Journal Watch

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**Association of androgenetic alopecia with metabolic syndrome in men: a community-based survey**
Su LH, Chen THH.

This was a population-based cross-sectional survey conducted in Taiwan between April and June 2005 to determine the association between metabolic syndrome and androgenetic alopecia (AGA).

Men with alopecia screened from the community-based survey on the prevalence of AGA in Tainan County and aged 40 years or above were included in the study. The AGA severity was assessed with Norwood classification and was categorized as normal to mild AGA (Norwood types I-III) and moderate to severe AGA (Norwood types IV-VII). Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III. Parameters including waist circumference and blood pressure were recorded. Blood sample of glucose and lipid profiles were collected. A total of 670 subjects aged 40-91 years participated in the survey.

In this study, the overall prevalence rate of metabolic syndrome among the 670 participants was 16.6% (n=111). The results revealed that the risk of having AGA type IV or above in subjects with metabolic syndrome was 1.51-fold increase (P=0.08) in the unadjusted model and 1.67-fold increase (P=0.04) in the adjusted model. It also showed that severe AGA conferred a 2.6-fold higher risk of metabolic syndrome compared with moderate AGA. Among lipid profiles, a negative gradient relationship between the level of high-density lipoprotein cholesterol (HDL-C) and the risk for moderate or severe AGA was demonstrated with odds ratio reducing from 0.55 to 0.32 (P<0.001).

The author suggested a significant association between AGA and metabolic syndrome and HDL-C was of particular importance among all lipid profiles.

**Probiotics in pregnant women to prevent allergic disease: a randomized, double-blind trial**
Dotterud CK, Storro O, Johnsen R, Oien T.

This was a randomized double-blind trial performed from September 2003 to December 2007 in Norway to investigate whether a probiotic supplement given to pregnant women would reduce the incidence of allergic disease and allergic sensitization in children both with and without a family history of atopy.

Eligible pregnant women were randomized in a double-blind manner to 250 mL probiotic low fat fermented milk or placebo milk per day during the last 4 weeks of pregnancy up until 3 months after birth. The probiotic milk, Biola, contained *Lactobacillus rhamnosus* GG, *Bifidobacterium animalis* subspecies *Lactis* Bb-12 and *L. acidophilus* La-5. The primary endpoint was diagnosed allergic rhinoconjunctivitis (ARC), asthma or atopic dermatitis (AD) according to the U.K Working Party’s diagnostic criteria for AD during the first 2 years of life. Atopic sensitization was assessed by a positive in skin prick test (SPT) or elevated specific IgE (≥0.35 kU) and defined as atopic sensitised if either was positive. Total 415 pregnant women were recruited into probiotic group (n=211) or placebo group (n=204). At 2 years, 138 and 140 children in the probiotic and the placebo groups, respectively, completed the study.
In the Intention to treat analysis, the odds ratio (OR) of the cumulative incidence of AD in the probiotic group to the placebo was 0.51 (P=0.013), but there was no significant effects on asthma, ARC or atopic sensitization. The AD severity was assessed using the Nottingham Eczema Severity Score and the children with AD in the probiotic group had a significantly (P=0.044) reduced risk of moderate AD. In the complete-case analysis, there was a significant difference in the cumulative incidence of AD between the probiotic and placebo groups (P=0.022) and the relative risk was 0.61. Subgroup analyses regarding family history of atopy showed that the effect of probiotic on AD was statistically significant (OR 0.09) among those without a family history of atopy.

The authors concluded that probiotics given to nonselected mothers reduced the cumulative incidence and severity of AD and the primary preventive effect was most evident in children without a family history of atopy.

A phase IIIb, multicentre, randomized, double-blind, vehicle-controlled study of the efficacy and safety of adalimumab with and without calcipotriol/betamethasone topical treatment in patients with moderate to severe psoriasis: the BELIEVE study

Thaci D, Ortonne JP, Chimenti S, Ghislain PD, Arenberger P, Kragballe K et al.

This is a randomized double-blind controlled trial enrolling patients from 15 countries across Europe. The aim is to assess the efficacy and safety of adalimumab (ADA) with and without topical calcipotriol/betamethasone (C/B) in patients with moderate to severe psoriasis.

Adult patients with chronic plaque psoriasis, who had previously failed or intolerant to at least two different systemic or biologic therapies, who fulfilled at least two of three severity criteria namely Psoriasis Area and Severity Index (PASI) ≥10; BSA ≥10%; and/or Dermatology Life Quality Index (DLQI) ≥10, were eligible for the study. A total of 730 patients were enrolled into the BELIEVE study; in which 366 were allocated ADA + C/B and 364 received ADA + vehicle. Efficacy was assessed at weeks 2, 4, 8, 12 and 16. The primary efficacy analysis compared the proportion of patients who achieved a 75% improvement in the PASI (PASI 75 response) at week 16 in each treatment group. Secondary efficacy endpoints included PASI 75, PASI 90 and PASI 100, mean PASI score, Physician’s Global Assessment, visual analogue scales for pruritus and pain, and the DLQI. Initial efficacy was measured throughout the study.

The proportion of patients achieved PASI 75 response at the first four weeks was significant higher in the combination therapy group. PASI 75 response rates were 14.8% vs. 5.8% at week 2 and 40.7% vs. 32.4% at week 4 for ADA + C/B and ADA + vehicle respectively. After week 4, the trend was towards a higher response with ADA monotherapy, with no statistical difference in the PASI 75 response at week 16 (64.8% for ADA + C/B vs. 70.9% for ADA monotherapy). Safety outcomes in this study were favourable and serious adverse events were observed in only 4.2% of patients overall (31/730), with similar rates in each treatment group (4.4% for ADA + C/B vs. 4.1% for ADA + vehicle).

The authors thus concluded that ADA + C/B resulted in a more rapid response and higher efficacy within the first 4 weeks; thereafter, the trend was towards a higher response with ADA monotherapy.

Infantile haemangiomas with minimal or arrested growth: a retrospective case series

Suh KY, Frieden IJ.
Arch Dermatol 2010;146:971-6.

This is a retrospective study to review the clinical features of infantile haemangioma with minimal or arrested growth (IH-MAG). The majority of infantile haemangiomas (IH) presented with lesions arising from normal skin or preceding skin mark such as patch of paleness or telangiectasia or bruise, followed by typical rapid growth phase. A small number of IH were noted to have minimal or arrested growth after the initial presented markings. The authors defined the IH-MAG as
growth portion of the IH equal to or less than 25% total surface area. These lesions were sometimes mistaken for port-wine stain or vascular malformation.

The cases were recruited from University of California, San Francisco. The case records and clinical photos with IH-MAG were retrieved over a period of three and a half years. A total of 42 patients with 47 IH-MAG were included. The female to male ratio was 2 to 1 and the majority (77%) was non-Hispanic white. About 68% of IH-MAG were below the waist. Most of the IH-MAG (45%) were smaller than 5 cm². It was 26-times more likely to have IH-MAG in lower body than classic IH. The most common appearance of IH-MAG was fine or coarse telangiectasia in a vasoconstricted patch. The proliferative component if present was usually small bright red papules in the periphery. Majority of IH-MAG was localised (64%) and 30% was segmental and 6% indeterminate. Proliferation was absent in 70%. Ulceration appeared in 9% of cases compare to 15-23% of previously reported series of IH. The presence of IH-MAG did not predict the proliferative potential of concomitant IH in the same individual.

This study is limited by small sample size and retrospective nature, further study with long term follow-up to determine the involution time of IH-MAG is necessary.

**Staphylococcus aureus carriage in the anterior nares of close contacts of patients with atopic dermatitis**
Chiu LS, Chow VC, Ling JM, Hon KL. Arch Dermatol 2010;146:748-52.

This is a prospective case-control study to determine the prevalence of Staphylococcus aureus (S. aureus) colonisation in close contacts of patients with atopic dermatitis (AD) and the effect in severity of disease. A total of 211 subjects were recruited, including 50 AD patients, 50 non-AD controls, 60 close contacts of AD patients and 51 close contacts of controls. Nasal swab and skin swab were taken to determine S. aureus colonisation state in AD patients, controls and contacts.

The demographic characteristics of patients and non-AD controls were of no significant difference. There was significantly more nasal colonisation of S. aureus in AD patients than non-AD controls. There was also significantly more colonisation of S. aureus in close contacts of AD patients than close contacts of non-AD controls. In addition, after exclusion of those close contacts of AD patients who had AD, there was still significantly more nasal colonisation of S. aureus in close contacts of AD patients than close contacts of non-AD controls. When comparing patients with severe AD and non-severe AD, there is significantly more nasal and skin colonisation of S. aureus in severe AD patients. The SCORAD of AD patients with S. aureus colonisation was significantly higher than those without S. aureus colonisation. Only skin colonisation with S. aureus was found to be the independent variable associated with severe AD.

The authors concluded that the anterior nares of close contacts of AD patients were important pool of S. aureus and the skin colonisation of S. aureus was independently associated with severe AD. This study is limited by small sample size and the recruitment of AD patients mainly with mild to moderate severity.

**A randomized, double-blind study comparing the efficacy of selenium sulfide shampoo 1% and cicloprox shampoo 1% as adjunctive treatments for tinea capitis in children**

Tinea capitis is not uncommon and its treatment goals include: to actively treat the dermatophyte infection, to eradicate the spores to prevent relapse or spread of disease, and to decrease the length of time of infectivity.

Selenium sulfide has a proven efficacy as adjuvant treatment in tinea capitis but has a sulfuric odor and drying effect. In contrast, cicloprox shampoo is odor-free and better tolerated. The objective of
this study was to compare the efficacy of selenium sulfide shampoo 1% and ciclopirox shampoo 1% as adjunctive treatments for tinea capitis in children. This was a randomized, double-blinded study. Forty children aged 1-11 years with clinically diagnosed tinea capitis were randomized to receive either shampoo twice a week as adjunct to an 8-week course of ultramicronized griseofulvin dosed at 10-12 mg/kg/day and then a follow-up period of 4 weeks. Patients were evaluated at week 2, 4, and 8 for clinical signs and scalp mycological cultures. Mycological cure was defined as having zero dermatophyte colonies on Mycosel agar. Subjects who had signs and symptoms of tinea capitis at week 8 continued with the study treatment protocol for another 4 weeks.

Among the forty children, seven were lost to follow-up at various points in the protocol and therefore thirty-three completed the study. Thirty out of thirty-three (90.9%) treated children demonstrated mycological cure. Selenium sulfide shampoo 1% and Cicloprox 1% shampoo seems to be equally effective as adjunctive treatment to tinea capitis.

This was overall a well-designed study. However, the number of subjects was small and the dropout rate was quite high at 17.5% (7/40). The authors suggested that the effects of both shampoos should be investigated further in larger studies.

Methotrexate (MTX), a folic acid antagonist, has been used in patients with psoriasis for more than 50yrs. However, the use of MTX carries risks of myelosuppression and hepatotoxicity in long term use. In our society, chronic psoriasis patients may turn to use alternative medicine or traditional Chinese herbal medicine (TCM) that has been used for centuries and was thought to be effective with little side effects.

This is a randomized, placebo-controlled trial comparing the use of MTX and ‘Wen-tong-hua-yu’ TCM formula in moderate to severe chronic plaque-type psoriasis. Sixty-one eligible patients with a minimum history of psoriasis involving >20% of body surface area were randomly allocated to receive MTX, TCM and placebo. TCM regime was administered by a specialist TCM physician experienced in the treatment of psoriasis with medicinal herbs. The standardized Wen-tong-hua-yu formulation was given in a capsule form which appearance is identical to that of the placebo and the treatment arm using MTX was unblinded. Except aqueous cream and 0.0125% topical flucinolone, all potent topical steroids, phototherapy, systemic therapies, vitamin D analogues, keratolytics and coal tar were stopped 2 weeks before and throughout the study. During the 6 months of study, blinded assessors evaluated the efficacy of treatment at monthly intervals using the Psoriasis Area and Severity Index (PASI), Physicians Global Assessment (PGA) and Psoriasis Disability Index (PDI). Baseline demographic characteristics and mean PASI were similar in different treatment groups.

Finally, 50 patients completed the study. Reasons for withdrawal included drug allergy, acute hepatitis, gastrointestinal side-effects, worries about possible side effects, and perceived lack of efficacy from the treatment. For the patients who completed the study, mean±SD PASI at baseline was 22.0±11.3 in the MTX group, 18.9±8.2 in the TCM group and 20.4±10.8 in the placebo group. After 6 months of treatment, the scores were 5.7±8.5, 16.0±9.8 and 13.9±10.1, an improvement of 73.9%, 15.1% and 32.1% respectively. The difference in response between MTX and TCM groups were significant at 2, 4 and 6 months (P<0.01, P<0.05, P=0.001 respectively). There was no difference between TCM and placebo groups (P>0.05).
The authors concluded that the results of this study verify the therapeutic effect of MTX for the management of psoriasis. Despite widespread belief and use of TCM in Asia for the treatment of psoriasis, this study (probably the first comparative study of MTX and TCM using PASI, PGA and PDI) was unable to confirm the efficacy of TCM.

**Evaluation of nail disease in psoriatic arthritis by using a modified nail psoriasis severity score index**


The Classification of Psoriatic Arthritis (CASPAR) Study Group had recently published new criteria for classifying psoriatic arthritis (PsA) which included five items: dactilitis, history of psoriasis and current psoriasis, nail psoriasis, rheumatoid factor negativity, and juxta-articular new bone formation. The aim of this study was to clarify the clinical importance of nail disease in PsA patients diagnosed by the new CASPAR criteria.

Twenty-three PsA patients and 23 patients with uncomplicated psoriasis as controls were included in the study. There were no significant differences in the Psoriasis Area and Severity Index (PASI) score between the two groups. Nail matrix psoriasis included pitting, leukonychia, red spots in the lunula and nail plate crumbling. Nail bed psoriasis included oil drop (salmon patch) discoloration, onycholysis, nail bed hyperkeratosis and splinter haemorrhage. The severity of nail psoriasis was determined by the modified Nail Psoriasis Severity Score Index (mNAPSI). The relationships of mNAPSI with nail fold psoriasis, PASI, swollen and/or tender joints counts (STJC), distal interphalangeal (DIP) joint disease, acute phase reactants and the score on the Japanese version of the Standard Health Assessment Questionnaire (J-HAQ) were analyzed.

Results shown that the mNAPSI in PsA patient was higher than that of controls (4.8±5.3 vs. 2.3±3.7, \( P<0.05 \)). The severity of fingernail disease in PsA patients was significantly associated with DIP joint disease (8.6±5.9 vs. 3.1±3.3, \( P<0.05 \)) and nail fold psoriasis (6.7±5.2 vs. 3.5±5.2, \( P<0.05 \)) when compared with controls. There were no correlations between the mNAPSI and other systemic involvements.

The authors concluded that the nail involvement and prolonged nail bed psoriasis were common in PsA patients and that nail involvement in PsA was among the disorders indicative of distal phalanx enthesitis.

**Impact of weight on the efficacy and safety of ustekinumab in patients with moderate to severe psoriasis: rationale for dosing recommendations**


Systemic therapies for psoriasis must accommodate a broad spectrum of weights because of the high prevalence of obesity among patients with psoriasis. As with many therapeutic agents, clinical response to ustekinumab is associated with serum ustekinumab concentration, which in turn is affected by body weight.

The authors sought to determine whether the optimal dose of ustekinumab is affected by weight in patients with psoriasis. Patients were randomized in two phase III trials (PHOENIX 1 and 2) to receive 45 mg or 90 mg of ustekinumab every 12 weeks (\( n=1331 \)) or placebo with crossover to ustekinumab at week 12 (\( n=665 \)). Efficacy and serum ustekinumab concentrations were to be evaluated by 10-kg increments of body weight at week 28 (steady-state trough level). The results showed that mean baseline weight was 93.9 and 91.0 kg in PHOENIX 1 and 2, respectively. Based on the analyses by 10-kg increments, a cutoff of 100 kg was determined to best differentiate the dose response. The proportion of patients with at least 75% improvement from baseline in Psoriasis Area and Severity Index score was 74.2% for 90 mg and 54.6% for 45 mg in heavier patients (\( \geq 100 \) kg), but the proportion with a response of at least 75% improvement from baseline in Psoriasis Area and Severity Index score was similar between doses (80.8% vs 76.9%) in lighter patients (\(<100 \) kg). Serum ustekinumab concentrations were also
affected by weight, with lower serum concentrations observed in heavier patients at each dose. Safety was not affected by weight. Based on the results of weight-based analyses of clinical and pharmacokinetic data, the authors concluded that fixed dosing of ustekinumab based on weight was appropriate for the treatment of patients with psoriasis. The low numbers of patients at the extremes of body weight may limit the analyses of these subgroups. For moderate to severe psoriasis, fixed dose administration of ustekinumab based on weight has the potential to optimize efficacy and minimize drug exposure while maintaining the convenience and potential safety advantages of using fixed doses.

Influence of evaluation of clinical pictures on the histopathologic diagnosis of inflammatory skin disorders

Clinical information on histologic referral sheets is usually very limited, and particularly for inflammatory skin disorders, dermatopathologists often ask referring physicians for clinical correlation. The authors tested in this study the value of clinicopathologic correlation in the histopathologic diagnosis of inflammatory skin disorders. One-hundred biopsy specimens were digitalized and stored on 3 DVDs along with the clinical images. All cases were evaluated by 9 independent full-time dermatopathologists, initially without looking at the clinical pictures and subsequently after checking them. All diagnoses were finally compared with the ‘reference’ diagnosis established in Graz, Austria, and the results were statistically analyzed. The results showed that after evaluation of the clinical images, the number of dermatopathologists making a correct diagnosis was increased in 70 cases, unchanged in 25 cases, and decreased in 5 cases. The total number of correct diagnoses increased from 332 (diagnoses before evaluation of clinical pictures) to 481 (diagnoses after evaluation of clinical pictures), with a 16.6% increase in the total. The limitation of this study could be due to its computerized setting as it is different from real-life dermatopathology and physical examination of patients. The authors concluded that clinical pictures should be added to biopsy request slips of inflammatory skin disorders whenever possible, as they allow a better interpretation of histopathologic findings.

Pilot, multicenter, double-blind, randomized placebo-controlled bilateral comparative study of a combination of calcipotriene and nicotinamide for the treatment of psoriasis

Calcipotriene has limited efficacy in treating psoriasis. By inhibiting proinflammatory cytokines such as interleukin-12, interleukin-23, and tumor necrosis factor-alpha, nicotinamide may enhance the efficacy of calcipotriene therapy when used in combination. The authors sought to determine if the combination of nicotinamide with calcipotriene is more effective than either component alone. A randomized, double-blinded, multicenter 7-arm bilateral comparison-controlled trial was performed. One hundred and sixty eight patients were randomized to two of 7 treatments: i) placebo, ii) calcipotriene 0.005% alone, iii) nicotinamide 1.4% alone, iv) calcipotriene plus nicotinamide 0.05%, v) calcipotriene plus nicotinamide 0.1%, vi) calcipotriene plus nicotinamide 0.7%, or vii) calcipotriene plus nicotinamide 1.4%, each administered to lesions on one side of the body or to one of two lesions at least 5 cm apart, for 12 weeks. Four patients (2.4%) discontinued the study: two because of patient noncompliance; one because of withdrawal of consent and one because of protocol violation. Efficacy was measured using a clear to almost clear outcome. In all, 50.0% of patients in the calcipotriene and nicotinamide 1.4% combination group achieved a clear to almost clear outcome at week 12, compared with only 18.8% of patients treated with placebo (P=0.002), 25% of patients treated with nicotinamide 1.4% alone (P=0.02), and 31.5% of patients treated with calcipotriene alone (P=0.096). A dose-response trend existed for
increasing concentrations of nicotinamide, but it was not significant. The relatively small patient number, relatively high placebo effect, and maximum in-life portion of only 12 weeks of dosing are weaknesses of the study. This study provides evidence that using the combination nicotinamide and calcipotriene may provide additional benefit in the topical treatment for patients with psoriasis and may be an adequate steroid-sparing substitute treatment.

Diabetes and genital warts: an unhappy coalition

Genital wart (GW) caused by Human Papilloma virus (HPV) infection is a common sexually transmitted disease. The defective cellular immune response such as in HIV infection, the use of immunosuppressants, pregnancy and diabetes mellitus (DM) may contribute to the recurrence, the extensiveness and the treatment responsiveness of the genital warts. The objectives of this study were (1) to investigate whether GW was more common in DM patients in comparison to the general population and (2) to determine whether female patients with DM and GW required more treatment than patients without DM.

This was a 2-year retrospective study done in a United Kingdom local sexual health clinic. Total 562 female patients were diagnosed to have GW during the study period. All these patients were documented in history whether they have DM or not. The data collected was then compared with the Sexual Health Audit and Education (SHAPE) data which was previously done for auditing the treatment of GW in the same unit. 2% (12 out of 562) of the patients had diabetes (8- type I , 4 - type II) and this prevalence was lower than the general population (4-5%). Nine out of the twelve patients were first time to have GW whereas the remaining three patients were recurrent cases. The median age was 32. About 66% (8/12) of these DM patients had moderate to extensive number of GW, in comparison to SHAPE data: 63% had only a single or few GW (<5 lesions). Also more DM patients (41%) had perianal GW in comparison to those without DM (12%). Ten patients received ablative treatment including cryotherapy and topical chemical treatments such as podophyllotoxin, imiquimod, trichloroacetic acid. One patient refused any treatment and 1 had surgical removal because of malignancy. Fewer patients with DM (60%) took less than 12 weeks to clear the GW when compared with SHAPE audit (94%).

In conclusion, although the number of patients with diabetes in the study was small, these data suggest that GW patients with DM did worse than those without DM. They had more extensive disease, required more treatments and lasted for longer period.

Association between smoking and genital wart: longitudinal analysis

Genital Warts (GW) are sexually transmitted caused mainly by Human Papillomavirus type 6 and 11. Smoking may influence the susceptibility to genital warts by immunosuppressive effects or an association with high risk sexual behaviour. The aim of this study is to assess the association between smoking and the reported clinical diagnosis of GW.

A random sample of total 69486 women aged 18-45 from Denmark, Iceland, Norway and Sweden participated in the study by self-administrated questionnaire. They were asked whether they had GW and the age at first diagnosis if they had. Smoking habit including age-specific smoking doses measured by the number of cigarettes smoked daily in the age interval was included. Other information such as debut age of smoking, alcohol drinking, first pregnancy, sexual behaviour including intercourse, condom use, and hormonal contraceptive use were collected. Total 58094 women were included (never-smoker=31908, ever-smoker=26186) and others were excluded as they did not respond to at least one of these questions. About 12.5% of ever-smoker reported to have GW whereas only 8.8% of never-smoker
had GW (p<0.0001). The smokers had an adjusted hazards ratio (HR) of 1.27 (95% CI 1.17-1.37) for having GW compared with non-smokers. The risk of GW also related to dose-response effect of smoking that risk was increased by 0.6% per additional cigarette smoked daily (HR=1.006, 95% CI 1.001 to 1.012). Moreover, smokers were positively associated with high risk sexual behaviour such as more lifetime coital partners (smoker=10.68 vs. non-smoker=5.81), alcohol drinking (smoker=98.7% vs. non-smoker =92.9%) and debut age of sexual intercourse (smoker=16.12 vs. non-smoker=17.48). All these differences were statistically significant and all these high risk sexual behaviour were affirmatively related to GW.

To conclude from this study, smokers had a high risk to have GW. It could be due to direct immunosuppressive effects of nicotine or the smokers participated in more high risk sexual behaviour.