

Journal Watch

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Patients with psoriasis have an increased amount of epicardial fat tissue

Balci A, Celik M, Balci DD, Karazincir S, Yonden Z, Korkmaz I, et al.

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Psoriasis is well-known to be associated with multiple cardiovascular risk factors and coronary artery disease. Recent research has focused on the increased amount of epicardial fat tissue (EFT) in patients with psoriasis which refers to perivascular visceral fat along the coronary arteries. This prospective study aimed to compare EFT and coronary artery calcium score (CACs) in patients with psoriasis with normal healthy controls. Thirty-eight psoriasis patients and 38 age- and gender-matched controls were enrolled in this study. Epicardial fat area (EFA) and CACS were investigated by multi-detector computed tomography. In the current study, a significantly higher mean EFA was observed in psoriasis patients than the controls (13.8 ± 8.4 vs. 9.7 ± 6.4 cm²) ($p=0.02$). However, the mean CACS did not show significant difference between the two groups of patients. EFA was positively correlated with coronary artery calcification and waist circumference in both groups. The authors concluded that patients with psoriasis had a higher level of EFA than normal individuals. This study also confirmed that EFA was an independent risk factor for the presence of coronary artery calcium. It was hypothesised that pro-inflammatory cytokines originated from EFA could have a local effect on the coronary arteries.

Efficacy of switching between tumour necrosis factor- α inhibitors in psoriasis: results from the Italian Psocare registry

Piaserico S, Cazzaniga S, Chimenti S, Giannetti A, Maccarone M, et al.

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Previous studies showed a beneficial role of switching to a second tumour necrosis factor- α inhibitor (TNF-I) in psoriasis patients with an inadequate response or an adverse event to the first TNF-I. The authors of this study investigated the predictors for the efficacy of the second TNF-I in patients discontinuing the first TNF-I. They used data from the Italian Psocare Registry. A total of 5423 consecutive patients starting TNF-I therapy for psoriasis in the period from September 2005 to September 2010 were analysed. In all, 105 patients had been switched to a second TNF-I in the study. Of these patients, 29% and 46% were able to achieve a 75% improvement in the Psoriasis Area and Severity Index score (PASI-75) by 16 weeks and 24 weeks respectively. The authors observed that patients who switched due to secondary loss of efficacy (loss of initial PASI-75 response) or adverse events and/or intolerance were more likely to achieve PASI-75 than those with primary drug failure (PASI-75 never been reached) (hazard ratio: 2.7 [95% CI 1.3-5.5] vs 2.0 [95% CI 1.0-3.9]). The authors suggested that it might be more advantageous to switch to another biologic with a different mechanism of action in patients with primary failure to a TNF-I.

Fields of effects of 2 commercial preparations of botulinum toxin type A at equal labeled unit doses: a double-blind randomized trial

Hexsel D, Hexsel C, Siega C, Schilling-Souza J, Rotta FT, Rodrigues TC.
[JAMA Dermatol 2013;149:1386-91.](#)

Commercially available preparations of botulinum toxin type A, abobotulinumtoxin A and onabotulinumtoxin A, have been used widely for wrinkle correction. Many studies showed controversial results about the fields of effect or diffusion between these two products. The objective of the present study was to assess the fields of effect or diffusion characteristics of abobotulinumtoxin A and onabotulinumtoxin A at the same dose (1:1 labelled unit equivalence) regarding muscle and sweat gland activities.

This prospective, single-centre, randomised, double-blind, non-commercially sponsored study evaluated the fields of effect of the two aforementioned botulinum toxins in 19 subjects. Each subject received two units of abobotulinumtoxin A on one side of the forehead and two units of onabotulinumtoxin A on the other side. The horizontal and vertical diameter and area of the fields of anhidrotic effect, the amplitude of evoked compound muscle action potentials, and the 4-point validated Wrinkle Severity Scale were assessed after 28 days.

It was found that onabotulinumtoxin A had significantly greater diffusion than abobotulinumtoxin A when isovolumetric injections of the same labelled unit doses of the products were injected. However, no significant differences between the products in the Wrinkle Severity Scale scores and evoked compound muscle action potentials were noted, suggesting that both products had similar results for cosmetic use and muscular effect after 28 days.

Prognostic value of skin manifestations of infective endocarditis

Servy A, Valeyrie-Allanore L, Alla F, Lechiche C, Nazeyrollas P, Chidiac C, et al.
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Dermatological manifestations of infective endocarditis include Osler's nodes, Janeway lesions, purpura, splinter and conjunctival haemorrhages. Despite the importance of dermatological manifestations in the diagnosis of infective endocarditis, few investigations have analysed the manifestations of cutaneous infective endocarditis and the prevalence of which remains unclear. This is an observational, prospective, population-based epidemiological study investigating the prevalence of the four main dermatological manifestations of infective endocarditis (Osler's nodes, Janeway lesions, purpura, and conjunctival haemorrhages) and their possible associated factors.

It was found that out of 487 cases, 58 (11.9%) had skin manifestations, including 39 (8.0%) with purpura, 13 (2.7%) with Osler's nodes, 8 (1.6%) with Janeway lesions and 3 (0.6%) with conjunctival haemorrhages. Patients with skin manifestations had a higher rate of infective endocarditis related extra-cardiac complications than patients without skin manifestations, in particular cerebral emboli. Moreover, patients with purpura had larger cardiac vegetations, and Janeway lesions were more associated with extra-cerebral emboli. In conclusion, classic skin manifestations of infective endocarditis are associated with a higher risk of complications that should alert physicians to look for secondary complications, in particular, cerebral imaging. The authors also suggested that in addition to their diagnostic contribution, dermatological manifestations may have a prognostic role in infective endocarditis and influence therapeutic decisions.

Durable remission of pemphigus with a fixed-dose rituximab protocol

Heelan K, Al-Mohammed F, Smith MJ, Knowles S, Walsh S, Shear NH.

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Rituximab is a chimeric murine/human monoclonal antibody which targets the B-lymphocyte surface protein CD20, resulting in B-lymphocyte apoptosis. It has been reported to be an effective treatment for autoimmune bullous dermatoses. However, the optimal dosage regimen and duration of response are unknown. The objective of this study is to assess the clinical response of patients with pemphigus vulgaris or pemphigus foliaceus to rituximab using a modified fixed-dose rheumatoid arthritis protocol.

This is a retrospective single-centre cohort study investigating 84 patients with pemphigus vulgaris and eight patients with pemphigus foliaceus who received rituximab 1 g intravenously on days 1 and 15, with a subsequent dose of 1 g or 500 mg intravenously administered 6 months or more after induction if clinically warranted. The response to treatment, time to relapse and adverse reactions were examined.

It was found that the complete remission rates with or without adjuvant treatment at final follow-up were 89%. The median time to relapse after the first treatment cycle was 15 months. No serious infectious adverse events occurred. The authors concluded that this modified, fixed-dose rheumatoid arthritis protocol of rituximab was well-tolerated and efficacious in patients with pemphigus. Patients who did not achieve remission after one cycle or patients who experienced relapse would benefit from further cycles. Rituximab appeared to be a safe therapeutic option with minimal serious adverse effects.

Malignant and benign forms of atrophic papulosis (Kohlmeier-Degos disease): systemic involvement determines the prognosis

Theodoridis A, Konstantinidou A, Makrantonaki E and Zouboulis CC.

Br J Dermatol 2014;170:110-5.

This prospective single-centre cohort study was conducted between 2000 and 2012 in Germany to assess the demographics, epidemiological data and prognosis of patients with atrophic papulosis. Demographic and clinical data were collected from 39 patients (16 male and 23 female) with atrophic papulosis diagnosed between 2000 and 2007 and followed until 2012. One defaulted follow-up at the end of the study. The mean age of onset was 35.4 ± 12.3 years (95% CI 31.5-39.4). Of these, 11/38 patients (29%) had systemic disease and the remaining had cutaneous signs only throughout the follow-up period. The gastrointestinal tract (73%, 8 of 11 patients) and central nervous system (64%) were the most commonly involved organs and the median time for development of systemic manifestations was one year (0.03-0.97 quartiles: 0-7 years) after the occurrence of cutaneous lesions. The mortality rate was 73% (8 of 11 patients) in systemic disease and no lethal cases were observed among those with only cutaneous involvement ($p < 0.05$). The cumulative 5-year survival rate in patients with systemic disease was 54.5%. The authors therefore concluded that the probability of having a benign form of the disease at onset is approximately 70%, increasing to 97% after 7 years of monosymptomatic cutaneous course.

Prognostic factors in pemphigus vulgaris and pemphigus foliaceus

Saha M, Bhogal B, Black MM, Cooper D, Vaughan RW, Groves RW.

Br J Dermatol 2014;170:116-22.

This retrospective single-centre study was conducted in 2007 to determine whether epidemiological and clinical factors, immunological parameters or genotype influence the clinical course of pemphigus. Patients with either pemphigus vulgaris (PV) or pemphigus foliaceus (PF) between 1975 and 2007 were recruited and finally 79 with PV and 16 with PF were identified. The endpoints were time to first disease remission (DR) and the disease duration (DD). This study showed that Indo-Asian patients were significantly associated with longer DD ($p=0.029$) than White European patients despite the fact that there was no impact on DR. The mean age at presentation of patients with DD less than five years was 49 years (standard error of the mean (SEM) 3.4) in contrast to an age of presentation of 40 years (SEM 1.9) in those who had a DD for over five years ($p=0.039$), which suggested a younger age of onset was associated with a worse prognosis. However, gender did not correlate with DD or DR. The baseline indirect immunofluorescence study (IIF) was not related to DD ($p=0.50$) but a higher initial normal human skin IIF titre was associated with a longer time to DR ($p=0.007$), and high anti-desmoglein 3 levels at baseline were associated with a longer total DD ($p=0.03$). The authors then concluded that ethnic group, age at presentation, initial intercellular antibody titre and initial desmoglein 3 antibody levels all had a significant impact on the prognosis of pemphigus.

Oral liarozole in the treatment of patients with moderate/severe lamellar ichthyosis: results of a randomised, double-blind, multinational, placebo-controlled phase II/III trial

Vahlquist A, Blockhuys S, Steijlen P, van Rossem K, Didona B, Blanco D, et al.

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This multi-centre randomised double-blind controlled study was conducted between January 2006 and April 2007 in nine countries to evaluate the efficacy and safety of two once-daily doses of oral liarozole (75 and 150 mg) in the treatment of patients with moderate to severe lamellar ichthyosis. Patients aged 14 years or above with moderate to severe lamellar ichthyosis (Investigator's Global Assessment (IGA) score ≥ 3) were recruited and IGA and Dermatology Life Quality Index (DLQI) were used for assessing lamellar ichthyosis. Sixty-four patients were included and randomised 3 : 3 : 1 to receive once-daily placebo or liarozole 75 mg, or 150 mg for 12 weeks. One of the nine (11%) patients in the placebo group responded (≥ 2 -point decrease in IGA from baseline) vs. 11/27 (41%) patients in the 75-mg liarozole group and 14/28 (50%) patients in the 150-mg group though the difference was not significant ($p=0.056$). Improvement in the DLQI score was observed in both liarozole groups. The authors thus concluded that scaling and DLQI were improved by once-daily oral liarozole 75 and 150 mg, and was well-tolerated in patients with moderate to severe lamellar ichthyosis.

Anal intraepithelial neoplasia: review and recommendations for screen and management

Smyczek P, Singh AE, Romanowski B.

Int J STD AIDS 2013;24:843-51.

Most of the malignancies in the anal region are squamous cell carcinoma (SCC, 65%) and transitional epithelial carcinoma (25%). Anal intraepithelial neoplasia (AIN), the precursor of anal SCC, can be broadly classified into low-grade anal squamous intraepithelial lesion (LSIL) including AIN I in which the nuclear abnormality

is limited to the lower third of the epithelium and high-grade anal squamous intraepithelial lesion (HSIL) including AIN II in which the epithelial changes involve the upper two-thirds of the epithelium and AIN III which involves the entire epithelium. Similar to cervical cancer, Human Papilloma Virus (HPV) 16 and 18 are the most commonly encountered strains. Receptive anal intercourse, smoking and immunocompromised state particularly HIV infection are other common risk factors. Study showed that HIV-positive patients were at a 37.9-fold increased risk of anal cancer compared to HIV-negative patients. There was also a 10-fold increase in the risk of anal cancer after organ transplantation.

In view of the parallelism of CIN and AIN, anal Pap smear is recommended as a screening test in the high risk groups. Anal Pap smear should be performed before other procedures such as digital examination or high resolution anoscopy (HRA) because lubricating jelly may influence the interpretation of the cytology sample. The patient should also be advised not to have receptive intercourse or enemas 24 hours before the anal Pap smear. Patients with abnormal cytology should be referred for HRA particularly focusing on the transformation zone where many dysplastic and cancerous lesions arise. Biopsy is considered for any ulcerative lesion, areas with irregular vascular patterns or aceto-white staining areas. Studies suggested that more than one-third of LSIL on anal Pap smear showed high-grade dysplasia on biopsy. Therefore, the authors suggested that all abnormal anal cytology should be followed by a HRA±biopsy. In cervical Pap smear, the HPV DNA testing has been used to further triage ASCUS. However, this is not recommended in anal Pap smear as HPV DNA testing for AIN shows good sensitivity but poor specificity and poor positive predictive value.

In conclusion, the authors suggested annual screening of anal Pap smear in HIV-positive patients and every two to three years for HIV-negative patients.

Human papillomavirus-associated balanoposthitis-a marker for penile intraepithelial neoplasia?

Wikstrom A, Hedblad MA, Syrjanen S.
Int J STD AIDS 2013;24:938-43.

Balanitis is an inflammation of the penile glans and posthitis is an inflammation of the inner side of the foreskin. It may associate with microbiological causes like like *Candida* and bacteria. Other causes may relate to plasma cell or may even be non-specific. Human Papilloma Virus (HPV)-associated balanoposthitis has been described. The aim of this study was to determine whether the incidence of balanoposthitis differed between men with histological benign and dysplastic lesions. A total of 292 male patients attending a STI clinic with clinical features of genital HPV planned for surgical treatment between 2004 and 2007 were included. Two clinically identical lesions from the same genital site were collected, one for histology examination and one for HPV PCR and genotyping. Of these, 16% (47/292) had penile intraepithelial neoplasia (PIN). Among those with PIN, 40% (19/47) had balanoposthitis which was only found in 6% (15/245) in those without ($p < 0.0001$). The authors found no significant difference among the PIN grading. However, balanoposthitis tended to be more common in advanced PIN grading (PIN I: 5, PIN II: 6, PIN III: 8). The authors divided the clinical manifestations of HPV infection into four categories: acuminate, papular, macular and seborrhoeic keratosis-like. There was no significant difference of balanoposthitis among different HPV clinical manifestations in the PIN group. However, in the non-PIN group, macular lesion was significantly associated with balanoposthitis while acuminate warts were not associated with balanoposthitis. The HPV lesion at foreskin was significantly commoner for balanoposthitis in both PIN and non PIN groups whereas the HPV lesions of the penile shaft and pubic region were significantly commoner for those without balanoposthitis in both groups. In the non-PIN group, HPV type 6 was the most common whereas HPV type 16 was the most common in PIN group. In conclusion, the authors suggested that one should be aware of the presence of genital dysplasia (PIN) in cases of genital warts and balanoposthitis compared to those without balanoposthitis.

Duration of efficacy increases with the repetition of botulinum toxin A injections in primary axillary hyperhidrosis : a study in 83 patients

Lecouflet M, Leux C, Fenot M, Celerier P, Maillard H.

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Intradermal injections of botulinum toxin have been shown to be an effective treatment for hyperhidrosis. However, its effect is not permanent and the duration of efficacy varies. This study aimed at evaluating whether repeated injections affected the duration of efficacy.

In this retrospective study, patients with primary axillary hyperhidrosis, as confirmed by iodine-starch test, who had failed first-line aluminum-based antiperspirant treatment, with no apparent cause found and had significant impairment in daily living, were recruited. Pregnant women and those with myasthenia gravis were excluded.

Each patient received intradermal botulinum toxin A (Dysport) at a dose of 120-130U per underarm. Subsequent treatment would be carried out if symptoms recurred with a moderate severity, as determined by Hyperhidrosis Disease Severity Scale (HDSS) of score more than two. The duration for symptoms to recur was recorded.

A total of 83 patients were recruited, with a follow-up period from three months to nine years (mean 2.73 years). Sixty-five percent had 2-4 injections while the rest had 5-10 injections. The median duration of efficacy of the last injection was significantly longer than the first injection (8.5 months vs. 5.5 months, $p=0.0002$). No adverse effects like compensatory sweating, myalgia, itching or headache were noted.

The authors concluded that repeated injections of botulinum toxin A were shown to safely and effectively prolong the duration of its efficacy in the treatment of primary hyperhidrosis. The authors postulated that repeated injections of toxin caused the degeneration of motor axon terminal and slowed down their regrowth.

Aspirin use and melanoma risk: a review of the literature

Femenini S, Young LC.

J Am Acad Dermatol 2014;70:187-91.

Use of non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, has been associated with a reduced risk of various cancers like colorectal, gastric and breast cancers. However, its association with melanoma risk is still controversial.

Several case-control studies have shown that aspirin is associated with reduced melanoma risk. This is particularly observed in women, with consistent use for more than five years but these studies were limited by the lack of control of various confounders like skin type, sun exposure and family history of skin malignancies.

On the other hand, there were several cohort and prospective studies that either showed no protective effect or even an increased risk of melanoma with aspirin. However, these results had to be cautiously interpreted as they were limited by sample bias, inadequate exposure of aspirin or short follow-up time.

Although there were inconsistent results regarding aspirin use and protection against melanoma, studies did show that consistent long-term use of aspirin reduced the risk of melanoma, especially in women. These findings were consistent with those aspirin use in colorectal cancer chemo-protection. The lack of effect in those cohort studies might be related to the inadequate dosage and duration of aspirin. Furthermore, various *in-vitro* studies also provided explanation for the potential protective role of aspirin in melanoma.

Hence, given the cardio-protective and colorectal cancer prevention benefits, the authors also recommended the daily use of aspirin, especially for those with an increased risk of melanoma like dysplastic nevus syndrome and positive family history of melanoma, with no contraindications to aspirin. However, more robust clinical studies are required to better assess this protective role in melanoma, and better delineate the dosage and duration of aspirin use.