



AARS **HOT TOPICS** MEMBER NEWSLETTER

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Industry News

FDA approves tretinoin lotion acne treatment. Dermatology Times Staff, Oct 3, 2018. Volume: 39 Issue: 10. <http://www.dermatologytimes.com/acne/fda-approves-tretinoin-lotion-acne-treatment>

The U.S. Food and Drug Administration has approved Ortho Dermatologic's new drug application for Altreno (tretinoin 0.05 percent) lotion for the treatment of acne vulgaris. Approved for use in patients ages nine and older, the formulation is the first of its kind in a lotion, according to a company news release. It is expected to be on the market by the fourth quarter of 2018. Noting that retinoids often result in skin irritation, physicians stated that the new lotion provides an attractive option for many patients suffering from acne. "With the efficacy expected from a retinoid plus a proven tolerability profile, Altreno will be an ideal choice for many of my patients," Joshua Zeichner, M.D., director of Cosmetic and Clinical Research in Dermatology at Mount Sinai Hospital, New York City, commented in the news release. Ortho Dermatologics states the lotion spreads easily and is quickly absorbed by the skin. In two multicenter, randomized, double-blind, vehicle-controlled phase 3 studies of 1,640 patients, Altreno demonstrated statistically significant reductions in inflammatory and noninflammatory lesions compared to vehicle. At week 12, 16.5 percent and 19.8 percent of patients in trials 1 and 2, respectively, demonstrated treatment success of at least a 2- grade improvement in global severity by Evaluator Global Severity Scores, compared to 6.9 percent and 12.5 percent with vehicle. Skin dryness, swelling, irritation, peeling and pain was reported by fewer than 4 percent of patients. "FDA approval of Altreno builds upon our strong acne portfolio, providing physicians and patients a trusted retinoid in a lotion formulated to enhance the user's experience with the inclusion of moisturizing attributes of hyaluronic acid, glycerin and collagen," stated Ortho Dermatologics President Bill Humphries.

Seysara: Oral antibiotic is first approved for dermatology in 40 years. DermWire, Practical Dermatology. Tuesday, October 02, 2018. <http://practicaldermatology.com/dermwire/2018/10/02/seysara-oral-antibiotic-is-first-approved-for-dermatology-in-40-years>

Seysara (sarecycline), a new, first in class tetracycline-derived oral antibiotic, is now approved for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older. Almirall, which recently acquired Seysara from Allergan, plans to launch the drug in January 2019. Seysara is an oral tablet that is taken once daily with or without food. It has proven significant reduction of inflammatory lesions as early as three weeks after start of treatment and is generally safe and well tolerated. "As dermatologists we are always seeking ways to improve the management of our patients' disease. The results of the studies are encouraging, with statistically significant efficacy vs placebo as early as 3 weeks. I'm looking forward to having this as an option for my patients when it becomes available in 2019," says Leon Kircik, MD, who participated in clinical trials for Seysara. With the approval of Seysara and its upcoming launch, Almirall says it will consolidate and reinforce its presence in the US, offering top dermatological products in the world's biggest market. Seysara is expected to reach peak sales of \$150-200 Million.

New Medical News

The assessment of the effects of the combination of microdermabrasion and cavitation peeling in the therapy of seborrheic skin with visible symptoms of acne punctata. Kołodziejczak A, Wieczorek A, Rotsztein H. *J Cosmet Laser Ther.* 2018 Oct 9:1-5. doi: 10.1080/14764172.2018.1525751. [Epub ahead of print]. <https://www.ncbi.nlm.nih.gov/pubmed/30300026>

Objective: The aim of this study was to assess objectively the effects of the combination of corundum microdermabrasion and cavitation peeling in the therapy of seborrheic skin with visible symptoms of acne punctata. **Material and methods:** The study involved a group of nine women. A series of six treatments with the combination of microdermabrasion and cavitation peeling were performed within facial skin at 10-14 days intervals. Corneometric measurements examining skin hydration level and sebumetric measurements analyzing skin sebum level were made before the series of treatments and after second, fourth and sixth procedure in five facial areas. Clinical assessment of the efficacy of the therapy was performed on the basis of photographic documentation (Fotomedicus). Anonymous questionnaires were used in order to evaluate patients' satisfaction rate. **Results:** Statistically significant improvement in skin sebum level was observed in all examined areas (forehead $p = 0.002$; nose $p = 0.001$, chin $p = 0.01$, left cheek $p = 0.009$, right cheek $p = 0.007$). In case of skin hydration, significant improvement was found only in the area of chin ($p = 0.03$). 78% of participants estimated that the improvement was in the range of 55-70%, while 22% of participants of 75-100%. The reduction in the amount and visibility of comedones and pimples were demonstrated on the basis of questionnaire and photographic documentation. **Conclusions:** Combined microdermabrasion and cavitation peeling treatments improve the condition of seborrheic skin.

Demographic and clinical features of hidradenitis suppurativa in Korea. Yang JH, Moon J, Kye YC, et al. *J Dermatol.* 2018 Oct 8. doi: 10.1111/1346-8138.14656. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30294846>

Hidradenitis suppurativa (HS) is a chronic, relapsing, inflammatory skin disorder. Although several epidemiological studies have been conducted in Western countries, such data regarding Asian populations are scarce. In this study, we sought to investigate the demographic and clinical features of HS in Korea. A total of 438 patients, diagnosed with HS from May 2007 to April 2017, were enrolled and the electronic medical record of each patient was reviewed. Male patients were predominant with a male:female ratio of 2.5:1. Mean age of disease onset was 23.9 years and most patients had no family history. The most frequently affected area was the buttocks, followed by axillae and groin. Acne and diabetes mellitus were the most prevalent associated diseases and no patients with inflammatory bowel diseases were observed. In the univariable analysis, male patients had severe diseases compared with females with an odds ratio (OR) of 1.790. Two or more affected body regions were associated with HS severity with an OR of 1.693. While involvement of the perineum (OR, 4.067) and buttocks (OR, 1.471) tended to be associated with increased severity of the disease, the inguinal area (OR, 0.620) showed a tendency to be inversely associated with the severity. In multivariable analysis, identified risk factors were the involvement of the perineum (OR, 3.819) and buttocks (OR, 2.288). Smoking status and high body mass index seemed to be associated with more severe diseases. Our results will provide clinical characteristics of HS patients in Asia and help to broaden understanding of HS.

Brimonidine displays anti-inflammatory properties in the skin through the modulation of the vascular barrier function. Bertino B, Blanchet-Réthoré S, Thibaut de Ménonville S, et al. *Exp Dermatol.* 2018 Oct 5. doi: 10.1111/exd.13793. [Epub ahead of print]. <https://www.ncbi.nlm.nih.gov/pubmed/30290018>

Background: Rosacea is a chronic inflammatory skin disease. Characteristic vascular changes in rosacea skin include enlarged, dilated vessels of the upper dermis and blood flow increase. Brimonidine is approved for symptomatic relief of the erythema of rosacea. It acts by selectively binding to α_2 -adrenergic receptors present on smooth muscle in the peripheral vasculature, resulting in transient local vasoconstriction. **Objectives:** To provide further evidence of the anti-inflammatory potential of brimonidine across preclinical models of skin inflammation and its ability to decrease the neutrophil infiltration in human skin after ultraviolet light exposure. **Methods:** The anti-inflammatory properties of brimonidine through modulation of the vascular barrier function were assessed using in vivo neurogenic vasodilation and acute inflammatory models and a well-described in vitro transmigration assay. A clinical study assessed the neutrophil infiltration in human skin after exposure to UV in 37 healthy Caucasian male subjects. **Results:** In vitro, brimonidine affects the transmigration of human neutrophils through the endothelial barrier by modulating adhesion molecules. In vivo, in the mouse, topical treatment with brimonidine, used at a vasoconstrictive dose, confirmed its anti-inflammatory properties and prevented leukocyte recruitment (rolling and adhesion) mediated by endothelial cells. Topical pre-treatment with brimonidine tartrate 0.33% gel once a day for four days significantly prevented neutrophil infiltration by 53.9% in human skin after exposure to UV light. **Conclusion:** Results from in vitro, in vivo and from a clinical study indicate that brimonidine impacts acute inflammation of the skin by interfering with neurogenic activation and/or recruitment of neutrophils.

Comparative efficacy of short-pulsed intense pulsed light and pulsed dye laser to treat rosacea. Kim BY, Moon HR, Ryu HJ. *J Cosmet Laser Ther.* 2018 Oct 4:1-6. doi: 10.1080/14764172.2018.1528371. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30285506>

Background: Laser and light-based therapies have often been used successfully to treat rosacea. Recently, short-pulsed intense pulsed light (IPL) that emitted pulse durations down to 0.5 ms was found to be effective for rosacea treatment. **Objective:** This study evaluated the efficacy of short-pulsed IPL in the treatment of rosacea compared with pulsed dye laser (PDL) using same pulse duration and fluence. **Materials and methods:** Nine patients with rosacea were enrolled in a randomized, split-face trial. Each treatment consisted of four sessions at three-week intervals and followed up until three weeks after the last treatment. Efficacy was assessed by erythema, melanin index, physician's subjective evaluation, and patient's satisfaction. **Results:** The mean change in erythema index was -4.93 ± 1.59 for the short-pulsed IPL group and -4.27 ± 1.23 for the PDL group. The mean change in melanin index was -2.52 ± 2.45 for the short-pulsed IPL group and -1.95 ± 1.41 for the PDL group. There was no significant difference in either melanin or erythema index between short-pulsed IPL and PDL treatments, and there were no noticeable adverse events. **Conclusions:** There was no significant difference between PDL and short-pulsed IPL treatment using the same energies and pulse. Both PDL and short-pulsed IPL were satisfactory and safe for rosacea treatment.

Estimated cost efficacy of US Food and Drug Administration approved treatments for acne. Tassavor M, Payette MJ. *Dermatol Ther.* 2018 Oct 4:e12765. doi: 10.1111/dth.12765. [Epub ahead of print]. <https://www.ncbi.nlm.nih.gov/pubmed/30288869>

Background: Standard of practice in patients with acne is generally to attempt topical and oral therapies, often in a

stepwise manner, before isotretinoin. Objective: To estimate the cost efficacy of US Food and Drug Administration approved treatments to facilitate comparison of therapeutic options, specifically against isotretinoin. Methods: Drug costs were obtained from the National Average Drug Acquisition Cost database maintained by the US Centers for Medicare & Medicaid Services (CMS). Laboratory fees were obtained from the CMS as well. Office fees are standard at our university. Cost calculations were standardized to seven months of treatment because this is when isotretinoin patients will have achieved the upper end of their weight-based cumulative dose. Results: Median prices for six classes of medications were calculated. Spironolactone was \$350. Oral antibiotics were \$501. Topical antibiotics were \$920. Topical retinoids were \$1,805. Topical combination antibiotics were \$2,282. Topical combination antibiotics and retinoids were \$3,770. The median cost for isotretinoin in males and females were \$3,227 and \$3,806 respectively. Conclusion: Our study provides meaningful cost efficacy data that may influence treatment selection. Isotretinoin can be more cost effective in moderate to severe acne, particularly over extended treatment periods.

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Licochalcone A attenuates acne symptoms mediated by suppression of NLRP3 inflammasome. Yang G, Lee HE, Yeon SH, et al. *Phytother Res.* 2018 Oct 3. doi: 10.1002/ptr.6195. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30281174>

Activation of the NACHT, LRR and PYD domains-containing protein 3 (NLRP3) inflammasome by *Propionibacterium acnes* (*P. acnes*) is critical for inducing inflammation and aggravating the development of acne lesions. We searched for available small-molecule inhibitors of the NLRP3 inflammasome that could be topically administered for the treatment of acne. We found that licochalcone A, a chalconoid isolated from the root of *Glycyrrhiza inflata*, was an effective inhibitor for *P. acnes*-induced NLRP3 inflammasome activation. Licochalcone A blocked *P. acnes*-induced production of caspase-1(p10) and IL-1 β in primary mouse macrophages and human SZ95 sebocytes, indicating the suppression of NLRP3 inflammasome. Licochalcone A suppressed *P. acnes*-induced ASC speck formation and mitochondrial reactive oxygen species. Topical application of licochalcone A to mouse ear skin attenuated *P. acnes*-induced skin inflammation as shown by histological assessment, ear thickness measurement, and inflammatory gene expression. Licochalcone A reduced caspase-1 activity and IL-1 β production in mouse ear injected with *P. acnes*. This study demonstrated that licochalcone A is effective in the control of *P. acnes*-induced skin inflammation as an efficient inhibitor for NLRP3 inflammasome. Our study provides a new paradigm for the development of anti-acne therapy via targeting NLRP3 inflammasome.

Improvement of dermal delivery of tetracycline using vesicular nanostructures. Hasanpour A, Lotfipour F, Ghanbarzadeh S, Hamishehkar H. *Res Pharm Sci.* 2018 Oct;13(5):385-393. doi: 10.4103/1735-5362.236831. <https://www.ncbi.nlm.nih.gov/pubmed/30271440>

The objective of this investigation was to study the potential use of nanoliposomes and nanotransfersomes in dermal delivery of tetracycline hydrochloride (TC) for acne treatment. Vesicular nanostructures were prepared by thin film hydration method and evaluated for their size, zeta potential, morphology, and entrapment efficiency. Minimal inhibitory concentration values of TC-loaded vesicles were evaluated and compared with TC aqueous solution against *Staphylococcus epidermidis*. In vitro drug release and ex vivo drug permeation through the excised rat skin were performed to assess drug delivery efficiency. Particle size, zeta potential, and entrapment efficiency of prepared nanoliposomes and nanotransfersomes were found to be 75 and 78 nm, 17 and 7 mV, and 45 and 55%, respectively. Antimicrobial analysis indicated that there was no difference between vesicular formulations and aqueous solution of

TC. In vitro drug release study indicated that nanoliposomes could release TC 2.6 folds more than nanotransfersomes, and skin permeation study showed that the permeability of TC-loaded nanotransfersomes was 1.6 times higher than nanoliposomes which was also confirmed by fluorescence microscope imaging. These findings concluded that nanoliposomal and especially nanotransfersomal formulations could be proposed as the potential approach for better therapeutic performance of TC against acne.

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Inhibitory effects of Euphorbia supina on Propionibacterium acnes-induced skin inflammation in vitro and in vivo. Lim HJ, Jeon YD, Kang SH, et al. BMC Complement Altern Med. 2018 Sep 27;18(1):263. doi: 10.1186/s12906-018-2320-8. <https://www.ncbi.nlm.nih.gov/pubmed/30261862>

Background: Euphorbia supina (ES) plant has been used as treatment for inflammatory conditions. The antibacterial effect and the anti-inflammatory mechanism of ES for Propionibacterium (P.) acnes-induced inflammation in THP-1 cells and acne animal model remain unclear. Therefore, the objective of the present study was to determine the antibacterial and anti-inflammatory activities of ES against P. acnes, the etiologic agent of skin inflammation. Method: The antibacterial activities of ES were tested with disc diffusion and broth dilution methods. Cytotoxicity of ES at different doses was evaluated by the MTT assay. THP-1 cells were stimulated by heat-killed P. acnes in the presence of ES. The pro-inflammatory cytokines and mRNA levels were measured by ELISA and real-time-PCR. MAPK expression was analyzed by Western blot. The living P. acnes was intradermally injected into the ear of BLBC/c mice. Subsequently, chemical composition of ES was analyzed by liquids chromatography-mass spectrometry (LC-MS). Result: ES had stronger antibacterial activity against P. acnes and inhibitory activity on lipase. ES had no significant cytotoxicity on THP-1 cells. ES suppressed the mRNA levels and production of IL-8, TNF- α , IL-1 β in vitro. ES inhibited the expression levels of pro-inflammatory cytokines and the MAPK signaling pathway. Ear thickness and inflammatory cells were markedly reduced by ES treatment. Protocatechuic acid, gallic acid, quercetin, and kaempferol were detected by LC-MS analysis in ES. Conclusions: Our results demonstrate antibacterial and anti-inflammatory activities of ES extract against P. acnes. It is suggested that ES extract might be used to treatment anti-inflammatory skin disease.

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Low-dose blue light irradiation enhances the antimicrobial activities of curcumin against Propionibacterium acnes. Yang MY, Chang KC, Chen LY, Hu A. J Photochem Photobiol B. 2018 Sep 26;189:21-28. doi: 10.1016/j.jphotobiol.2018.09.021. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30273795>

Propionibacterium acnes (P. acnes) is an opportunistic infection in human skin that causes acne vulgaris. Antibiotic agents provide the effective eradication of microbes until the development of drug-resistant microbes. Photodynamic inactivation (PDI) is a non-antibiotic therapy for microbial eradication. In this study, the visible blue light (BL, λ_{max} = 462 nm) was used to enhance the antimicrobial activities of curcumin, a natural phenolic compound. Individual exposure to curcumin or BL irradiation does not generate cytotoxicity on P. acnes. The viability of P. acnes was decreased significantly in 0.09 J/cm² BL with 1.52 μ M of curcumin. Furthermore, the low-dose blue light irradiation triggers a series of cytotoxic actions of curcumin on P. acnes. The lethal factors of photolytic curcumin were investigated based on the morphology of P. acnes by SEM and fluorescent images. The membrane disruption of microbes was observed on the PDI against P. acnes. Chromatography and mass spectrometry techniques were also used to identify the photolytic metabolites. Curcumin could be photolysed into vanillin through BL irradiation, which presents a strong linear relationship in quantitation. Because the safety of blue light in mammalian cell has been

proven, the photolytic curcumin treatment could support non-antibiotic therapy to eradicate *P. acnes* on clinical dermatology.

Comparative analyses of biofilm formation among different *Cutibacterium acnes* isolates. Kuehnast T, Cakar F, Weinhäupl T, et al. *Int J Med Microbiol.* 2018 Sep 22. pii: S1438-4221(18)30056-0. doi: 10.1016/j.ijmm.2018.09.005. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30268774>

The Gram-positive anaerobic bacterium *Cutibacterium acnes* is a commensal of the human skin, but also an opportunistic pathogen that contributes to the pathophysiology of the skin disease acne vulgaris. Moreover, *C. acnes*, in addition to other skin-colonizing bacteria such as *S. epidermidis* and *S. aureus*, is an emerging pathogen of implant-associated infections. Notably, *C. acnes* isolates exhibit marked heterogeneity and can be divided into at least 6 phylotypes by multilocus sequence typing. It is becoming increasingly evident that biofilm formation is a relevant factor for *C. acnes* virulence, but information on biofilm formation by diverse *C. acnes* isolates is limited. In this study we performed a first comparative analysis of 58 diverse skin- or implant-isolates covering all six *C. acnes* phylotypes to investigate biofilm formation dynamics, biofilm morphology and attachment properties to abiotic surfaces. The results presented herein suggest that biofilm formation correlates with the phylotype, rather than the anatomical isolation site. IA1 isolates, particularly SLST sub-types A1 and A2, showed highest biofilm amounts in the microtiter plate assays, followed by isolates of the IC, IA2 and II phylotypes. Microscopic evaluation revealed well-structured three-dimensional biofilms and relatively high adhesive properties to abiotic surfaces for phylotypes IA1, IA2 and IC. Representatives of phylotype III formed biofilms with comparable biomass, but with less defined structures, whereas IB as well as II isolates showed the least complex three-dimensional morphology. Proteinase K- and DNase I-treatment reduced attachment rates of all phylotypes, therefore, indicating that extracellular DNA and proteins are critical for adhesion to abiotic surfaces. Moreover, proteins seem to be pivotal structural biofilm components as mature biofilms of all phylotypes were proteinase K-sensitive, whereas the sensitivity to DNase I-treatment varied depending on the phylotype.

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Clinical Reviews

Approaches to limit systemic antibiotic use in acne: Systemic alternatives, emerging topical therapies, dietary modification, and laser and light-based treatments. *J Am Acad Dermatol.* 2018 Oct 5. pii: S0190-9622(18)32671-9. doi: 10.1016/j.jaad.2018.09.055. [Epub ahead of print]. Barbieri JS, Spaccarelli N, Margolis DJ, James WD. <https://www.ncbi.nlm.nih.gov/pubmed/30296534>

Acne is one of the most common diseases worldwide and affects approximately 50 million individuals in the United States. Oral antibiotics are the most common systemic agent prescribed for the treatment of acne. However, their use may be associated with a variety of adverse outcomes including bacterial resistance and disruption of the microbiome. As a result, multiple treatment guidelines call for limiting the use of oral antibiotics in the treatment of acne, although actual prescribing often does not follow these guidelines. In this review, the rationale for concerns regarding the use of oral antibiotics for the management of acne is reviewed. In addition, we will discuss our approach to complying with the intent of the guidelines, with a focus on novel topical agents, dietary modification, laser and light-based modalities, and systemic medications such as spironolactone, combined oral contraceptives, and oral isotretinoin.

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Acute localised exanthematous pustulosis due to metronidazole. Kostaki M, Polydorou D, Adamou E, et al. *J Eur Acad Dermatol Venereol.* 2018 Oct 5. doi: 10.1111/jdv.15274. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30288796>

A 78-year-old male patient known for hypertension consulted for a pustular eruption of the face of acute onset. The patient was receiving oral metronidazole as a treatment for rosacea and reported the sudden development of multiple pustules on the face 2 days after the initiation metronidazole. Physical examination revealed the presence of multiple minuscule, non-follicular pustules of the face on an erythematous, edematous background.

Long-term clinical safety of clindamycin and rifampicin combination for the treatment of hidradenitis suppurativa: A critically appraised topic. Albrecht J, Baine PA, Ladizinski B, et al. *Br J Dermatol.* 2018 Oct 3. doi: 10.1111/bjd.17265. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30281779>

Clinical question: Can therapy with clindamycin and rifampicin be safely continued long term beyond the recommended 10 week course? Background: Clindamycin and rifampicin are used in combination to treat hidradenitis suppurativa (HS). There is no data on the efficacy and safety of clindamycin/rifampicin combination therapy for HS beyond 10 weeks. Methods: We identified the following major concerns that still lack a proper evidenced based analysis: For rifampicin: drug induced liver injury, interstitial nephritis, drug interaction and hepatic p450 3A4 enzyme induction; for clindamycin the concern was community acquired clostridium difficile infection (CA-CDI); and experience with long-term treatment. Data sources were used as appropriate to answer the question. Systematic searches were used to assess the risk of CA-CDI and experience with long term treatment with Clindamycin. Results: The risk for rifampicin induced liver injury is highest in the first 6 weeks of treatment, whereas interstitial nephritis is primarily observed during intermittent treatment. Enzyme induction due to rifampicin is usually complete after about 2 weeks of treatment, and reduces clindamycin blood levels by about 90%. Three meta-analyses identified antibiotic use as a risk factor for CA-CDI. Two of them assigned the highest risk to clindamycin. None of them stratified by the length of treatment. There is extensive experience with rifampicin, primarily for the treatment of tuberculosis. Long-term experience with clindamycin is limited. Recommendation for clinical care: The analyzed risks associated with a combination of clindamycin and rifampicin for hidradenitis suppurative cluster within the first 10 weeks. Treatment can be continued beyond 10 weeks, if clinically necessary.

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Host-microbiome interactions and recent progress into understanding the biology of acne vulgaris. O'Neill AM, Gallo RL. *Microbiome.* 2018 Oct 2;6(1):177. doi: 10.1186/s40168-018-0558-5. <https://www.ncbi.nlm.nih.gov/pubmed/30285861>

Acne is one of the most common skin diseases worldwide and results in major health care costs and significant morbidity to severely affected individuals. However, the pathophysiology of this disorder is not well understood. Host-microbiome interactions that affect both innate and adaptive immune homeostasis appear to be a central factor in this disease, with recent observations suggesting that the composition and activities of the microbiota in acne is perturbed. *Staphylococcus epidermidis* and *Cutibacterium acnes* (*C. acnes*; formerly *Propionibacterium acnes*) are two major inhabitants of the skin that are thought to contribute to the disease but are also known to promote health by inhibiting the growth and invasion of pathogens. Because *C. acnes* is ubiquitous in sebaceous-rich skin, it is typically labeled as the etiological agent of acne yet it fails to fulfill all of Koch's postulates. The outdated model of acne progression proposes that increased sebum production promotes over-proliferation of *C. acnes* in a plugged hair follicle, thereby

driving inflammation. In contrast, growing evidence indicates that *C. acnes* is equally abundant in both unaffected and acne-affected follicles. Moreover, recent advances in metagenomic sequencing of the acne microbiome have revealed a diverse population structure distinct from healthy individuals, uncovering new lineage-specific virulence determinants. In this article, we review recent developments in the interactions of skin microbes with host immunity, discussing the contribution of dysbiosis to the immunobiology of acne and newly emerging skin microbiome-based therapeutics to treat acne.

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Trends in utilization of topical medications for treatment of rosacea in the United States (2005-2014) - a cohort analysis. Lev-Tov H, Rill JS, Liu G, Kirby JS. *J Am Acad Dermatol.* 2018 Oct 1. pii: S0190-9622(18)32650-1. doi: 10.1016/j.jaad.2018.09.039. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/30287319>

Rosacea is a common inflammatory skin disorder (1.3-2.1% prevalence). In addition to gentle skin care and sun protection, metronidazole or azelaic acid are considered first-line topical therapy for papulopustular rosacea and topical alphaagonists are first-line topical therapy for erythrotelangiectatic rosacea. The aim of this study is to evaluate real-world topical rosacea therapy utilization and costs. We carried a retrospective cohort analysis of the MarketScan® Commercial Claims and Encounters database (“the database”). The validated Database consists of reimbursed claims of approximately 50 million employees per year covered under private insurance plans across the United States. Uniquely the database can track an individual across payers, geographical locations, and contains demographic data, dates, and costs for services, procedures, and pharmacy claims. Costs were adjusted for inflation and are reported in 2015 US dollars. During 1/1/05-12/31/14, 72,173 adults were continuously enrolled with a diagnosis of rosacea, defined as two or more claims for ICD-9 695.3 over 18 months by a dermatologist, primary care provider and/or an ophthalmologist. Most patients (86%, n= 62,074) were treated with topical agents and only 6% (n= 4463) were treated with oral therapy exclusively (a discussion of oral therapy in this cohort is presented elsewhere). Single agent topical therapy was used for 75.8% (n=47,035), while 24.2% (n=15,039) received combination topical therapy. Metronidazole and azelaic acid was the most common combination regimen. Branded topical medications were utilized by more patients than generic versions (n=50,334 versus n=39,621, respectively). The mean (standard deviation [SD]) annual cost of topical therapy per patient was \$308.02 (314.71) and \$160.37 (209.53) for branded and generic medications, respectively (p<0.0001). The potential annual per patient cost saving by switching from branded medication to a generic was \$147.65. Our study is limited by its retrospective nature, lack of Medicare and Medicaid claims and dependency on ICD-9 code of rosacea that has not been validated. However, validity is supported by the high proportion with dermatologist care. In summary, an important proportion of patients (24.2%) received combination topical therapy. These medications are thought to work by similar mechanisms (anti-inflammatory, anti-oxidant and KLK5 modulation) and to our knowledge have not been studied together. Also, combination therapy is not discussed in most guidelines. We defined the cost of a topical medication as the sum of insurance payments, patient copay and deductible per medication, over a year. We found the mean annual cost of topical therapy for branded medications per person was nearly twice the cost of generics, despite the rise in generic drug costs. Thus, there is an opportunity to save healthcare costs, nearly \$7.5 million annually for this cohort. Importantly, we analyzed the data from a healthcare system point-of-view which provides more realistic overall cost analysis and is different from patient point-of-view in which for example coupons and other discounts reduce immediate out-of-pocket expense, but increase societal cost. Our analysis suggests there is an opportunity to increase utilization of generic medications and that combination topical therapy is commonly used. In addition, more research is needed to determine the most efficacious rosacea therapies. Topical therapy is common, 86% in this study, and may have lower adverse effects, yet topical agents can be more expensive than systemic medications.

This is pertinent given that about 24% of patients received combination topical therapy. More cost-effectiveness studies for rosacea therapy could inform providers, patients, and future guidelines.

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Overall and subgroup prevalence of acne vulgaris among patients with hidradenitis suppurativa. Wertenteil S, Strunk A, Garg A. *J Am Acad Dermatol.* 2018 Oct 1. pii: S0190-9622(18)32651-3. doi: 10.1016/j.jaad.2018.09.040. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/?term=Overall+and+Subgroup+Prevalence+of+Acne+Vulgaris+Among+Patients+with+Hidradenitis+Suppurativa>

Background: Evidence establishing the link between acne vulgaris (AV) and hidradenitis suppurativa (HS) is limited, and the burden of AV in this group is unknown. Objective: To determine prevalence of AV among adults with HS, and to determine the strength of this association. Methods: Cross-sectional analysis identifying adults with AV among HS and non-HS patients using electronic health records data from a population-based sample of over 55 million patients. Results: Prevalence of AV among adults with HS was 15.2% (7,315 /48,050), compared to 2.9% (497,360 /16,899,470) for adults without HS ($p < 0.001$). Prevalence was greatest among HS patients who were female (5,870/35,790; 16.4%), ages 18-44 years (5,260/28,870; 18.2%), non-white (3,120/17,825); 17.5%), obese (5,430/35,135; 15.5%), and had PCOS (685/2,385; 28.7%). HS patients had 4.51 [95% CI 4.40-4.63] times the odds of having AV compared to non-HS patients, and the higher likelihood of having AV persisted across all HS subgroups. The association between HS and AV was generally stronger for patients who were male, aged ≥ 65 years, non-whites, and obese. Limitations: Influence of disease severity in HS, or in acne, on the strength of the association could not be assessed. Conclusion: Patients with HS may benefit from assessment of acne status and optimization of co-management strategies.

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Patient Counseling/Communication

Acne stigma linked to lower overall Q of L. DermWire, Practical Dermatology. Wednesday, October 03, 2018. <http://practicaldermatology.com/dermwire/2018/10/03/acne-stigma-linked-to-lower-overall-q-of-l>

Acne patients perceived social stigma negatively affects their quality of life, according to a new study from the University of Limerick. In the survey of 271 people with acne, those whose negative perceptions of how society viewed their appearance had higher psychological distress levels and further physical symptoms such as sleep disturbance, headaches and gastrointestinal problems. Females in the study reported greater impairment of life quality and more symptoms than males. Acne severity was significantly correlated with health-related quality of life and psychological distress, the study showed. University of Limerick researchers Aisling O'Donnell and Jamie Davern conducted the study to investigate whether acne sufferers' perceptions of stigmatization significantly predicts psychological and physical health outcomes; specifically health-related quality of life, psychological distress, and somatic symptoms. "We know from previous research that many acne sufferers experience negative feelings about their condition, but we have never before been able to draw such a direct link between quality of life and perception of social stigma around acne," says Aisling O'Donnell of the Department of Psychology and Centre for Social Issues Research at UL, in a news release. "The findings of this study echo previous research showing that individuals with

visible physical distinctions, which are viewed negatively by society, can experience impaired psychological and physical well-being as a result,” Dr O’Donnell says. According to the article’s lead author, PhD student Jamie Davern, a lack of representation of people with acne in popular culture can increase the perceived stigma around the condition. “Like many physical attributes that are stigmatized, acne is not well represented in popular culture, advertising or social media. This can lead people with acne to feel that they are ‘not normal’ and therefore negatively viewed by others. Online campaigns like #freethepimple and the recent ‘acne-positive’ movement emerging on social media is an encouraging development for people of all ages that are affected by acne,” he explains. “Importantly, the findings provide further support for the comparatively limited amount of studies investigating physical health problems experienced by acne sufferers. This is important information for clinicians dealing with acne conditions. It’s also useful for those who are close to acne sufferers. The wider negative impacts some acne sufferers experience are very challenging and require sensitivity and support,” Mr Davern concludes.

Is teen acne a sign of future financial success? DermWire, Practical Dermatology. Tuesday, October 02, 2018. <http://practicaldermatology.com/dermwire/2018/10/02/is-teen-acne-a-sign-of-future-financial-success>

The love of books, the need for glasses and high intelligence are traits found among the top earners in many fields across the country, and now, a Ball State University researcher suggests that teen acne may also be on this list. In his study, “Do Pimples Pay? Acne, Human Capital, and the Labor Market Abstract,” Erik Nesson, a Ball State economics professor, found that having acne is positively associated with overall grade point average in high school, grades in high-school English, history, math and science, and the completion of a college degree. The study also found evidence that acne is associated with higher personal labor market earnings for women, said Nesson, who conducted the study with Hugo M. Mialon, an economics professor at Emory University. Their work is forthcoming in the Journal of Human Capital. “Acne has been the scourge of teenage boys and girls as long as there have been teenagers,” Nesson says in a news release. “Our study finds evidence for the theory that having acne leads teens to be less social and to focus more on studying or brainwork, which may increase their educational attainment. “Specifically, we find that having acne is associated with feeling less socially accepted and is associated with participating less in sports clubs and more in non-sports clubs, suggesting a possible shift from physical to intellectual pursuits.” Acne is also strongly associated with depression and suicidal ideation among teenagers, but Nesson said some teenagers could be comforted if they knew the association between having acne and educational attainment and getting better jobs. While acne in adolescence is likely to subside, the benefits of higher educational attainment persist. The researchers used data from the National Longitudinal Study of Adolescent to Adult Health to analyze the effects of acne on educational outcomes and labor market earnings. In the sample, nearly 50 percent of high school students reported having pimples occasionally, often, or every day.