

Recent Abstracts from International Journals

Matrix metalloproteinase-9: a novel biomarker for monitoring disease activity in patients with chronic urticaria patients?

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BACKGROUND: Matrix metalloproteinase (MMP)-9, an enzyme that contributes to inflammatory responses and subsequent tissue remodelling, has recently been suggested to be a good biomarker for monitoring disease activity in patients with chronic urticaria (CU). Here, we assessed whether total MMP-9 and/or active MMP-9 plasma levels are increased and correlated to disease activity in patients with CU. **METHODS:** Total MMP-9 and active MMP-9 plasma levels were determined by ELISA in 70 CU patients and control subjects (patients with psoriasis and healthy controls). CU activity was measured using weekly and daily composite symptom scores (urticaria

activity score) calculated from the number of wheals and the intensity of pruritus.

RESULTS: Significantly increased levels of total and active MMP-9 were detected in patients with CU as compared to healthy controls. Interestingly, patients with psoriasis also had clearly elevated plasma levels of total and active MMP-9, indicating that MMP-9 plasma levels do not specifically reflect CU activity. Most notably, total and active MMP-9 levels were not correlated with disease activity in CU or psoriasis patients. **CONCLUSION:** Plasma MMP-9 is not a good CU biomarker and should not be used for assessing the efficacy of treatment in CU patients or their spontaneous changes in disease activity.

Vascular endothelial growth factor in psoriasis: an indicator of disease severity and control.

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Background: Psoriasis is a chronic disease characterized by abnormal epidermal proliferation, inflammation and angiogenesis. It has been reported that vascular endothelial growth factor (VEGF) is overexpressed in lesional psoriatic skin and its serum levels are significantly elevated in patients with moderate to severe disease. **Objective:** This study aims to evaluate the possible role of VEGF in the pathogenesis of psoriasis, and its significance as an indicator of disease severity and control.

Methods: Thirty patients with moderate to severe psoriasis and 10 healthy controls were subjected to baseline evaluation of VEGF. Patients were divided into three groups according to the received treatment: psoralen plus ultraviolet A (PUVA) thrice weekly (group 1), acitretin 50 mg daily (group 2), and combined PUVA twice weekly and acitretin 25 mg daily (group 3). Treatment continued

for 16 weeks or up to clinical cure. Every patient was subjected to severity evaluation by Psoriasis Area and Severity Index (PASI) and measurement of serum VEGF before and after treatment. **Results:** Mean serum levels of VEGF were significantly elevated in patients (327 +/- 66.2 pg/mL) than control subjects (178 +/- 83.4 pg/mL). A highly significant correlation was found between VEGF and PASI score, but not with other variables. The best clinical response, the least side-effects and the highest reduction of VEGF serum levels were achieved by the combined therapy. **Conclusion:** The present study supported the proposed role of VEGF in the pathogenesis of psoriasis, and suggested that it could serve as a good indicator of disease severity and control.

Pruritus measurement and treatment.

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Pruritus measurement is problematic, because of its subjective nature and poor localization. Ratio scales enhance the usefulness of the visual analogue scale (VAS) by reducing variation; other scales such as the generalized labelled magnitude scale may also be useful. Pruritus neuroanatomy includes peripheral receptors, peripheral and central nerves, ascending and descending spinal pathways, and

several brain regions. Pruritus receptors include Merkel discs and free nerve endings, and itch receptors have fast or slow adaptation. In this review, we discuss the pathophysiology of pruritus in atopic dermatitis, psoriasis and scabies. Pruritus treatment is reviewed for topical agents and antihistamines. Future research directions are suggested.

Melanocyte as a possible key cell in the pathogenesis of psoriasis vulgaris.

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Current research in pathogenesis of psoriasis vulgaris suggests that the inflammatory mechanisms are immune based and most likely initiated and maintained by T cells. However, the question of lymphocyte being an initiator of psoriatic events remains open so far. Clinical observations such as plaque symmetry, stress-induced onset or exacerbations, pruritus, and possibility of generalization, suggest a role of the nervous system and neurogenic inflammation in pathogenesis. A key to understanding the role of melanocyte in psoriasis is their ability to act as regulatory cell in maintaining epidermal homeostasis. In suggested hypothetic event, melanocyte, acting as a local "stress sensor", provide communicatory link between CNS and

skin. The disease probably begins with so far unknown signal directed through neuronal network to the melanocyte, placed in the center of epidermal unit. That signal governs keratinocyte cellular activities and lead to reactive abnormal epidermal differentiation and hyperproliferation. Increased proliferation of basal keratinocytes and high metabolic demands creates angiogenesis in papillary dermis and elongation of dermal papillae. Stimulated melanocytes and basal keratinocytes become an important source of proinflammatory cytokines that attract lymphocytes in dermis. In conclusion, according to our hypothesis, lymphocyte infiltrate in psoriasis is secondary event rather than vice versa as presented in the literature.

Comorbidities in dermatology.

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Recently, comorbidities have been rediscovered in dermatology. Although numerous associations between skin diseases and other conditions have been reported, only a few are well documented. The association of comorbidities and dermatoses is complex and multifactorial. Life-style factors, impaired health-related quality of life, depression, therapeutic interventions, and several biases may

confound the relationship between skin diseases and comorbidities. This article discusses observational studies that assess comorbidities in psoriasis, atopic dermatitis, vitiligo, and nonmelanoma skin cancer, and the likelihood of the observed associations and their clinical consequences.

Oral lesions in 166 patients with cutaneous psoriasis: a controlled study.

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Objectives: This study was aimed to test if the frequency of oral lesions bears statistical correlation or not with the condition of cutaneous psoriasis. **Study design:** Two groups were examined, one made up of 166 patients with skin psoriasis and the other with the same number of individuals with a negative history of skin diseases (control group), matched by age, race, and sex. Patients with psoriasis were grouped according to their having localized or generalized forms of the disease. The oral mucosa was thoroughly examined in both groups. Data were analyzed using chi-square test, Fisher's test, the odds ratio (OR) with a 95% confidence interval (CI), and the Ryan-Holm step-down Bonferroni procedure. The overall significance was set at $P \leq 0.05$.

Results: The oral lesions significantly associated with psoriasis were fissured tongue (FT, OR =

2.7; 95% CI: 1.3-5.6), and geographic tongue (GT, OR = 5.0; 95% CI: 1.5-16.8). Other factors analyzed, such as topical and/or systemic medication for treatment of psoriasis versus nontreated patients, and localized versus generalized forms of psoriasis presented no statistical association with the frequency of FT or GT lesions ($p > 0.05$).

Conclusions: Patients with psoriasis presented no specific oral lesion different from those seen in the control group. Although further investigation is warranted to establish whether or not either FT or GT can be characterized as an oral expression of psoriasis, the present investigation did find for both these types of lesions that the frequency of each bore a statistically significant relation with the presence of cutaneous psoriasis.

Evaluation of the efficacy of acitretin therapy for nail psoriasis.

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Arch Dermatol. 2009 Mar;145(3):269-71.

OBJECTIVE: To evaluate the therapeutic efficacy of acitretin in patients with isolated nail psoriasis. **DESIGN:** Open study involving 36 patients with moderate to severe nail psoriasis treated with acitretin. **SETTING:** University-based outpatient dermatology clinic specializing in nail diseases. **PATIENTS:** A total of 27 men and 9 women (mean age, 41 years) with nail psoriasis.

INTERVENTION: Therapy consisted of acitretin, 0.2 to 0.3 mg/kg/d, for 6 months.

MAIN OUTCOME MEASURES: Clinical evaluation, and Nail Psoriasis Severity Index (NAPSI) and modified NAPSI scores before therapy, every 2 months during therapy, and 6 months after treatment. **RESULTS:** The mean percentage of reduction of the NAPSI score after treatment was 41%; the mean percentage of

reduction of the modified NAPSI score of the target nail was 50%. Clinical evaluation at 6 months showed complete or almost complete clearing of the nail lesions in 9 patients (25%), moderate improvement in 9 (25%), mild improvement in 12 (33%), and no improvement in 6 (11%). **CONCLUSION:** Results from low-dose acitretin therapy show NAPSI score reductions comparable with those studies evaluating biologic drugs for nail psoriasis and suggest that low-dose systemic acitretin should be considered in the treatment of nail psoriasis.

Psoriasis treatment in difficult locations: scalp, nails, and intertriginous areas.

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Psoriasis comprises a broad spectrum of different clinical courses among which the chronic stable psoriasis by far occurs most frequently. The clinical presentation ranges from mild disease to more serious forms involving large areas of skin and/or joint disease. A number of modifying factors may impact on treatment choice in individual cases (eg, location of the lesions, disease phase, treatment history, response to previous treatments, comorbidity). Aside from this consideration, there are special localizations that remain some of the most difficult regions to control. Such entities are the scalp, nails, and intertriginous areas. Topical treatment of such different-to-treat areas has to be considered as a first-line intervention strategy, at least in those patients who are presenting an exclusively isolated involvement. In some situations (eg, in severe psoriasis or in patients who are refractory to topical treatment), however, a systemic treatment is indicated. Most obvious difficulties in treating these locations are due to unrealistic expectations from the patients' perspectives, time-consuming applications, side effects, cosmetic injuries, and restricted bioavailability of active compounds. Aside from hair care, initial use of keratolytics for scalp psoriasis, corticosteroids,

and vitamin D3 and analogues are currently standard treatments. Recently developed new formulations of both active ingredients such as foam or gel appear to be more acceptable to patients than traditional creams or ointments. Current treatment options for nail psoriasis are very often poorly efficacious, associated with undesirable effects, or time consuming. Success has to be measured in terms of months. Topical treatments (eg, corticosteroids, vitamin D analogues, tazarotene) are mainly used, but impressive improvement rates mostly will be achieved by systemic treatment of conventional and biologic agents. Finally, the usefulness of corticosteroids, vitamin D and analogues, and calcineurin inhibitors in treating intertriginous psoriasis clearly is demonstrated. Especially the use of calcineurin inhibitors exhibits efficacy in intertriginous regions and therefore may be seen as a promising treatment option in the future. Besides the important innovations in the last years, there is a need for new effective and well-tolerated treatment modalities, especially for long-term use in the 3 difficult-to-treat locations, which encompass cosmetic acceptability.

Nickel allergy as risk factor for hand eczema: a population-based study.

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Background: In population-based studies using self-reported nickel allergy, a hand eczema prevalence of 30-43% has been reported in individuals with nickel allergy. In a previous Swedish study, 958 schoolgirls were patch tested for nickel. In a questionnaire follow up 20 years later no association was found between nickel allergy and hand eczema.

Objectives: To investigate further the relation between nickel allergy and hand eczema.

Methods: Three hundred and sixty-nine women, still living in the same geographical area, now aged 30-40 years, were patch tested and clinically investigated regarding hand eczema.

Results: Patch testing showed 30.1% nickel-positive individuals. The adjusted prevalence proportion ratio (PPR) for hand eczema after age 15 years in relation to nickel patch test results was 1.03 (95% confidence

interval, CI 0.71-1.50). A history of childhood eczema was reported by 35.9%, and the PPR for hand eczema in relation to childhood eczema was 3.68 (95% CI 2.45-5.54). When analysing the relation separately in women with and without a history of childhood eczema a statistical interaction was found. The hand eczema risk was doubled in nickel-positive women without a history of childhood eczema, with a PPR of 2.23 (95% CI 1.10-4.49) for hand eczema after age 15 years.

Conclusions: A doubled risk for hand eczema was found in nickel-positive women without a history of childhood eczema. When analysing all participants, there was no statistically significant difference between nickel-positive and nickel-negative women regarding occurrence of hand eczema. The most important risk factor for hand eczema was childhood eczema. The risk for hand eczema in nickel-positive women may previously have been overestimated.

Does tobacco smoking influence the occurrence of hand eczema?

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Br J Dermatol. 2009 Mar;160(3):514-8. Epub 2008 Nov 25.

BACKGROUND: Tobacco smoking is known to influence various inflammatory skin diseases and an association between tobacco smoking and hand eczema has been proposed in some studies. **OBJECTIVES:** To examine a possible association between reported current tobacco smoking and the occurrence of hand eczema.

SUBJECTS AND METHODS: Previously collected questionnaire data on the occurrence of hand eczema in three occupational cohorts and corresponding controls from the general population were studied. The questionnaires used included questions on 1-year prevalence of hand eczema and questions on smoking habits. For one occupational group, hairdressers and their controls, information on amount of smoking was obtained. Information on age, sex and history of atopy was also available.

RESULTS: In total, answers regarding smoking and hand eczema were obtained from 13,452 individuals. Out of 3493 smokers, 437 (12.5%) reported hand eczema compared with 1294 out of 9959 nonsmokers (13.0%) ($P = 0.51$). With regard to the number of cigarettes smoked, 22.6% of the hairdressers smoking more than 10 cigarettes per day reported hand eczema compared with 17.4% of those smoking 0-10 cigarettes per day ($P = 0.01$). Corresponding figures for the controls were 14.5% and 11.7%, respectively ($P = 0.06$).

CONCLUSIONS: No clear association was found between 1-year prevalence of hand eczema and smoking. Heavy smoking, more than 10 cigarettes per day, may give a slightly increased risk of hand eczema. Further studies with information on the amount of tobacco consumption and on possible confounders are needed to evaluate smoking as a risk factor for hand eczema.

Nine cases of omeprazole allergy: cross-reactivity between proton pump inhibitors.

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Although rare, anaphylactic reactions induced by proton pump inhibitors have been reported. The presence of cross-reactivity between different members of the group is not clear. We studied 9 patients with adverse reactions to omeprazole. Clinical symptoms appeared immediately in 8 patients and after 4 hours in 1. Symptoms ranged from urticaria/angioedema in 7 cases to anaphylaxis in 2 cases. Skin prick tests and oral controlled challenge tests with omeprazole, lansoprazole, and pantoprazole were performed. Skin prick or

intradermal tests with omeprazole were positive in 8 patients. Four were also positive to pantoprazole. Prick tests with lansoprazole were always negative. Lansoprazole was administered to all 9 patients, with good tolerance in 8. Only 3 patients were challenged with pantoprazole and developed widespread urticaria. We present 9 patients with immunoglobulin E-mediated allergy to omeprazole. In most of our cases, lansoprazole proved to be a good alternative treatment.

Classification and design of teledermatology practice: What dermatoses? Which technology to apply?

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Dermatologists are mostly confined to urban regions and rural population is deprived of specialist care. Teledermatology Practice (TDP) is a solution to overcome this global problem. Tools for TDP includes video conference, store and forward, hybrid, mobile, satellite communication, integration model, nurse-led teledermatology, teledermatology focusing on difficult-to-manage cases, teledermoscopy, and teledermatopathology with combined applications. This article reviews the feasibility studies focusing teledermatology tools and analyses the possible options in designing TDP. Categorizing dermatoses for TDP depends on the purpose and types of technology. The dermatoses presenting from a remote geographic regions requires any of the following approaches (i) only TDP, (b) initial TDP followed by face-to-face, (iii) initial face-to-face followed by TDP and (iv) only face-to-face examination. The technology should suit the dermatoses, meet the purpose, be cost-effective and provide better management with follow-up

care. We recommend store and forward as a basic TDP model as most dermatoses are diagnosed and follow-up care is delivered. Leprosy, pigmented skin lesions, leg ulcers, HIV and endemic dermatoses require screening and triage services using mobile teledermatology. Counselling and education require videoconference. Rural dermatology's camps require satellite communication mounted on a vehicle. Objective assessment (vitiligo and leg ulcer) after treatment requires integration model at a tertiary centre. Difficult-to-manage cases require second opinion using hybrid/store and forward TDP. Lower rural centre are provided with mobile/ store and forward teledermatology services. Selected or major community centre should be equipped with hybrid teledermatology and linked to a tertiary centre. This process helps healthcare administration to plan a TDP to cover all dermatoses, utilizing the available health care professional (HCP) and technology with minimum budget investment.

Skin penetration enhancement by a microneedle device (Dermaroller) in vitro: dependency on needle size and applied formulation.

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This study focused on the in vitro evaluation of skin perforation using a new microneedle device (Dermaroller) with different needle lengths (150, 500 and 1500 microm). The influence of the microneedle treatment on the morphology of the skin surface (studied by light and scanning electron microscopy), on the transepidermal water loss (TEWL) and on the penetration and permeation of hydrophilic model drugs was investigated using excised human full-thickness skin. Furthermore, invasomes - highly flexible phospholipid vesicles containing terpenes and ethanol as penetration enhancer - were compared with an aqueous solution. Elevated TEWL values were measured after Dermaroller treatment compared to untreated human skin with a gradual increase of the TEWL

over the first hour whereas afterwards the TEWL values decreased probably caused by a reduction of the pore size with time. Skin perforation with the Dermarollers enhanced drug penetration and permeation for both formulations tested. Invasomes were more effective to deliver hydrophilic compounds into and through the skin compared to the aqueous drug solutions and the combination with skin perforation further enhanced drug penetration and permeation. In conclusion, Dermarollers being already commercially available for cosmetic purposes appear also promising for drug delivery purposes particularly those with medium (500 microm) and shorter (150 microm) needle lengths.