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AARS Special Highlight

Special Highlight: Please see recently published data from former AARS Grantee Dr. Alison Paine!

Evolution of the facial skin microbiome during puberty in normal and acne skin. Schneider AM, Nolan ZT, Banerjee K, et al. J Eur Acad Dermatol Venereol. 2022 Sep 27. doi: 10.1111/jdv.18616. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36165604/>

Background: The composition of the skin microbiome varies from infancy to adulthood and becomes most stable in adulthood. Adult acne patients harbour an 'acne microbiome' dominated by specific strains of *Cutibacterium acnes*. However, the precise timing of skin microbiome evolution, the development of the acne microbiome, and the shift to virulent *C. acnes* strain composition during puberty is unknown. Objectives: We performed a cross-sectional pilot study in a paediatric population to understand how and when the skin microbiome composition transitions during puberty and whether a distinct 'acne microbiome' emerges in paediatric subjects. Methods: Forty-eight volunteers including males and females, ages 7-17 years, with and without acne were enrolled and evaluated for pubertal development using the Tanner staging criteria. Sebum levels were measured, and skin microbiota were collected by sterile swab on the subject's forehead. DNA was sequenced by whole genome shotgun sequencing. Results: A significant shift in microbial diversity emerged between early (T1-T2) and late (T3-T5) stages of puberty, coinciding with increased sebum production on the face. The overall relative abundance of *C. acnes* in both normal and acne skin increased during puberty and individual *C. acnes* strains were uniquely affected by pubertal stage and the presence of acne. Further, an acne microbiome signature associated with unique *C. acnes* strain composition and metabolic activity emerges in late puberty in those with acne. This unique *C. acnes* strain composition is predicted to have increased porphyrin production, which may contribute to skin inflammation. Conclusions: Our data suggest that the stage of pubertal development influences skin microbiome composition. As children mature, a distinct acne microbiome composition emerges in those with acne. Understanding how both puberty and acne influence the microbiome may support novel therapeutic strategies to combat acne in the paediatric population.

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Industry News

Cutera's AviClear now broadly available to US physicians and practitioners. DermWire, Practical Dermatology. November 7, 2022. <https://practicaldermatology.com/news/cuteras-aviclear-now-broadly-available-to-us-physicians-and-practitioners?c4src=news-landing:feed>

AviClear is the first and only energy device to be both U.S. Food and Drug Administration cleared, and Health Canada approved for the treatment of mild, moderate, and severe acne, with additional approval in Canada for acne scars. Cutera, Inc.'s AviClear is now broadly available to physicians and practitioners treating patients throughout North America. AviClear is the first and only energy device to be both U.S. Food and Drug Administration cleared, and Health Canada approved for the treatment of mild, moderate, and severe acne, with additional approval in Canada for acne scars. AviClear has seen widespread interest from physicians and patients following its FDA clearance in March 2022 and was recently awarded the "Best Laser Treatment for Acne" by Cosmopolitan Magazine. In conjunction with greater availability, Cutera is also announcing a new, monthly financing plan to US consumers starting at \$99 a month*. "I was an early AviClear adopter because I know this treatment will change the way my acne patients face the world," says Sonia Batra, MD, founder of Batra Dermatology in Santa Monica, Calif., in a news release. "I am thrilled my colleagues nationwide will now have access to this device, and I am even happier for their patients who have not wanted or could not proceed with prescription options. What makes the treatment even more

appealing is that it can be used on all skin types and acne severities without adverse effects. I have no doubt it will be the treatment of choice for many acne sufferers.” “We are pleased to see AviClear praised as a groundbreaking treatment by physicians, patients, and the media,” adds Dave Mowry, CEO of Cutera. “Pairing the commercial launch with the new patient financing option will enable us to extend the reach of AviClear to more people who want an effective, chemical-free, and durable solution to their acne. “Based on our market feedback to date, we are confident that patient demand and practice installations will continue to grow over the next several quarters beginning in the first quarter of 2023,” said Mowry. “Affordability, efficacy, and durability will help establish AviClear as the gold standard of care for acne sufferers.” AviClear is now broadly available to physicians and practitioners across the United States, with a limited commercial release in Canada. Visit www.AviClear.com to find out more information.

New Medical Research

Evaluation of the efficacy and relapse rates of treatment protocols for moderate acne using isotretinoin based on the global acne grading system: Randomized, controlled, comparative study. Kassem B, Ismail M, Hassan F. *Dermatol Ther.* 2022 Nov 8;e15974. doi: 10.1111/dth.15974. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36346039/>

Protocols for treating acne with isotretinoin have varied widely because some factors associated with relapse and treatment duration have not yet been fully determined. This paper evaluates the effectiveness of conventional, low, and intermittent isotretinoin dosage protocols in the treatment of moderate acne and investigates the relationships between GAGS score, treatment duration and relapse rate. The 107 patients with moderate acne were randomly divided into three groups who received isotretinoin for 24 weeks (Group A: 0.5-1 mg/kg/day; Group B: 0.25-0.4 mg/kg/day; Group C: 0.5-0.7 mg/kg/day for 1 week out of every 4 weeks). The results show that both conventional and continuous low doses achieved full clinical effectiveness with minimum relapse rates. However, fewer side effects and better patient satisfaction were reported with the low dose. Significant differences in GAGS scores after 24 weeks were found between groups B and C ($p = 0.037$) and between groups A and C ($p < 0.001$), while no significant differences were found between groups A and B ($p = 0.153$). It was observed that relapse rate increased with initial GAGS score. The average relapse rate was 58.0% for those with initial GAGS scores of 25-30 compared with 5.5% for those with scores of 19-24. It was also noticed that, among the patients who relapsed, the highest percentage (56.3%) were in the age group <20 years. However, GAGS ($\beta = 0.646$, $t = 8.323$, $p < 0.001$) was found to be a better predictor of relapse than age ($\beta = 0.083$, $t = 1.073$, $p = 0.286$). These results suggest that initial GAGS score is an important factor in determining the treatment protocol for moderate acne. Furthermore, this study recommends that a low-dose treatment is most suitable when GAGS <25, as it can achieve complete clearance of acne with minimal relapses and side effects.

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Microneedling combined with botulinum toxin-A versus microneedling combined with platelet-rich plasma in treatment of atrophic acne scars: A comparative split face study. Albalat W, Ghonemy S, Saleh A, Elradi M. *Arch Dermatol Res.* 2022 Nov 5. doi: 10.1007/s00403-022-02446-9. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36334117/>

Background: Atrophic post-acne scarring constitutes a troublesome cosmetic concern for both patients and dermatologists. Old and new therapies as well as combinations are being introduced to achieve a satisfactory response. Microneedling has been used either alone or under different combinations for its treatment. The aim was to compare its combination with topical platelet-rich plasma versus its combination with topical Botulinum Toxin-A.

Methods: 30 subjects with different types and grades of atrophic post-acne scars completed the study. Right side of the face was treated with microneedling and platelet-rich plasma while the left side was treated microneedling and Botox. Response was assessed using two different scales. Patient satisfaction and pain were also assessed. Results: Regarding response to therapy and according to the quartile grading scale, there was no statistically significant difference between the two sides where (23.4% & 13.3%) of the right and left sides, respectively, had an excellent response. Regarding the difference in the qualitative global scarring grading system before and after treatment, there was a highly statistically significant improvement on both sides with higher improvement on the right side than left side but in a non-statistically significant way. Conclusions: Both combinations present efficacious options for treating acne scars with comparable efficacy.

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Efficacy of microneedling with 35% glycolic acid peels versus microneedling with 15% trichloroacetic acid peels in treatment of atrophic acne scars: A randomized controlled trial. Dayal S, Kaur R, Sahu P. *Dermatol Surg.* 2022 Nov 1;48(11):1203-1209. doi: 10.1097/DSS.0000000000003556. Epub 2022 Aug 23.

<https://pubmed.ncbi.nlm.nih.gov/36342251/>

Background: Combination of microneedling and chemical peeling is a simple cost-effective treatment for acne scars. Objective: To compare efficacy and safety of combining microneedling with 35% glycolic acid (GA) peel versus microneedling with 15% trichloroacetic acid (TCA) peel in facial atrophic acne scars. Methods: Forty acne scars patients were randomly divided into 2 groups of 20 each. Patients underwent microneedling followed by 35% GA peeling in Group 1 and 15% TCA peeling in Group 2 at 2 weekly intervals. Improvement was graded by Goodman and Baron's qualitative and quantitative global acne scar grading systems, physician's global assessment, and visual analogue scale (VAS). Skin texture was graded by VAS. Results: On comparing qualitative and quantitative acne scar grading within groups, there was significant difference from the baseline. When the two groups were compared for quantitative and qualitative acne scar grading, the difference was statistically not significant at the end of therapy. In VAS, greater number of patients assessed response as excellent and good in Group 1 than in Group 2 indicating better skin texture improvement in Group 1. Conclusion: Both combinations were equally efficacious in treating acne scars. Glycolic acid peel delivered additional advantage of improvement in skin texture.

Patient preferences for acne vulgaris treatment and barriers to care: A survey study. Perche P, Singh R, Feldman S. *J Drugs Dermatol.* 2022 Nov 1;21(11):1191-1195. doi: 10.36849/JDD.6940.

<https://pubmed.ncbi.nlm.nih.gov/36342733/>

The associated direct and indirect costs of acquiring acne vulgaris (acne) treatment from a clinician may prohibit some patients from doing so. Barriers to care may also influence patient preferences for treatment, and while both over-the-counter (OTC) and prescription acne treatments are efficacious, preferences for OTC or prescription acne medications are not well established. We recruited 529 adult subjects from the United States through Amazon Mechanical Turk (MTurk), and subjects were surveyed about acne, their acne treatment preferences, and any barriers to care. A total of 450 subjects passed the attention check and were included in the analysis. Of respondents who had tried both OTC and prescription treatments (n=223), more respondents reported that they preferred prescription treatments (130/223, 58.3%), compared with OTC treatments (64/223, 28.7%); or no preference (29/223, 13.0%; P=0.00001). Almost half of all respondents also stated that they experienced barriers to accessing medical care for acne treatment (192/450 42.7%); cost and transportation were the top 2 factors. Considering how common barriers are, and their everchanging nature, some patients may benefit from a discussion of alternative non-prescription acne treatments, serving as a bridge to therapy or while patients are unable to reach a medical provider.

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Racial/ethnic variations in acne: A practical algorithm for treatment and maintenance, including skincare recommendations for skin of color patients with acne. Alexis A, Woolery-Lloyd H, Andriessen A, et al. *J Drugs Dermatol.* 2022 Nov 1;21(11):s13223-s132214. <https://pubmed.ncbi.nlm.nih.gov/36342741/>

Background: Racial/ethnic differences in the clinical presentation, sequelae, and desired treatment outcomes for acne have been reported. Post-inflammatory hyperpigmentation (PIH) frequently occurs in patients with richly pigmented skin complexions and can frequently be the most bothersome aspect of acne in this population. Methods: The project used a modified Delphi hybrid process comprising face-to-face discussions followed by an online follow-up. A structured literature search was conducted to identify publications on racial/ethnic differences in the clinical presentation, sequelae, and desired treatment outcomes for skin of color (SOC) patients with acne. The advisors subsequently convened to review the results and draft an algorithm for the treatment and maintenance, including skincare recommendations, for SOC patients with acne. Online, the panel reviewed and adopted the algorithm using published evidence coupled with the panel's expert opinion and clinical experience. Results: Studies suggest that strategies for improving outcomes in patients with acne who have SOC include: the early initiation and maintenance of treatment regimens; careful consideration of the tolerability of active ingredients, vehicle formulations, and dosing; and the use of skin care (eg, pH balanced, non-irritating cleansers, and non-comedogenic moisturizers) to minimize irritation or dryness. Conclusion: Acne treatment in patients with SOC involves unique therapeutic considerations, including management of PIH through efficacious longitudinal acne treatment, prevention of irritation, and potential active treatment of PIH. Skincare products are recommended as an adjunct to prescription therapy to maximize tolerability and may also play a role in maintenance therapy.

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Value of high-frequency ultrasound in the treatment of moderate and severe acne vulgaris. Luo Y, Wang J, Gao Y, et al. *Skin Res Technol.* 2022 Nov;28(6):833-839. doi: 10.1111/srt.13208. Epub 2022 Oct 25. <https://pubmed.ncbi.nlm.nih.gov/36281955/>

Background: Acne treatment may fail or cause undesirable side effects due to inaccurate evaluation. High-frequency ultrasound (HFUS) can monitor systemic treatment in patients with moderate-to-severe acne vulgaris. Materials and methods: In this prospective study, consecutive patients with moderate-to-severe acne vulgaris were recruited. Patients were graded by a comprehensive clinical assessment before and after therapy. Simultaneous HFUS grading was independently evaluated according to the sonographic scoring system for acne (SSSA). Clinical and HFUS grades were compared through kappa analysis. Results: A total of 70 patients were enrolled. At baseline, 36 (51.4%) and 34 (48.6%) patients were graded as moderate and severe, respectively, through clinical assessment. However, 27 patients (38.6%) scored SSSA-Grade II and 43 (61.4%) scored SSSA-Grade III in the HFUS grading. Sixty-one patients (87.1%) were in the consistent category as per clinical assessment and HFUS grades, with Kappa1 = 0.745, whereas higher HFUS grades were observed in nine patients. By the end of the observation, 65 of all patients (92.9%) showed significant improvement and 5 (7.1%) showed no apparent improvement after the treatment. According to the clinical assessment, 14, 52, and 4 patients were graded as mild, moderate, and severe, respectively. On the other hand, 11, 51, and 8 patients had SSSA-Grade I, II, and III, respectively. Of all patients, 63 (90.0%) had consistent evaluation results, with Kappa2 = 0.762, whereas the remaining seven patients had an HFUS grade higher than the clinical. Conclusion: HFUS is a useful tool for dermatologists to monitor the treatment of moderate and severe acne vulgaris.

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Ivermectin treatment in rosacea: How novel smartphone technology can support monitoring rosacea-associated signs and symptoms. Schaller M, Riel S, Bashur R, et al. *Dermatol Ther.* 2022 Nov;35(11):e15869. doi: 10.1111/dth.15869. Epub 2022 Oct 7. <https://pubmed.ncbi.nlm.nih.gov/36177738/>

Rosacea lessens patients' quality of life not only by visible symptoms like erythema, papules, and pustules but also by invisible symptoms like stinging, burning, and dryness. Ivermectin 1% cream has recently been introduced as an efficient therapy for papules and pustules in rosacea patients. To investigate the potential of ivermectin 1% cream to improve rosacea-associated erythema and invisible symptoms by combining established questionnaires with the novel photography and analysis tool Scarletred®Vision. We performed an open monocentric pilot study including 25 Caucasian patients presenting with moderate to severe rosacea with erythema, less than 10 papules and/or pustules, and ≥ 15 Demodex mites/cm². Patients applied 1 g of ivermectin 1% cream (Soolantra®) once a day for ≥ 16 weeks. Skin symptoms were recorded at baseline, week 8 and \geq week 16. Grade of erythema was determined by clinician erythema assessment (CEA) and patient self-assessment (PSA). Severity of invisible skin symptoms (stinging and/or burning, dryness, itching) were assessed by questionnaire. Erythema and skin texture were additionally quantified using Scarletred®Vision. Ivermectin 1% cream significantly reduced invisible symptoms of rosacea (stinging and/or burning, dryness: $p < 0.0001$; itching $p < 0.001$; at ≥ 16 weeks). Analysis with Scarletred®Vision confirmed CEA and PSA results for improvement of erythema ($p < 0.0001$; at ≥ 16 weeks) and skin roughness ($p < 0.001$; at ≥ 16 weeks). Treatment with ivermectin 1% cream is efficient in treating not only rosacea-associated papules and pustules but also erythema and invisible skin symptoms.

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A randomized split-face comparative study of long-pulsed alexandrite plus low-fluence Nd:YAG laser versus pulsed-dye laser in the treatment of rosacea. Park S, Lee JH, Kang E, et al. *Lasers Surg Med.* 2022 Nov;54(9):1217-1225. doi: 10.1002/lsm.23605. Epub 2022 Oct 2. <https://pubmed.ncbi.nlm.nih.gov/36183378/>

Objectives: To compare the effectiveness of long-pulsed alexandrite laser (LPAL) with that of pulsed-dye laser (PDL) for rosacea. Methods: This was a single-blind randomized controlled trial on 27 patients who were clinically diagnosed with rosacea. Randomly assigned split face in each patient received four times monthly treatment of LPAL plus low-fluence Nd:YAG with the contralateral side serving as the control treated with PDL. At every visit, the erythema index (EI) was measured with skin analysis systems, and two independent dermatologists evaluated digital photographs for five-point global aesthetic improvement scale (GAIS). Results: The EI significantly decreased on both treated sides (LPAL 366.5 ± 101.0 vs. 295.8 ± 90.2 , $p < 0.001$, PDL 369.0 ± 124.3 vs. 302.7 ± 92.1 , $p < 0.001$) 1 month after fourth treatment (visit 5). Also 3 months after the fourth treatment (visit 6), the reduction in the EI was well maintained on both sides (LPAL 360.3 ± 96.8 vs. 282.0 ± 89.2 , $p < 0.001$, PDL 364.3 ± 121.6 vs. 281.6 ± 97.8 , $p < 0.001$). When comparing the improvement in the EI between the two groups, the percentage reduction in the EI on the LPAL-treated side was not inferior to the PDL-treated side (visit 5: LPAL $18.7 \pm 15.7\%$ vs. PDL $16.4 \pm 12.9\%$, $p = 0.501$ and visit 6: LPAL $21.7 \pm 13.9\%$ vs. PDL $21.9 \pm 15.2\%$, $p = 0.943$). The GAIS and patient satisfaction were comparable between the LPAL and PDL sides and did not show any significant difference. No serious adverse events occurred on either of the treated sides. Conclusion: This study showed that the decrease in EI in the treatment of rosacea was comparable between PDL and LPAL. Therefore, LPAL could be a promising alternative treatment option with good merits for rosacea, considering no consumables are required for device maintenance.

Anti-IL-17A blockade did not significantly reduce inflammatory lesions in a placebo-controlled pilot study in adult patients with moderate to severe acne. Thiboutot DM, Craft N, Rissmann R, et al. *J Dermatolog Treat.* 2022 Oct 28;1-27. doi: 10.1080/09546634.2022.2138691. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36305633/>

Background: CJM112 is a potent anti-IL-17A monoclonal antibody, whose clinical efficacy in psoriasis was recently documented. This study aimed to assess the effect of IL-17A blockade, using CJM112, in patients with moderate to severe acne. Methods: A randomized, placebo-controlled, double-blind, parallel-group, proof-of-concept study was conducted on patients with moderate to severe acne. Patients received CJM112 300 mg, 75 mg, or placebo subcutaneously during Treatment Period1 (0-12 weeks). Patients receiving placebo were re-randomized to receive CJM112 300 mg or 75 mg during Treatment Period 2 (12-24 weeks). The primary endpoint was the number of inflammatory facial lesions at Week 12. Results: As the futility criterion was met during the interim analysis, only 52/75 (69.3%) patients were recruited. In total, 48/52 (92.3%) and 26/41 (63.4%) completed Treatment Periods 1 and 2, respectively. All groups exhibited a reduction in facial inflammatory lesions, with no difference observed between CJM112 and placebo (CJM112 300 mg 27.6 ± 20.7 ; CJM112 75 mg 30.4 ± 34.8 ; placebo 23.6 ± 13.6 ; primary endpoint). Additionally, no differences were observed between groups in other secondary and exploratory endpoints at Week 12. Conclusions: Anti-IL-17A therapy was not significantly different compared to the placebo in reducing inflammatory lesions in patients with moderate to severe acne.

The relevant of sex hormone levels and acne grades in patients with acne vulgaris: A cross-sectional study in Beijing. Zhang R, Zhou L, Lv M, et al. *Clin Cosmet Investig Dermatol.* 2022 Oct 18;15:2211-2219. doi: 10.2147/CCID.S385376. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/36281268/>

Background: The tests of sex hormones play pivotal roles in the clinical diagnosis and treatment of acne vulgaris, but the majority of patients with acne vulgaris present regular sex hormone levels within the normal reference range. Objective: To determine the correlation among levels of sex hormones, ratio of androgen to estrogen and acne grades in patients with acne vulgaris. Methods: A cross-sectional study was applied to collect 693 patients with acne vulgaris. All samples were screened by cluster sampling among those who underwent tests of sex hormones at Beijing Jingcheng Skin Hospital from July 2021 to June 2022. A gender stratified analysis was performed to classify acne grades I-IV. Spearman correlation analysis was used to analyze the relationship between age, sex hormones, ratio of androgen to estrogen and acne grades, with multinomial logistic regression to analyze the association of sex hormones with acne grades in patients with acne. Results: (1) The testosterone levels were mostly within normal reference values for both males and females with varying degrees of acne. For females, the serum follicle-stimulating hormone, estradiol, progesterone, testosterone, and ratio of androgen to estrogen were significantly different between acne grades. For males, there were significant differences in serum estradiol, testosterone, and ratio of androgen to estrogen across acne grades. (2) The acne grade was negatively correlated with estradiol and positively correlated with the ratio of androgen to estrogen; the female acne grade was also negatively correlated with age and progesterone, but positively correlated with follicle-stimulating hormone. (3) Multivariate logistic regression analysis indicated that the ratio of androgen to estrogen was independently correlated with the grade of acne and that acne grade worsened as the ratio increased. Conclusion: The increase in the ratio of androgen to estrogen may aggravate the acne grade in patients with acne vulgaris.

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Oral zinc as a novel adjuvant and sparing therapy for systemic isotretinoin in acne vulgaris: A preliminary comparative study. Salah E. J Clin Aesthet Dermatol. 2022 Oct;15(10):58-61. <https://pubmed.ncbi.nlm.nih.gov/36312827/>

Background: Systemic isotretinoin is the most effective treatment for acne vulgaris (AV). However, numerous side effects are associated with isotretinoin. Oral zinc has a better safety profile and has been used to treat AV with variable results. Objective: We sought to evaluate the safety and efficacy of combining oral zinc to low-dose systemic isotretinoin in AV patients. Methods: Sixty AV patients were divided into two groups. Group A received oral zinc sulfate plus low-dose isotretinoin and Group B received the standard isotretinoin dosage. At each visit acne severity, photos, side effects, and patient-reported satisfaction were recorded. Results: In the two groups, no significant difference in reduction of lesion count and Global Acne Grading System scores. The frequency of treatment-related side effects was (20%) in Group A and (76.7%) in Group B. Furthermore, there was no difference regarding the relapse rates between both groups ($p>0.05$). Finally, the patients' satisfaction rates did not differ between the two groups. Conclusion: Oral zinc plus low-dose isotretinoin resulted in satisfactory improvement in AV patients with fewer side effects. Further studies are recommended to compare the efficacy of other zinc preparations if combined with systemic isotretinoin at different concentrations.

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A split face comparative study to evaluate the efficacy of 40% pyruvic acid vs. microdermabrasion with 40% pyruvic acid on biomechanical skin parameters in the treatment of acne vulgaris. Rusztowicz M, Chilicka K, Szygula R, et al. J Clin Med. 2022 Oct 14;11(20):6079. doi: 10.3390/jcm11206079. <https://pubmed.ncbi.nlm.nih.gov/36294402/>

The synergy of cosmetic acids, with their keratolytic and antibacterial properties, with the mechanical exfoliation of the epidermis brings faster and better treatment results. The aim of the study was to compare the effects of using only pyruvic acid and the synergy of microdermabrasion and chemical exfoliation. In total, 14 women diagnosed with acne took part in the study. Two areas were marked on the participants' faces: the right side (microdermabrasion treatment and a preparation containing pyruvic acid 40%) and the left side (preparation containing pyruvic acid 40%) without mechanical exfoliation. A series of four treatments was performed at 2-week intervals. Skin parameters such as stratum corneum hydration and sebum secretion were measured. Before the treatments, all patients had moderate acne according to GAGS (Min: 19, Max: 22, Md: 20), and after the treatments, it decreased to mild acne according to GAGS (Min: 13, Max: 17, Md: 14). On the right side of the face, there was a statistically significant reduction in sebum secretion in all the examined areas of the face and increase in the hydration of the stratum corneum. On the left side of the face, the differences were also observed in the decrease of sebum value and increase of hydration level; however, they were smaller than on the right side. The use of microdermabrasion in combination with pyruvic acid led to better results in the case of increased hydration and reduction of sebum secretion than using only pyruvic acid treatment.

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Efficacy of diammonium glycyrrhizinate in the treatment of rosacea with papules and pustules: A randomized, double-blind, placebo-controlled study. Xie Y, Huang J, Liu J, Zhang Q. Dermatol Ther. 2022 Oct 6;e15905. doi: 10.1111/dth.15905. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36200523/>

Rosacea is a kind of chronic inflammatory skin disease that usually occurs in the middle of the face. Diammonium glycyrrhizinate (DG), an effective monomer component extracted from licorice, has extensive anti-inflammatory, antioxidant, anti-allergic, and immunomodulatory effects. There is no research on its therapeutic effect on rosacea. In this study, we divided rosacea patients mainly characterized by papules and pustules randomly into three groups.

Group A received clarithromycin 500 mg once a day, isotretinoin 10 mg once a day; Group B received DG 150 mg three times a day, other medicines were the same as Group A; Group C received clarithromycin 250 mg once a day, isotretinoin 10 mg once every 2 days, and DG 150 mg three times a day. All patients' symptom scores and laboratory tests were evaluated when followed up. We found that DG combined with clarithromycin and isotretinoin in the treatment of rosacea was more effective and quicker than clarithromycin and isotretinoin alone. Moreover, half common dosage of clarithromycin and isotretinoin combined with DG could achieve the same therapeutic effect as the conventional dose and brought about lower incidences of adverse events (AEs). Therefore, it is recommended to use half common dosage of routine medication combined with DG for rosacea patients mainly characterized by papules and pustules.

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Severe papulopustular rosacea successfully treated with a combination of oral azithromycin and isotretinoin.

Ring HC, Zachariae C, Thomsen SF, et al. *J Dermatolog Treat.* 2022 Oct 5;1-3. doi: 10.1080/09546634.2022.2129953. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36165496/>

Papulopustular rosacea is notoriously a challenge to treat, and treatment options are scarce. Only limited data exist on the use of azithromycin in treatment of papulopustular rosacea. However, the unique pharmacokinetics of azithromycin may have several indications in the treatment of papulopustular rosacea. We here report a case of hard-to-treat papulopustular rosacea which was successfully treated with pulsed oral azithromycin in addition to maintenance isotretinoin.

Analysis of the epidemiological burden of acne vulgaris in China based on the data of global burden of disease 2019.

Wang Y, Xiao S, Ren J, Zhang Y. *Front Med (Lausanne).* 2022 Oct 4;9:939584. doi: 10.3389/fmed.2022.939584. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/36267619/>

Acne vulgaris is a chronic, inflammatory skin disease, which has brought an increasing disease burden to patients and society. But there is no systematic study on the disease burden and social development of acne vulgaris in China. This study aimed to analyze the epidemiological burden and trend of acne vulgaris in China from 1990 to 2019 based on the data in the global burden of disease 2019 (GBD 2019). The number of incidences/illnesses, age-standardized incidence/prevalence rates, disability-adjusted life years (DALYs), and DALY rate of acne vulgaris in China from 1990 to 2019 were obtained from the GBD 2019 to evaluate the epidemiological trends and age-period-cohort trends. The associations between disease burden and social development degrees were analyzed using a sociodemographic index. In 2019, the age-standardized prevalence and incidence of acne vulgaris in China were both at low levels in the world. From 1990 to 2019, the prevalent cases and incident cases of acne vulgaris in China rose firstly and then fell (peaked in 2005 and 2003, respectively), and the age-standardized prevalence/incidence/DALY rates showed growth trends continuously. The prevalence of acne vulgaris peaked in the 15-19 age group while the incidence peak age was 10-14 years old and there was an obvious gender difference, females were higher than males. With the increase of sociodemographic index (SDI) value, the morbidity of acne vulgaris showed a linear growth trend ($P < 0.05$). From 1990 to 2019, the disease burden of acne vulgaris is increasing in China, which is correlated with social and medical development. Active research on the epidemiological data of acne vulgaris and its relationship with the level of social development is important for both the diagnosis and treatment of acne vulgaris and for the development of health policies.

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Clinical Reviews

Treatment strategies, including antibiotics, to target the immune component of rosacea. Delans K, Kelly K, Feldman SR. *Expert Rev Clin Immunol.* 2022 Dec;18(12):1239-1251. doi: 10.1080/1744666X.2022.2128334. Epub 2022 Sep 27. <https://pubmed.ncbi.nlm.nih.gov/36137266/>

Introduction: Recent advances in the understanding of the pathophysiology of rosacea have led to increased focus on the disease's immunologic etiology and to the development of immunologically based treatments. With many patients suffering from incomplete control, addressing the immune components of the disease process may provide a more effective treatment option for rosacea patients that may improve quality of life. Areas covered: This review will provide a brief overview of the pathophysiology of rosacea, as well as specific immunologic contributions to the disease state. Current standard-of-care treatments will be described, including anti-parasitic, anti-inflammatory agents, and antibiotics. Emphasis will be placed on treatments that target the immune components of the disease process. Expert opinion: Rosacea remains a difficult dermatologic disease to treat, partially due to an incomplete understanding of the disease pathophysiology. The immune pathophysiology of rosacea, particularly the key role of inflammation, has been clarified over the past decade. Identification of specific molecules, including cytokines and nuclear transcription factors, may allow for the development of targeted rosacea-specific biologic and topical treatments. However, medication nonadherence is a limiting factor to achieving symptomatic control among rosacea patients. Focusing on the development of oral or injectable forms of therapy may circumvent poor adherence.

Tofacitinib for the treatment of erythematotelangiectatic and papulopustular rosacea: A retrospective case series. Sun YH, Man XY, Xuan XY, et al. *Dermatol Ther.* 2022 Nov;35(11):e15848. doi: 10.1111/dth.15848. Epub 2022 Oct 10. <https://pubmed.ncbi.nlm.nih.gov/36175135/>

Rosacea is a chronic inflammatory skin disease characterized by facial erythema, papules, pustules, telangiectasia, and flushing. The Janus kinase (JAK) signal transducer and activator of transcription (STAT) pathway appears to play a role in the pathogenesis of rosacea. Our study preliminarily explored the efficacy of JAK inhibitor tofacitinib in the treatment of rosacea. We retrospectively reviewed the cases of 21 patients with rosacea who were treated with oral tofacitinib. Patients received oral tofacitinib 5 mg as either monotherapy or adjunctive therapy. We have observed that 15 out of 21 patients (71.4%) patients experienced significant regression of erythema on the face (IGA \leq 1), and a mean change of -2.24 in the Investigator's Global Assessment (IGA) score was significant improvement from baseline. Treatment with oral tofacitinib might be a potentially effective treatment to ameliorate the symptoms of rosacea.

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Utilization of light-emitting diodes for skin therapy: Systematic review and meta-analysis. Ngoc LTN, Moon JY, Lee YC. *Photodermatol Photoimmunol Photomed.* 2022 Oct 31. doi: 10.1111/phpp.12841. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36310510/>

This study investigates the dermatological as well as the esthetic potential of light-emitting diodes (LEDs) by performing a systematic review and meta-analysis. From the electronic databases, 554 articles were assessed; however, only 31 studies were selected after manually screening and eliminating unnecessary studies. The potential effectiveness of LEDs for skin therapies was assessed by evaluating the standardized mean differences (SMDs) and funnel plots of this meta-analysis. It was discovered that both red and blue LED lights play an important role in the treatment of acne vulgaris with an overall statistically significant SMD of -2.42 [-2.64, -2.15] and I² = 17% < 50%. Additionally, other LEDs (e.g., yellow LEDs and near-infrared devices) showed outstanding levels of effectiveness, not only in reducing the lesions of herpes simplex and psoriasis but also in improved skin rejuvenation with highly

consistent analytical results (I2 = 0% and 33%, respectively). However, the analysis of LED-based skin wound healing and atopic dermatitis treatments exhibited heterogeneity (I2 = 85% and 90%) due to the lack of unpublished articles. In conclusion, it is suggested that LEDs are useful for dermatology and could be potential candidates for future cosmetic applications.

Use of patient-reported outcomes in acne vulgaris and rosacea clinical trials from 2011 to 2021: A systematic review. Ly S, Miller J, Tong L, et al. *JAMA Dermatol.* 2022 Oct 26. doi: 10.1001/jamadermatol.2022.3911. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/36287541/>

Importance: Acne and rosacea have substantial implications for quality of life, and it is therefore important to ensure the patient's voice is being captured in pivotal randomized clinical trials (RCTs). Although patient-reported outcome measures (PROMs) are a valuable tool to capture the patient perspective, little is known about use of PROMs in RCTs on acne and rosacea. Objective: To characterize the use of PROMs in RCTs on acne and rosacea. Evidence review: A systematic literature search was conducted using the search terms acne vulgaris and rosacea in the following databases: MEDLINE through PubMed, Embase, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews. A modified search hedge for RCTs from the McGill Library was applied. All phase 2, 3, and 4 RCTs published between December 31, 2011, through December 31, 2021, that evaluated the efficacy and safety of therapies for acne and rosacea vs any comparator were eligible for inclusion. Findings: A total of 2461 publications describing RCTs were identified, of which 206 RCTs met the inclusion criteria (163 trials [79%] on acne and 43 [21%] on rosacea). At least 1 PROM was used in 53% of trials (110) included; PROM use was more common in rosacea RCTs (67% [n = 29]) compared with acne RCTs (50% [n = 81]). At least 1 dermatology-specific (13% [n = 27]) or disease-specific (14% [n = 28]) PROM was included in the RCTs analyzed. Only 7% of trials (14) included a PROM as a primary outcome measure. There was no statistically significant increase in PROM inclusion over the study period (11 of 21 trials in 2011 vs 5 of 12 trials in 2021). Conclusions and relevance: In this systematic review, PROMs were included in approximately one-half of acne and rosacea RCTs performed over the study period. In addition, PROMs were rarely used as a primary outcome measure, and inclusion of PROMs has not increased substantially over the past 10 years. Increasing use of PROMs in RCTs can ensure that the patient's perspective is captured during the development of new treatments for acne and rosacea.

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Prevalence and demographics of truncal involvement among acne patients: Survey data and a review of the literature. Tan J, Del Rosso JQ, Weiss JS, et al. *J Clin Aesthet Dermatol.* 2022 Oct;15(10):62-67. <https://pubmed.ncbi.nlm.nih.gov/36312821/>

Background: Truncal acne is frequently underdiagnosed despite affecting around half of those with facial acne. The objective was to provide an overview of the literature on the incidence of truncal acne according to age, gender, and acne severity. Methods: A narrative review of data from recent large surveys and a literature search in PubMed on the incidence of truncal acne across subgroups of age, gender, and acne severity. Results: The prevalence of truncal acne alone was low, ranging from <1% to 14%, but approximately 30 to 60 percent of individuals with facial acne also had truncal acne depending on the population. In an online survey in the United States of 2,000 respondents aged between 14 -29 years with self-reported active facial and/or truncal acne, the incidence of truncal acne was lower in the 14-20 years subgroup than in the 21-29 years subgroup (49% vs 54%). The incidence of truncal acne was similar in both males and females, while 46 percent of respondents with self-declared clear and mild acne indicated having truncal involvement compared to 60 percent of those with moderate or severe acne. Limitations: Online surveys have inherent limitations, such as self-reporting and potential confounders. Conclusion: Data suggests that patients with both facial and truncal involvement have earlier onset of acne and more severe acne. Additional adverse

psychological impact may arise from having the impression that the disease is spreading and becoming more severe. Raising awareness of truncal acne prevalence and demographics could improve its clinical management to reduce the negative psychological impact.

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Minocycline-induced gum pigmentation during treatment for acne vulgaris. Wang J, Brown I, Goodarzi H. Case Rep Pediatr. 2022 Oct 14;2022:9493061. doi: 10.1155/2022/9493061. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/36276924/>

Minocycline, a type of tetracycline, is a broad-spectrum antibiotic that is commonly prescribed in dermatology for the treatment of acne vulgaris. Common side effects of minocycline include nausea, vertigo, and dizziness while less common side effects include hyperpigmentation. In this case study, we found an 18-year-old female who presented with dark blue pigmentation in her upper gum after using minocycline on and off for 4 years. After discontinuation of the minocycline for 2 years, the pigmentation decreased gradually.

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Acne vulgaris, atopic dermatitis and rosacea: The role of the skin microbiota-a review. Condrò G, Guerini M, Castello M, Perugini P. Biomedicines. 2022 Oct 9;10(10):2523. doi: 10.3390/biomedicines10102523. <https://pubmed.ncbi.nlm.nih.gov/36289784/>

The skin harbors a huge number of different microorganisms such as bacteria, fungi and viruses, and it acts as a protective shield to prevent the invasion of pathogens and to maintain the health of the commensal microbiota. Several studies, in fact, have shown the importance of the skin microbiota for healthy skin. However, this balance can be altered by intrinsic and extrinsic factors, leading to the development of skin disease, such as acne vulgaris (AV), atopic dermatitis (AD) and rosacea (RS). Although these diseases are widespread and affect both adolescents and adults, the scientific correlation between these disorders and the skin microbiota and physiological parameters (TEWL, hydration and lipid composition) is still unclear. This review aims to investigate the current literature regarding the correlation between the skin microbiota and its imbalance underlying microbiological aspects, how the skin microbiota changes over the course of the disease and the current possible treatments. The following reported studies show a general imbalance of the bacterial flora. For this reason, more in-depth studies are necessary to explore the different subspecies and strains involved in all three diseases.

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Treatment and maintenance of cutaneous rosacea in Latino skin types with prescription medications and non-prescription cleansers and moisturizers as adjuncts: A review. Gonzalez C, Andriessen A, Antelo D, et al. J Drugs Dermatol. 2022 Oct 1;21(10):1111-1118. doi: 10.36849/JDD.7010. <https://pubmed.ncbi.nlm.nih.gov/36219059/>

Background: Rosacea is an inflammatory dermatosis with at least a ten percent prevalence reported among white adults. Rosacea occurs in nonwhite populations, but prevalence data is limited. Methods: Five dermatologists from Latin America (the panel) met virtually after completing a survey of their prescription and adjunctive therapy practices when managing Latin American patients with rosacea. Panel members were chosen based on their dermatology expertise in treating a range of skin phototypes. Survey results were reviewed and discussed, along with a review of published guidelines for rosacea treatment. Results: The panel addressed diagnostic challenges in richly pigmented skin individuals. Pathophysiology and treatment of rosacea were reviewed, with a primary focus on how to treat the skin barrier dysfunction in those affected, using prescription and over-the-counter measures. Conclusions: Appropriate skincare is crucial for effective rosacea management. Cleansers and moisturizers with ingredients such as ceramides, hyaluronic acid, and niacinamide promote a healthy skin barrier, improving rosacea control.

A rare case of acne medication-induced drug reaction with eosinophilia and systemic symptoms. Hamel BL, Mason SF, Burek AG, Holland KE. WMJ. 2022 Oct;121(3):E53-E56. <https://pubmed.ncbi.nlm.nih.gov/36301660/>

Introduction: Acne vulgaris is the most common skin condition in late adolescence and frequently requires systemic treatment with antibiotics or androgen receptor blockers in moderate to- severe cases. Case presentation: We report the case of a 17-year-old adolescent female with new onset fever, headache, and pruritic rash 1 month after she started doxycycline and spironolactone for the treatment of acne vulgaris. Later, she developed eosinophilia and transaminitis. Infectious workup was negative. Discussion: This presentation was consistent with a definite case of drug reaction with eosinophilia and systemic symptoms (DRESS). DRESS is a severe, systemic hypersensitivity drug reaction that typically occurs 2 to 8 weeks following exposure to the offending medication. Conclusions: Although doxycycline and spironolactone are uncommon triggers of DRESS, they are common medications used to treat acne, and clinicians should be aware of this potential complication when counseling patients, especially adolescents.

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