

## Journal Watch

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### **Association Between Pediatric Psoriasis and Waist-to-Height Ratio in the Absence of Obesity: A Multicenter Australian Study**

Lee A, Smith SD, Hong E, Garnett S, Fischer G. JAMA Dermatol 2016 Sep 28. doi: 10.1001/jamadermatol.2016.3432. [Epub ahead of print]

Psoriasis is an autoimmune-mediated inflammatory and hyperproliferative skin disorder, posing a cardiometabolic risk in children. The aim of this study is to determine whether children with psoriasis are more likely to have increased Waist-to-Height Ratio (WtHR), obesity and metabolic syndrome relative to children without psoriasis.

This multicentre cross-sectional prospective case-control study was done in a paediatric dermatology clinic in Australia between February 2014 and July 2015. Two hundred and eight children, aged from 5 to 16 years were evaluated. Study subjects consisted of 135 children with psoriasis and 73 controls with non-inflammatory skin conditions. Increased central adiposity indicated by WtHR of 0.5 or higher, metabolic syndrome and increased body mass index (BMI) were the parameters studied.

There was a significantly increase prevalence of WtHR greater than or equal to 0.5 in children with

psoriasis (29%; n=39) compared with controls (11%; n=8) ( $p=0.002$ ). The OR for having a WtHR of 0.5 or greater in children with psoriasis compared with controls was 3.30 (95% CI, 1.45-7.52). Moreover, the prevalence of WtHR of 0.5 or greater was higher in children with moderate to severe psoriasis (35%; n=13) than those with mild psoriasis (27%; n=26). A higher mean WtHR was more common in paediatric cases of moderate to severe psoriasis had than in those with mild psoriasis (0.48 vs 0.46;  $p=0.04$ ). There were four children with psoriasis who also had metabolic syndrome. Among them, three children had moderate to severe psoriasis while one had mild psoriasis. There was no significant difference in the prevalence of BMI-determined overweight and obesity in the paediatric cases of psoriasis and in the controls.

The authors concluded the WtHR is a simple and valid tool for identifying children with increased central adiposity. A WtHR of 0.5 or greater had been shown to be associated with future cardiometabolic risk. This finding in psoriasis children should alert the physician to provide counselling on a more healthy lifestyle and early intervention. Besides, cardiometabolic screening is suggested for children older than 10 years with increased WtHR.

## **Clinical features associated with individuals at higher risk of melanoma A population-based study**

Watts CG, Madronio C, Morton RL, Goumas C, Armstrong BK, Curtin A, et al.

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This study characterised melanoma patients and clinical features associated with their melanomas in relation to patient risk factors. In addition, it aimed to improve the identification and treatment of high-risk patients.

This study was a population-based study. It reported 2727 patients in New South Wales, Australia. It described patient and melanoma characteristics of high and low-risk patients, as well as the differences in melanoma characteristics for higher-risk patients. Multiple naevi, personal history and family history were risk factors in the higher-risk group. Higher-risk patients had a higher proportion of superficial spreading melanoma compared with lower-risk patients (49% vs 45%), fewer lentigo maligna melanoma (12% vs 15%,  $p=0.007$ ), a lower proportion of melanomas larger than 1 mm thick (29% vs 32%,  $p<0.001$ ). The higher-risk group had a younger mean age at diagnosis (62 years vs 65 years,  $p<0.001$ ). Higher-risk patients were less likely to have a melanoma situated on the head and neck and were more likely to have lesion on the trunk and limbs. The pattern of melanomas on different body sites also differed by sex. Males were more likely to have lesion on the trunk, head and neck. Among higher-risk patients, those with many naevi were more likely to have lesions on the trunk, and those with family history were more likely to have lesions on the limbs. The mean age at diagnosis was 56 years, 59 years, 69 years for patients with family history, those with many naevi, as well as those with a previous melanoma respectively.

This study provides information on which a personalised screening strategy could be based.

## **In vitro test to confirm diagnosis of allopurinol-induced severe cutaneous adverse reactions**

Klaewsongkram J, Thantiworasit P, Suthumchai N, Rerknimitr P, Sukasem C, Tuchinda P, et al.

Br J Dermatol 2016;175:994-1002.

Allopurinol is one of the commonest drug causing severe cutaneous adverse reactions (SCARs). It may cause severe drug reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS) or toxic epidermal necrolysis (TEN). Human leucocyte antigen (HLA)-B\*58:01 is positive for most patients with Steven Johnsons syndrome (SJS) or TEN but is only positive in 77% of patients with allopurinol-related DRESS. As drug re-challenge is not feasible, an in vitro test to confirm the diagnosis of allopurinol induced SCAR would be preferable.

This study investigated interferon (IFN)- $\gamma$  by enzyme-linked immunospot (ELISpot) test for confirmation of allopurinol-induced SCARs. Peripheral blood mononuclear cells (PBMCs) were incubated with allopurinol or oxypurinol (metabolite of allopurinol) with or without anti-programmed death ligand 1 antibody (anti-PD-L1) and the number of IFN- $\gamma$  releasing cell were measured by ELISpot. IFN- $\gamma$  level is low in acute stage of SCARs from other drug reaction. PD-L1 signal negatively regulates drug-antigen specific T cells. Hence, anti-PD-L1 will stimulate drug antigen-specific T cell activity and increases IFN- $\gamma$  production by stimulated drug-specific cell clones.

In this study, 24 patients with allopurinol-induced SCAR were studied. Twenty-one patients with a history of DRESS/SJS/TEN caused by other drugs

were as controls. Oxypurinol-specific IFN- $\gamma$  releasing cells level after stimulation with oxypurinol 100 ug per ml and after anti-PD-L1 (i.e. OXY100/anti-PD-L1) augmentation was significantly increased and higher in the allopurinol-allergic group than control group with a sensitivity 79.2% and specificity 95.2% by using 16 spot-forming cells per  $10^6$  PBMCs as a reference value for OXY100/anti-PD-L1 stimulation. IFN- $\gamma$  releasing cell was increased in almost all patients with allopurinol-induced DRESS and two thirds of patients with allopurinol-induced SJS/TENS. The authors concluded that this test was useful to confirm the diagnosis of allopurinol-induced SCARs in patients taking multiple drugs.

### **Clinical and immunological features and outcome of anti-p200 pemphigoid**

Commin MH, Schmidt E, Duver-Lehembre S, Lasek A, Morice C, Estival JL, et al.  
Br J Dermatol 2016;175:776-81.

This study investigated the clinical course and characteristics of anti-p200 pemphigoid. Anti-p200 pemphigoid is rare dermo-epidermal autoimmune blistering disease (AIBD) in which serum antibodies against 200-kDa band (corresponding to anti-laminin  $\gamma$  1 antibodies) are found.

Fourteen patients with mean age of  $81.6 \pm 6.5$  years old were included in this retrospective study. Anti-p200 pemphigoid has been associated with psoriasis in previous studies but only one patient in this study had psoriasis. The most frequent associated diseases were cardiovascular disorder (78%). Most patients had large blisters and extensive involvement. Over half of patients (57%) had mucosal involvement and which may be related to high laminin  $\gamma$  1 in the mucosa. Twelve patients had other skin presentations such as urticarial, eczematous, prurigo-like lesions and scar. One patient developed rosette-like

herpetiform, dyshidrosis-like presentation. The clinical presentation was heterogeneous and may resemble bullous pemphigoid, mucous membrane pemphigoid, IgA linear bullous dermatoses, dyshidrosis or prurigo. It was difficult to differentiate anti-p200 pemphigoid from other AIBD of dermoepidermal junction (e.g. bullous pemphigoid, IgA linear bullous dermatosis) solely by clinical presentation. Subepidermal blisters were found in all patients. Dermal infiltrate were also variable as follows: neutrophilic in two patients, eosinophilic in five patients, neutrophilic and eosinophilic in seven patients. It ran a more severe course than previously reported and relapse (50%) was frequently found even after systemic treatment. Thirty-six percent of patients died and only one patient had complete remission. High mortality rate may be related to old age, use of systemic steroid or immunosuppressants.

In conclusion, anti-200 pemphigoid is a more severe disease than previously reported and runs a heterogeneous course.

### **Combined treatment of anogenital HPV infection with cryodestruction, podophyllin 25% and post-ablation immunomodulation with sinecatechins 15% ointment – a retrospective analysis**

Juhl ME, Seferovic V, Antonijevic S, Kronic A.  
Int J STI AIDS 2016;27:1071-8.

Anogenital warts (GW) are caused mainly by low-risk type human papillomavirus (HPV). Recently sinecatechins which is a green tea leaf derivative with possible immunostimulatory, antiviral and anti-proliferative activity was approved as 15% ointment and 10% ointment in United States and Europe respectively in treatment of GWs. The aim of this retrospective study was to evaluate the clearance rate (CC) and recurrence rate (RR) of this combination of cryodestructive method and sinecatechins.

Adult patients aged 18-65 years with first-time diagnosis of GW, not previously treated, in good past health and immunocompetent were included. Patients with warts affecting greater than 10 cm<sup>2</sup> area, pregnant, breastfeeding, with cardiac, pulmonary, renal and other chronic diseases were excluded. All were advised to use condom or abstain from sexual intercourse during treatment and women were advised to use contraception as well.

All cases were treated with cryosurgery using a spray method with 20-30 seconds of direct freeze in two cycles after 30 to 40 seconds of thaw time. After freezing, 25% podophyllin (max 0.5 ml) was applied to all lesions after which patients were advised to wash off 6 hours later. Sinecatechins were applied two weeks later, three times daily until the lesions were completely cleared or for a maximum of 16 weeks. If lesions persisted or recurred, the treatment was repeated after four weeks.

A total of 27 patients were included. The clearance rate was 96.3% and recurrence rate was 7.4%. Sixteen patients required two treatment cycles. Only two patients had severe side-effects including severe oedema and vesiculation and stopped the sinecatechins after four weeks. However, there was no recurrence at the end of the study period. Six patients had mild adverse effects like mild oedema, itching and erythema but were able to continue the sinecatechins after one-week break until complete clearance of warts.

The authors concluded that as this combination may achieve a high clearance rate further randomised controlled trials may be considered.

### **A Scottish multi-centre service evaluation examining the prevalence and diagnosis of *Trichomonas vaginalis* in symptomatic women attending sexual health clinics**

Shone J, Winter A, Jones BL, Butt A, Brawley D, Cunningham C, et al.

[Int J STD AIDS 2016;27:1066-70.](#)

Trichomoniasis, caused by *Trichomonas vaginalis* (TV) is a common sexually transmitted infection. Microscopy is a highly specific but low sensitivity in diagnosis of TV infection. Nowadays, molecular testing improves its diagnostic sensitivity. In this study, three methods: (1) TV APTIMA (TVA); (2) in-house real-time PCR and (3) microscopy were used to evaluate the prevalence of TV infection.

Female patients aged over 16 presented with vaginal discharge attending three Scottish sexual health clinics were recruited. In addition to routine swabs, two additional swabs were collected for TVA and in in-house real-time PCR. A case was defined as true positive if two of the three TV investigated methods were positive.

In total, 398 patients were tested. The prevalence of TV by microscopy, TVA, and in-house real-time PCR was 2.3% (n=9), 3.3% (n=13) and 3.0% (n=12) respectively. The sensitivity by microscopy, TVA, and in-house real-time PCR was 81.8%, 100% and 100% and the specificity was 100%, 99.5% and 99.7% respectively. The positive predicted value was 100%, 84.6% and 91.7% in microscopy, TVA and in-house real-time PCR respectively.

Co-infections were noted in two TV patients: one had both TV and Herpes Simplex infection and one had TV and Chlamydial infection. One patient had co-infection with chlamydia and gonococcus but without TV. Among those had TV, 73% were aged over 29 whereas 97% of chlamydia infection were aged below 30 years.

The authors concluded that they provided supportive evidence that both commercial and in-house molecular assays showed increased sensitivity in TV detection when compared with microscopy even within centres with expert microscopists.

### **Clinical outcomes and response of patients applying topical therapy for pyoderma gangrenosum: A prospective cohort study**

Thomas KS, Ormerod AD, Craig FE, Greenlaw N, Norrie J, Mitchell E, et al.  
*J Am Acad Dermatol* 2016;75:940-9.

Pyoderma gangrenosum (PG) is a painful ulcerating disease. Treatment usually requires systemic immunosuppressive agents which can be associated with significant morbidity and mortality. Topical agents have been advocated for localised disease but there is limited clinical evidence for this. In this multi-centre prospective cohort study, the authors aimed at investigating the efficacy of topical therapies in treatment of PG.

Patients with a diagnosis of PG confirmed by a dermatologist and skin biopsy done to exclude other aetiologies, and who presented with one or more measureable ulcers were included. Those who had pustular or granulomatous variants and had received oral prednisolone, cyclosporine or intravenous immunoglobulin for the treatment of PG in previous months were excluded. Patients were freely prescribed topical treatments according to local practice. Those with more severe disease were also eligible if systemic treatments were contraindicated or the patient preferred topical treatment. The ulcers were measured at weeks 2, 6 and 24, and the speed of healing at 6 weeks was assessed. The proportion healed by 6 months, time to healing, global assessment of improvement and inflammation were also assessed at weeks 6 and 24. Pain and quality of life assessments were measured and included as outcome assessment.

A total of 66 participants enrolled. Forty-nine cases received 0.05% clobetasol propionated, 10 received tacrolimus and the rest received other topical corticosteroids and lymecycline. Five participants were also on concurrent anti-inflammatory treatment including azathioprine, tetracycline and anti-tumour necrosis factor for underlying comorbid conditions. Overall 43.8% of ulcers had healed on topical treatment alone by 6 months, with a median time to healing was 145 days. Thirty-three percent required systemic treatment. Initial ulcer size was a significant predictor of time to healing and four patients showed recurrence at 6 months.

The authors concluded some patients can be managed effectively with topical agents alone and the size of ulcers was the most important predicting factors. However, whether more severe disease will respond adequately to topical agents alone still remains unclear. This study was limited by the lack of a control arm and comparison between the topical agents could not be performed due to the small sample size.

### **American Academy of Ophthalmology Statement: Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision)**

Marmor MF, Keller U, Lai TYY, Melles RB, Mieler WF; American Academy of Ophthalmology.  
*Ophthalmology* 2016;123:1386-94.

Hydroxychloroquine (HCQ) and Chloroquine (CQ) are known to lead to irreversible retinopathy. However, when the retinopathy is recognised early, the damage is mild and the fovea is not threatened after discontinuing the medications. Recent publications have shown that toxicity is not rare among long-term users and the risk is highly dependent on the daily dose by real body weight. The American Academy of Ophthalmology revised the recommendations on screening for CQ and HCQ retinopathy in 2016 and goal of screening

for retinopathy is not to stop HCQ or CQ at the first borderline abnormality, but to recognise definitive signs of toxicity at the early enough stage to prevent a loss of visual acuity.

The academy recommends a maximum daily dose of HCQ  $\leq 5.0$  mg/kg. It is because studies have shown that patients taking HCQ  $\leq 5.0$  mg/kg have less than 1% risk in the first 5 years of therapy and less than 2% up to 10 years. The risk increases sharply to around 20% after 20 years. Although the risk is smaller with lower doses, there is no truly "safe" dosage for long term use. Moreover, the annual incremental risk for a patient taking  $\leq 5.0$  mg/kg HCQ who shows no signs of toxicity

is less than 1% during the first 10 years of therapy and increases to only approximately 4% after 20 years. Since there are no similar studies on CQ, HCQ 5.0 mg/kg is estimated to be equivalent to 2.3 mg/kg CQ.

As a result, the academy suggested baseline screening for all patients on long-term HCQ or CQ and baseline screening should be performed within the first year of starting the drugs and annual screening after five years of use or sooner in case of the presence of major risk factors including (1) HCQ  $> 5$  mg/kg or CQ  $> 2.3$  mg/kg; (2) impaired renal function; (3) on tamoxifen and (4) underlying retinal and macular diseases.