.

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Difference in vasoconstrictors: oxymetazoline vs brimonidine. Okwundu N, Cline A, Feldman SR. *J Dermatolog Treat.* 2019 Jul 11:1-23. doi: 10.1080/09546634.2019.1639606. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31294643>

Objective: Topical oxymetazoline and brimonidine are the only medications approved for treating persistent facial erythema of rosacea. This review aims to investigate the efficacy, safety, pharmacodynamics, and pharmacokinetic properties of oxymetazoline and brimonidine. Method and materials: Phase II and phase III clinical studies evaluating oxymetazoline and brimonidine were assessed to compare their efficacy and safety. Results: In their respective phase III trials, both oxymetazoline and brimonidine met the primary efficacy outcome of having at least a 2-grade decrease from baseline on both the Clinician Erythema Assessment and the Subject Self-Assessment Scales compared to the vehicle control. Treatment related adverse events of oxymetazoline and brimonidine are most often mild and localized. Conclusion: Topical oxymetazoline and brimonidine are effective for the management of persistent facial erythema associated with rosacea with a few mild and localized adverse effects. Further long-term research is imperative to further understand their long-term effects.

Potential role of the microbiome in acne: a comprehensive review. Lee YB, Byun EJ, Kim AHS. *J Clin Med.* 2019 Jul 7;8(7). pii: E987. doi: 10.3390/jcm8070987. <https://www.ncbi.nlm.nih.gov/pubmed/31284694>

Acne is a highly prevalent inflammatory skin condition involving sebaceous sties. Although it clearly develops from an interplay of multiple factors, the exact cause of acne remains elusive. It is increasingly believed that the interaction between skin microbes and host immunity plays an important role in this disease, with perturbed microbial composition and activity found in acne patients. *Cutibacterium acnes* (*C. acnes*; formerly called *Propionibacterium acnes*) is commonly found in sebum-rich areas and its over-proliferation has long been thought to contribute to the disease. However, information provided by advanced metagenomic sequencing has indicated that the cutaneous microbiota in acne patients and acne-free individuals differ at the virulent-specific lineage level. Acne also has close connections with the gastrointestinal tract, and many argue that the gut microbiota could be involved in the pathogenic process of acne. The emotions of stress (e.g., depression and anxiety), for instance, have been hypothesized to aggravate acne by altering the gut microbiota and increasing intestinal permeability, potentially contributing to skin inflammation. Over the years, an expanding body of research has highlighted the presence of a gut-brain-skin axis that connects gut microbes, oral probiotics, and diet, currently an area of intense scrutiny, to acne severity. This review concentrates on the skin and gut microbes in acne, the role that the gut-brain-skin axis plays in the immunobiology of acne, and newly emerging microbiome-based therapies that can be applied to treat acne.

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Uncommon pretibial bilateral manifestation of Hidradenitis suppurativa (Hurley III) after discontinuation of systemic treatment with adalimumab: a serious reason to prefer surgery as a primary approach? Tchernev G, Temelkova I, Wollina U. *J Eur Acad Dermatol Venereol.* 2019 Jul 5. doi: 10.1111/jdv.15773. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/31273867>

By definition, three distinct areas of acne inversa / hidradenitis suppurativa, namely the axillary, anogenital and inguinal area are mentioned (1,2). The axillary, inguinal and anogenital regions are the major areas affected by hidradenitis suppurativa (HS)(2). However, there are literature data describing atypical cases of HS affecting the face, neck, retroauricular area, and legs (3,4). We present a 73- year- old male with type 2 diabetes mellitus, who was hospitalized

for painful nodular changes, on erythematous basis, located on the skin of the two lower limbs, the two axils and the abdomen.

Increased infection rates associated with tetracycline therapy given for epidermal growth factor receptor inhibitor (EGFRI)-associated acneiform eruption: a retrospective study of data from two cancer centers.

Magnino MZ, Perry DJ, Subramaniam DS, DeKlotz CMC. *J Am Acad Dermatol.* 2019 Jul 4. pii: S0190-9622(19)32310-2. doi: 10.1016/j.jaad.2019.06.1310. [Epub ahead of print]. <https://www.ncbi.nlm.nih.gov/pubmed/31279812>

Epidermal growth factor receptor (EGFR)-targeted therapies, including tyrosine kinase inhibitors (TKIs) and monoclonal antibodies (MABs), cause acneiform eruptions often managed with oral tetracyclines as first line therapy. We evaluated whether use of tetracyclines increased rates of any infection when given as prophylaxis or treatment for EGFRI-associated eruption. All patients included in this retrospective analysis received at least one dose of an EGFRI. Exclusion criteria include HIV or other immunocompromised state. EGFRI was used as monotherapy, concomitant with chemotherapy, or with intermittent corticosteroids but not continuous corticosteroid use. Infection was defined as symptoms warranting systemic antibiotic therapy with documented positive culture. Impetigo was excluded as an infection due to the association with acneiform eruptions. Patients were divided into those who received tetracycline for treatment of EGFRI associated cutaneous sequelae (Treatment-Tetracycline, T-TC), those who received tetracycline prophylaxis upon initiation of EGFRI (Prophylaxis-Tetracycline, P-TC), and patients who did not receive tetracycline (No-Tetracycline, No-TC). When T-TC plus P TC are combined, they are referred to as patients who received tetracycline for any use (All-TC). Infection was recorded only after starting tetracycline for All-TC. Data were analyzed with one-way unpaired student's t-test.

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Hidradenitis suppurativa and polycystic ovarian syndrome: systematic review and meta-analysis. Phan K, Charlton O, Smith SD. *Australas J Dermatol.* 2019 Jul 1. doi: 10.1111/ajd.13110. [Epub ahead of print]

<https://www.ncbi.nlm.nih.gov/pubmed/31261440>

Background/objectives: Hidradenitis suppurativa has been associated with a number of pathologies, including various endocrine and autoimmune disorders. Although signs of hyperandrogenism are common in hidradenitis suppurativa, few formal studies have assessed the relationship between hidradenitis suppurativa and polycystic ovarian syndrome. Therefore, we performed a systematic review and meta-analysis to assess the association between hidradenitis suppurativa and polycystic ovarian syndrome. Methods: We performed a systematic review and meta-analysis according to PRISMA guidelines. Odds ratio was used as the effect size, with random-effects meta-analysis. Results: We identified five case-control studies for inclusion. From pooled data, we found a significantly higher proportion of polycystic ovarian syndrome in hidradenitis suppurativa cases compared with controls (OR 2.64; 95% CI 1.69-4.11; $P < 0.00001$). There was significant heterogeneity noted ($I^2 = 88\%$, $P < 0.00001$). Limitations included that studies reviewed were observational by design which are susceptible to bias, and lack of randomisation. Conclusions: In summary, pooled analysis of existing case-control studies supports a significant association between hidradenitis suppurativa and polycystic ovarian syndrome. Our results imply that hidradenitis suppurativa patients with signs of hyperandrogenism may benefit from screening for polycystic ovarian syndrome and may potentially benefit from anti-androgen therapy.

New evidence but still unmet medical needs in rosacea treatment. Le Cleach L, Cribier B. *Br J Dermatol.* 2019 Jul;181(1):11-12. doi: 10.1111/bjd.17865. <https://www.ncbi.nlm.nih.gov/pubmed/31259410>

In this issue of the BJD, van Zuuren and colleagues have published the update of their systematic review of efficacy and tolerance of interventions for rosacea, a prevalent facial dermatosis that has a significant impact on quality of life. The number of included randomized controlled trials (RCTs) has increased from 22 in the first version in 2003 to 152 in this current update, illustrating the dynamism of contemporary therapeutic research. Of note, two-thirds of these trials were funded by the pharmaceutical industry. Following the recent recommendations regarding diagnostic criteria, while using similar primary and secondary outcomes to the previous version of the review, the authors chose to present their results according to individual features. In other words, they used a phenotypic approach (such as papules/pustules; telangiectasia/ erythema) and not diagnostic subtypes. Important new evidence that has appeared since the last update in 2015 is highlighted. For erythema, the authors confirmed that there was moderate certainty of evidence for efficacy of topical oxymetazoline, an alpha-adrenoceptor agonist compared with placebo. For rosacea with papules/pustules the authors concluded with a moderate degree of certainty the efficacy of topical minocycline compared with placebo and a high degree of certainty of efficacy for 0.25 mg kg⁻¹ of systemic isotretinoin for treating patients with difficult-to-treat papular/pustular rosacea. For both erythema and papules/pustules the authors concluded that the combination of topical brimonidine and ivermectin was efficacious compared with placebo (certainty of evidence not assessed).

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