

## Journal Watch

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### **Satellite lesions accompanying herpes zoster: a new prognostic sign for high-risk zoster**

el Hayderi L, Bontems S, Nikkels-Tassoudji N, Arrese JE, Seidel L, Meex C, et al.  
[Br J Dermatol 2015;172:1530-4.](#)

The incidence, clinical relevance and pathogenesis of the single, isolated, varicella-like skin lesions appearing far away from the primary herpes zoster (HZ) affected dermatome are not well understood. The aim of this study was to investigate the satellite lesions in 120 patients with HZ and tried to correlate their presence with different clinical, histological and virological data.

In this study, 109 HZ patients confirmed by using immunohistochemistry methods on Tzanck smears were included. In addition, skin biopsies and blood samples for histology, serology, immunohistology, and polymerase chain reaction were obtained from a subgroup of patients presenting with primary HZ with and without satellite lesions.

Satellite lesions were present in 21.1% of the patients with HZ in which there was a statistically significant relative risk (RR) for severe (RR 3.27,  $p < 0.001$ ), multi-dermatomal (RR 10.6,  $p < 0.001$ ) and multi-stage HZ (RR 3.30,  $p < 0.001$ ); systemic signs (RR 2.08,  $p = 0.0031$ ); immunosuppression (RR 2.38,  $p = 0.0014$ ) and hospitalisation (RR 2.94,  $p < 0.001$ ). Furthermore, in HZ with satellite lesions, varicella-zoster virus (VZV) viraemia was higher (mean 4075 copies  $\text{mL}^{-1}$ ) than in those without (mean 1466 copies  $\text{mL}^{-1}$ ). VZV immunostaining in endothelial cells was often positive in satellite lesions. The limitation of this study was that it might have recruited more immunocompromised patients with more severe diseases in the tertiary care centre and therefore the prevalence of the satellite lesions might have been overestimated.

In summary, complete examination of the skin of the whole body for satellite lesions was a fast, simple and effective means for identifying patients with high-risk HZ.

### **Skin reaction and regeneration after single sodium lauryl sulphate exposure stratified by filaggrin genotype and atopic dermatitis phenotype**

Bandier J, Carlsen BC, Rasmussen MA, Petersen LJ, Johansen JD.  
[Br J Dermatol 2015;172:1519-29.](#)

Filaggrin plays a major role in maintaining the normal function of the stratum corneum. As a result, mutation in the filaggrin gene (FLGnull) is an important cause of atopic dermatitis (AD). It had been noted that patients with AD were more vulnerable to irritants. In addition, few data is available on the effect of filaggrin genotype and AD phenotype on irritant reaction and skin repair.

The aim of this study was to study the role of FLGnull and AD groups for skin reaction and recovery after sodium lauryl sulphate (SLS) irritation. A case-control study comprising 67 subjects, including healthy controls and patients with and without FLGnull and AD was performed. Transepidermal water loss (TEWL) was measured and laser Doppler flowmetry (LDF) was used to see the effects of different doses of SLS at 24, 48, 72 and 145 h after its application. Univariate and pattern analysis were used to study the reactivity.

All patient groups were found to have a higher extent of skin-barrier disruption and inflammation compared to controls in response to SLS. The authors assessed the reactivity by the delta value of the area under the curve for both TEWL and LDF which showed significant differences between

healthy controls and in cases with the AD phenotype, regardless of filaggrin mutation. Patients with the AD phenotype showed the poorest regeneration.

In summary, there was a significant difference in skin reaction and regeneration between the patient population and healthy controls. Besides, response severity and regeneration were determined more by AD phenotype than filaggrin genotype.

### **Histopathology of drug rash with eosinophilia and systemic symptoms syndrome: a morphological and phenotypical study**

Ortonne N, Valeyrie-Allanore L, Bastuji-Garin S, Wechsler J, de Feraudy S, Duong TA, et al.  
*Br J Dermatol* 2015;173:50-8.

The purpose of this study was investigate the histopathological features of DRESS syndrome, the phenotype of the effector cells in the skin and to compare the phenotype with the maculopapular rash (MPR).

A retrospective study was carried out on 50 skin biopsies from patients with DRESS syndrome (n=36). The authors studied the histopathological and immunophenotypical features and then compared with a series of MPRs (n=20).

The results showed that various spots of interface dermatitis, involving cutaneous adnexae, were commonly found in patients with DRESS. Furthermore, eosinophils were detected in 20% of cases and neutrophils in 42% of cases. Interestingly, acute generalised exanthematic pustulosis-like (20%), interface dermatitis (74%), eczematous (40%) and erythema multiforme-like (24%) patterns were seen. Cases of DRESS were significantly associated with the presence of two or three of histological patterns in a single biopsy when compared to cases of nondrug-induced dermatoses ( $p < 0.01$ ). These were more obvious in DRESS syndrome with severe cutaneous lesions ( $p = 0.01$ ) than in mild cases of DRESS and MPR. There was a higher percentage of CD8<sup>+</sup> and granzyme B<sup>+</sup> lymphocytes seen in patients with the severe form of DRESS. In addition, 28% of biopsies showed atypical lymphocytes which expressed CD8 in most cases and a cutaneous T-cell clone was uncommon (6%).

In conclusion, different inflammatory forms in a single biopsy may be present in DRESS syndrome. It was noted that polyclonal CD8<sup>+</sup> granzyme B<sup>+</sup> lymphocytes were found among the cutaneous effector lymphocytes.

### **Pemphigus and associated comorbidities: a cross-sectional study**

Heelan K, Mahar AL, Walsh S, Shear NH.  
*Clin Exp Dermatol* 2015;40:593-9.

Pemphigus is a severe, debilitating autoimmune blistering condition with a significant mortality. It is well-known to be associated with other autoimmune diseases such as alopecia areata, vitiligo, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, thyroid dysfunction and myasthenia gravis. The present study aimed to investigate the prevalence of various comorbidities in a cohort of patients with pemphigus. The relative risk of occurrence of individual comorbidities among the patients were also studied. A total of 295 Canadian patients with pemphigus were included in this single-centre, cross-sectional study. The prevalence of 15 comorbid diseases were analysed. The age-standardised prevalence ratio (SPR) of individual comorbidities in the studied cohort was determined and compared to the prevalence rates of the general Canadian population. In this study, the authors demonstrated that the most frequently occurring comorbidities were diabetes mellitus, hypertension, hypothyroidism, solid-organ tumour (excluding non-melanoma skin cancer), heart disease and asthma. Statistical analyses confirmed that there is a higher prevalence rate of diabetes mellitus (SPR, 2.20 [95% CI, 1.64-2.87]), hypothyroidism (SPR, 1.53 [95% CI, 1.08-2.10]) and inflammatory bowel diseases (SPR, 1.48 [95% CI, 0.40-3.80]). The authors concluded that potential associations with other autoimmune diseases exist among patients with pemphigus. Active screening of blood sugar, thyroid dysfunction and bowel symptoms should be considered in all patients with this autoimmune blistering condition. Given the retrospective nature of this study, future prospective trials with a larger sample size are required to confirm the findings.

## Phototherapy in the elderly

Powell JB, Gach JE.

Clin Exp Dermatol 2015;40:605-10.

The geriatric population often presents with a unique pattern of skin conditions when compared to the general adult patients. With an ageing population, there is an immense need to understand the specific physical structures and physiological functions of the aged skin. It is largely unknown whether similar clinical responses and improvements to phototherapy could be achieved among elderly patients. Also, the overall safety profile of UV radiation in the elderly is unknown. The present study aimed to determine the clinical efficacy and safety of phototherapy among geriatric patients. This was a retrospective, single-centre study of 249 patients, who had completed a course of phototherapy in a tertiary centre in the United Kingdom in 2014. Among them, 31 patients were above the age of 65 and had received phototherapy. The underlying indications were eczema (11%), psoriasis (51%), others (11%), prurigo nodularis (11%), pruritus (11%) and Grover's disease (5%). They received a total of 739 sessions of phototherapy (narrow-band UVB [nbUVB] in 88%; psoralen plus UVA [PUVA] in 12%). The acute adverse event rate was 1.89% (mild erythema, n=13; moderate erythema, n=1). Two patients had terminated the phototherapy prematurely. One was due to a scheduled surgery and the other was due to difficulties in transportation. Among those who finished their courses of phototherapy, 84% achieved clear, near-clear or moderate skin clearance responses. Only two patients (8%) had minimal responses and they had the underlying diseases of polymorphic light eruption and psoriasis. For those who had completed treatment with nbUVB, 91% achieved a clear or near-clear response after an average of 30 treatment sessions. The authors concluded that phototherapy was in general a well-tolerated, safe, and effective treatment modality for a variety of dermatological conditions in the elderly. Apparently, no specific alteration in the treatment protocol appeared necessary for these patients.

## Cardiovascular comorbidities in patients with rosacea: A nationwide case-control study from Taiwan

Hua TC, Chung PI, Chen YJ, Wu LC, Chen YD, Hwang CY, et al.

J Am Acad Dermatol 2015;73:249-54.

Rosacea is a chronic inflammatory skin disorder. As shown in psoriasis, chronic inflammation plays a role in atherosclerosis and cardiovascular disease. However, this association had not been well-studied in rosacea. In this nation-wide case-control study, the authors investigated the association of rosacea with cardiovascular risk factors and coronary artery disease (CAD). Data was collected from the National Health Insurance Research Database (NHIRD) in Taiwan, which covered 99.6% of Taiwan population. Individuals who were diagnosed to have rosacea by dermatologists on at least two occasions between 1997 and 2010 were recruited to ensure diagnostic validity. Those with the diagnoses of acne, seborrhoeic dermatitis and lupus erythematosus, which are clinical mimickers of rosacea, were excluded. Equal numbers of age- and gender-matched controls were selected from the Longitudinal Health Insurance Database 2000, which was a random sample from NHIRD.

A total of 33,553 patients with rosacea were selected, 74.4% were females and 25.6% males. Patients with rosacea had a significantly higher risk of dyslipidaemia (OR 1.41, 95%CI 1.36-1.46), CAD (OR 1.35, 95%CI 1.29-1.41) and hypertension (OR 1.17, 95%CI 1.12-1.21). CAD was independently associated with rosacea after adjustment for other cardiovascular risk factors.

Chronic inflammation causes structural changes in lipoproteins, which may affect their ability to clear cholesterol. Also, paraoxonase-1 (PON1) activity was found to be significantly lowered in patients with rosacea. This was also found in dyslipidaemic and hypertensive patients, and was a known predictor of CAD. The authors concluded that patients with rosacea are more likely to have dyslipidaemia, hypertension and CAD and clinicians should screen for CVD risk factors in these patients. However, since the data was collected from NHIRD, clinical information about the severity and subtype of the disease was lacking.

Also, misclassification of the disease or miscoding may be a source of error from this nationwide database.

### **Liver injury in patients with DRESS: A clinical study of 72 cases**

Lin IC, Yang HC, Strong C, Yang CW, Cho YT, Chen KL, et al.

*J Am Acad Dermatol* 2015;72:984-91.

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe drug reaction characterised by multi-organ involvement. Liver injury accounts for the most common visceral involvement. However, clinical characteristics of liver injury and relationships with culprit drugs have not been well-studied. In this retrospective study, the authors reviewed clinical records from the National Taiwan University Hospital database from year 2000-2013. Seventy-two cases were included and 86.1% had liver injury. The most common culprit drugs were allopurinol, phenytoin and dapsone. Atypical lymphocytosis was shown to be significantly associated with liver injury. Among those with liver damage, 37% had cholestatic type, 27.4% mixed type and 19.4% hepatocellular type. Older patients tend to have cholestatic type which is associated with interface changes in skin pathology. Moreover, different drugs might give different patterns of liver damage, e.g allopurinol-DRESS showed cholestatic pattern, while carbamazepine-DRESS had hepatocellular damage.

The authors concluded that atypical lymphocytosis might be an indicator for liver injury in DRESS and they postulated that the association of atypical lymphocytosis with liver injury might be due to the reactivation of human herpes virus or other viral reactivation and the activation of inflammatory cytokine cascade. Moreover, the difference in liver injury in different age groups could be explained by the difference in culprit drugs, variation in immune function and ageing of the hepatobiliary system.

This study showed that liver injury is commonly associated with DRESS and early diagnosis and management may improve the outcome of these patients. However, the small number of cases and the retrospective nature limited this study.

### **Association of psoriatic disease with uveitis. A Danish nationwide cohort study**

Egeberg A, Khalid U, Gislason GH, Mallbris L, Skov L, Hansen PR.

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The relationship between uveitis and spondyloarthropathies has been well-established. However, evidence about the risk of uveitis in patients with psoriasis with or without arthritis is lacking. Moreover, the risk of psoriasis or psoriatic arthritis in patients with uveitis is not known. The associations among uveitis, mild psoriasis, severe psoriasis, and psoriatic arthritis were examined in this cohort study.

This was a 15-year cohort study investigating the relationship between psoriatic disease and uveitis in Denmark. A total of 74,129 patients with incident psoriasis and 13,114 patients with incident uveitis were identified. It was found that there was an overall increased risk for uveitis in patients with psoriasis and psoriatic arthritis. An increased risk (reported as incidence rate (IR) ratio [95% CIs]) was demonstrated for uveitis in mild psoriasis (1.38 [1.11-1.70]) and psoriatic arthritis (2.50 [1.53-4.08]) but not for severe psoriasis (1.40 [0.70-2.81]) ( $p=0.34$ ). Moreover, increased risks for mild psoriasis, severe psoriasis and psoriatic arthritis in patients with uveitis were identified. In patients with uveitis, the IR ratios (95% CIs) were 1.59 (1.32-1.91 [ $p<0.001$ ]) for mild psoriasis, and 2.17 (1.40-3.38 [ $p<0.001$ ]) for severe psoriasis respectively. For psoriatic arthritis, the IR was 3.77 (2.66-5.34 [ $p<0.001$ ]).

This study demonstrated a bidirectional association between psoriatic disease and uveitis. It is suggested that a shared pathogenic pathway and increased systemic inflammation may contribute to the observed relationship. The authors suggested that attention should be paid to eye symptoms in patients with psoriasis and psoriatic arthritis, while patients with uveitis should be enquired about skin and joint symptoms.

## Vaginal douching and sexually transmitted infection among female sex workers: a cross-sectional study in three provinces in China

Li J, Jiang N, Yue X, Gong X.

*Int J STD AIDS* 2015;26:420-7.

Vaginal douching is misperceived as a method to maintain personal hygiene and prevent sexually transmitted infections (STIs). It is commonly practised among female sex workers (FSW). The aims of this study are to understand the correlates of douching practice among FSW in China and to explore the associations between vaginal douching, STIs and condom use. A convenience sample of FSW who aged 16 or above and self-reported to have exchanged sex for money in the past year and who were willing to undergo STI testing and examinations were eligible for study. Blood samples were taken for syphilis serology and endocervical swabs were taken for *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) polymerase chain reaction (PCR). Vaginal douching was defined as having douched the vagina with disinfectants including soapy water, household bleach or detergents after sex with clients in the past six months. Consistent condom use was defined as the FSW using condom every time when having sex with client in the past four weeks while all those who only occasionally or never used condoms were classified as inconsistent condom users. FSW were also asked about any STI symptoms including ulcers, sores, genital warts and abnormal vaginal discharge and any STI diagnosis they had in the past 12 months.

A total of 1,032 FSW were enrolled. Of these, 23.1% of FSW had practised vaginal douching and 31.2% of FSW believed that it could prevent HIV/STI infection and 65.9% of FSW reported consistent condom use. The overall prevalence of syphilis, GC and CT was 3.8%, 3.0% and 18.7% respectively. In the vaginal douching group, it was more common in FSW aged 25 or above (25.9% vs. 20.3%  $p < 0.05$ ) compared to those aged below 25. It was also more common in FSW who had a regular sex partner (29.5% vs. 12.7% of those without regular partner,  $p < 0.001$ ). FSW who reported STIs symptoms (37.9% vs. 16.3% of those without symptoms,  $p < 0.001$ ) and had STI diagnosis (54.9% vs 20.7% of those without STI diagnosis,  $p < 0.001$ ) were more prevalent to have

vaginal douching. In contrast, vaginal douching was not significantly associated with FSW who believed douching could prevent HIV/STI infection (24.1%) and those who did not think so or did not know (22.6%). It was also not associated with education levels or positivity of STI tests.

## Should we screen heterosexuals for extra-genital chlamydial and gonococcal infections?

Garner AL, Schembri G, Cullen T, Lee V.

*Int J STD AIDS* 2015;26:462-6.

Although nucleic acid amplification tests (NAATs) for *Neisseria gonorrhoea* (GC) and *Chlamydia trachomatis* (CT) are not approved by Food and Drugs Administration (FDA) for extra-genital samples, many studies showed the importance of these NAATs in testing the extra-genital samples, especially in high risk groups such as men who have sex with men (MSM) and female sex workers. This study is to review the significance of extra-genital site infections with CT and GC in heterosexual women.

A total of 1,567 patients (heterosexual men=553, MSM=365, women=649) who attended the UK sexual health centre were offered extra-genital site screening for CT and GC according to their sexual history of oral sex and anal sex practice during the three-month study period. The overall positive rate for CT was 5.9% in women, 6.5% in heterosexual men and 4.5% in MSM. Slightly more women had extra-genital CT when compared with MSM (2.5% vs 2.2% in pharyngeal CT, 6.6% vs 6.5% for rectal CT). There were only few cases of GC in women (0.7%) and non-MSM men (0.6%). However, there were more GC cases in MSM (6.1%). The subgroup analysis also showed that rectal and pharyngeal GC were  $< 1\%$  in women and non-MSM men while rectal and pharyngeal GC in MSM were 9.0% and 5.2% respectively. The authors concluded that this study demonstrated that both MSM and heterosexual women were possible reservoirs for extra-genital chlamydial and gonococcal infections. They suggested the extra-genital screening for CT and GC is not necessary in heterosexual men but should be considered in MSM and women if there is a history of oral or anal sexual intercourse.