Psoriasis Research Review™

Making Education Easy

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In this issue:

Abbreviations used in this issue:

BMI = body mass index; **CI** = confidence interval; **DLQI** = Dermatology Life Quality Index; **HR** = hazard ratio; **HRQoL** = health-related quality of life; **IL** = interleukin; **NB-UVB** = narrow-band ultraviolet B phototherapy; **PASI** = Psoriasis Area Severity Index; **PGA** = Physician Global Assessment; **QoL** = quality of life; **RR** = risk ratio.

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Welcome to issue 82 of Psoriasis Research Review.

A large retrospective analysis of data from over 38,000 patients in North America has revealed allergic contact dermatitis in one-third of patients referred for patch testing with a final diagnosis of psoriasis. In a case-control study from Egypt, we discover that IL-36γ and cathepsin G expression is upregulated in psoriatic lesions, supporting their role as mediators of inflammation in psoriasis, with both proteins decreasing significantly, along with clinical improvement, following NB-UVB therapy. Other topics covered in this issue include pregnancy outcomes after ixekizumab exposure, musculoskeletal pain in patients with psoriasis, apremilast for palmoplantar pustulosis, and the coprevalence of hidradenitis suppurativa and psoriasis.

We hope you find the latest issue of Psoriasis Research Review stimulating reading and we look forward to any feedback.

Kind Regards,

Clinical Associate Professor Kurt Gebauer
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Prevalence and trend of allergen sensitization in patients referred for patch testing with a final diagnosis of psoriasis: North American Contact Dermatitis Group data, 2001-2016

Authors: Silverberg JA et al.

Summary: This retrospective analysis of data from 38,723 patients in the North American Contact Dermatitis Group examined relationships between psoriasis and allergic contact dermatitis, clinical characteristics, and common positive and clinically relevant allergens among patients finally diagnosed with psoriasis who were referred for patch testing. Patients finally diagnosed with psoriasis had lower proportions of allergic contact dermatitis than those without psoriasis (32.7% vs 57.8%). Multivariate analysis suggested that psoriasis was inversely associated with female sex, Black or Asian race, and a history of atopic dermatitis and hay fever. Psoriasis patients were less likely to have ≥1 positive allergic patch-test reaction or to have a clinically relevant patch-test reaction to common positive and/or relevant allergens including nickel sulphate, methylisothiazolinone, and Fragrance mix I.

Comment: There has been clinical concern with the emergence of the newer systemic atopic dermatitis drugs that some prescribing practitioners may fail to consider the possibility of allergic contact dermatitis either as a primary diagnosis or a confounding additive diagnosis. This is an interesting paper out of the United States summarising the North American Contact Dermatitis Group data from 2001 to 2016. I put this article in to highlight that the possible presence of allergic contact dermatitis is always there in our patients. Certainly, with hyperkeratotic hand dermatitis it behoves all of us to consider allergic contact dermatitis and test.

Reference: Contact Dermatitis. 2021;85(4):435-445
Abstract

Downregulation of interleukin 36γ and its cleaver cathepsin G following treatment with narrow-band ultraviolet B phototherapy in psoriasis vulgaris

Authors: El-Kalioby M et al.

Summary: This case-control study examined expression of IL-36γ and cathepsin G in 26 patients with moderate-severe psoriasis and 25 healthy volunteers and quantified the impact of treatment with NB-UVB. Expression of IL-36γ and cathepsin G was higher before NB-UVB therapy in psoriasis patients than in controls ($p < 0.001$). Both proteins decreased with clinical improvement after NB-UVB therapy ($p < 0.001$), but expression levels remained higher than in controls ($p < 0.001$).

Comment: In my clinic, phototherapy is still used a lot for chronic plaque psoriasis. Many of our patients prefer not to take systemic medication and despite the inconvenience on their lifestyle, have elected to utilise phototherapy. I have always told patients that phototherapy is a predominantly cutaneous immunosuppressant and does have some mild systemic immunosuppressant effects. I haven't really thought further about how, on a biochemical level, phototherapy works. This paper has been submitted for those who think a little bit deeper as to what inflammatory mediators are altered/improved by phototherapy. One for the more academic.

Reference: J Dermatolog Treat. 2021;Aug 23 [Epub ahead of print]
Abstract

Pregnancy outcomes in patients with psoriasis, psoriatic arthritis, or axial spondyloarthritis receiving ixekizumab

Authors: Egeberg A et al.

Summary: This analysis of data from the Eli Lilly Global Safety Database was conducted to examine pregnancy outcomes after maternal or paternal ixekizumab exposure in 193 pregnancies in patients with psoriasis, psoriatic arthritis, or axial spondyloarthritis. 51.3% of pregnancies had maternal exposure (58 in clinical trials; 41 in post-marketing reports) while most paternal exposure events occurred in clinical trials (91 of 94). Live births were reported for 53.8% of clinical trial pregnancies and 61.1% of post-marketing surveillance reports. No congenital malformations were reported in clinical trials. One case not causally related to ixekizumab therapy was recorded in post-marketing reports.

Comment: Biologics have been used by dermatologists and rheumatologists for many decades now. The original anxieties regarding pregnancy and biologics arose from the absence of any clinical studies. This is a Danish paper. I welcome a thorough detailed review of all biologics both in assessing the safety of conception as well as the logic of altering therapy as delivery approaches. Most of our guidelines and consensus statements are based on opinion not scientific data. This paper also has its author, Professor A Kimball, a very well-known American psoriasis expert, as co-author. It provides reassuring data that patients conceiving on ixekizumab had no increased congenital malformations.

Reference: J Dermatolog Treat. 2021.Sep 21 [Epub ahead of print]
Abstract

Long-term proactive treatment of plaque psoriasis with calcipotriene/betamethasone dipropionate foam prolongs remission and reduces relapses irrespective of patient baseline characteristics

Authors: Lebwohl MG et al.

Summary: This analysis of the open label, randomised, phase III PSO LONG study of proactive management (PM) versus reactive management (RM) of plaque psoriasis using calcipotriene/betamethasone dipropionate foam examined the effect on time to first relapse (TTFR), number of relapses, and treatment interactions of baseline parameters including body surface area, modified PASI (mPASI), PGA, BMI, age, sex, DLQI, and duration of psoriasis. Overall, TTFR did not vary with treatment across any baseline parameters. TTFR varied with treatment group (PM vs RM HR 0.56; $p < 0.001$), PGA (moderate vs mild HR 1.42; severe vs mild HR 2.32; $p = 0.009$), mPASI (moderate vs mild HR 1.19; severe vs mild HR: 1.77; $p = 0.009$), and sex (women vs men HR 1.26; $p = 0.030$). Variables that affected the number of relapses included treatment group (RR 0.52; $p < 0.001$), PGA at baseline (moderate vs mild RR 1.38; severe vs mild RR 2.22; $p < 0.001$) and mPASI (moderate vs mild RR 1.25; severe vs mild, HR 1.70; $p = 0.002$).

Comment: In considering the long-term proactive topical treatment of plaque psoriasis, I did put a similar paper in a month or so ago regarding how we can/should be using calcipotriene/betamethasone dipropionate foam. My habit has always been to treat patients until they are happy and then get them to stop. Invariably the psoriasis will inevitably recur. In my hands this is usually within 2-4 weeks. The authors of this paper are getting their patients to use therapy twice-weekly ongoing. I believe that I will be changing my management practice with this drug.

Reference: Dermatol Ther (Heidelb). 2021;11(5):1657-1665
Abstract

Musculoskeletal pain in patients with psoriasis and its influence on health-related quality of life: Results from a Danish population-based survey

Authors: Felbo S et al.

Summary: This Danish study used a nationwide e-based survey of 561 psoriasis patients to assess musculoskeletal pain and patient-reported outcomes, including HRQoL. 81% of respondents had psoriasis without arthritis (29% pain now, 23% pain previously, 39% no pain ever), and 19% had psoriatic arthritis. Patients with psoriasis with musculoskeletal pain 'now' had poorer QoL than patients without pain and similar QoL to psoriatic arthritis patients. Patients with pain now or previously had higher self-assessed severity of psoriasis and lower satisfaction with treatment. Two-thirds of psoriasis patients with pain now or previously and one-third of psoriatic arthritis patients had never seen a rheumatologist, highlighting the unmet need for appropriate evaluation of this group of patients.

Comment: We have got a Scandinavian study. I like Scandinavian studies as their entire populations are in medical databases. This means that a number of challenging clinical scenarios can be scientifically assessed and investigated. In my clinic, I struggle with my middle aged, obese patients with cutaneous psoriasis. I worry about axial psoriatic disease. Inflamed fingers and joints are now relatively easy to diagnose as psoriatic arthritis. I have concerns about other deeper systemic factors. The authors of this paper make the point that in their socialistic system, two-thirds of the patients with musculoskeletal pain have never seen a rheumatologist. I personally find this a daunting clinical issue and generally if there is a history of joint aches and pains, I try to prescribe medications that are effective systemically on arthritis.

Reference: Acta Derm Venereol. 2021;101(9):adv00553
Abstract

Clinical analysis of generalized pustular psoriasis in Chinese patients: A retrospective study of 110 patients

Authors: Zheng J et al.

Summary: This Chinese, single-centre, retrospective analysis examined precipitating factors, clinical manifestations, laboratory data, relapse patterns, and prognosis in 110 patients (mean age 46.5 years) with generalised pustular psoriasis. A psoriasis vulgaris history was observed in 85.5% of patients, 10.9% had a history of psoriatic arthritis, 4.5% had a history of erythrodermic psoriasis, and 14.5% had a family history of psoriasis. Infections triggered 10.0% of cases and 15.5% were caused by discontinuation of systemic drugs. During hospitalisation, the hyperlipidaemia rate was higher after acitretin treatment ($p < 0.05$), while the rate of abnormal liver function was higher after methotrexate treatment ($p > 0.05$). Age at onset was younger in patients without prior psoriasis ($p < 0.05$) and mean time to pustular clearance was shorter in patients with prior psoriasis ($p > 0.05$). In patients with fever, skin lesion clearance rates were highest in those receiving biological agents (81.8%). Among patients without fever, skin lesion clearance rates were highest with acitretin treatment (86.7%).

Comment: Generalised pustular psoriasis is rare. We have a large Chinese patient load. Most studies come out of America and Northwest Europe which are different genetic subgroups to what we see in Australia in our clinic. Essentially there is nothing in this paper that suggests that Chinese patients have any significant differences between the patients that I manage either in clinic or hospital practice. It is reassuring for our multicultural nation.

Reference: J Dermatol. 2021;48(9):1336-1342
Abstract

A multicentre open-label study of apremilast in palmoplantar pustulosis (APLANTUS)

Authors: Wilsmann-Theis D et al.

Summary: The 20-week, multicentre, single-arm, phase II APLANTUS study tested the phosphodiesterase-4 inhibitor apremilast in 21 patients with moderate-to-severe palmoplantar pustulosis. Palmoplantar Pustulosis Psoriasis Area and Severity Index (PPPASI) decreased by a median of 57.1% ($p < 0.001$), and 61.9% of patients had a ≥50% improvement relative to baseline. Total number of pustules decreased relative to baseline by ≥50% in 76.2% of patients. There was also a decrease in the DLQI from a median of 8.5 at baseline to 2.0 at week 20 ($p = 0.030$). Apremilast was generally well tolerated and there were no serious adverse events.

Comment: Apremilast is an oral medication that is finding a wider role in dermatology. It's use in oral ulcers associated with Bechet's disease has made me consider prescribing this medication for severe oral aphthae. I look forward to a paper on this specific condition. Palmoplantar pustulosis is not that uncommon in the clinic. This was a study looking at a small number of patients. However, after using oral antibiotics and then acitretin, there are a limited number of options that we can utilise. This paper was selected to suggest that maybe apremilast can be trialled in this patient group and is something that we may all wish to consider.

Reference: J Eur Acad Dermatol Venereol. 2021;35(10):2045-2050
Abstract

Serum lactate dehydrogenase level as a possible predictor of treatment preference in psoriasis

Authors: Koguchi-Yoshioka H et al.

Summary: This small Japanese study used clinical and laboratory data from 58 psoriatic patients to identify indices predicting apremilast efficacy and the impact of immune cell metabolic activity on the psoriatic pathogenesis. Clinical improvement was correlated with serum lactate dehydrogenase (LDH) level in apremilast but not biologic recipients. Serum LDH level was not correlated with cutaneous disease severity but was correlated with oxygen consumption rate of T cells.

Comment: There is a lot of research work on biomarkers or other indices that will help us as clinicians decide on prescribing one systemic agent over another. This is a very small study out of Japan looking at only 58 psoriatic patients. It seems to suggest that patients with a higher serum LDH level respond better to apremilast than to a biologic. This may be a way of helping assess which patients respond to apremilast. I look forward to the days when I can do a test and the answer will tell me what to treat my patients with.

Reference: J Dermatol Sci. 2021;103(2):109-115
Abstract

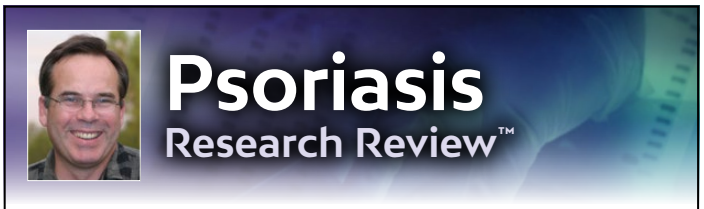
Coprevalence of hidradenitis suppurativa and psoriasis: Detailed demographic, disease severity and comorbidity pattern

Authors: Pinter A et al.

Summary: This small retrospective study (2015-19) examined terms of onset, disease course, severity, concomitant diseases and therapeutical management in 28 patients (mean age 44.4 years) with a co-diagnosis of hidradenitis suppurativa and plaque psoriasis. Hidradenitis suppurativa was the first diagnosis in 15 patients at an average age of 22.8 years; 13 patients first showed symptoms of plaque psoriasis at a mean age of 21.7 years. Average time to onset of the second disease was 14.3 years. Patients with hidradenitis suppurativa first had a more severe form of the disease than those with a first diagnosis of plaque psoriasis (mean highest International Hidradenitis Suppurativa Severity Score System 23.5 vs 8.2; $p = 0.02$). In patients with hidradenitis suppurativa first, the severity of psoriatic disease was numerically but not significantly lower than those with plaque psoriasis first (mean highest PASI 7.8 vs 13.2). Across all patients, the most frequent comorbidity was obesity (64.3%; mean BMI 32.2) followed by psychiatric complaints (25%) and psoriatic arthritis (21.4%). Adalimumab was the most effective agent with a positive effect on both diseases.

Comment: Another German article. Frankfurt is a very big centre and they had only 28 patients reviewing two university hospitals collecting patients over 4 years. To date, I have read a number of papers that link hidradenitis suppurativa and psoriasis. Certainly, in my practice both conditions are quite common. I must say that I have not linked these clinically in my head. Certainly, the conclusions of this review are not particularly stunning as 64% of patients were obese, 25% had psychiatric complaints and one in five had psoriatic arthritis. In this group of patients, they use adalimumab as do we.

Reference: Dermatology. 2021;237(5):759-768
Abstract



Selection of papers and comments are provided by Clinical Associate Professor Kurt Gebauer, *MBBS, FACD, FACP*

Clinical Associate Professor Kurt Gebauer has been practicing dermatology for 20 years in Australia. Dr. Gebauer has a busy private practice located in Fremantle and can also be found lecturing locally and internationally on different medical topics. As a contributing author on many publications, Dr. Gebauer is a well-known authority on dermatological conditions. Along with his dermatology practice Dr. Gebauer also participates in clinical research studies in order to offer new and innovative treatments for dermatological conditions including acne, atopic dermatitis, psoriasis, actinic keratoses, onychomycosis, and skin cancer.

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