AARS Hot Topics Member Newsletter
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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.

Institute scientists have revealed a potent inflammatory molecule released by dying cells triggers inflammation during necroptosis, a recently described form of cell death linked to inflammatory disease. The discovery could lead to new and existing medicines that target the molecule being investigated as a way of treating inflammatory diseases, such as psoriasis and inflammatory bowel disease. Dr Lisa Lindqvist, Dr Kate Lawlor, Dr James Vince and PhD student Ms Stephanie Conos led research that showed interleukin-1 beta (IL-1) triggers inflammation during necroptotic cell death. Necroptosis is important for protecting us against infections, by sacrificing infected or diseased cells 'for the greater good'. However, necroptosis can become inappropriately or excessively activated, triggering damaging inflammation that leads to inflammatory disease. Dr Lindqvist said the discovery challenged a long-standing dogma that inflammation triggered by necroptosis was a byproduct of dead cell debris. "Our research has pinpointed that, during necroptosis, dying cells release IL-1, a potent inflammatory signal," Dr Lindqvist said. "Now that we have discovered IL-1 is the 'root' of the inflammation associated with necroptosis, we speculate that targeting this molecule could be an effective way of treating inflammatory diseases." Future treatments: The findings suggest that targeting IL-1 could suppress inflammation associated with multiple inflammatory diseases, including multiple sclerosis, ischemia-reperfusion injury, atherosclerosis, liver disease, pancreatitis, psoriasis, inflammatory bowel disease, and infectious diseases. "Our research suggests that existing drugs that block IL-1 might be useful in treating these diseases," Dr Lindqvist said. "We are also exploring how IL-1 is signalled to be secreted during necroptosis, so that we can create new drugs to stop its release and reduce inflammation to treat inflammatory diseases." Source: Walter Reed Army Institute of Research


Hologic and Cynosure announced today that they have signed a definitive agreement in which Hologic will acquire the medical aesthetics company, according to a press release. Hologic, with core business units focusing on diagnostics, breast health, GHN surgical and skeletal health, has agreed to acquire all shares of Cynosure for $66 per share in cash, corresponding to an equity value of approximately $1.65 billion and an enterprise value of $1.44 billion net of cash, according to the release. The transaction has been approved by the boards of directors of both companies. “Acquiring Cynosure will accelerate our transformation into a higher-growth company by leveraging our core women’s health expertise and OB/GYN channel leadership into an adjacent, cash-pay segment that is expanding at a low double-digit rate,” Steve MacMillan, Hologic’s chairman and CEO, stated in the release. “We identified medical aesthetics as an attractive and complementary growth opportunity through our strategic planning process, and are pleased to have agreed to acquire Cynosure.” Cynosure has reported revenues of $433.5 million in 2016, and has a product portfolio in categories including non-invasive body contouring, hair removal, skin revitalization and women’s health. Cynosure’s has introduced SculpSure, the world’s first FDA-laser treatment of non-invasive body contouring, and markets MonaLisaTouch, a novel CO2 laser for women’s health. “Strategically, this deal enables Cynosure to further capitalize on growth
opportunities in the core and non-core aesthetic market, rapidly strengthens our position in women’s health – where Helogic has a leading commercial presence and accelerates our R&D initiatives," Michael Davin, Cynosure's president and CEO, stated in the release. Reference: www.hologic.com

**New Medical Research**

**Excessive serous retinal detachment during the use of isotretinoin.** Citirik M, Tekin K. Int Ophthalmol. 2017 Feb 25. doi: 10.1007/s10792-017-0482-x. [Epub ahead of print]  
**PURPOSE:** To report a case unilateral excessive subretinal fluid during the use of isotretinoin. **METHOD:** A case report. A patient who used isotretinoin orally for nodular-cystic acne vulgaris developed concurrent unilaterally excessive subretinal fluid and serous retinal detachment. **RESULTS:** Fluorescein angiography did not demonstrate the leakage points throughout the subretinal fluid. Spectral-domain optical coherence tomography showed the excessive subretinal fluid and serous retinal detachment at macula. Two weeks after presentation, visual acuity was partially increased and subretinal fluid was disappeared at macula. **CONCLUSION:** Isotretinoin may affect the functioning of the RPE and can cause the development of subretinal fluid and serous retinal detachment.

**BACKGROUND:** Hidradenitis suppurativa (HS) has recently been described as a component of two autoinflammatory syndromes: PASH (pyoderma gangrenosum, acne, and HS) and PAPASH (pyoderma gangrenosum, acne, pyogenic arthritis, and HS). These associations together with others such as inflammatory bowel diseases suggest that defects in autoinflammatory pathways may play a role in the pathogenesis of HS. **OBJECTIVES:** To describe clinical and genetic characteristics of two unrelated patients with HS and familial Mediterranean fever (FMF). **METHODS:** Case study. **RESULTS:** Besides FMF and HS, the first patient had acne conglobata, and the second patient had pyoderma gangrenosum and ankylosing spondylarthropathy. Both patients had M694V/V726A MEFV gene mutations. **CONCLUSION:** PASH and PAPASH have recently been associated with genetic alterations of gene encoding proline-serine-threonine phosphatase-interacting protein 1 (PSTPIP1), which interacts with the product of MEFV gene in the autoinflammatory pathway. This intriguing molecular interaction may explain shared phenotypic characteristics seen in genetic defects. Association of one more autoinflammatory disorders with HS adds another brick to the wall.

The microbial community exhibits remarkable diversity on topographically distinct skin regions, which may be accompanied by differences in skin immune characteristics. Our aim was to compare the immune milieu of healthy sebaceous gland rich (SGR) and sebaceous gland poor (SGP) skin areas, and to analyze its changes in an inflammatory disease of SGR skin. For this purpose, immunohistochemical, immunocytochemical and quantitative real-time PCR analyses of thymic stromal lymphopoietin (TSLP)
and other cytokines, phenotypic immune cell markers and transcription factors were carried out in samples from SGP, SGR skin and from papulopustular rosacea (PPR). TSLP mRNA and protein production was also studied in cultured keratinocytes. In SGR skin, higher TSLP expression, dendritic cell (DC) appearance without prominent activation and T cell presence with interleukin (IL)-17/IL-10 cytokine milieu were detected compared to SGP skin. Linoleic acid, a major sebum component, was found to induce TSLP expression dose-dependently in keratinocytes. In PPR, significantly decreased TSLP level and influx of inflammatory DCs and T cells with IL-17/interferon-γ cytokine milieu were observed. According to our results, SGR skin is characterized by a distinct, non-inflammatory immune surveillance, which may explain the preferred localization of inflammatory skin diseases, and can influence future barrier repair therapeutic concepts.


Propionibacterium acnes (P. acnes), the sebaceous gland and follicular keratinocytes are considered the three actors involved in the development of acne. This exploratory study investigated the characteristics of the skin microbiota in subjects with acne and determined microbiota changes after 28 days of application of erythromycin 4% or a dermocosmetic. Skin Microbiota were collected under axenic conditions from comedones, papulo-pustular lesions and nonlesional skin areas from subjects with mild to moderate acne according to the GEA Grading using swabs. Samples were characterised using a high-throughput sequencing approach that targets a portion of the bacterial 16S rRNA gene. RESULTS: Overall, microbiota samples from 26 subjects showed an overabundance of Proteobacteria and Firmicutes and an underrepresentation of Actinobacteria. Staphylococci were more abundant on the surface of comedones, papules and pustules (p=0.004 and p=0.003 respectively) than on nonlesional skin. Their proportions increased significantly with acne severity (p<0.05 between GEA-2 and GEA-3). Propionibacteria represented less than 2% of the bacteria on the skin surface. At Day 28, only the number of Actinobacteria had decreased with erythromycin while the dermocosmetic decreased also the number of Staphylococci. A significant reduction (p<0.05) from Day 0 of comedones, papules and pustules with no significant difference between the products was observed. CONCLUSION: The bacterial diversity on all sampling areas was similar. The dermocosmetic decreased the number of Actinobacteria and Staphylococcus spp. after 28 days. Staphylococcus remained the predominant genus of the superficial skin microbiota. No significant reduction of Staphylococcus spp. was observed with the topical antibiotic.


Propionibacterium acnes is an anaerobic bacterium that causes deep infection in organs and prosthetic joints, in addition to acne vulgaris. Many tetracycline-resistant P. acnes strains have been isolated because oral tetracyclines are frequently used as an acne treatment against P. acnes. In this study, we found a novel tetracycline resistance mechanism in P. acnes. Three doxycycline-resistant (MIC: 16 µg ml-1) strains were isolated from 69 strains in acne patients in Japan between 2010 and 2011. Additionally, six insusceptible strains (MIC: 1-2 µg ml-1) that had reduced susceptibility compared to susceptible...
strains (MIC: ≤0.5 µg ml\(^{-1}\)) were identified. All doxycycline-resistant strains had a G1036C mutation in the 16S rRNA gene in addition to an amino acid substitution in the ribosomal S10 protein encoded by rpsJ. By contrast, insusceptible strains had an amino acid substitution in the S10 protein but no mutation in the 16S rRNA. When the mutant with decreased susceptibility to doxycycline was obtained in vitro, only the mutated S10 protein was found (MIC: 4 µg ml\(^{-1}\)), not the mutated 16S rRNA gene. This result shows that the S10 protein amino acid substitution contributes to reduced doxycycline susceptibility in P. acnes and suggests that tetracycline resistance is acquired through a 16S rRNA mutation after the S10 protein amino acid substitution causes reduced susceptibility.


BACKGROUND: Rosacea is a chronic, multifactorial, dermatological condition. Increased density of Demodex folliculorum mites in the skin of rosacea patients suggests a possible role for these mites in the pathophysiology of rosacea. OBJECTIVE: To evaluate the effects of permethrin 5% topical gel vs. placebo on Demodex density (Dd) and clinical presentations of rosacea patients, and also to further refine the quantitative assessment of Dd in the non-invasive standard skin surface biopsy (SSSB). METHODS: Twenty patients with bilateral papulopustular rosacea and ≥5 mites/cm\(^2\) were enrolled in the study. Participants and physicians were blinded to the group assignments. Each patient applied permethrin on one side and placebo on the other side of the face twice daily for 12 weeks. SSSB and photography and Rosacea Clinical Scorecard of the National Rosacea Society were used to assess the patients at the baseline, 2nd, 5th, 8th, and 12th weeks for both sides of the face. Causality and severity of adverse drug reactions (ADRs) were assessed by WHO Scale and Hartwig Scale, respectively. RESULTS: Dd was not significantly different between the two groups at the baseline. In both groups, Dd significantly decreased after 12 weeks compared to the baseline. At the end of the 12th week, the Dd in the permethrin group was significantly lower than the placebo group. Severity of the clinical presentations decreased in both groups at the end of week 12 in comparison to the baseline, particularly in the permethrin group. ADRs were all mild and in most cases unlikely related to permethrin. CONCLUSION: Permethrin 5% gel can significantly reduce the Dd and severity of presentations in rosacea patients and can be a safe and effective option in the management of this chronic disorder. This new SSSB technique offers an easy, quick, inexpensive, and non-invasive sampling method proper for quantitative assessment of Dd.


CONTEXT: Rosacea fulminans is a rare skin disorder with a multifactorial etiology. Stress is one of the common precipitating factors of this condition but is not often targeted in treatment. Isotretinoin is considered part of the first-line therapy for this condition but, in cases where its use is restricted, other therapeutic interventions as part of an integrative approach may be effective. PATIENT CONCERNS: A 38-y-old female presented with rosacea fulminans brought on by an acutely stressful event. After multiple failed therapies, she experienced resolution of her symptoms with a combination of systemic corticosteroids, antibiotics, diet modification, and stress reduction, with the treatment of stress playing
a significant role. CONCLUSIONS: Stress management and diet modification are key adjunctive therapies in the treatment of rosacea fulminans and need to be addressed more often in treatment. In cases where patients are reluctant or unable to take isotretinoin, an integrative approach may be effective in achieving symptomatic improvement.

Acne can lead to severe physical and psychological implications on chronic sufferers if not treated promptly and properly. Ramli et al. proposed a k-means cluster based algorithm to provide computer-assisted support for the manual grading of digital images. We propose an improved, automated, and more objective, grading method which involves optimizing the k-means clustering algorithm by identifying the actual number of clusters rather than basing analysis on a fixed $K=3$ assumption for all images. The Hough transform was used to further analyze the found acne cluster leading to an approach to more accurately automatically determine the number and type of lesions. A quantitative comparison of the two approaches showed that the new approach provided a better match to the stated specialist analysis. We found it inappropriate to use accuracy and specificity performance analysis metrics to compare the algorithms. A better matching of the algorithms' accuracy to the specialist's analysis of the skin condition was found by modifying the sensitivity metric to account for the Michelson acne grading scale. This robustness suggests that the tool might be a first-step towards patient self-monitoring between visits to a specialist; potentially reducing visits frequency, decreasing wait times, and lead to a definitive standardized assessment scale.

Idiopathic facial aseptic granuloma (IFAG) is a rare, benign pediatric dermatological lesion that occurs in children between 8 months and 13 years of age. The pathogenesis of IFAG is still unclear but it is likely to be associated with granulomatous rosacea in childhood. Here we describe a case of IFAG in a 13-year-old boy who showed a dramatic response to oral doxycycline and topical metronidazole, which supports the hypothesis that IFAG may belong to the spectrum of rosacea.

Clinical Reviews

Safe and effective treatment options for acne vulgaris are needed to address side effects and increasing rates of antibiotic resistance from current treatments. Nicotinamide is a vitamin with potent anti-inflammatory properties that could offer a potential treatment option. We aim to summarize the
relevant literature on the role of nicotinamide in acne vulgaris and discuss the next steps necessary to move this approach into clinical practice. We searched PubMed for clinical studies using nicotinamide for treatment of acne vulgaris. We summarized the 10 studies that met our search criteria. Six of eight studies using topical nicotinamide led to a significant reduction in acne compared with the patient's baseline or performed similarly to another standard-of-care acne treatment. Both studies using an oral supplement containing nicotinamide resulted in a significant reduction in acne compared with baseline. No major adverse side effects were noted. Our review suggests that topical and oral nicotinamide has an unclear effect on acne vulgaris due to the limited nature of the available literature. Additional studies are needed comparing nicotinamide to other first-line acne treatments and evaluating the efficacy and side effect profile of nicotinamide over an extended period of time.

BACKGROUND: In 2010, the British Association of Dermatologists (BAD) published clinical guidelines for the safe introduction and continued use of isotretinoin in patients with acne in the UK. The BAD provides UK dermatologists with a facility for national audit, and it undertook an audit on compliance with these guidelines in 2012. AIM: To determine current clinical practices relating to use of isotretinoin among dermatologists in the UK (including geographical variations) as measured against BAD standards, and to ascertain any improvement since the 2012 audit. METHODS: The 2012 isotretinoin audit proforma was used, with additional questions on clinical setting, complaints and litigation. A web-based survey tool was used for data entry and submission, with email invitation to working, UK-based BAD members (n = 1226) in December 2013 and weekly reminders during the 8.5-week data collection period. Responders were requested to enter data for the three most recent consecutive patients (including one male and one female patient) who had completed treatment within the previous 6 months. RESULTS: In total, 338 (27.6%) respondents provided data on 1013 patients. Serum lipids were checked in 93.4% of patients and documentation of mental health and/or mood state was recorded in 82.1%. Regarding the Pregnancy Prevention Programme (PPP), 91.6% of female patients of childbearing potential had signed the PPP information form, while 93.3% who had followed the PPP had taken pregnancy tests both before and during treatment, and 54.7% had taken a pregnancy test 5 weeks post-treatment. CONCLUSION: Overall, there is currently good compliance with standards. Certain aspects of care that are less frequently preformed, such as pregnancy testing post-treatment, are highlighted.

Friends or Foes? Host defense (antimicrobial) peptides and proteins in human skin diseases.
Host defense peptides/proteins (HDPs), also known as antimicrobial peptides/proteins (AMPs), are key molecules in the cutaneous innate immune system. AMPs/HDPs historically exhibit broad-spectrum killing activity against bacteria, enveloped viruses, fungi and several parasites. Recently, AMPs/HDPs were shown to have important biological functions, including inducing cell proliferation, migration and differentiation; regulating inflammatory responses; controlling the production of various
cytokines/chemokines; promoting wound healing; and improving skin barrier function. Despite the fact that AMPs/HDPs protect our body, several studies have hypothesized that these molecules actively contribute to the pathogenesis of various skin diseases. For example, AMPs/HDPs play crucial roles in the pathological processes of psoriasis, atopic dermatitis, rosacea, acne vulgaris, systemic lupus erythematosus and systemic sclerosis. Thus, AMPs/HDPs may be a double-edged sword, promoting cutaneous immunity while simultaneously initiating the pathogenesis of some skin disorders. This review will describe the most common skin-derived AMPs/HDPs (defensins, cathelicidins, S100 proteins, ribonucleases and dermcidin) and discuss the biology and both the positive and negative aspects of these AMPs/HDPs in skin inflammatory/infectious diseases. Understanding the regulation, functions and mechanisms of AMPs/HDPs may offer new therapeutic opportunities in the treatment of various skin disorders.


Propionibacterium acnes is associated with purulent skin infections, and it poses a global problem for both patients and doctors. Acne vulgaris (acne) remains a problem due to its chronic character and difficulty of treatment, as well as its large impact on patients’ quality of life. Due to the chronic course of the disease, treatment is long lasting, and often ineffective. Currently there are data regarding isolation of P. acnes phages, and there have been numerous studies on phage killing of P. acnes, but no data are available on phage application specifically in acne treatment. In this review, we have summarized the current knowledge on the phages active against P. acnes described so far and their potential application in the treatment of acne associated with P. acnes. The treatment of acne with phages may be important in order to reduce the overuse of antibiotics, which are currently the main acne treatment. However, more detailed studies are first needed to understand phage functioning in the skin microbiome and the possibility to use phages to combat P. acnes.


Acne, the most common skin disease, is a disorder of pilosebaceous units that affects adolescents mainly and adults occasionally. The pathogenesis is multifactorial. Besides genetic predisposition, other major factors include the action of androgens, pro-inflammatory lipids acting as ligands of peroxisome proliferator-activated receptors in the sebocytes, toll-like receptor-2 acting on keratinocytes, recognition of pathogen-associated molecular patterns, cytokines, chemokines, inflammasomes, neuroendocrine regulatory mechanisms, diet and other pro-inflammatory targets implicated in the activation of immune detection and response. Most of these factors converge on mammalian target of rapamycin complex1 (mTORC1) activation which is further enhanced by the nutrient signaling of Western diet. This multitude of pathogenic factors has led to a new armamentarium of drugs for the treatment of acne. Topical anti-androgens, insulin-like growth factor-1 inhibitors, peroxisome proliferator-activated receptor-modulators, acetylcholine inhibitors, topical retinoic acid metabolism-
blocking agents, vitamin D analogues, antimicrobial peptides, interleukin-1α and interleukin-1β blockers and immunotherapy are some of the novel treatment options.


Photodynamic therapy (PDT) is a noninvasive treatment that utilizes light treatment along with application of a photosensitizing agent. In dermatology, PDT is commonly used and approved for the treatment of oncological conditions such as actinic keratosis, Bowen disease and superficial basal cell carcinoma. In the last 2 decades however, PDT has also been used for the treatment of several nonneoplastic dermatological diseases. The present review summarizes published data on PDT application in skin appendage disorders. Our literature review shows that: (a) PDT may be a suitable treatment for acne, folliculitis decalvans, hidradenitis suppurativa, nail diseases, and sebaceous hyperplasia; (b) there is a lack of agreement on PDT features (type, concentrations and incubation period of used substances, number and frequency of PDT sessions, optimal parameters of light sources, and patient characteristics [e.g., failure to previous treatments, disease severity, body surface area involved, etc.] which should guide PDT use in these diseases); (c) further research is needed to establish international guidelines helping dermatologists to choose PDT for the right patient at the right time.


Acne vulgaris (acne) is a common affliction in adolescence and is a growing problem in adult women. Despite an increasing awareness of acne in the adult female population, there is a lack of good prospective studies assessing the severity, distribution, and differential response to treatment in this group. The long-held dogma that acne in adult women develops on the lower one-third of the face has been recently challenged, and here the authors critically review data from available literature. Moreover, while adult female acne has traditionally been defined as disease in women over age 25, it is the authors' experience that this group is subdivided into women ages 25 to 44 years, separate from perimenopausal patients, ages 45 years and up. While there is no data specifically comparing these two groups, the authors will review the existing data and provide practical recommendations based on our experience in treating these groups of patients. Finally, while there is a lack of data on this subject, it is the group's opinion that adherence to medication regimens is likely higher in women than men, which influences therapeutic outcomes.


Rosacea is a chronic cutaneous inflammatory disease that affects the facial skin. Clinically, rosacea can be categorized into papulopustular, erythematotelangiectatic, ocular, and phymatous rosacea. However, the phenotypic presentations of rosacea are more heterogeneous. Although the pathophysiology of rosacea remains to be elucidated, immunologic alterations and neurovascular dysregulation are thought
to have important roles in initiating and strengthening the clinical manifestations of rosacea. In this article, we present the possible molecular mechanisms of rosacea based on recent laboratory and clinical studies. We describe the genetic predisposition for rosacea along with its associated diseases, triggering factors, and suggested management options in detail based on the underlying molecular biology. Understanding the molecular pathomechanisms of rosacea will likely aid toward better comprehending its complex pathogenesis.

**Patient Communication / Counseling**


BACKGROUND: Acne vulgaris is common and can significantly impair quality of life, yet little is known about patients' understanding of acne and its treatments. Oral antibiotics are widely used for acne, despite concerns about antibiotic resistance. People are increasingly turning to online discussion forums for advice and information on these sites may influence health beliefs and treatment adherence.

OBJECTIVE: To explore understandings about the use of oral antibiotics for acne and advice shared amongst messages posted on online forums.

METHODS: We systematically searched for online forums and identified four where acne was frequently discussed. Discussion threads relating to oral antibiotics were analysed thematically. NVivo 11 facilitated data handling.

RESULTS: We extracted 136 pages of data; 65 discussions amongst 294 participants. We found a wide range of perceptions around effectiveness of antibiotics for acne and concerns about adverse effects. The delayed onset of action of antibiotics was a source of frustration and compounded dissatisfaction with healthcare providers, who people perceived as 'fobbing them off' with prolonged courses of ineffective treatment. Advice ranged from costly cleansers to when to ask for, or insist on, referral. Posts related to a wide range of severities, from 'spots' to severe acne, which may make it confusing for users to assess appropriateness of information.

CONCLUSIONS: Online forums offer opinions that could be confusing or lead to early abandonment of treatments, challenging consultations and patient dissatisfaction. Users expressed frustration about the delayed onset of action of antibiotics for acne, perceptions of only temporary effectiveness and adverse effects.


Growing incentives to control health care costs may cause accountable care organizations (ACOs) to reconsider how skin disease is best managed. Limited data have suggested that disease management by a primary care physician (PCP) may be less costly than seeing a specialist, though it is not clear if the same is true for the management of skin disease. This study assessed the cost of seeing a dermatologist...
versus a PCP for diagnosis of psoriasis and rosacea. Practice Points: - Growing health care costs are causing accountable care organizations (ACOs) to reconsider how to best manage skin disease. - There is little difference in average diagnosis-related cost between primary care physicians and dermatologists in diagnosing psoriasis or rosacea. - With diagnosis costs essentially equal and increased dermatologist diagnostic accuracy, ACOs may encourage skin disease to be managed by dermatologists.