Journal Watch

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Association of pediatric psoriasis severity with excess and central adiposity: an international cross-sectional study

Paller AS, Mercy K, Kwasny MJ, Choon SE, Cordoro KM, Girolomoni G, *et al.*
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Children with psoriasis have been shown to be at risk of obesity. The waist circumference (WC) and waist-to-height ratio (WHR) are better predictors of cardiovascular risk than body-mass index (BMI) and they are of more sensitive predictors of metabolic diseases. This international cross-sectional study aimed to determine whether psoriasis severity in children was associated with excess adiposity by measuring WC and WHR. Excess adiposity was defined by overweight or obese (overweight: BMI 85-95th percentile; obese: BMI>95th percentile).

A total of 409 children with moderate to severe psoriasis were recruited and another 205 children were recruited as controls. Psoriasis children of all severities showed a higher risk of excess adiposity compare to controls (OR=2.65, 95% CI: 1.70-4.15). The risk of obesity in psoriasis children with all severities compare to controls was even higher (OR=4.29, 95% CI: 1.96-9.39). The risk of obesity was higher in those with severe psoriasis compared to controls (OR=4.92, 95% CI: 2.20-10.99) while the risk of obesity in moderate psoriasis was high but not as severe psoriasis (OR=3.60, 95% CI: 1.56-8.30). The risk of central adiposity (WC>90th percentile) was higher in psoriasis of all severities compared to controls (OR=2.52, 95% CI: 1.24.5.12). The risk of higher WHR (>0.539) was significantly greater in psoriasis of all severity compared to controls (OR=3.10, 95% CI: 1.39-6.90).

The authors also found that childhood-onset psoriasis was associated with higher risk for obesity than adult-onset psoriasis. In conclusion, children with psoriasis, in particular severe psoriasis, were at increased risk of obesity and thus at risk of complications such as metabolic and cardiovascular diseases.

Tumor recurrence five years after treatment of cutaneous basal cell carcinoma and squamous cell carcinoma

Chren MM, Linos E, Torres ES, Stuart SE, Parvataneni R, Boscardin WJ.
J Invest Dermatol 2013;133:1188-96.

This was a prospective study to compare the efficacy of common treatments of non-melanoma skin cancers (NMSC), namely basal cell carcinoma and squamous cell carcinoma, with respect to prevention of recurrences. There is currently insufficient data to allow any evidence-based decision making in the treatment of NMSC.

The study recruited 1253 patients during 1999-2000, of which 1174 patients were finally analysed with available follow-up information. The treatment modalities were destruction (electrodessication and curettage), excision and Mohs surgery. The median follow-up time was 7.4 years. A total of 652 patients were alive and

522 patients had died up to December 2011. The unadjusted five year recurrence rate overall was 3.3% (95% CI=2.3-4.4). The recurrence rate did not differ significantly among different treatments: 4.9% after destruction, 3.5% after excision and 2.1% after Mohs surgery (p=0.26). There was also no significant difference in terms of risk of recurrence at five years between excision and Mohs surgery after adjustment for conventional risk factors in patients, tumour and type of care.

In conclusion, this study showed that there was no significant difference in terms of tumour recurrence at five years for NMSC among the three treatments described. The limitations of this study included non-randomised basis, limited centres and patients and dermatologists involved; causing less generalisability of the results. Further studies to guide the choice of treatment for various clinical subgroups of NMSC are required.

Use of emollients in dry-skin conditions: consensus statement
Moncrieff G, Cork M, Lawton S, Kokiet S, Daly C, Clark C.
Clin Exp Dermatol 2013;38:231-8.

Dry skin is a common symptom of skin conditions that can be aggravated by environmental factors, which in turn lead to a flare of underlying condition. In diseased skin, there is a raised stratum corneum (SC) pH level and decrease in natural moisturising factor. Simple emollients, such as petrolatum, provide a fine occlusive layer of non-physiological lipid on skin surface to reduce water loss. Emollients could be added with additional formulation include: humectants (urea and glycerol, which hold water in SC), physiological lipids (ceramides, cholesterol and free fatty acid, which restore intercellular lipid matrix) and antipruritic agents.

The general consensus is that emollients should be used as the first-line therapy for all dry-skin conditions. Emollient therapy should be initiated at an early stage, with adequate quantity and

applied generously. The recommendation is 250-500 g/week, in a 10:1 ratio of emollient to steroid (as emollients have a steroid-sparing effect).

In general, leave-on occlusive emollient creams should be used as first-line therapy in atopic dermatitis, and ointment formulation for severe dry-skin conditions. Humectant-containing emollients should be used as first-line therapy for cases where simple emollients are not effective, or greasier products are unacceptable. Antipruritic emollients should be used as an adjuvant in pruritic dermatoses. Emollient products like emulsifiers for bathing and bath oils should be used in conjunction with leave-on emollients. In particular, due to the irritation property and damage of epidermal barrier of sodium lauryl sulphate (SLS), emollient with SLS as leave-on or washing product should not be used. In atopic eczema, application of emollients and topical steroids should be separated by 30 minutes, and topical tacrolimus by one hour.

Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria
Maurer M, Rosen K, Hsieh HJ, Saini S, Grattan C, Gimenez-Arnau A, et al.
N Engl J Med 2013;368:924-35.

Some patients with chronic idiopathic urticaria (CIU) do not respond despite high dose off-label use of H1-antihistamines. Omalizumab is a recombinant humanised monoclonal antibody that reduces the levels of free IgE and high-affinity receptor for the Fc region of IgE (FceRI) in basophils and mast cells. It has been shown in phase II studies to be effective in CIU patients.

A multicentre, randomised, double-blind, placebo-controlled, industry-sponsored study was carried out to evaluate the efficacy and safety of omalizumab in patients with moderate-to-severe CIU who remained symptomatic despite H1-antihistamine therapy. Total 323 patients between the ages of 12 and 75 years were recruited. They

were randomised to receive one of three doses of subcutaneous omalizumab (75 mg, 150 mg, or 300 mg) or matching placebo. They received a dose once every four weeks for 12 weeks, followed by a 16-week untreated follow-up period. The primary outcome was the change in weekly itch-severity scores on a 21-point scale.

The baseline weekly itch-severity score was approximately 14 in all four groups. At week 12, the score dropped significantly in the 150-mg dose group (-8.1±6.4, p=0.001) and more in the 300-mg group (-9.8±6, p<0.001), while the 75-mg group and the placebo group did not show significant improvement. Both Dermatology Life Quality Index and Chronic-Urticaria Quality-of-Life Questionnaire improved slightly for the 150-mg and 300-mg groups compared with placebo. Patients in the 300-mg group took four fewer 25-mg diphenhydramine tablets than those in the placebo group. The frequency of adverse events was similar across all groups (about 60%). Adverse events were more common in the 300-mg dose group (6% vs. 3% in placebo; statistical significance not reported).

The onset of effect was noted to be within one week of initiation of omalizumab. Within the 28 weeks, there was no rebound increase in symptoms after completing treatment though gradual recurrence of symptoms (itch and urticaria) after discontinuation of treatment was noted.

Dermatomyositis is associated with an increased risk of cardiovascular and cerebrovascular events: a Taiwanese population-based longitudinal follow-up study

Lai YT, Dai YS, Yen MF, Chen LS, Chen HH, Cooper RG, et al.

Br J Dermatol 2013;168:1054-9.

This prospective age- and sex-matched case-control study was conducted in Taiwan to investigate the risks of acute myocardial infarction (AMI) and ischaemic stroke in patients with dermatomyositis (DMS) by using the data from the National Health Insurance claim database between 2000 and 2003. The study included a DMS group of 907 subjects and a non-DMS control group of 4535 subjects. During the 2-year follow-up period, fourteen patients with DMS (1.5%) and 18 control subjects (0.4%) developed AMIs. The crude hazard ratio (HR) for AMI in patients with DMS was thus 3.96 and the adjusted HR was 3.37 (95% CI 1.67-6.80, p=0.0007) after adjusting group demographic and comorbidity differences. Forty-six (5.1%) subjects with DMS developed ischaemic stroke compared with 133 (2.9%) in the control group, giving the crude HR of ischaemic stroke 1.78 and the adjusted HR was 1.67 (95% CI 1.19-2.34, p=0.0028) after adjusting the between-group demographic and comorbidity differences. The AMI-free and stroke-free survival were significantly lower in DMS patients (p<0.0001). The adjusted relative mortality ratio of DMS group was 2.13 (95% CI= 1.53-2.96, p<0.0001).

The author thus concluded that DMS is associated with increased risk of acute myocardial infarction and ischaemic stroke. This study is limited by lack of data regarding other lifestyle confounding factors such as smoking and alcohol consumption. The study subjects were all of Chinese ethnicity; results may not be applicable to other ethnic group.

Self-collected swabs of the urinary meatus diagnose more *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections than first catch urine from men

Chernesky MA, Jang D, Portillo E, Smieja M, Gilchrist J, Ewert R, et al.

Sex Transm Infect 2013;89:102-4.

Self-collection of samples in Sexually Transmitted Infection (STI) management is particularly useful for point-of-care testing. The aim of this study was to compare the first-catch-urine (FCU) and self-

collected meatal-flocked swabs and Dacron APTIMA swabs in diagnosing urogenital *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC) infection.

A total of 511 men aged from 15-24 years who first attended a youth clinic in Canada were included. More than 80% were asymptomatic. First-catch-urine and self-collected APTIMA swabs were collected in Group A (n=293). In addition to those specimens in Group A, self-collected flocked swabs were also collected in Group B (n=218). The specimens were tested by APTIMA Combo 2 assay. The prevalence of CT and GC were 6.8% (20/293) and 4.4% (13/293) in Group A and 9.1% (20/218) and 0.5% (1/218) in Group B respectively. For the sensitivity of CT, it was 90% (Group A) and 85% (Group B) in swab samples whereas only 85% and 80% in FCU respectively. For the sensitivity of GC, it was 100% in both Group A and B swab samples whereas only 84.6% in FCU. Overall 92% of patients expressed no difficulty collecting either FCU or meatal swab and 63% preferred FCU. Amongst those who preferred swabbing, 60% chose the flocked swabs.

This study concluded that regardless of the swab type, swabbing from the meatus had a higher sensitivity than FCU, thus enabling more cases of CT and GC to be identified.

How likely is environmental or patient cross-contamination of *Chlamydia trachomatis* DNA to lead to false positive results in patients attending our clinic?

Chan SY, Jose S, King R, Pakianathan MR, Sabin C, Sadiq ST, et al.
Sex Transm Infect 2013;89:105-7.

Chlamydia trachomatis (CT) can survive on surfaces up to 30 hours. This raises the concern of contamination of specimens in the Sexually Transmitted Infection (STI) clinic. The aim of this study was to investigate environmental and patient cross-contamination of specimen in STI clinic.

The potential contaminations were tested by two ways: (1) A run of dummy samples processed as normal: 60 dummy urine samples and 10 dummy swabs. Two vials of sterile water and the universal container were taken to the toilet which was flushed with the containers opened. The sterile water was emptied into the container and processed identically as the usual specimen. The dummy CT swabs not used before were opened and placed on the tray of examination room for a week before sending to the laboratory as usual. (2) A patient-throughput analysis was performed to assess the patient attendance on a given day. It was classified as low (<100), moderate (100-149) or high (>150).

About 9.6% (2860 / 29748 new attendance) had positive CT infection. Those under age 25 years had a statistically significant higher rate of CT infection (16.7%) than those older than 25 years (7.4% 25-40; 3.4% >40). Around 11% positive results were obtained on low-attendance days compared with 9.0% and 9.7% on moderate and high attendance days respectively. However, after adjustment for age and sex, busy and moderate throughput did not show any significance of the positive result compare with low attendance days. All dummy urine and swabs samples were negative for CT.

Although there may be a hypothesis that contamination was more likely on busier days due to high throughput, this study found no evidence to support the hypothesis of any detectable cross-contamination of specimen in STI clinic.

Food patch testing for irritable bowel syndrome

Stierstorfer MB, Sha CT, Sasson M.
J Am Acad Dermatol 2013;68:377-84.

Irritable bowel syndrome (IBS) used to be classified as a functional disorder. With the evidence of ongoing low-grade gastrointestinal tract inflammation in IBS patients demonstrated in recent studies, this classification was challenged.

The authors hypothesised that food and food additives may cause allergic contact enteritis that may result in IBS symptoms. In this study, patients with physician-diagnosed IBS or those with gastrointestinal symptoms of unknown aetiology were recruited. Standard skin patch testing was done using raw vegetables and common food allergens. Results were read and recorded by two-board of dermatologist investigators on day 3 and day 4 or 5. Those with one or more doubtful and confirmed food allergens were instructed to avoid the allergens in question for one week. Afterwards, they were asked to complete a brief follow-up self-administered questionnaire concerning the compliance of food avoidance, symptom change and grading of symptom improvement after one-week of food avoidance.

Among 51 participants, 30 (58.8%) of them showed one or more doubtful and positive reactions. Garlic showed the most postive reactions. Fourteen of those who had positive patch test reactions did report various degrees of improvement in bowel symptoms after one week of food avoidance (3 slight, 8 moderate and 3 great improvement), while 9 showed no improvement and seven did not complete the food avoidance phase.

With the demonstration of positive skin patch tests and the improvement of symptoms after avoiding the possible food allergens, the authors concluded that food-related type IV hypersensitivity reaction should be considered in the pathogenesis in IBS. However, this study was limited by the small sample size, unblinded nature of assessment and short duration of follow-up.

Histopathology and correlates of systemic disease in adult Henoch-Schönlein purpura: a retrospective study of microscopic and clinical findings in 68 patients at Mayo Clinic

Poterucha TJ, Wetter DA, Gibson LE, Camilleri MJ, Lohse CM.
J Am Acad Dermatol 2013;68:420-4.

Henoch-Schönlein purpura (HSP) is an IgA-mediated leukocytoclastic vasculitis (LCV), and may be associated with renal or gastrointestinal involvement. Previous studies had focused on the prognostic implications of various clinical and laboratory findings with renal involvement, but the correlation with histopathological findings were lacking.

In this retrospective study, the authors reviewed the clinical records and pathological slides of adult patients with HSP who had been seen at the Mayo Clinic between 1992 and 2011. A total of 68 patients were included. Systemic involvement, namely renal, gastrointestinal and joint involvement were found in 44%, 40% and 47% of cases respectively. Furthermore, patients older than 40 years old and those with the absence of eosinophils on skin biopsy specimens were at significantly higher risk of renal involvement (75% vs 27%, p<0.001), while those who showed LCV with an absence of histiocytes were at higher risk of gastrointestinal involvement (p=0.03). Young patients (age<40) were having more gastrointestinal involvement and joint involvement (p=0.004 and p=0.06 respectively).

The presence of eosionophils could be a marker of drug-induced HSP, and it had been shown in previous studies that drug-induced vasculitis had a lower risk of renal involvement. The authors concluded that as the cause of HSP could not be easily identified in most of the adult cases, the presence of eosinophils may be helpful in determining the risk of renal involvement in those cases. This study was limited by the retrospective nature and in most cases, the cause of HSP could not be attributed to drug administration.

Efinaconazole 10% solution in the treatment of toenail onychomycosis: two phase III multicenter, randomized, double-blind studies

Elewski BE, Rich P, Pollak R, Pariser DM, Watanabe S, Senda H, et al.

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Onychomycosis can result in patient distress, pain and disability. However, topical nail lacquers are of negligible efficacy, while oral antifungal agents are associated with hepatotoxicity and various drug interactions.

Patients with mild to moderate toenail distal lateral subungual onychomycosis (DLSO) were recruited. Inclusion criteria included age of 18-70 years, clinical diagnosis of DLSO affecting at least one great toenail, target toenail should have an uninfected length of 3 mm or more from proximal nailfold and thickness less than 3 mm, positive potassium hydroxide microscopy results and culture showing dermatophyte or mixed dermatophyte/ Candida infection. Eligible patients were then randomised to receive efinaconazole 10% solution or vehicle self-applied once daily for 48 weeks without debridement.

A total of 1655 patients were recruited in these two studies of which 1239 patients were randomised to efinaconazole group while 416 to vehicle group. Overall, 86.8% of patients completed the active treatment and 85.8% completed the 4-week post-treatment follow-up. In both studies, patients received efinaconazole showed a significantly higher rate of complete cure at week 52 (study 1: 17.8% vs. 3.3%; study 2: 15.2% vs. 5.5%; both p<0.001). Similar findings were also shown mycologically (study 1: 55.2% vs. 16.8%; study 2: 53.4% vs. 16.9%; both p<0.001). Efinaconazole was generally well-tolerated and only 2% experienced local site reactions resulting in discontinuation of treatment.

The authors concluded that topical efinaconazole can be considered as an alternative to oral treatments. However, this study was limited by its short treatment period and the lack of follow-up to assess recurrence. Also, the highly-selected patient group compromised its generalisability.

Propranolol in a case series of 174 patients with complicated infantile haemangioma: indications, safety and future directions

Hermans DJ, Bauland CG, Zweegers J, van Beynum IM, van der Vleuten CJ.

Br J Dermatol 2013;168:837-43.

This case series was prospectively collected between September 2008 and January 2012 in a tertiary centre in Netherlands to provide data on indications and side-effects of propranolol for complicated infantile haemangioma (IH). A total of 174 children with potentially life-threatening and/or complicated IH were included in the study. Propranolol was administered from the starting dosage up to a maximum of 2.5 mg/kg daily and was stopped at the age of 12-18 months. One hundred and twenty-three patients were girls (70.7%) and thirty-nine patients (22.4%) were premature babies. Treatment was successful within 72 hours in 168 patients (96.6%). The mean age at the start of the treatment was 4.8 months and the mean duration of treatment was 10.7 months. Possible side-effects during treatment were recorded for 108 patients (62.1%) and most adverse reactions were not serious and reversible and dose dependent. The most important adverse effects were hypotension (3.4%), wheezing (9.2%), nocturnal restlessness (22.4%) and cold extremities (36.2%). The author concluded that propranolol is an effective and safe therapeutic option for IH. The limitation of this study is that the effect of treatment by propranolol was not quantified objectively and this was not a controlled trial.

Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses

Samarasekera EJ, Sawyer L, Wonderling D, Tucker R, Smith CH.

This Network meta-analysis was conducted to summarise the evidence on topical treatments in chronic plaque psoriasis and to find the data on the efficacy of topical treatment so as to inform the health authority about the cost-effectiveness and recommendations for treatment. The study was conducted through systematic literature search of Medline, Embase, Cinahl and The Cochrane Library for randomised, placebo-controlled or head-to-head trials of U.K.-licensed topical therapies. Interventions included were vitamin D containing combination therapies, corticosteroids, tar, dithranol and retinoids. Data were stratified according to the site: trunk and limbs, and scalp. Total 48 studies were included for trunk and limb psoriasis and 17 for scalp psoriasis (totally 22,028 patients). The majority included patients with moderate to severe psoriasis.

The combination of potent topical steroid and vitamin D analogue was the most effective treatment for trunk and limbs. For scalp psoriasis, very potent topical steroid was the most effective treatment while coal-tar shampoo was the least effective. Increasing treatment frequency did not improve efficacy in scalp psoriasis. There was discordance between physician and patient assessed outcome, hence both should be included in the evaluation of efficacy. The authors concluded that potent or very potent topical corticosteroids are the most effective when used continuously for up to 8 weeks and intermittently for up to 52 weeks. However there were no long-term safety and efficacy data including relapse rate. There were also no data to indicate the optimal time to restart treatment for relapse and how to maintain remission with topical treatment.