AARS HOT TOPICS MEMBER NEWSLETTER

March 15, 2019 Issue

American Acne and Rosacea Society
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We encourage you to invite your colleagues and patients to get active in the American Acne & Rosacea Society! Visit www.acneandrosacea.org to become member and donate now on www.acneandrosacea.org/donate to continue to see a change in acne and rosacea.

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AARS Announcements

Thank you for attending the 14th Annual AARS Member Networking Reception during AAD! The AARS is honored to have an evening devoted to recent announcements and a chance to spend time with friends and colleagues! Some of the highlights included:

- Wear your AARS apparel with pride! Dr. Julie Harper helped design and launch new "AARS Dr. Pimple Stopper' t-shirts for Members! Please contact us at info@aarsmember.org to purchase yours today! Found in ladies and men's sizes, these shirts are a tax-deductible donation of $20 to AARS and available today. Get them for you and your office staff today!

- It was night of celebration to say thank you to Dr. Julie Harper for her service as AARS President. We shared a recent highlight video of some of the recent accomplishments of the AARS, too.
- We are very excited to welcome founding AARS Board Member and now President Dr. Mark Jackson and President-Elect Dr. Andrea Zaenglein our new leadership of the AARS!

- The AARS announced plans for our inaugural AARS Global Research Summit for 2020! This is envisioned as a three-day meeting in the US for university and private practice researchers, clinicians, dermatology drug, devices, and diagnostics, major investment firms, and other contract organizations to translate the science and provide exposure to acne, rosacea, and hidradenitis suppurativa research. A strategic planning meeting among AARS Committees and the scientific and commercial representatives of invited Corporate Benefactors will take place after the AARS Scientific Symposium in May 2019. Email Stacey Moore at info@aarsmember.org for more information!

Register Now for the 8th Annual AARS Scientific Symposium at the Society for Investigative Dermatology co-hosted by AARS President Mark Jackson and Past President Diane Thiboutot!

This will feature acne, HS, and rosacea presentations during a luncheon symposium on Wednesday, May 8, 2019 from 10:00 AM – 2:00 PM at the Hilton Chicago in the Waldorf room, 2nd floor. This is free to all SID attendees and AARS members. Register Here!

Industry News

Ortho Dermatologics launches 2019 Aspire Higher scholarship program for students with dermatologic conditions. Ortho Dermatologics. Press Room. March 11, 2019. http://ortho-dermatologics.com/about-us/press-room/

Ortho Dermatologics, one of the largest prescription dermatology health care businesses, today announced the opening of applications for its 2019 Aspire Higher scholarship program, which will award $90,000 total in scholarships to nine students who have been treated for a dermatologic condition. Students can apply for the scholarship through April 26, 2019.

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New mouse model validates how "good" and "bad" bacteria affect acne. DermWire, Practical Dermatology. Thursday, March 07, 2019. http://practicaldermatology.com/dermwire/2019/03/07/new-mouse-model-validates-how-good-and-bad-bacteria-affect-acne/?c=111&t=

Researchers at University of California San Diego School of Medicine, Cedars-Sinai and UCLA have developed a new mouse model that closely resembles human acne by adding one new factor — a synthetic sebum. Researchers have long believed that Propionibacterium acnes causes acne. But these bacteria are plentiful on everyone's skin and yet not everyone gets acne or experiences it to the same degree. Genetic sequencing recently revealed that not all Propionibacterium acnes are the same — there are different strains, some of which are abundant in acne lesions and some that are never found there. Acne research and therapeutic development have been hampered by the lack of an animal model that replicates the human condition until now. For the first time, the new model, described in JCI Insight, allowed the researchers to directly compare "good" (and "bad" strains of P. acnes bacteria in a way that is more relevant to human acne than in previous attempts. "Since we know exactly which genes differ between these strains, next we can pinpoint exactly what it is about the acne-associated strains that allows them to cause skin lesions," says George Y. Liu, MD, PhD, professor and chief of the Division of Pediatric Infectious Diseases at UC San Diego School of Medicine, in a news release. "And that information will help us develop new therapies that specifically block those acne-promoting factors or tip the balance of a person's skin chemistry in favor of the healthy strains." (Dr. Liu was a faculty member at Cedars-Sinai at the time of the study.) Dr. Liu and team prepared synthetic sebum by following a recipe they found in a previous scientific study, a simple concoction of four ingredients — fatty acid, triglyceride, wax and squalene, a precursor compound to sterols, such as cholesterol and steroid hormones — in ratios that resemble human sebum. (Mice produce skin sebum, too, but its makeup is different.) "When we started working with these bacteria and checked out the animal models others have been using over the years, we thought 'we've got to come up with something better than this,'" Dr. Liu says. "Acne typically occurs when a person hits their teenage years…What's the difference between a child's skin and a teenager's skin? Increased sebum production.

And we were surprised to find how such a simple addition made a big difference in our ability to study acne." The researchers inoculated mice with P. acnes and applied fresh sebum daily. Without the sebum, the mice had minimal lesions and the bacteria were rapidly cleared from the site of administration. With the sebum alone, there was no effect on the skin. But when Dr. Liu and team applied both sebum and acne-associated strains of P. acnes, they saw what looked like human acne, and the bacteria survived for weeks. These P. acnes strains also caused inflammation in the skin, as measured by elevated levels of inflammatory cytokines. Then the researchers tried the same with health-associated strains of P. acnes — strains that aren't found in human acne lesions. The same amount of bacteria was still present on the skin three days after inoculation, no matter the strain applied. But researchers could clearly see the differences between strains just by looking at the mice, Dr. Liu said. Lesions caused by acne-associated P. acnes strains scored approximately two times higher than lesions caused by health-associated strains in a measure that takes into account a lesion's size, redness, dryness and degree of skin sloughing. Unlike people, the mice in these experiments were all genetically identical. Dr. Liu says that's important because it means that the differences in acne severity were due only to differences between the bacterial strains, not differences in the mice's innate ability to react to the bacteria. Next, the team hopes to improve upon its acne mouse model so they can achieve similar results when the bacteria are applied topically rather than administered by injection under the skin. They also want to study the genes that are unique to acne-associated P. acnes strains and determine what it is about human sebum that promotes these strains. Dr. Liu says this information could help the team better understand who is at increased risk for acne, and how to develop personalized therapies and vaccines that target the acne-promoting bacterial factors or sebum components. Co-authors of this study include: Stacey L. Kolar, Juan Torres, Xuemo Fan, Cedars-Sinai; Chih-Ming Tsai, Cedars-Sinai and UC San Diego; and Huiying Li, UCLA.

Study: isotretinoin does not raise depression risk. DermWire, Practical Dermatology. Friday, March 01, 2019. http://practicaldermatology.com/dermwire/2019/03/01/study-isotretinoin-does-not-raise-depression-risk

Isotretinoin is not an independent risk factor for depression in adult acne patients, finds new research presented at the 2019 American Academy of Dermatology (AAD) Annual Meeting in Washington. "There has been mixed evidence and much debate around the impact of isotretinoin on mood change," says Bethanee Schlosser, MD, PhD, FAAD, an associate professor in the department of dermatology at the Northwestern University Feinberg School of Medicine in Chicago. "There's also a lot of misinformation out there, particularly on social media, so we hope this large-scale study can shed some light on the issue." Dr. Schlosser and her colleagues evaluated medical records for more than 38,000 patients age 18-65 who were diagnosed with acne between January 2001 and December 2017. Forty-one of the 1,087 patients exposed to isotretinoin (3.77 percent) developed depression, compared to 1,775 of the 36,929 who were not exposed to isotretinoin (4.81 percent). "These results showed no significant difference in frequency of depression between acne patients treated with isotretinoin and those who receive other types of therapy," Dr. Schlosser says. "Further, we know the mere presence of acne can be associated with mood disorders, including depression, and isotretinoin can provide significant relief for patients whose acne is not responding to other treatments and causing severe psychosocial distress." No studies to date have established a causal relationship between isotretinoin and depression, Dr. Schlosser says, and her research indicates that the drug's effect on mood is limited. She says more research in this area is necessary, however, and she encourages those with acne to see a board-certified dermatologist to discuss their treatment options and let their doctors know if they experience symptoms of depression.

New Medical Research

Pulsed-dye laser as an adjuvant treatment for papulopustular eruptions from epidermal growth factor receptor inhibitors, a randomized blinded split-faced controlled trial. Rerknimitr P, Suphankong Y, Panchaprateep R, et al. Lasers Surg Med. 2019 Mar 7. doi: 10.1002/lsm.23080. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30843231

Objectives: To investigate the efficacy of pulsed-dye laser (PDL) as an adjunctive treatment for facial papulopustular eruptions from EGFR inhibitors (EGFRi). Methods: Fourteen patients with facial acneiform eruptions were recruited. Half side of the face was randomized to receive PDL treatment while the other side served as a control. The treatments were delivered every 2 weeks for 4 sessions. The patients were seen at baseline, weeks 2, 4, 6, 8, and 10. Erythema index (EI) measured by colorimeter, the papulopustular lesion count and physician global assessment (PGA) were obtained. Patients were allowed to use their standard treatments for their eruptions. Results: Both arms had a significant decrease in EI from baseline at each subsequent visit. In the laser treated side, the mean (95%CI) EI decreased from 23.5 (22.24-24.76) at baseline to 16.3 (15.01-17.59) at week 10, while those of the sham were 23.49 (22.23-24.75) to 20.51 (19.22-21.8), respectively. The mean change was significantly lower in the PDL arm from week 4 onwards. The lesion counts in both groups also decreased significantly, but the mean difference between the arms was not different. PGA scores followed the same pattern as EI. Conclusions: Adjunctive treatment with PDL was a safe and effective treatment.

Transfollicular delivery of gold microparticles in healthy skin and acne vulgaris, assessed by in vivo reflectance confocal microscopy and optical coherence tomography. Fuchs CSK, Ortner VK, Mogensen M, et al. Lasers Surg Med. 2019 Mar 5. doi: 10.1002/lsm.23076. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30835885 Introduction: Topical application of gold microparticles (GMPs) for selective photothermolysis is a recently FDA-cleared therapy for acne vulgaris. Current evidence indicates the potential of optical imaging to non-invasively visualize GMPs and describe photothermal tissue effects. Objectives: To qualitatively and quantitatively describe GMP delivery in vivo and visualize laser-mediated thermal effects of GMPs in facial skin of acne patients and healthy participants, using reflectance confocal microscopy (RCM) and optical coherence tomography (OCT). Methods: Patients with facial acne (n = 14), and healthy participants (n = 7) were included. RCM and OCT images were acquired at baseline, after GMP application, and after diode laser exposure. All images were evaluated qualitatively and quantitatively with regards to GMP delivery in skin layers and morphological thermal effects. Lastly, skin biopsies were obtained to compare RCM and OCT findings to histology. Results: GMPs were delivered equally in healthy participants and acne patients, and in lesional and non-lesional acne skin. In RCM images, GMPs appeared as hyperreflective aggregates inside hair follicles and eccrine ducts, corresponding to natural skin openings (NSOs). The fraction of NSOs with hyperreflective content increased significantly after GMP application compared to baseline (50-75% increase, $P = 8.88 \times 10\text{-}16$). Similarly, in OCT images, GMPs appeared as hyperreflective columns inside hair follicles and were not detected in surrounding skin. GMPs reached a maximum depth of 920 µm (median 300 µm). After laser exposure, RCM and histology revealed selective perifollicular tissue changes around NSOs. Conclusion: Optical imaging visualizes GMP delivery and thermal tissue response following laser exposure and enables bedside monitoring of transfollicular microparticle delivery.

A new Th-17 cytokine in hidradenitis suppurativa: antimicrobial and pro-inflammatory role of IL-26. Scala E, Di Caprio R, Cacciapuoti S, et al. Br J Dermatol. 2019 Mar 4. doi: 10.1111/bjd.17854. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30829398

Background: IL-26 is a signature Th-17 cytokine described as a pro-inflammatory and antimicrobial mediator. So far, IL-26 has been reported in several immune-mediated inflammatory diseases, but its involvement in inflammatory skin disorders is poorly known. Objectives: Investigation of IL-26 in HS, through its involvement in the antimicrobial activity. Methods: IL-26 was assessed in HS patients through gene expression and protein analysis at skin and circulating levels. Ex vivo HS organ skin cultures, together with IL-26 antibody treatment, were performed to determine the activity. HS and HC PBMC were even or no silenced with IL-26 siRNA in order to measure antimicrobial, cytotoxic and phagocytic activities against S. aureus. Results: First, we observed that IL-26 is able to modulate pro-inflammatory response at immune cell levels. IL-26 was increased in the plasma of HS patients compared to healthy subjects. Subsequently, we explored PBMC bactericidal, cytotoxic and phagocytic activities against S. aureus in HS and HC subjects. These activities were lower in HS subjects compared to HC ones. Remarkably, killing activities were reduced when HC PBMC were transfected with IL-26 siRNA. However, the transfection did not affect the killing activity of HS PBMC, supporting the idea that IL-26 cargo lacks of efficiency in HS. Conclusions: Our findings suggest that infection susceptibility in HS might be related to IL-26. Despite the role of bacteria remains controversial in HS, this paper supports that there is a defect of antimicrobial response in these patients.

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What is the most relevant factor during ALA-PDT？ A multi-center, open clinical pain score research about actinic keratosis, acne and condylomatata acuminata. Zheng Z, Zhang LL, Shi L, et al. Photodiagnosis Photodyn Ther. 2019 Mar 2. pii: S1572-1000(19)30061-4. doi: 10.1016/j.pdpdt.2019.03.001. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30836211

Background: To date, it has been reported that the intrinsic factors (lesions location, lesions area, disease types) and extrinsic factors (fluence rate) contribute to the pain during 5-aminolevulinic acid photodynamic therapy (ALA-PDT). But there are few studies on pain during ALA-PDT and lack of sufficient clinical evidence related to the pain intensity. Objective: To investigate pain intensity and its relative factors during ALA-PDT and to provide clinical implication. Methods: The pain numeric rating scale (PNRS) score was used to evaluate the patients' pain intensity at different times during ALA-PDT irradiation from 0 to 10 minutes during treatment. Gender, age, lesions location, lesions area, ALA concentration and fluence rate were recorded. Results: The trial enrolled 274 patients in total, including 118 acne patients (in face), 30 actinic keratosis (AK) patients (in face), 126 Condylomatata acuminate patients(in genitalia). The average pain score in PDT was highest in the patients with actinic keratosis (7.3 ± 0.7), and that of condylomata acuminata was the lowest (4.5 ± 1.1) ($p < 0.05$). The highest pain score in patients with AK, acne and condylomata acuminata was 8, 6 and 6 respectively which occurred at 4 min, 4 min and 6 min respectively. The pain score of males was higher compared with females in all of the three diseases ($p < 0.05$). The pain score of facial diseases (5.6 ± 1.2) was higher than that of the genitalia (4.5 ± 1.1) ($p < 0.05$). The lesions area was positively correlated with the pain score ($p < 0.05$). In facial diseases, the pain score of patients with high fluence rate (7.3 ± 0.7) was higher than patients with low fluence rate (5.1 ± 0.9) ($p < 0.05$). Conclusions: Intrinsic and extrinsic factors both correlate with pain during PDT. Intrinsic factors are difficult to change, so extrinsic factors is the key point to control. Maybe we can reduce the fluence rate and extend the treatment time to relieving pain intensity while ensuring efficacy at the same time.

Optimization of hydrogel containing toluidine blue O for photodynamic therapy in treating acne. Zheng Y, Yu E, Weng Q, et al. Lasers Med Sci. 2019 Mar 1. doi: 10.1007/s10103-019-02727-2. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30825010

Antibiotics and photodynamic therapy (PDT) are widely employed in curing acne. However, antibiotics as an effective treatment would lead to bacterial resistance and severe side effects. In this study, we aimed to develop a novel TBO hydrogel, which could prolong the retention time of photosensitizer (TBO) at the lesion site and improve therapeutic effect. In vitro antibacterial experiments (against Staphylococcus aureus and Escherichia coli), the response surface methodology was used to optimize the formulation of TBO hydrogel. The results indicated that the optimal formulation was 0.5% (v/v) carbomer, 0.01 mg/mL TBO, 0.5% (v/v) ethanol concentration, 0.5% (v/v) Tween 80, the mass ratio of NaOH to carbomer of 0.4 (w/w). The TBO hydrogel formulation showed the strong antibacterial activity for Propionibacterium acnes. The stability, pH, and antibacterial activity of TBO hydrogel did not significantly change under 4 °C, 25 °C, and 40 °C during 6-week storage. Furthermore, TBO combined with carbomer hydrogel showed the 51.28% (4 h) and 69.80% (24 h) release. In summary, the hydrogel TBO might be a vital therapeutic strategy to promote the PDT applied in the topical therapy of acne. Graphical abstract A TBO hydrogel for photodynamic therapy in the treatment of acne.

Case of coincident severe acne and psoriasis in AIDS patient successfully treated with antiretroviral therapy. Li YY, Dong RJ, Cao LJ, et al. J Dermatol. 2019 Feb 27. doi: 10.1111/1346-8138.14823. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30811070

Cutaneous disorders remain a major problem in HIV-infected patients, even under antiretroviral therapy (ART). Patients at any stage of HIV/AIDS may suffer from skin lesions. Acnes and psoriasis are both common chronic and inflammatory skin diseases, and the treatment becomes more challenging and complex when combined with HIV infection. Whether the incidence and severity of acne and psoriasis are related to HIV infection is still controversial. Here, we report a rare case of an AIDS patient who developed severe acne along with psoriasis. The patient had initially received multiple systemic and topical antipsoriatic and anti-acne treatments which failed. Ultimately, he achieved dramatic clinical improvement after initiation of ART for main treatment. An 8-year follow up demonstrated that the patient has been free of symptoms of both psoriasis and acne till now.

The efficacy of glycolic acid, salicylic acid, gluconolactone, and licochalcone A combined with 0.1% adapalene vs adapalene monotherapy in mild-to-moderate acne vulgaris: a double-blinded within-person comparative study. Kantikosum K, Chongpison Y, Chottawornsak N, Asawanonda P. Clin Cosmet Investig Dermatol. 2019 Feb 19;12:151-161. doi: 10.2147/CCID.S193730. eCollection 2019. https://www.ncbi.nlm.nih.gov/pubmed/30858720 Background: Acne vulgaris is a common and chronic disease that impacts on physical and psychological perceptions. Cosmeceutical products are widely used as adjunct therapy to standard treatments. Objective: To evaluate the efficacy of cosmeceutical products comprising glycolic acid, salicylic acid, gluconolactone, and licochalcone A as adjunct therapy to adapalene in mild-to-moderate acne vulgaris. Materials and methods: A 28-day, double-blind, within-person comparative study was conducted with a total of 25 subjects. Each participant received two products, consisting of (1) a cosmeceutical product mixed with 0.1% adapalene, and (2) 0.1% adapalene, and was asked to apply them separately on each hemi-side once nightly for 28 days. The number of acne lesions, severity of acne vulgaris, physician's and patient's global assessment of acne severity, visual analog scale of radiance, skin biophysics, safety assessment, and VISIA® camera system were evaluated. The primary efficacy outcome was to compare the reduction of inflammatory lesions between two

treatments at day 7 by using non-inferiority comparison. Results: The mean differences of inflammatory lesions reduction at day 7 between the two groups was 0.391 (90% CI = 0.253-0.530). The differences between two groups fell within our acceptable margin for the 90% CI. The spot score from VISIA® showed higher statistically significant improvement in the combination side. Conclusion: The results showed no hindrance of using a cosmeceutical combined with standard treatment. Nevertheless, this cosmeceutical product showed some benefits in reducing complications from acne. Clinical trial registration: Thai Clinical Trials Registry (primary site), no. TCTR20171031005.

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Hidradenitis suppurativa (Hurley I/II): serial excisions with primary wound closure under local anesthesia as most adequate treatment approach. Tchernev G, Temelkova I. Open Access Maced J Med Sci. 2019 Feb 11;7(3):400-402. doi: 10.3889/oamjms.2019.148. eCollection 2019 Feb 15. https://www.ncbi.nlm.nih.gov/pubmed/30834010

Background: Acne inversa as a chronic inflammatory disorder can be divided into three stages according to Hurley's classification. It affects the axillary and anogenital region predominantly, and its chronic course of development is associated with a major negative impact on quality of life, especially in young patients. We discuss the different types of treatment in patients with acne inversa and the benefits of two-stage surgical treatment by serial excisions with primary wound closure under local anaesthesia. Case report: We present a 28-year-old man with hidradenitis suppurativa stage I in the right axillary region and also in the pubic area. The patient is an active smoker. The patient was treated with Rifampicin 2x 300mg / day without any particular effect and preoperatively, systemic therapy with Clindamycin 4x 600mg / day was performed, combined with daily dressings with jodasept ointment for 7 days. The patient was treated through two surgical sessions under local anaesthesia with elliptical excision of the lesions located in the right axillary and the pubic area. Both of the two surgical defects were initially closed with single interrupted sutures. Histological examination of both lesions revealed the presence of suppurative folliculitis. Conclusion: The literature describes various methods for treating acne inversa which include both systemic and local approaches. However, it is considered that drug therapy achieves only a temporary improvement in patients with hidradenitis suppurativa. For this reason, the surgical treatment of acne inversa is indicated as the only curative treatment, especially for recurrent lesions and serial excisions under local anaesthesia, followed by primary wound closure is a valuable treatment for patients with mild to moderate HS (Hurly stage I & II).

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Polymethylmethacrylate collagen gel-injectable dermal filler for full face atrophic acne scar correction. Joseph JH, Shamban A, Eaton L, et al. Dermatol Surg. 2019 Feb 15. doi: 10.1097/DSS.0000000000001863. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30829754

Background/objectives: This trial evaluated the effectiveness and safety of Bellafill for full-face acne scar treatment. Patients and methods: In this open-label, nonrandomized, multicenter pilot study investigating the use of polymethylmethacrylate for full-face atrophic acne scar correction, 42 adult subjects with a mean age of 43 years were treated and assessed for safety and effectiveness at Months 4 and 7. There were no hypersensitivity reactions to pretreatment skin testing or during scar treatments. Results: At 4 and 7 months after initial treatment, 92% and 95% of subjects, respectively, were responders with ≥1-point improvement on the 5-point Acne Scar Assessment Scale. Subjects reported very high levels of improvement on the Global Aesthetic Improvement Scale (GAIS), with 95% of subjects reporting "improved or better" at 4 months and 90% at 7 months. The outcome of the physician GAIS

was also high with 92% of patients classified as "improved or better" at 4 months and 97% at 7 months. There were only 2 device-related adverse events, both mild events related to Bellafill skin test (bruising, ecchymosis). There were no serious adverse events in response to the treatment product in this short-term follow-up study. Conclusion: Polymethylmethacrylate is effective for treating full-face acne scarring. Clinicaltrials.gov #NCT02642627.

Apremilast for the treatment of mild-to-moderate hidradenitis suppurativa in a prospective, open-label, phase 2 study. Kerdel FR, Azevedo FA, Kerdel Don C, et al. J Drugs Dermatol. 2019 Feb 1;18(2):170-176. https://www.ncbi.nlm.nih.gov/pubmed/30811140

Background: Treatment options are limited for patients with hidradenitis suppurativa (HS). Apremilast, an oral phosphodiesterase 4 inhibitor, may offer an attractive therapeutic option for patients with mild-to-moderate HS. Methods: This open-label, phase 2 clinical trial enrolled adults (≥18 years of age) with mild-to-moderate HS. Patients received apremilast 30mg twice daily for 24 weeks after a 5-day titration period. Therapy was discontinued at week 24; data were collected up to week 28. Hidradenitis Suppurativa Clinical Response 30 (HiSCR30), ie, proportion of patients with a ≥30% reduction in abscesses and nodules at week 16, was the primary endpoint. HiSCR50, ie, ≥50% reduction, was also explored. Mean changes from baseline to week 24 in the modified Sartorius, Physician's Global Assessment, visual analog scale (VAS) for pain, and Dermatology Life Quality Index (DLQI) scores were analyzed using the Wilcoxon Rank-Sum test. Adverse events (AEs) were summarized. Results: Twenty patients (mean age, 32.5 years) were enrolled in the study. HiSCR30 was achieved in 65% of patients at weeks 16 and 24. A similar proportion of patients achieved HiSCR50. Significant mean improvements from baseline were observed for all assessments. At week 24, the overall Sartorius score improved from 35.6 to 13.9 (-21.7 change; P<0.001), the PGA score from 2.7 to 1.6 (-1.1 change; P<0.01), the VAS pain score from 27.6 to 10.9 (-16.8 change; P<0.05), and the DLQI score from 11.6 to 5.4 (-6.2 change; P<0.01). Diarrhea (20%), nausea (15%), and depression (10%) were the most commonly reported AEs. No serious AEs or deaths were reported. Conclusions: Apremilast was safe and effective in improving HS disease activity, pain, and QoL in patients with mild-to-moderate HS. These data suggest that apremilast may have a role in the early treatment of less severe HS.

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Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris in an adult and adolescent female population. Kircik LH, Baldwin H, Lain E, et al. J Drugs Dermatol. 2019 Feb 1;18(2):178-188. https://www.ncbi.nlm.nih.gov/pubmed/30811141

Background: Acne vulgaris (acne) is a common dermatological condition typically associated with adolescents, affecting about 85% of young people. However, it is also prevalent and persistent into adulthood, particularly in females. The efficacy of tretinoin in acne is well documented with large pivotal studies. The first lotion formulation of tretinoin was developed to provide an important alternative option to treat acne patients who may be sensitive to the irritant effects of other tretinoin formulations. Objective: To determine whether efficacy and safety of tretinoin 0.05% lotion was similar in adolescent (<18 years) and adult (>=18 years) women with moderate-to-severe acne. Methods: Post hoc analysis of two multicenter, randomized, double-blind, vehicle-controlled Phase 3 studies in moderate or severe acne. Female subjects (aged 9 to 58 years, N=909) randomized (1:1) to receive tretinoin 0.05% lotion or vehicle, once-daily for 12 weeks. Efficacy assessments included changes in baseline inflammatory and noninflammatory lesions and treatment success (at least 2-grade reduction in Evaluator's Global Severity Score [EGSS] and clear/almost clear). Safety, adverse events (AEs), and cutaneous tolerability were evaluated throughout.

Results: At week 12, mean percent reduction in inflammatory and noninflammatory lesion counts in female subjects were 56.9% and 51.7%, respectively, compared with 47.1% and 34.9% with vehicle (P=<0.001). Similar results were seen in adult and adolescent females in terms of reduction in inflammatory lesion counts with tretinoin 0.05% lotion; reduction in noninflammatory lesions was significantly greater in adult females (P=0.002). Treatment success was achieved by 23.6% of female subjects by week 12, compared with 13.5% on vehicle (P<0.001). Although treatment success was somewhat greater in adult females (24.6% versus 21.6%), the difference was not significant. The majority of AEs were mild and transient. There were five serious AEs (SAEs) reported (4/1, adult/adolescent, respectively). The most frequently reported treatment related AEs with tretinoin 0.05% lotion were application site pain (3.0%/5.7%), and application site dryness (4.9%/6.4%). Local cutaneous safety and tolerability assessments were generally mild-to-moderate and improved by week 12. Slight increases in mean scores were observed for scaling, burning and stinging within the first four weeks and appeared to be transient. Conclusions: Tretinoin 0.05% lotion was significantly more effective than its vehicle in achieving treatment success and reducing inflammatory and noninflammatory lesions in female acne. Noninflammatory lesion count reduction was significantly greater in adult females compared with adolescent females. The new lotion formulation was well-tolerated.

New indications for topical ivermectin 1% cream: a case series study. Barańska-Rybak W, Kowalska-Olędzka E. Postepy Dermatol Alergol. 2019 Feb;36(1):58-62. doi: 10.5114/ada.2019.82825. Epub 2019 Feb 22. https://www.ncbi.nlm.nih.gov/pubmed/30858780

Introduction: Topical ivermectin is an effective treatment for inflammatory papulopustular rosacea in adults. Positive therapeutic effects of ivermectin due to its potential anti-inflammatory properties could be achieved in the other facial dermatoses. Aim: To assess the efficacy of topical ivermectin 1% cream therapy in mild and moderate perioral dermatitis (PD), seborrheic dermatitis (SD) and acne vulgaris (AV). Material and methods: The study comprising 20 patients diagnosed with PD (8), SD (8) and AV (4) was conducted between November 2016 and July 2017. Two scales were applied to establish efficacy of the treatment: Investigator Global Assessment score (IGA) and Patient Global Assessment of Treatment (PGA). Results: All patients responded to the treatment with topical ivermectin very well with a gradual reduction in inflammatory skin lesions. Complete or almost complete clearance (IGA score 0-1) was achieved in 20 cases. Four patients with PD achieved IGA 0-1 after 4 weeks of treatment, 1 patient after 5 weeks, 2 patients after 6 weeks and 1 patient after 12 weeks. In the total group of 8 patients with SD, 4 presented IGA 0 after 4 weeks of therapy, while 4 patients demonstrated IGA 1 after 6 weeks. Patients with AV required 8 and 10 weeks to obtain IGA 1. Nineteen patients of the studied group reported "very good" or "excellent" response to the therapy, only one patient with AV assessed therapy with topical ivermectin as "good". The adverse events were transient and manifested as mild-moderate desquamation, stinging and burning in 2 patients with PD. Conclusions: Topical ivermectin was well tolerated and beneficial for treatment of mild and moderate PD, SD and AV.

Clinical Reviews

From pathogenesis of acne vulgaris to anti-acne agents. Cong TX, Hao D, Wen X, et al. Arch Dermatol Res. 2019 Mar 11. doi: 10.1007/s00403-019-01908-x. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30859308 Acne vulgaris is a cutaneous chronic inflammatory disorder with complex pathogenesis. Four factors play vital roles in acne pathophysiology: hyperseborrhea and dysseborrhea, altered keratinization of the pilosebaceous duct, Cutibacterium acnes (C. acnes) and inflammation. The main hormones responsible for the development of acne vulgaris include androgens, insulin and insulin-like growth factor-

1. Other factors involved in this process are corticotropin-releasing hormone, α-melanocyte-stimulating hormone and substance P. Wnt/β-catenin signaling pathway, phosphoinositide 3-kinase (PI3K)/Akt pathway, mitogen-activated protein kinase pathway, adenosine 5'-monophosphate-activated protein kinase pathway and nuclear factor kappa B pathway participate in the modulation of sebocyte, keratinocyte and inflammatory cell (e.g. lymphocytes, monocytes, macrophages, neutrophils) activity. Among all the triggers and pathways mentioned above, IGF-1-induced PI3K/Akt/Forkhead box protein O1/mammalian target of rapamycin (mTOR) C1 pathway is the most important signaling responsible for acne pathogenesis. Commonly used anti-acne agents include retinoids, benzoyl peroxide, antibiotics and hormonal agents (e.g. spironolactone, combination oral contraceptive and flutamide). New approaches including peroxisome proliferator-activated receptor γ modifier, melanocortin receptor antagonists, epigallocatechin-3-gallate, metformin, olumacostat glasaretil, stearoyl-CoA desaturase inhibitor omiganan pentahydrochloride, KDPT, afamelanotide, apremilast and biologics have been developed as promising treatments for acne vulgaris. Although these anti-acne agents have various pharmacological effects against the diverse pathogenesis of acne, all of them have a synergistic mode of action, the attenuation of Akt/mTORC1 signaling and enhancement of p53 signal transduction. In addition to drug therapy, diet with no hyperglycemic carbohydrates, no milk and dairy products is also beneficial for treatment of acne.

Vitamin D and the skin: a review for dermatologists. Navarro-Triviño FJ, Arias-Santiago S, Gilaberte-Calzada Y. Actas Dermosifiliogr. 2019 Mar 8. pii: S0001-7310(18)30531-3. doi: 10.1016/j.ad.2018.08.006. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30857638

In recent years, the growing interest in the role played by vitamin D in skin disease has given rise to the publication of many studies of the relationship between this vitamin and certain skin conditions. As dermatologists, we need to understand, among other aspects, how vitamin D is synthesized and the main sources in humans, as well as plasma levels and the factors that can modify them. Of particular interest are the latest discoveries about the role of vitamin D in skin diseases such as lupus erythematosus, ichthyosis, atopic dermatitis, hidradenitis suppurativa, acne, alopecia areata, androgenetic alopecia, melanoma, and nonmelanoma skin cancer. Also of interest is the importance of vitamin D as adjuvant therapy in patients on long-term treatment with corticosteroids. In this review, we provide an overview of the most important and most recent information regarding the relationship between vitamin D and skin disease and discuss the importance of assessing individual vitamin D status and correcting deficiencies.

New and emerging drugs for the treatment of acne vulgaris in adolescents. Valente Duarte De Sousa IC. Expert Opin Pharmacother. 2019 Mar 8:1-16. doi: 10.1080/14656566.2019.1584182. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30848961

Acne vulgaris is the most common skin disease worldwide, yet current treatment options, although effective, are associated with unwanted side effects, chronicity, relapses and recurrences. The adequate control of the four pathogenic mechanisms involved in the appearance of acne lesions is key to treatment success. This paper aims to discuss the novel treatment modalities that have surfaced in consequence of new knowledge obtained in acne pathogenesis. Areas covered: Pathogenic pathways are evaluated and discussed throughout the paper in relation to the mechanisms of action of novel molecules being investigated for the treatment of acne vulgaris. A comprehensive search was made in PubMed and Clinicaltrial.gov using a different combination of keywords, which included acne vulgaris, treatment, therapy, and therapeutic. Expert opinion: In the near future, more effective treatments with less side effects are expected. The use of topical anti-androgens, coenzyme-A carboxylase inhibitors, and insulin growth factor-1inhibitors to control sebum production seem promising. Selective RAR-agonists have the potential of

becoming an alternative to the currently available retinoid therapy in the management of infundibular dyskeratosis with a better safety profile. Antibiotic use will probably decline as more effective options for controlling Cutinebacterium acnes colonization and the inflammation cascade emerge.

Minimize the regular laboratory monitoring during the systemic isotretinoin treatment: data of 704 patients with acne vulgaris. Öktem A, Hayran Y, Arı E, Yalçın B. J Dermatolog Treat. 2019 Mar 6:1-15. doi: 10.1080/09546634.2019.1591578. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30836808 Backround: Despite extensive usage of systemic isotretinoin in patients with acne for many years, laboratory monitoring protocols for adverse effects depend on the centers and there is no standardized practice for frequency and type of laboratory testing. We aimed to decrease unnecessary monitoring and to standardize our general clinical practice of our department as well as to provide patient comfort and cost saving. Material and method: The medical charts of 704 acne patients treated with systemic isotretinoin were reviewed retrospectively. The National Cancer Institute common terminology criteria for adverse events v3.0 grading system was used in order to categorize the laboratory abnormalities of liver functions and lipid levels. Results: All laboratory abnormalities were grade I. Abnormal liver function was seen in 7.2% of the patients (n = 51), maximum values were ALT: 87 IU/L, AST: 97 IU/L (normal values, ALT: 5-41 IU/L, AST: 5-40 IU/L) and median time of the abnormalities in liver function tests was in the second month. Lipid profile abnormalities were detected in 58% of the patients (n = 401). Maximum values during the laboratory monitoring were Tg: 481mg/dL CHOL: 314mg/dL, LDL: 259 mg/dL (normal values, Tg:0-200 mg/dL, CHOL.: 0-200mg/dL, LDL: 0-100 mg/dL). The median time of lipid abnormalities was in the first month (1-3 months). Abnormalities related to CBC were seen in 8.2% of the patients (n = 58). The median time of CBC abnormality was the second month of treatment. Anemia, leukopenia and thrombocytopenia were seen in 3.4%, 3.7%, and 1.6% of the patients respectively. Conclusion: Clinically insignificant and revers CBC abnormalities, mild to moderate elevation of liver transaminases and serum lipids are the most common laboratory abnormalities in patients with acne treated with oral isotretinoin. Due to these abnormalities are reversible even the isotretinoin therapy continued, and generally there is no need to discontinuation of treatment due to laboratory abnormalities, frequent biochemical monitoring is not recommended.

Biologics for chronic inflammatory skin diseases: an update for the clinician. Yao Y, Jørgensen AR, Thomsen SF. J Dermatolog Treat. 2019 Mar 2:1-49. doi: 10.1080/09546634.2019.1589643. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30827126

The introduction and continuous development in biological drugs has greatly improved the therapeutic quality for patients with chronic inflammatory skin conditions. Current approaches to the biologic treatment of psoriasis, atopic dermatitis, chronic spontaneous urticaria, and hidradenitis suppurativa include licensed use of traditional anti-tumor necrosis factor agents, selective interleukin antagonists (IL-4, IL-12/23, IL-17), and the IgE inhibitor omalizumab, and as the knowledge on the pathogenesis of these diseases expands, off-label uses of the currently available biologics are becoming increasingly attractive, and the number of investigational drugs is growing progressively plentiful. In recent years, small molecule inhibitors, many of which are used in cancer therapy, have emerged as valuable future prospects in the treatment of inflammatory diseases. Inhibitors of PGD2, JAK, Syk, and C5a all have, to some extent, theorized efficacy in the treatment of chronic skin conditions, and multiple clinical trials are ongoing. The extensive research of the novel targets' roles in the pathogenesis of dermatological conditions should, in the future, further improve the therapeutic options for both the patients and physicians involved.

A review and update of treatment options using the acne scar classification system. Boen M, Jacob C. Dermatol Surg. 2019 Mar;45(3):411-422. doi: 10.1097/DSS.0000000000001765. https://www.ncbi.nlm.nih.gov/pubmed/30856634

Background: An unfortunate consequence of acne vulgaris is residual scarring that can negatively affect a patient's quality of life. Objective: Jacob and colleagues have previously described an acne scar classification system based on acne scar pathology that divided atrophic acne scars into icepick, rolling, and boxcar scars, and this review will evaluate new and developing treatment options for acne scarring. Methods: A Medline search was performed on the various treatments for acne scars, and particular attention was placed on articles that used the acne scar classification system of icepick, rolling, and boxcar scars. Results: Therapies for acne scarring included surgical modalities, such as subcision, and punch excision and elevation, injectable fillers, chemical peels, dermabrasion, microneedling, and energy-based devices. In the past decade, there has been a trend toward using cosmetic fillers and energy-based devices to improve acne scarring. Conclusion: There were few high-quality evidence-based studies evaluating the management of acne scarring. Many disparate acne severity scores were used in these studies, and the acne scar type was frequently undefined, making comparison between them difficult. Nonetheless, research into interventions for acne scarring has increased substantially in the past decade and has given patients more therapeutic strategies.

Topical, systemic and biologic therapies in hidradenitis suppurativa: pathogenic insights by examining therapeutic mechanisms. Frew JW, Hawkes JE, Krueger JG. Ther Adv Chronic Dis. 2019 Mar1;10:2040622319830646. doi: 10.1177/2040622319830646. eCollection 2019. https://www.ncbi.nlm.nih.gov/pubmed/30854183

Hidradenitis suppurativa (HS) is a chronic inflammatory disease of the skin, manifesting in chronic, recurrent painful pustules, nodules, boils and purulent draining abscesses. Our current understanding of the pathogenesis of the disease is incomplete. This review aims to identify available treatment options in HS and discuss the pharmacological mechanisms through which such agents function. Identifying common pathways may inform our understanding of the pathogenesis of HS as well as identify future therapeutic targets. The pharmacological mechanisms implicated in topical therapies, antibiotic, hormonal, systemic immunomodulatory and biologic therapies for HS are discussed. Significant differences exist between agents and implicated pathways in therapy for mild and severe disease. This is an expression of the possible dichotomy in inflammatory pathways (and treatment responses) in HS. Studies involving monoclonal antibodies provide the greatest insight into what these specific mechanisms may be. Their variable levels of clinical efficacy compared with placebo bolsters the suggestion that differential inflammatory pathways may be involved in different presentations and severity of disease. Nuclear factor kappa B (NF-κB), tumor necrosis factor (TNF)-α and other innate immune mechanisms are strongly represented in treatments which are effective in mild to moderate disease in the absence of scarring or draining fistulae, however complex feed-forward mechanisms in severe disease respond to interleukin (IL)-1 inhibition but are less likely to respond to innate immune inhibition (through NF-κB or TNF-α) alone. It is unclear whether IL-17 inhibition will parallel TNF-α or IL-1 inhibition in effect, however it is plausible that small molecule targets (Janus kinase1 and phosphodiesterase 4) may provide effective new strategies for treatment of HS.

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Antibacterial and antifungal properties of resveratrol. Vestergaard M, Ingmer H. Int J Antimicrob Agents. 2019 Feb 27. pii: S0924-8579(19)30045-7. doi: 10.1016/j.ijantimicag.2019.02.015. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30825504

Resveratrol is a naturally occurring polyphenolic antioxidant that has received massive attention for potential health benefits, including anti-carcinogenesis, anti-aging and antimicrobial properties. The compound is well tolerated by humans and has in recent years been widely used as a nutraceutical. The common use makes it interesting to investigate with respect to antimicrobial properties both as a single agent and in interactions with conventional antibiotics. Resveratrol displays antimicrobial activity against a surprisingly wide range of bacterial, viral and fungal species. At sub-inhibitory concentrations, resveratrol can alter bacterial expression of virulence traits leading to reduced toxin production, inhibition of biofilm formation, reduced motility and interference with quorum sensing. In combination with conventional antibiotics, resveratrol enhances the activity of aminoglycosides against Staphylococcus aureus, whereas it antagonizes the lethal activity of for example fluoroquinolones against S. aureus and Escherichia coli. While the antimicrobial properties of the compound have been extensively studied in vitro, little is known of its efficacy in vivo. Nonetheless, following topical application, resveratrol has alleviated acne lesions caused by the bacterium Propionibacterium acnes. In combination with antibiotics there is currently no in vivo studies addressing its effect, but recent research suggests that there may be a potential for enhancing antimicrobial efficacy of certain existing antibiotic classes in combination with resveratrol. Given the difficulties associated with introducing new antimicrobial agents to the market, nutraceuticals, such as resveratrol, may prove to be interesting candidates when searching for solutions for the growing problems of antibiotic resistance.

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Efficacy of autologous platelet-rich plasma combined with ablative fractional carbon dioxide laser for acne scars: a systematic review and meta-analysis. Chang HC, Sung CW, Lin MH. Aesthet Surg J. 2019 Feb 27. pii: sjz048. doi: 10.1093/asj/sjz048. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30809666

Background: Acne scars are common and challenging clinical complications of acne vulgaris. Ablative fractional carbon dioxide (CO2) laser is a well-established treatment for acne scars; however, some postlaser adverse effects have been noted. Autologous platelet-rich plasma (PRP) can improve tissue regeneration. Several studies have investigated the efficacy of combination therapy of CO2 laser and PRP for acne scars. Objective: To conduct a meta-analysis of the efficacy of PRP combined with ablative fractional CO2 laser for treating acne scars by examining clinical trial results. Methods: A systematic review was performed by searching PubMed, Embase, Cochrane Library, and Web of Science, and a meta-analysis was conducted to assess the clinical outcomes after combination therapy of PRP and ablative fractional CO2 laser compared with laser alone. Results: We identified 4 eligible studies for the meta-analysis, including 3 randomized controlled trials. Our results demonstrated that clinical improvement after combination therapy was significantly higher than that after laser alone (odds ratio [OR] = 2.992, P = 0.001). Regarding major side effects, patients undergoing combination therapy experienced significantly shorter duration of crust compared with CO2 laser alone (standard mean difference = -1.140, P < 0.001); relatively shorter durations of erythema and edema were also noted after combination therapy. Furthermore, patient satisfaction rates were significantly higher after combination therapy than after laser alone (OR = 3.169, P = 0.002). Conclusions: The combination of autologous PRP and ablative fractional CO2 laser has synergistic positive effects on the clinical outcomes for acne scars and can accelerate the recovery of laser-damaged skin.

Global rosacea treatment guidelines and expert consensus points: the differences. Juliandri J, Wang X, Liu Z, et al. J Cosmet Dermatol. 2019 Feb 26. doi: 10.1111/jocd.12903. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30809947

Background: Rosacea is a highly prevalent, chronic inflammatory disease. The treatment of rosacea remains a challenge to dermatologists. Therapies include skin care, medications, lasers, and various combinations of these modalities. The appropriate treatment depends on clinical types and patient's various clinical symptoms. Purpose: The purpose of this study was to review and compare current therapies for rosacea of all severities from four different guidelines. Methodology: We searched PubMed using the keywords "rosacea," "treatment" AND ["erythema rosacea" OR "papulopustular rosacea" OR "ocular rosacea" OR "phymatous rosacea"]. We selected randomized controlled trials, observational studies, controlled clinical trials, and clinical trials. We indentified further studies (including the guidelines) by hand-searching relevant publications and included those that met the inclusion criteria. Results: The total number of records identified was 421. We limited our search to the specific abovementioned study types. Twenty-five of these studies met with our inclusion criteria. An additional five manuscripts were selected using the abovementioned method, and four guidelines were included in this review. Conclusion: Diagnosing and choosing the appropriate treatment options of rosacea according to guidelines is the basis of scientific criteria. More large-scale randomized controlled clinical trials on new treatment methods, new drugs, or new dosage forms provide a new guideline for future rosacea treatment. Although there are some differences in the treatment of rosacea, it is generally based on anti-demodex, anti-inflammatory, and anti-angiogenesis.

An overview of acne therapy, part 1: topical therapy, oral antibiotics, laser and light therapy, and dietary interventions. Marson JW, Baldwin HE. Dermatol Clin. 2019 Apr;37(2):183-193. doi: 10.1016/j.det.2018.12.001. Epub 2019 Feb 14. https://www.ncbi.nlm.nih.gov/pubmed/30850041

Therapeutic actives for acne have changed little in the last decade. Recognition that acne is an inflammatory condition, not an infectious one, has led to a call for reduction in antibiotic use. This has culminated in a re-evaluation of highly efficacious combination topical therapy and improved vehicle technology. Laser and light modalities, although not sufficiently studied for first-line use, show promise for the future. The role that diet plays in the initiation and continuation of acne is unclear but remains one of our patients' most frequently asked questions.

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An overview of acne therapy, part 2: hormonal therapy and isotretinoin. Marson JW, Baldwin HE. Dermatol Clin. 2019 Apr;37(2):195-203. doi: 10.1016/j.det.2018.12.002. Epub 2019 Feb 14. https://www.ncbi.nlm.nih.gov/pubmed/30850042

Therapeutic actives for acne have changed little in the last decade. Recognition that acne is an inflammatory condition, not an infectious one, has led to a call for reduction in antibiotic use, which has culminated in a re-evaluation of our nonantibiotic choices. Spironolactone and oral contraceptives have become more acceptable first-line choices, and earlier use of isotretinoin has been proposed.

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Psychiatric and developmental effects of isotretinoin (retinoid) treatment for acne vulgaris. Suuberg A. Curr Ther Res Clin Exp. 2019 Feb 10;90:27-31. doi: 10.1016/j.curtheres.2019.01.008. eCollection 2019. https://www.ncbi.nlm.nih.gov/pubmed/30828405

Background: An association between isotretinoin (13-cis-retinoic acid, sold under trade names including Accutane [Hoffmann-La Roche Inc, Basel, Switzerland]) and birth defects, depression, and suicide is well documented but controversial. A link to psychosis and exacerbation of bipolar symptoms is less extensively addressed in the literature. Objective: Given recent conceptualization of psychotic disorders as neurodevelopmental, and current interest in possible shared etiology of different neurodevelopmental disorders such as psychosis, autism, and intellectual disability, this review concurrently examines the literature on developmental (primarily teratogenic) and psychiatric side effects of isotretinoin exposure. The goal of concurrent review is to identify shared mechanisms in the literature that may inform future efforts to clarify the neurocognitive and psychiatric effects of isotretinoin exposure at different developmental stages or given different genetic backgrounds. Methods: Literature was obtained by PubMed search for the term isotretinoin in combination with each of the terms psychosis, psychiatric, and teratogenic. Resulting articles met inclusion criteria for review if they addressed psychiatric side effects of isotretinoin treatment or the neurobehavioral teratology of isotretinoin. Results: The association of isotretinoin exposure with prenatal developmental toxicity is well established. Although numerous reports also link isotretinoin treatment with psychiatric side effects, this association remains controversial. Conclusions: The extent to which isotretinoin influences pediatric and adult development and cognition, and whether and why certain individuals may be susceptible to psychiatric side effects, remains to be clarified.

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