AARS HOT TOPICS MEMBER NEWSLETTER

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AARS Special Announcements

Register Now: AARS 14th Annual Member Reception, Friday, March 1, 2019 6P – 8PM, Washington, DC

Join your AARS colleagues and President Julie Harper and President-Elect Mark Jackson for a wonderful evening! We will be at Hotel Monaco, 700 F Street Northwest in Washington DC in the Paris Ballroom. All members and Corporate Benefactors are welcome! Click here to register now!

AARS Grantee Publication

We are happy to announce AARS Grant Awardee Dr. William McCoy has published his work in Journal of Investigative Dermatology!

Skin Ecology During Sebaceous Drought-How Skin Microbes Respond to Isotretinoin. McCoy WH 4th, Otchere E, Rosa BA, et al. *J Invest Dermatol*. 2018 Oct 24. pii: S0022-202X(18)32693-9. doi: 10.1016/j.jid.2018.09.023. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30579608

Twenty-five percent of acne vulgaris patients are prescribed oral antibiotic courses lasting longer than 6 months (Barbieri et al., 2017). These courses can cause significant collateral damage (dysbiosis, antibiotic resistance) (Leyden et al., 2014). Acne antibiotics target Cutibacterium (formerly Propionibacterium) acnes (Scholz and Kilian, 2016). This bacterium is associated with acne and can cause opportunistic infections (Achermann et al., 2014).

New Medical Research

Gender- and age-related differences in facial sebaceous glands in Asian skin, as observed by non-invasive analysis using three-dimensional ultrasound microscopy. Sugawara T, Nakagawa N, Shimizu N, et al. Skin Res Technol. 2019 Jan 4. doi: 10.1111/srt.12657. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30609153

Background: While determining sebaceous gland morphology is useful in the treatment of skin disorders such as acne, a non-invasive assessment method has not been developed. Since age and gender affect sebum level, differences in sebaceous gland morphology according to these factors were investigated. Methods: Facial skin was measured using a high-frequency three-dimensional ultrasound microscope. First, the ultrasound images were compared with skin sections. Next, we assessed sebaceous gland morphology. Images of sebaceous gland in the cheeks of young male, young female and elderly female subjects were obtained using ultrasound microscopy, and en face images were processed to measure the sebaceous gland area. Results: In the ultrasound images, sebaceous glands and also thin collagen fibers, which surrounded the glands, could be detected as low-intensity regions. We called them sebaceous units. In young male subjects, the sebaceous unit areas 900-μm beneath the skin surface were larger than those at 700 μm. In contrast, depth-dependent differences in sebaceous unit area were not observed in young female subjects, indicating that males had cauliflower-shaped sebaceous glands while young females had somewhat more cylindrical and smaller sebaceous glands than the young males. Regarding age, the areas of sebaceous units at 900 μm were diminished and the depth of maximum area was shallower in elderly female subjects compared to young female subjects. Hence, sebaceous glands are considered to shrink with age. Conclusion: Differences in facial sebaceous unit morphology between genders as well as by age groups could be observed using high-frequency ultrasound microscopy.

A microtube array membrane (MTAM) encapsulated live fermenting staphylococcus epidermidis as a skin probiotic patch against Cutibacterium acnes. Yang AJ, Marito S, Yang JJ, et al. Int J Mol Sci. 2018 Dec 20;20(1). pii: E14. doi: 10.3390/ijms20010014. https://www.ncbi.nlm.nih.gov/pubmed/30577530

Antibiotics without selectivity for acne treatment may destroy the beneficial microbes in the human microbiome that helps to fight Cutibacterium acnes (C. acnes), a bacterium associated with inflammatory acne vulgaris. Probiotic treatment by direct application of live Staphylococcus epidermidis (S. epidermidis) onto the open acne lesions may run the risk of bloodstream infections. Here, we fabricated the polysulfone microtube array membranes (PSF MTAM) to encapsulate probiotic S. epidermidis. We demonstrate that the application of the encapsulation of S. epidermidis in PSF MTAM enhanced the glycerol fermentation activities of S. epidermidis. To mimic the granulomatous type of acne inflammatory acne vulgaris, the ears of mice were injected intradermally with C. acnes to induce the secretion of macrophage inflammatory protein-2 (MIP-2), a murine counterpart of human interleukin (IL)-8. The C. acnes-injected mouse ears were covered with a PST MTAM encapsulated with or without S. epidermidis in the presence of glycerol. The application of S. epidermidis-encapsulated PST MTAM plus glycerol onto the C. acnes-injected mouse ears considerably reduced the growth of C. acnes and the production of MIP-2. Furthermore, no S. epidermidis leaked from PSF MTAM into mouse skin. The S. epidermidis-encapsulated PST MTAM functions as a probiotic acne patch.

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Tranexamic acid ameliorates rosacea symptoms through regulating immune response and angiogenesis. Li Y, Xie H, Deng Z, et al. Int Immunopharmacol. 2018 Dec 19;67:326-334. doi: 10.1016/j.intimp.2018.12.031. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30578968

Rosacea is a chronic inflammatory cutaneous disease characterized by immune system anomalies and vascular hyperreactivity. Recently, therapy of rosacea has improved substantially with the approval of Tranexamic acid (TXA), an antifibrinolytic agent. However, we know little about the underlying mechanism. In this study, we evaluated the effects of TXA and its molecular mechanism on rosacea by using LL37-induced mouse model and HaCaT cell model. Rosacea-like symptoms including skin erythema and histopathological alterations, as well as the elevated pro-inflammatory cytokines (IL-6 and TNFα) and MMP9 expression were significantly ameliorated by TXA treatment. In addition, TXA reduced the expression levels of innate immune gene (TLR2, KLK5 and Camp) and neutrophils relative gene in rosacea-like lesion. For adaptive immune, CD4+ T cell infiltration and the gene expression of Th cytokines and chemokines were regulated by TXA in skin lesion. Furthermore, the anti-inflammatory effects of TXA were associated with the inhibition of TLR2, pro-inflammatory cytokines (IL-6 and TNFα) and chemokines (CCL10) expression in LL37-activated HaCaT cells. Finally, TXA repressed the angiogenesis by reducing the number of CD31+ cell and downregulating the expression levels of VEGF in rosacea. In conclusion, our finding defines a treatment mechanism by which TXA ameliorates rosacea symptoms by regulating the immune response and angiogenesis.

Treatment of acne with a combination of propolis, tea tree oil, and aloe vera compared to erythromycin cream: Two double-blind investigations. Mazzarello V, Donadu MG, Ferrari M, et al. Clin Pharmacol. 2018 Dec 13;10:175-181. doi: 10.2147/CPAA.S180474. eCollection 2018. https://www.ncbi.nlm.nih.gov/pubmed/30588129

Introduction: Antibiotics that suppress Propionibacterium acnes are the standard treatment for acne but are becoming less effective, due to the appearance of antibiotic-resistant strains. Many plants are known to have innate antimicrobial action and can be used as alternatives to antibiotics; thus, it is necessary to prove their effectiveness in vivo. This study aimed to evaluate the anti-acne efficacy of a new cream based on three natural extracts, comparing it to

erythromycin cream and placebo. Patients and methods: Sixty patients with mild to moderate acne vulgaris were randomly divided into three groups: treated with cream containing 20% propolis, 3% "tea tree oil", and 10% "Aloe vera" (PTAC) (n=20); or with 3 % erythromycin cream (ERC) (n=20); or with placebo (n=20). At baseline, after 15 and 30 days, investigators evaluated response to treatment by counting acne lesions through noninvasive measurements and macrophotography. Results: All the clinical and instrumental values studied were statistically different from placebo except for sebometry, pHmetry, and erythema index values, measured on healthy skin. Unlike in the placebo group, papular and scar lesions showed high erythema reduction after 15 and 30 days of PTAC and ERC application. Conclusion: The PTAC formulation was better than ERC in reducing erythema scars, acne severity index, and total lesion count.

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New study to assess treatments for antibiotic-resistant skin infections. Practical Dermatology. December 2018. http://practicaldermatology.com/2018/11/recent-developments

Investigators from LA BioMed have scored a $5.3M grant from the National Institutes of Health to study the effectiveness of treatments for antibiotic-resistant skin infections. The study, Short and Long Term Outcomes of Doxycycline Versus Trimethoprim-Sulfamethoxazole for Skin and Soft Tissue Infections Treatment, is slated to enroll 462 patients with skin infections who will be monitored for a year. The investigators will examine how well certain antibiotics treat infections, how infections recur, and how those that do recur can be prevented. The first participants will be enrolled in the clinical trial later this month. Along with studying the effectiveness of skin infection therapies, the grant funding will also allow investigators to give comprehensive and accurate descriptions detailing individual and group outcomes from the clinical trials. Additionally, investigators will use professional and experienced community partners throughout the trial, to ensure patient needs are met while they are enrolled in the trials.

Microneedling by dermapen and glycolic acid peel for the treatment of acne scars: Comparative study. Saadawi AN, Esawy AM, Kandeel AH, El-Sayed W. J Cosmet Dermatol. 2018 Dec 9. doi: 10.1111/jocd.12827. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30548170

Background: Many methods have been performed to achieve a satisfying outcome in acne scars but some of them were high cost and also were associated with low results and some complications. Objectives: To evaluate and compare the efficacy and safety therapy of glycolic acid (GA) peel, microneedling with dermapen and a combination of both procedures in treatment of atrophic acne scars. Patents and methods: This study was conducted on 30 patients suffering from acne scars. They were randomly assigned into three groups, each group included 10 patients; group I was treated with GA peel, group II treated was with microneedling. Group III received a combination of both procedures. All patients received six sessions with 2-week intervals. The clinical assessment was based on the qualitative global scar grading system before and after treatment, quartile grading scale, and degree of patient satisfaction. Results: There was a statistically significant decrease in acne scars grade after treatment among the studied groups (P = 0.04) but it was higher in group III. There was improvement in boxcar, ice pick, and rolling scars in all groups, respectively (P = 0.03, P = 0.04, P = 0.04). Patients' satisfaction was higher in group III (P = 0.04). Conclusion: The combination of dermapen and GA peel is more effective than monotherapy.

Association of caffeine intake and caffeinated coffee consumption with risk of incident rosacea in women. Li S, Chen ML, Drucker AM, et al. JAMA Dermatol. 2018 Dec 1;154(12):1394-1400. doi: 10.1001/jamadermatol.2018.3301.
https://www.ncbi.nlm.nih.gov/pubmed/?term=Association+of+Caffeine+Intake+and+Caffeinated+Coffee+Consumption+With+Risk+of+Incident+Rosacea+in+Women

Importance: Caffeine is known to decrease vasodilation and have immunosuppressant effects, which may potentially decrease the risk of rosacea. However, the heat from coffee may be a trigger for rosacea flares. The relationship between the risk of rosacea and caffeine intake, including coffee consumption, is poorly understood. Objective: To determine the association between the risk of incident rosacea and caffeine intake, including coffee consumption. Design, setting, and participants: This cohort study included 82 737 women in the Nurses' Health Study II (NHS II), a prospective cohort established in 1989, with follow-up conducted biennially between 1991 and 2005. All analysis took place between June 2017 and June 2018. Exposures: Data on coffee, tea, soda, and chocolate consumption were collected every 4 years during follow-up. Main outcomes and measures: Information on history of clinician-diagnosed rosacea and year of diagnosis was collected in 2005. Results: A total of 82 737 women responded to the question regarding a diagnosis of rosacea in 2005 in NHS II and were included in the final analysis (mean [SD] age at study entry, 50.5 [4.6] years). During 1 120 051 person-years of follow-up, we identified 4945 incident cases of rosacea. After adjustment for other risk factors, we found an inverse association between increased caffeine intake and risk of rosacea (hazard ratio for the highest quintile of caffeine intake vs the lowest, 0.76; 95% CI, 0.69-0.84; P < .001 for trend). A significant inverse association with risk of rosacea was also observed for caffeinated coffee consumption (HR, 0.77 for those who consumed ≥4 servings/d vs those who consumed <1/mo; 95% CI, 0.69-0.87; P < .001 for trend), but not for decaffeinated coffee (HR, 0.80; 95% CI, 0.56-1.14; P = .39 for trend). Further analyses found that increased caffeine intake from foods other than coffee (tea, soda, and chocolate) was not significantly associated with decreased risk of rosacea. Conclusions and relevance: Increased caffeine intake from coffee was inversely associated with the risk of incident rosacea. Our findings do not support limiting caffeine intake as a means to prevent rosacea. Further studies are required to explain the mechanisms of action of these associations, to replicate our findings in other populations, and to explore the relationship of caffeine with different rosacea subtypes.

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Association between market competition and prices of generic topical dermatology drugs. Li DG, Joyce C, Mostaghimi A. JAMA Dermatol. 2018 Dec 1;154(12):1441-1446. doi: 10.1001/jamadermatol.2018.3798.
https://www.ncbi.nlm.nih.gov/pubmed/?term=Association+Between+Market+Competition+and+Prices+of+Generic+Topical+Dermatology+Drugs

Importance: During the last decade, increases in drug prices for commonly prescribed dermatologic medications have outpaced the rate of inflation, national health care growth, and reimbursements. Among nondermatologic medications, studies have shown a role for robust generic market competition in reducing drug prices. The association between competition and the costs of topical dermatologic generic drugs has not been evaluated. Objective: To characterize the association between changes in drug price and the number of US Food and Drug Administration (FDA)-approved manufacturers among the most commonly used topical dermatologic generic products. Design, setting, and participants: This retrospective cost analysis of the most commonly prescribed topical dermatologic generic drugs used cumulative annual claims data from the Medicare Part D Prescriber Public User File to identify 597 dermatologist-prescribed drugs with more than 10 claims. The number of manufacturers and the price per unit were identified from the FDA Orange Book and the National Average Drug Acquisition Cost (NADAC) database,

respectively, for 2013 through 2016. Drugs that were nondermatologic, were not topically administered, were missing NADAC data, were lacking a generic formulation, or had fewer than 400 claims were excluded. Main outcomes and measures: Primary outcomes included per-unit drug price and number of FDA-approved manufacturers. Pricing measures were adjusted for inflation and are reported in 2016 dollars. Results: The present analysis included 116 topical dermatologic generic formulations, representing 70.5% of the total Medicare Part D dermatologist-coded claims from 2015. Drug formulations with 1 to 2 manufacturers during the study period sustained a median percentage increase in price of 12.7%, whereas those with more than 6 manufacturers had a median percentage decrease in price of 20.5%. Formulations with 1 to 2 manufacturers had a 20.6%, 19.5%, and 33.2% higher percentage increase in price than those with 3 to 4 manufacturers, 5 to 6 manufacturers, and more than 6 manufacturers, respectively. There was a statistically significant inverse association between the percentage change in drug price and median number of manufacturers (Spearman correlation coefficient, -0.26; P = .005). Conclusions and relevance: The negative association between the change in drug price and the median number of manufacturers of generic topical dermatologic drugs indicates a role for market competition in controlling the costs of generic drug prices within dermatology. These findings support policies that facilitate robust market competition among topical dermatologic generic drugs produced by a limited number of manufacturers.

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BPX-01 minocycline topical gel shows promise for the treatment of moderate-to-severe inflammatory acne vulgaris. Alexis A, Del Rosso JQ, Desai SR, et al. J Clin Aesthet Dermatol. 2018 Nov;11(11):25-35. Epub 2018 Nov 1. https://www.ncbi.nlm.nih.gov/pubmed/30588271

Background and objectives: Acne vulgaris is a highly prevalent and multifactorial skin disorder that can adversely impact health-related quality of life. Factors that contribute to the pathogenesis of acne include pilosebaceous proliferation of proinflammatory Propionibacterium acnes (P. acnes) bacteria, presence of circulating androgens, excess sebum production, abnormal follicular keratinization, and multiple inflammatory cascades. Oral tetracyclines-especially doxycycline and minocycline-are frequently prescribed for the treatment of moderate-to-severe acne, given their anti-inflammatory properties and their effect on P. acnes reduction. Notwithstanding their established efficacy in the management of acne vulgaris, there is a desire to limit systemic exposure to antibiotics given growing concerns regarding bacterial resistance as well as the potential for serious side effects. This report describes outcomes of two randomized, vehicle-controlled trials (Phases IIa and IIb) of BPX-01, a topical minocycline gel, in the treatment of moderate-to-severe acne. Methods: In Study 1 (NCT02709096), at a single center, 33 subjects with highly fluorescing facial skin were randomized 2:1 to BPX-01 1% or vehicle control once-daily treatment for four weeks. Changes in P. acnes quantitative bacteriological cultures were assessed, as well as cutaneous tolerance to the study drug by both subjects and the investigator. In Study 2 (NCT02815332), subjects with moderate-to-severe inflammatory nonnodular acne (n=226) at 15 centers were randomized 1:1:1 to treatment with BPX-01 1%, BPX-01 2%, or vehicle control once-daily for 12 weeks. The primary endpoint was reduction in the number of inflammatory lesions; other endpoints included the number of noninflammatory lesions, Investigator's Global Assessment (IGA) of severity, and subjective ratings (investigator and subject) of acne. In both studies, cutaneous tolerability and safety were assessed, and plasma minocycline levels were tracked with a highly sensitive assay. Results: In Study 1, BPX-01 treatment reduced P. acnes colonization by 90.9 percent, which exceeded the reduction in the vehicle control group (65.53%; p=0.020). In Study 2, treatment with BPX-01 2% reduced the number of inflammatory lesions by 58.5 percent, exceeding the reduction in the vehicle control group (43.8%; p=0.0256). Trends toward an improvement preferential to BPX-01 2% were observed in the other endpoints. Across both studies, BPX-01 treatment was well-tolerated, with no photosensitivity, postinflammatory hyperpigmentation, or skin discoloration reported. A single subject (out of 259 study

participants) was identified to have detectable levels of plasma minocycline at low levels (42ng/mL) after 12 weeks of treatment but had no signs or symptoms associated with systemic administration of minocycline. Conclusion: BPX-01 appears to exhibit an effectiveness profile for reduction of inflammatory (nonnodular) acne lesions similar to that of oral minocycline formulations. However, because BPX-01 is topical and exhibits negligible systemic exposure, the likelihood of adverse events associated with oral minocycline use is much lower. These results demonstrate effectiveness of BPX-01 topical minocycline gel in reducing P. acnes colonization, suggesting that the BPX-01 2% formulation is a promising treatment for moderate-to-severe nonnodular, inflammatory acne vulgaris in both reduction of inflammatory lesions and also overall improvement in facial acne according to IGA.

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Clinical Reviews

Metabolic Syndrome in Dermatology: Treatment and Management for Dermatologists. Engin B, Özkoca D, Kutlubay Z, Serdaroğlu S. Dermatol Ther. 2019 Jan 8:e12812. doi: 10.1111/dth.12812. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30620081

Metabolic Syndrome is a commonly observed pathology and a global health issue. A great spectrum of dermatologic diseases is linked with metabolic syndrome. The diseases with the strongest association are psoriasis, hidradenitis suppurativa, acne vulgaris, acanthosis nigricans, and (Karadağ et al., 2017). Their management is an important and challenging issue for dermatologists.

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Dermatology today and tomorrow: From symptom control to targeted therapy. Blume-Peytavi U, Bagot M, Tennstedt D, et al. J Eur Acad Dermatol Venereol. 2019 Jan;33 Suppl 1:3-36. doi: 10.1111/jdv.15335. https://www.ncbi.nlm.nih.gov/pubmed/30561009

For many decades and until recently, medical approach to dermatologic diseases has been based on the physician's ability to recognize and treat symptoms. Nowadays, advances in the understanding of the biology of diseases and in technologies for intervening against them have allowed physicians to diagnose and treat underlying disease processes rather than simply addressing the symptoms. This means that rather than addressing 'the disease in humans', physicians can now address the particular pathologic (biologic, molecular) disturbance as it presents in the individual patient, i.e., physicians now can practice something much closer to 'personalized medicine', leading to greater benefits for the patients and the health of society in general. The deeper understanding of ultraviolet radiation, the importance of photoprotection and increased knowledge about signalling pathways of melanoma and carcinoma have led to more complete care for the dermatologic patient. The current popularity for excessive exposure to the sun, without adequate application of the appropriate photoprotection remedies, is the origin of melanoma, but also for the weakening of the structure and functions of the skin. Indeed, fragility of the skin can affect humans around the world. In the senior population, this skin fragility is accompanied by pruritus, whereas atopic dermatitis is an inflammatory disease with highest prevalence in children and adolescents. Acne, the number one reason for dermatologic consultations worldwide, increases its prevalence in adolescents and in females. Senescent alopecia affects humans after menopause and andropause. The articles in this publication present an overview of the current advanced understanding of the diagnosis and therapeutic approaches in 6 fields of dermatology - dermatopaediatry and gerontodermatology, oncodermatology, hair loss, atopic dermatitis, photoprotection and acne - and thereby serve

as a useful compendium of updated information and references for all healthcare professionals who see patients with presentations of the symptoms of these diseases.

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A 12-Year Experience of Hidradenitis Suppurativa Management. Vankeviciute RA, Polozovaite B, Trapikas J, et al. Adv Skin Wound Care. 2019 Jan;32(1):1-7. doi: 10.1097/01.ASW.0000549611.06727.52. https://www.ncbi.nlm.nih.gov/pubmed/30570558

Background: Although treatment recommendations for hidradenitis suppurativa (HS) are well known, practical experience implementing them in Lithuania has not been reported yet. Objective: To review clinical findings and treatment options used in patients with HS in the largest center of dermatology and venereology in Lithuania from 2005 to 2016. Methods: A retrospective single-center medical file analysis was conducted on 46 patients with HS. Demographic information, patient history, and treatment results were included in the final analysis. χ Tests were used. Statistical significance was set at P ≤ .05. Main results: Of the 46 patients, 52.2% were male. Percentages of patients with Hurley stages I, II, and III were 41.3%, 30.4%, and 28.3%, respectively. Patients with Hurley III HS were more likely to be smokers and obese. The most commonly prescribed medications were systemic antibiotics (76.1%) and systemic retinoids (37.0%). Systemic corticosteroids (19.6%) were more often prescribed to patients with Hurley III. Surgical procedures were performed in 54.3% of patients. The most common complication of the disease was contracture (13.0%). Conclusions: This study revealed an association between smoking and obesity and the most severe stage of HS. Results showed that traditional medications used in this study were not effective for severe HS.

New concepts, concerns, and creations in acne. Marson JW, Baldwin HE. Dermatol Clin. 2019 Jan;37(1):1-9. doi: 10.1016/j.det.2018.07.002. https://www.ncbi.nlm.nih.gov/pubmed/?term=New+Concepts%2C+Concerns%2C+and+Creations+in+Acne

Laboratory monitoring for patients on isotretinoin should include creatinine kinase in athletic males and the more liver-specific gamma glutamyltransferase. There is mounting evidence that acne pathophysiology includes a barrier defect and subsequent microbiome disruption. Avoidance of acne scars with early and aggressive treatment is a more efficient and cost-effective option than subsequent treatment. Laser and light treatments for acne and acne scars are plentiful but poorly supported by evidence-based medicine. The acne pipeline is rich with new chemical entities, new formulations, and combinations of older agents. The gold standard for acne therapy may be changing its face.

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Comorbidities in dermatology: What's real and what's not. Qureshi A, Friedman A. Dermatol Clin. 2019 Jan;37(1):65-71. doi: 10.1016/j.det.2018.07.007. https://www.ncbi.nlm.nih.gov/pubmed/?term=Comorbidities+in+Dermatology+What%E2%80%99s+Real+and+What%E2%80%99s+Not

Comorbidities affecting dermatologic patients are of significant importance to providers and highly relevant for appropriate patient counseling, screening practices, prevention, and treatment. This article seeks to highlight several of the newest findings in the literature regarding comorbidities associated with dermatologic diseases including atopic dermatitis, hidradenitis suppurativa, alopecia areata, chronic urticaria, and the pemphigus family of immunobullous diseases. Further investigation is needed for associations between atopic dermatitis and pancreatic cancer and

pemphigus family diseases and chronic obstructive pulmonary disease in order to better characterize the strength of these associations and clinical relevance.

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Interventions for rosacea based on the phenotype approach: An updated systematic review including GRADE assessments. van Zuuren EJ, Fedorowicz Z, Tan J, et al. Br J Dermatol. 2018 Dec 26. doi: 10.1111/bjd.17590. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30585305

Background: Rosacea is a common chronic facial dermatosis. Classification of rosacea has evolved from subtyping to phenotyping. Objectives: Updating our systematic review on interventions for rosacea. Methods: We searched: CENTRAL in The Cochrane Library, MEDLINE, EMBASE, LILACS, Science Citation Index, and ongoing trials registers (March 2018) for randomised controlled trials. Study selection, data extraction, risk of bias assessment and analyses were carried out independently by two authors. GRADE was used to assess certainty of evidence. Results: We included 152 studies (46 were new), comprising 20,944 participants. Topical interventions included: brimonidine, oxymetazoline, metronidazole, azelaic acid, ivermectin and other topical treatments. Systemic interventions included: oral antibiotics, combinations with topical treatments or other systemic treatments. Several studies evaluated laser or light-based treatment. We present the most current evidence for rosacea management based on a phenotype-led approach. Conclusions: For reducing temporarily persistent erythema: there was high certainty evidence for topical brimonidine and moderate certainty for topical oxymetazoline; for erythema and mainly telangiectasia: low to moderate certainty evidence for laser and intense pulsed light therapy.

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British Association of Dermatologists guidelines for the management of hidradenitis suppurativa (acne inversa) 2018. Ingram JR, Collier F, Brown D, et al. Br J Dermatol. 2018 Dec 15. doi: 10.1111/bjd.17537. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30552762

The overall objective of the guideline is to provide up-to-date, evidence-based recommendations for the management of hidradenitis suppurativa (HS). The document aims to: offer an appraisal of all relevant literature up to July 2018, focusing on any key developments. address important, practical clinical questions relating to the primary guideline objective. provide guideline recommendations and if appropriate research recommendations.

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Hidradenitis suppurativa: A systematic review integrating inflammatory pathways into a cohesive pathogenic model. Vossen ARJV, van der Zee HH, Prens EP. Front Immunol. 2018 Dec 14;9:2965. doi: 10.3389/fimmu.2018.02965. eCollection 2018. https://www.ncbi.nlm.nih.gov/pubmed/30619323

Background: The pathogenesis of hidradenitis suppurativa (HS) is not fully understood. This systematic review examined the latest evidence for molecular inflammatory pathways involved in HS as a chronic inflammatory skin disease. Methods: A systematic literature search was performed in PubMed/Medline and EMBASE from January 2013 through September 2017, according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA). Findings on HS pathogenesis were also compared with those of other immune-mediated inflammatory diseases (IMIDs) in a non-systematic review. In addition, current therapeutic options for HS are briefly discussed on the basis of the findings for the inflammatory pathways involved in HS. Results: A total of 32 eligible publications were

identified by the systematic search; these were supplemented with three additional publications. The extracted data indicated that four key themes underlie the pathogenesis of HS and related syndromic conditions. First, nicastrin (NCSTN) and PSTPIP1 mutations are directly associated with auto-inflammatory disease. Secondly, the up-regulation of several cytokines including tumor necrosis factor-α and T helper-17/interleukin-23 are connected to auto-inflammatory mechanisms in the pathogenesis of HS. Thirdly, the microbiome of lesional skin differs significantly vs. normal-appearing skin. Fourthly, HS risk is enhanced through physiological and environmental factors such as smoking, obesity, and mechanical friction. There is significant overlap between the pathogenesis of HS, its syndromic forms and other IMIDs, particularly with respect to aberrations in the innate immune response. Conclusions: The evidence presented in this review supports HS as an auto-inflammatory skin disorder associated with alterations in the innate immune system. Based on these most recent data, an integrative viewpoint is presented on the pathogenesis of HS. Current management strategies on HS consist of anti-inflammatory therapies, surgical removal of chronic lesions, and lifestyle changes such as smoking cessation and weight loss. As large gaps remain in the understanding of the pathogenesis of HS, further research is warranted to ultimately improve the management and treatment of patients with HS and related syndromic conditions.

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Propionibacterium (cutibacterium) acnes bacteriophage therapy in acne: Current evidence and future perspectives. Castillo DE, Nanda S, Keri JE. Dermatol Ther (Heidelb). 2018 Dec 11. doi: 10.1007/s13555-018-0275-9. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30539425

Acne vulgaris is the most common dermatological disorder worldwide. It is a multifactorial disease that involves increased sebum production, hyperkeratinization of the pilosebaceous unit, Propionibacterium acnes (Cutibacterium acnes) colonization, and inflammation. The human skin microbiome hosts a wide variety of microorganisms, including bacteria, viruses, and fungi. A delicate balance of these microorganisms is essential for the barrier function of the skin. Propionibacterium acnes represents nearly 90% of the human skin microbiome of healthy adults. Acne is a chronic recurrent disease that requires long-lasting treatment, which has led to the emergence of antibiotic resistance. New alternatives to traditional therapy are emerging, including antimicrobial peptides, natural engineered antibodies, and bacteriophages. Bacteriophages have been shown to play a role in human skin health and disease. There is evidence supporting phage therapy in many types of skin infections. P. acnes bacteriophages have been isolated and characterized. However, only a few in vitro studies have tested the ability of bacteriophages to kill P. acnes. Furthermore, there is no evidence on bacteriophage therapy in the treatment of acne in humans. In this review, we summarize the most recent evidence regarding P. acnes bacteriophages and the potential role of these bacteriophages in the treatment of acne. Further research on this field will provide the evidence to use phage therapy to decrease rates of antibiotic resistance and restore antibiotic susceptibility of P. acnes.

A brief compendium of some long-forgotten remedies for dermatology. Is it time to drop the one-size-fits-all approach and consider remedies of the past? Arnold K, Lio PA. Practical Dermatology. December 2018. http://practicaldermatology.com/2018/11/a-brief-compendium-of-some-long-forgotten-remedies-for-dermatology

The pace of innovation in modern medicine is truly extraordinary, with novel treatment modalities helping revolutionize patient outcomes. However, even with these impressive strides, physicians may need to reach back into history on occasion to find a fitting therapy when the patient's disease has not read the proverbial play book. Those treatments with the best evidence are not mentioned here; indeed, those are what we already know and use. Herein we focus on fringe therapies, most with little or mixed evidence, because sometimes, as Celsus reminds us, "Satius est enim

anceps auxilium experiri quam nullum" (It is better to try a doubtful remedy than to try none). We seek to expand the clinician's armamentarium beyond a one-size-fits-all approach, presenting long-forgotten remedies as diverse as the conditions and patients we treat. We realize that this can be upsetting in an era where evidence is king, and we in no way wish to impugn evidence-based medicine—we're simply here to dust off some older approaches and explore, particularly for those cases where things are getting desperate. While this is clearly not an exhaustive collection, we hope it will serve as a useful reference, inspiring further investigation and application of these therapies and perhaps sparking ideas for new ones.

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Rosacea update: New findings on risks and impact. Understanding rosacea risk factors can allow for earlier, more effective treatment. Zeichner J. Practical Dermatology. December 2018. http://practicaldermatology.com/2018/12/rosacea-update-new-findings-on-risks-and-impact

Despite how common rosacea is, we have a poor understanding of its causes. Rosacea is a common, chronic skin condition characterized by flushing and blushing that may lead to persistent facial erythema as well as inflammatory papules and pustules. Data from the National Rosacea Society (NRS) estimate that approximately 16 million Americans and 415 million people worldwide are affected by rosacea. Despite how common rosacea is, we have a poor understanding of the causes. Symptoms of rosacea tend to appear after age 30 and, if untreated, may worsen over time and can significantly impact quality of life. New findings in risk factors for rosacea: Rosacea has been associated with several systemic comorbidities, including metabolic, cardiovascular, gastrointestinal, and psychiatric disturbances. However, there is limited real-world data available that evaluates potential risk factors for developing rosacea. New data was recently presented at the 2018 European Academy of Dermatology and Venereology (EADV) Congress in Paris. In a multivariate analysis, potential socio-demographic, geographic, and clinical risk factors were evaluated and matched to rosacea-free controls by age, gender, primary payer (commercial or Medicare), index year, and geographic region in a US claims database. The analysis looked at rosacea patients 30 years and older in the 36 months prior to receiving the rosacea diagnosis. In total, 103,269 rosacea patients (mean age 55 years), were directly matched to an equal number of controls. Patients were primarily women (69 percent), had commercial insurance (81 percent), and lived in middle latitudes of the US. Potential risk factors for rosacea found in the study included gastroesophageal reflux disease (GERD), hyperlipidemia, and migraines. Certain medications were also shown to be associated with the development of rosacea. These include gastrointestinal medications, such as proton pump inhibitors and laxatives, anxiolytic/sedative/hypnotics, and benzodiazepines. Interestingly, Helicobacter pylori, cardiovascular disease, and peptic ulcer were associated with a reduced risk of developing rosacea. Despite these findings, further studies are needed to examine both pre- and post-diagnosis periods to explore any causal relationships between potential risk factors and rosacea.

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Acne and scarring: Facing the issue to optimize outcomes. Tan J. J Drugs Dermatol. 2018 Dec 1;17(12):s43. https://www.ncbi.nlm.nih.gov/pubmed/30586480

Acne scarring can affect patients across the spectrum of acne severity. Of multiple potential risk factors, the most important is acne severity followed by time to effective treatment, manipulation of lesions, and a family history of acne scarring. These factors reflect the intensity and duration of inflammation as well as an intrinsic tendency to scar.

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Evaluation, prevention, and management of acne scars: Issues, strategies, and enhanced outcomes. Fabbrocini G, Cacciapuoti S. J Drugs Dermatol. 2018 Dec 1;17(12):s44-48. https://www.ncbi.nlm.nih.gov/pubmed/30586481

Acne is a common disease affecting a high percentage of the younger population. Without appropriate and effective primary prevention of scarring, post-acne scars occur in about 80-95% of all patients. Acne scarring is the result of an alteration of the healing process and it can have deep psychosocial implications for patients. Scars can involve textural change in the superficial and deep dermis and it can also be associated with erythema or pigmentation. While the most effective strategy to reduce acne scarring is to prevent its formation, over the past decades, numerous aesthetic and surgical techniques have been proposed to improve the appearance of acne scarring. However, scar treatment still remains suboptimal; indeed, acne scarring management is a difficult therapeutic challenge for dermatologists. Several treatment options have been described to treat various acne scar types and clinical responses may differ from various factors, such as skin types. Treatment approaches for acne scarring should be individualized and primarily determined by the morphological features of each patient's scars. Dermatologists need to better organize their assessment of acne scarring and develop a multistep treatment plans tailored to address patients' individual needs.

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Micromanagement: Microparticles enhance outcomes of energy-based acne care. With recent FDA-clearance, microparticles are available to support Nd:YAG based treatment of inflammatory acne. Bhatia A, Lain T. Practical Dermatology. December 2018. http://practicaldermatology.com/2018/12/micromanagement-microparticles-enhance-outcomes-of-energy-based-acne-care

Use of energy-based devices to treat acne is a well-established practice, despite variations in reported efficacy between devices or operators. Recently FDA-cleared for use in the treatment of acne, Sebacia Microparticles are intended to enhance the outcomes of energy-based interventions for acne using the 1064nm laser. Sebacia Microparticles selectively target the sebaceous glands where they facilitate photothermal heating of the glands for the improvement of mild to moderate inflammatory acne vulgaris. "Historically there have been three different strategies for using energy-based devices to help clear or reduce acne," observes Ted Lain, MD. Sebacia Microparticles offer a new, fourth approach. Previous energy-based approaches attempted either to kill P. acnes bacteria with blue light or to reduce inflammation and potentially increase blood flow with red light, Dr. Lain explains. "The third approach uses the heat of longer wavelength devices to kill, or at least reduce, the size of the sebaceous glands. At its most basic form, the Sebacia Microparticles act as a heat sump, so they absorb the laser energy and help to heat up, and thereby reduce the size and output of the sebaceous glands." The microparticles consist of a silica-coated gold core. "The microparticles are specifically tuned to be activated by laser light from a 1064nm Nd:YAG laser, which is commonly found in most dermatology practices, where it is used for hair removal and other applications," says Ashish Bhatia, MD. The microparticles are applied during a 10- to 12-minute process using a massaging device. Heating of the microparticles is achieved using an Nd:YAG laser at a low fluence. The result is selective thermal injury in the pilosebaceous unit, where the microparticles are located. "We know the common mechanism of all types of acne really occurs in the pilosebaceous unit, when the follicle gets plugged and inflamed. By causing selective thermal damage of the sebaceous glands and pilosebaceous unit, we can significantly improve acne," Dr. Bhatia observes.

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Retinoids in acne management: Review of current understanding, future considerations, and focus on topical treatments. Chien A. J Drugs Dermatol. 2018 Dec 1;17(12):s51-55. https://www.ncbi.nlm.nih.gov/pubmed/30586483

Acne vulgaris is the most common skin condition affecting adolescents and young adults with a tremendous psychosocial impact. Its pathogenic hallmarks include follicular dyskeratosis, increased sebum production, and inflammation induced by Cutibacterium (formerly Propionibacterium) acnes within the follicle. Retinoids, derived from vitamin A, are the mainstays of acne treatment given they address the key pathogenic pathways of acne. Retinoids exert their effects through the binding of their nuclear receptors leading to downstream biological effects. The understanding of retinoid pharmacology has increased the diversity of retinoids with now both natural and synthetic retinoids available for use. For acne, retinoids can be administered both topically in a variety of formulations and combinations as well as systemically. With judicious use, this class of medication is well tolerated and very efficacious in managing acne. Furthermore, there is evidence showing its role in improving and preventing one of the most challenging post-acne changes, atrophic acne scarring. With a promising topical retinoid, trifarotene, on the horizon, the acne armamentarium will be further broadened to better manage acne and its related sequelae.

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