Isotretinoin does not induce insulin resistance in patients with acne

Isotretinoin (13-cis-retinoic acid) is an effective and generally well-tolerated medication for the treatment of severe acne. However, isotretinoin may increase serum levels of total cholesterol (TC) and triglycerides, and reduce serum levels of high-density lipoprotein cholesterol (HDL-C). Insulin resistance is known to be associated with hypertriglyceridaemia. Whether isotretinoin treatment causes insulin resistance has not been studied directly.

This study aimed to evaluate the relationship between isotretinoin treatment and insulin resistance in patients with acne vulgaris (AV). A total of 48 patients with moderate to severe nodulocystic AV unresponsive to topical therapies and systemic tetracyclines were included. Potential participants were excluded if they reported previous treatment with oral retinoids, medications known to affect insulin metabolism, hormone treatment for any reason in the previous 3 months, cigarette smoking, thyroid dysfunction, and a history of diabetes, hypertension, atherosclerotic vascular disease, malignancy, amyloidosis or any other systemic inflammatory diseases. Patients were started on isotretinoin at a dose of 0.5-0.75 mg/kg body weight, which was then adjusted to 0.88 mg/kg/day as maintenance dosage after 1 month. Screening for biochemical parameters was performed just before the start of treatment and after 4 months of isotretinoin treatment. The parameters measured were insulin, C-peptide, fasting blood glucose, aspartate and alanine aminotransferases (AST, ALT), total cholesterol (TC), triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol. Insulin resistance was measured using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) method available from the Oxford Centre for Endocrinology and Diabetes.

When comparing pre- and post-treatment value, AST, ALT, TC, LDL-C and triglyceride levels were significantly increased ($P<0.01, <0.05, <0.01, <0.05$ and $<0.01$ respectively), but there was no significant change in fasting blood glucose, insulin, C-peptide levels or HOMA-IR. The authors concluded that isotretinoin does not induce insulin resistance in patients with AV.

The importance of checking for delayed reactions in pediatric patch testing

Allergic contact dermatitis (ACD) is a T-cell mediated delayed hypersensitivity reaction in which re-exposure of the skin to a recognized allergen in a previously sensitized person leads to a complex reaction involving lymphocyte proliferation and release of inflammatory mediators, which clinically manifests as dermatitis. After re-exposure, these effects often begin within 12 to 24 hours, typically peak at 3 to 5 days, and may last up to 4 weeks if left untreated. Patch testing is the diagnostic tool to evaluate ACD. In adults, the standard protocol is to remove the patch tests after 48 hours followed by a delayed reading at 72 to 96 hours after application. Late-delayed positive reactions appearing at 168 to 216 hours have been reported in adult populations to have clinical relevance.
The purpose of this study was to prospectively examine the frequency and relevance of positive reactions at different time intervals and to check for late-delayed patch test reactions in children. Thirty-eight children aged 6 to 17 with presumed allergic contact dermatitis were recruited in the study. The patients were required to return at 48 hours for patch test removal and assessment of early reactions, at 72 to 96 hours for evaluation of delayed reactions, and again at 168 to 216 hours for a final delayed reading. The strength of the reactions was graded on the International Contact Dermatitis Research Group (IC-DRG) grading scale with a maximum intensity of ++++. Patients with +/−, +, ++ and +++ were regarded as a positive reaction.

Twenty-five of the 38 (66%) children had a positive reaction at 48 hours. Among these, 10 children (26%) had reactions that resolved by 72 hours and were thus considered to be likely irritant in nature. The most common irritants were potassium dichromate, carba mix and diazolidinyl urea. Thirty-two children (84%) had a positive reaction at 72 hours; 19 children (50%) had a positive reaction at 168 to 216 hours. Of those 19 children with positive reaction, 16 (42%) had persistent reactions, while 5 children (13%) had new delayed reactions. Among the new late-delayed reactions, there were six allergens identified, four of which were considered clinical significant. The authors suggested that physicians should be aware of the late-delayed patch test reactions and additional studies should be conducted to assess optimal reading schedules. This study is limited by small sample size.

Relevance of autoimmune thyroiditis in children and adolescents with vitiligo
Uncu S, Yayl S, Bahadir S, Ökten A, Alpay K.

Vitiligo is the most common pigmentation-related disorder worldwide. An increased prevalence of autoimmune thyroiditis has been shown in vitiligo patients, as it has been shown in patients with other autoimmune diseases such as pernicious anaemia, Addison’s disease and systemic lupus erythematosus. However, only few and controversial data have been reported about the association of vitiligo and autoimmune thyroiditis in pediatric population. The purpose of this study was to assess the presence of thyroid dysfunction and auto-immune thyroiditis in children and adolescents with vitiligo, and to identify any factors related to this association.

Fifty children with vitiligo and 50 controls were enrolled into the study. The diagnosis of vitiligo was based on clinical and Wood’s light examination. Data on age, onset, duration, disease activity, presence of thyroid disorder, other autoimmune diseases, halo nevi, poliosis, and mucosal vitiligo were determined. Serum free triiodothyronine, free thyroxine, total T3, total T4, thyroid-stimulating hormone, and antibodies to thyroperoxidase and thyroglobulin were measured. Patients with positive thyroid antibodies, thyroid dysfunction, or both were examined by a pediatric endocrinologist to evaluate thyroid gland efficiency.

Results showed that the mean age at onset of vitiligo was 7.26±4.43 years and the duration of vitiligo was 2.26±2.95 years. Vulgaris-type vitiligo was the most common form (56%) and 42% reported at least one family member with thyroid disorder, autoimmune disease or both. Overt hypothyroidism or hyperthyroidism was not detected. Significant association was found between autoimmune thyroiditis and vitiligo in both sex and disease duration (P=0.046 and P=0.07, respectively). No association was found between autoimmune thyroiditis and age, age of onset of vitiligo, halo nevi, poliosis, mucosal involvement, disease activity, or family history of vitiligo, autoimmunity, or thyroid disorders. The authors suggested that children with vitiligo, especially girls and subjects with generalized, vulgaris-type vitiligo, should be screened annually for thyroid function and antithyroid antibodies to assist in early diagnosis and therapy of autoimmune thyroiditis.
Influence of Aqueous Cream BP on corneocyte size, maturity, skin protease activity, protein content and transepidermal water loss

This is a prospective study that examine the changes in size of corneocyte, maturity of corneocyte, selected protease activities, protein content and transepidermal water loss (TEWL) in normal skin after a 28-day application of Aqueous Cream BP. Six female Caucasian volunteers without any history of skin diseases were recruited. The mid-volar surfaces of both forearms in the volunteers were used as control and treatment sites. Aqueous Cream BP was applied twice daily for 28 days continuously. Standardized tapes were then applied to the treatment and control sites after 28 days. Twenty consecutive tape strippings were done in the treatment and control areas to obtain sample of corneocytes for further analysis. Protein content was calculated from a formula determined by protein absorption obtained from strippings at 850 nm using an infrared densitometer. The maturity of corneocyte was analyzed by immunofluorescence and Nile Red staining of tape strips. The measurement of corneocyte surface area and protease activities were also performed using samples of stratum corneum obtained from tape strippings by methods previously published. TEWL was measured using a standard instrument initially and after removal of series of four strips.

The TEWL was found to be greater in sites treated with Aqueous Cream BP (P<0.05) when more amount of stratum corneum was removed by stripping. There were significant differences (P<0.05) in the maturity of corneocytes when comparing the treatment site with the control site with the corneocytes always more mature in the control sites. The corneocytes-size were significantly larger in the control sites than in the treatment sites, which was consistent with the observation in the maturity study. The protein content of the control sites was found to be significantly more than the treatment sites as well. Finally, sites treated with Aqueous Cream BP were found to have significant increased activity (P<0.05) of the desquamatory kallikreins and the inflammatory enzymes, plasmin and trypase at all depths analyzed. The study also found that the depth of the skin that could be probed in treatment sites was approximately 0.7 µm less than for control sites. The authors concluded that application of Aqueous Cream BP in normal skin is associated with increase in desquamatory and inflammatory proteases activity. This will increase stratum corneum turnover and TEWL and resulted in skin irritation, inflammation and thinning. Further study for the exact component in Aqueous Cream BP that cause the reaction and the mechanism is recommended.

Very severe psoriasis is associated with increased noncardiovascular mortality but not with increased cardiovascular risk

In recent years studies in specialized population have showed an association of psoriasis, in particular severe psoriasis, with cardiovascular disease (CVD). However, the severity of psoriasis in these populations was mainly based on the therapy employed rather than an objective assessment scale. Recent studies in European population had failed to demonstrate psoriasis as an significant independent risk factors for CVD. This study utilized a 30 years-cohort of patients with severe psoriasis to determine cause-specific mortality, whether excess mortality due to CVD was more significant than other causes and the risk of mortality in relation to extent of psoriasis.

A total of 1376 patients who entered the cohort of psoralens with ultraviolet-A (PUVA) study in 1975-76 were analyzed. The mean age was 46 and about 92% had at least 10% body surface area affected by psoriasis. This cohort documented a total of 617 deaths from 1977 to 2005. The expected deaths of general population were 560 and the standard mortality ratio (SMR) is 1.1 (95% CI=1.02-1.20). The causes of death in this cohort were almost similar to those in general population except for the liver-related mortality. The deaths related to CVD and cancer were of no significant difference between the psoriasis
patients and the expected general population (SMR=1.02, 95\%CI=0.90-1.16 and SMR=1.02, 95\%CR=0.86-1.20 respectively). The patients with the most severe psoriasis (BSA>42\%) were at slightly higher but not statistical significant risk of dying from CVD. However, patients with the most severe psoriasis (BSA>42\%) were at higher and significant risk of dying from other causes (other than CVD and cancer) when compare with general population and those with less severe psoriasis. The authors concluded that causes of deaths other than CVD and cancer are more significant in patients with severe psoriasis. Patients with most severe psoriasis are having high prevalence of CVD risk factors and increase overall mortality, screening and treatment for the risk factors is of significant importance.

Love TJ, Qureshi AA, Karlson EW, Gelfand JM, Choi HK.

There are studies that indicate the association between psoriasis and metabolic syndromes such as hypertension, diabete mellitus, obesity and dyslipidaemia. Some studies had showed a prevalence of 15-24\% of metabolic syndrome in general population. This population-based study aimed at comparing the prevalence of metabolic syndrome and the associated characteristics in people with and without psoriasis. The study data came from the United States National Health and Nutrition Examination Survey (NHANES). This survey was conducted every 2 years and 2 cycles of data from 2003 to 2006 were analyzed. National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria were employed to define metabolic syndrome. Self-reporting of the diagnosis of psoriasis was used to determine the prevalence.

A total of 2456 subjects were included in this study. Seventy-one subjects were diagnosed to have psoriasis previously and the prevalence was 4\%. It was found that age, body mass index, waist circumference and systolic blood pressure were significantly greater in the psoriatic subjects. About 40\% of the psoriatic subjects had metabolic syndrome with reference to the NCEP ATP III criteria and only 23\% of normal subjects had metabolic syndrome. The adjusted odds ratio (adjusted for age, sex, race, smoking, C-reactive protein level) for subjects with psoriasis and metabolic syndrome was 1.96 with reference to the revised NCEP ATP III criteria. There was a higher prevalence of metabolic syndrome among female subjects with psoriasis than that of male subjects. The most prevalent metabolic syndrome among the psoriatic subjects was abdominal obesity, followed by hypertriglycerideremia and low high-density-lipoprotein level. There are evidences that the risk of cardiovascular disease is increased among patients with psoriasis, the presence of metabolic syndrome is nevertheless an important risk factor for development of cardiovascular diseases. The authors also implied that individuals diagnosed with psoriasis should be evaluated for the presence of metabolic syndrome and the presence of metabolic syndrome should be considered as a more serious health hazard than psoriasis itself. This study is however surveying subjects in the US and the majority is non-Hispanic White, application to Chinese population should rely on further studies.

Acitretin revisited in the era of biologics
Booij MT, Van De Kerkhof PC.

This is a review article reminding us the importance of acitretin in the treatment of psoriasis. The use of biologics in treating psoriasis has reached a new height in recent years. Despite the promising results produced by biologics, there are still a significant number of patients not responding to treatment. Acitretin has a unique position that it is not immunosuppressive. The mechanism of action of acitretin is not completely understood. It has antiproliferative and immunomodulatory properties. It decreases the epidermal proliferative activity and promotes keratinocyte differentiation. Acitretin can inhibit production of vascular endothelial growth factor, decrease intraepidermal neutrophil migration, inhibits IL-6 driven activation of Th17 cells.
When comparing the treatment efficacy of acitretin with other systemic therapies and biologics, the level of evidence for acitretin is limited by the study design and not enough long-term data available. It is generally believed that acitretin monotherapy is highly effective in treating pustular psoriasis. The safety of acitretin is high because most side effects are dose dependent and reversible. It is important that some psoriatic patients are contraindicated for immunosuppressive therapy and acitretin is the drug of choice in this clinical context. In the combination therapy with acitretin and photochemotherapy, increased efficacy is noted compared to monotherapy and a reduced dose and exposure of acitretin and UVA or UVB can be achieved. The combination of acitretin and biologics has been reported in few case reports and one randomized controlled trial.

The authors concluded that acitretin combined with photochemotherapy is an important non-immunosuppressive therapeutic option in the era of biologics. Further study on the use of acitretin with other immunosuppressants and biologics is beneficial.

Is it useful to perform a chest X-ray in asymptomatic patients with late latent syphilis?
Dabia R, Radcliffe K.
Int J STD AIDS 2011;22;105-6.

A Chest X-ray (CXR) is recommended in the patients with late latent syphilis (LLS) so as to exclude the cardiovascular complications according to the British Association for Sexual Health and HIV (BASHH) guidelines. The aims of this study are to audit the physicians’ compliance to perform the CXR in LLS patients and to review clinical usefulness of performing the CXR.

The case notes of 456 patients who were given the diagnosis of LLS since 1994 were available for review. Only 65.4% (298/456) cases had CXR performed and 34.6% (158/456) had not. Fifty-six cases were pregnant women so CXRs were not done. Three patients refused the offer and 24 defaulted the CXR appointments. CXR was not requested in 72 patients without stating the reasons. It was not clear whether or not the CXR was requested in 3 patients.

Linear calcification of the ascending aorta is the specific radiological sign of syphilitic aortitis. Only 6.7% (20/298) showed abnormality in the CXRs: 11 showed cardiomegaly and heart enlargement, 3 had unfolded aorta and 2 have thoracic aortic tortuous. The remaining was for old tuberculosis, interstitial shadowing, mitral valve replacement and aortic arch calcification. None of the CXR findings suggested the diagnosis of cardiovascular syphilis. In view of the lack of positive CXR findings in asymptomatic LLS patients, the authors proposed a change in the current guidelines that a CXR be requested only if there are symptoms or clinical signs of cardiovascular disease.

Int J STD AIDS 2011;22;80-4.

The prevalence of Sexually Transmitted Infections (STIs) is increased with the prevalence of HIV infection across the China. The association between HIV and STIs causing genital ulceration like herpes infection, syphilis and chancroid is strong. However, the association between HIV and non-ulcerative STIs such as Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) is not obvious. The objectives of this study were to estimate the prevalence of CT and NG infection among female sex workers (FSWs) in an HIV / AIDS high-risk area in China and to examine the risk factors associated with CT or NG infection.

A cross-sectional study of 568 FSWs was carried out in a city of China. Blood for HIV testing and endocervical swab for CT and NG polymerase chain reaction (PCR) were taken. Questionnaires were given and completed by the FSWs. The median age was 28 years old and median age for the first commercial sex act was 24. Total
85.9% responders reported always use condoms in commercial sex, 23.4% reported to have STIs symptoms and 2.8% reported using illicit drugs in whom 12.1% had the experience of needle sharing.

The prevalence rates of HIV, CT and NG in the study was 11.1%, 7.4% and 8.3% respectively. Age <25 (adjusted OR=3.0), low class sex work (adjusted OR=2.8), age at the first commercial sex <20 (adjusted OR=2.4) and positive NG (adjusted OR=7.1) were the risk factors for CT infection. Also, low class sex work (adjusted OR=4.6), positive CT infection (adjusted OR=6.8) and positive HIV infection (adjusted OR=2.5) were the risk factors for NG infection.

From this study, the HIV infection is significantly associated with NG infection. It has been postulated that the presence of NG may give rise to heightened mucosal HIV viral load. Thus, it may increase the chance of HIV acquisition and progression of the virus in those NG infected patients. Finally, the authors suggested that concomitant CT, NG and HIV testing should be carried out in all high risk group populations and further studies are required to examine the prevalence and the spread of CT and NG infection on the potential impact on the HIV infection.

Propranolol, a very promising treatment for ulceration in infantile hemangiomas: a study of 20 cases with matched historical controls
Hermans DJ, van Beynum IM, Schulzte Kool LJ, van de Kerkhof PC, Wijnen MH, van der Vleuten CJ.

Ulceration is a common complication of infantile hemangiomas (IH) and can be difficult to manage. The authors investigated the possible role of propranolol monotherapy for ulcerating IH. Propranolol was given to 20 patients with IH, who suffered from ulceration at the start of treatment (mean age at onset of treatment, 3.5 months; standard error of the mean: 0.4). After cardiac screening, propranolol was administered in a progressive schedule to 2 to 2.5 mg/kg per day, divided in 3 doses. Blood pressure, heart rate, and fasting glucose levels were monitored during the first 3 days in hospital and, in the absence of complications, treatment was continued at home until the age of approximately 1 year. The 20 propranolol-treated patients were matched to patients from a historical control group, seen before the ‘propranolol era’. These matches were randomly made by using clinical pictures based on type, location and size of the IH, extent of ulceration, and age at the start of ulceration. The results showed that propranolol significantly shortened the ulceration time when compared with a group of matched historical controls. The time to complete healing from the onset of ulceration was significantly shorter for the propranolol-treated patients, compared with the control group (8.7 vs 22.4 weeks; t test: P=0.015). In the propranolol group, a tendency to shorter ulceration duration was seen in patients starting propranolol at an earlier stage of disease. The authors proposed that early administration of propranolol in the proliferation phase may possibly prevent ulceration by limiting expansile growth of the hemangioma. The study was limited by the partially retrospective design and the small number of patients.

Early treatment of cold sores with topical ME-609 decreases the frequency of ulcerative lesions: a randomized, double-blind, placebo-controlled, patient-initiated clinical trial

Prior pilot studies support the use of antiviral medications with topical corticosteroids for herpes simplex labialis (HSL). ME-609 (Xerese, Xerclear) is a combination of 5% acyclovir and 1% hydrocortisone developed for the topical treatment of HSL. In this study the primary end point was the prevention of ulcerative HSL lesions. In all, 2437 patients with a history of HSL were randomized to self-initiate treatment with ME-609, 5% acyclovir in ME-609 vehicle, or ME-609 vehicle (placebo) at the earliest sign of a cold sore
Cream was applied 5 times per day for 5 days. A total of 1443 patients experienced a recurrence and initiated treatment with ME-609 (n=601), acyclovir (n=610), or placebo (n=232). The results showed that in patients receiving ME-609, 42% did not develop an ulcerative lesion compared with 35% of patients receiving acyclovir in ME-609 vehicle (P=0.014) and 26% of patients receiving placebo (P<0.0001). In patients with ulcerative lesions, healing times were reduced in the ME-609 and acyclovir groups compared with placebo (P<0.01 for both). The cumulative lesion area for all lesions was reduced 50% in patients receiving ME-609 compared with the placebo group (P<0.0001). There were no differences among groups in the number of patients with positive herpes simplex virus cultures. The side-effect profile was similar among treatments. The authors concluded that ME-609 prevented progression of cold sores to ulcerative lesions and significantly reduced the cumulative lesion area compared with acyclovir and placebo. ME-609 treatment offers additional therapeutic benefit compared with therapy with topical acyclovir alone. The study was limited by the lack of a test group treated with a topical corticosteroid alone.

Effect of intravenous immunoglobulin with or without cytotoxic drugs on pemphigus intercellular antibodies
Lolis M, Toosi S, Czernik A, Bystryn JC.

Intravenous immunoglobulin (IVIG) lowers serum levels of pemphigus antibodies and is a relatively new approach to treat pemphigus. The optimal way to use this agent, however, is unknown. The authors sought to examine whether co-administration of a cytotoxic drug to patients with pemphigus improves the ability of IVIG to decrease serum levels of intercellular (IC) antibodies. In this retrospective study, the authors analyzed changes in IC antibody levels in 20 patients with pemphigus who were treated with 24 courses of IVIG administered alone (n=10) or with a cytotoxic drug (n=14). Each course of IVIG consisted of 400 mg/kg daily of immunoglobulin given over 5 days every other week; this cycle was repeated 3 to 4 times. Serum levels of IC antibodies were measured at baseline, before treatment, and 1 week and 1 month after the last IVIG cycle. The results showed that one week after the last IVIG cycle IC antibodies decreased by an average of 77% in the group treated with IVIG and cytotoxic drug compared with 48% in the group treated with IVIG alone (P=0.54), and by 90% versus 43% 1 month later (P=0.03). The authors concluded that these observations confirm that IVIG can rapidly lower serum levels of auto-antibodies in patients with pemphigus and its ability to do so is improved by the co-administration of a cytotoxic drug. These findings imply that the clinical effectiveness of IVIG in treating pemphigus, and possibly other autoantibody-mediated diseases, may be improved by the concurrent administration of a cytotoxic drug. Larger sample size is suggested for future studies.