

Journal Watch

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Comparative evaluation of the INNO-LIA syphilis score and the MarDx Treponema pallidum immunoglobulin G Marblot test assays for the serological diagnosis of syphilis

Lam TK, Lau HY, Lee YP, Fung SM, Leung WL, Kam KM.

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The laboratory diagnosis of syphilis depends mainly on two types of serology tests: (1) treponemal tests which detect specific anti-treponemal antibody such as enzyme immunoassay (TP EIA), Treponema pallidum particle agglutination (TPPA) test and fluorescent treponemal antibody absorption assay (FTA-abs); and (2) non-specific anti-lipoidal antibody like Venereal Disease Research Laboratory (VDRL) assay and rapid plasma regain (RPR) assay.

The aim of this study is to evaluate the two immunoblot assays: (1) INNO-LIA syphilis Score (LIA) which uses three recombinant antigens and one synthetic peptide (Tp47, Tp17, Tp15, TmpA) to detect IgG anti-treponemal antibody and (2) the MarDx T. pallidum IgG Marblot Test (TWB) which uses three native antigens to detect TP antibody. The results generated by these two immunoblot assays were compared with the results from TP EIA / TPPA / FTA-abs. The consensus result of a positive syphilis case (LIA / TWB positive) was defined as at least two out of three tests (TP EIA / TPPA / FTA-abs) showed positive while a negative case (LIA / TWB negative) was defined as at least two tests (TP EIA / TPPA / FTA-abs) showed negative or otherwise indeterminate. A total of 135 newly diagnosed syphilis (39 primary, 20 secondary, 18 early latent and 58 late latent) and 43 normal healthy subjects were included. In this study, the TP EIA had an overall sensitivity of 98.5% (95%

CI 94.8-99.6) and the LIA had an overall sensitivity of 94.1% (95% CI 88.7-97.0). The difference was not statistically significant whereas, the sensitivity of TWB was only 65.2% (95% CI 56.8-72.7) which was statistically lower than TP EIA and LIA. All 43 normal subjects were negative so the specificity was 100%. Therefore, the authors concluded that the LIA assay performed significantly better than the TWB assay. It can be considered to be a valid alternative confirmatory test for the serological diagnosis of syphilis.

Oropharyngeal gonorrhoea: rate of co-infection with sexually transmitted infection, antibiotic susceptibility and treatment outcome

Manavi K, Zafar F, Shahid H.

Int J STD AIDS 2010;21:138-40.

Oropharyngeal gonorrhoea (GC) is seldom symptomatic and is difficult to diagnosis unless the clinician has high index of suspicion, indicates by history and does proper culture. The aim of this retrospective study was to investigate the co-infection rate of oropharyngeal GC with other sexually transmitted diseases, antibiotic susceptibility and the treatment in a genitourinary medicine clinic. Oropharyngeal GC was diagnosed by positive culture. Case notes for those positive culture were reviewed for demographic data, antibiotic regime and susceptibility, result of test-of-cure, concomitant chlamydia, HIV and syphilis infections.

A total of 131 patients were diagnosed to have oropharyngeal GC. These included 63% men who have sex with men. About 52% had oropharyngeal symptoms like sore throat and 31% were younger than 24 years old. Around one third of these

patients co-infected with urethral GC or rectal GC. About 14% of male and 19% of female patients were co-infected with chlamydia. About 10% of male patients had newly diagnosed HIV infection whereas none was found in female. Only one patient had concomitant syphilis infection.

Among these 131 oropharyngeal GC patients, 128 (98%) were treated. About 17% was identified to have penicillin resistance, 5% had ciprofloxacin resistance and 2% had tetracycline resistance. However, no isolated specimen had resistance to azithromycin, spectinomycin or ceftriaxone. In the present study, antibiotic susceptibility to cefixime was not included but among 46 patients treated with cefixime, 59% had test-of-cure done and all were negative.

The authors commented that oropharyngeal GC was associated with high co-infection rates of anogenital GC and chlamydial infection. Antibiotic susceptibility, patient counselling, partner notification and test-of-cure after initial treatment were all important in management of oropharyngeal GC.

A randomized and controlled trial about the use of oral isotretinoin for photoaging

Bagatin E, Parada MO, Miot HA, Hassun KM, Michalany N, Talarico S.
Int J Dermatol 2010;49:207-14.

Topical tretinoin or all-trans-retinoic acid had been documented to be useful for the prevention and repairing of aged skin. Oral isotretinoin has been used for severe acne and other dermatoses. Despite the known adverse effects, some authors suggested the use of low-dose oral isotretinoin to control photoaging. This study is a randomized controlled trial on the effectiveness and safety of oral isotretinoin for the treatment of photoaging.

The study population comprised of 32 menopausal or sterilized women of aged 40-55, divided into 2 groups: first group included 21 participants received 20 mg isotretinoin, 3 times per week, nightly moisturizer and daily sunscreen; the second group included 11 participants received just moisturizer and sunscreen. Efficacy

was measured by 1) investigator and patients' self clinical evaluation on photoaging; 2) digital standardized photographs blinded and evaluated by two independent dermatologists; 3) profilometry, through the average difference between the baseline and the highest peak of final profile; 4) corneometer test for skin hydration, also used for evaluation of skin dryness related to isotretinoin; 5) skin elasticity and dermal viscosity tests; 6) skin biopsies from dorsal aspect of left forearm, stained to Hematoxylin and Eosin, Verhoeff, picosirius, and immunomarker to p53 (a tumor suppressor gene that could be activated by UV induced DNA damage) were evaluated in 19 subjects randomly selected from the two groups, before and after treatment.

At the end of the study, most of the variables showed no differences between both groups. There was slight but statistically significant average reduction in p53 expression in the patients who received oral isotretinoin. The author concluded that oral isotretinoin seemed safe but not effective to treat photoaging, and special caution should be considered for women prone to pregnancy.

Premenarchal vulvar ulceration: is chronic irritation a causative factor?

Cebesoy FB, Balat O, Inaloz S.
Pediatr Dermatol 2009;26:514-8.

Vulval ulcers are uncommon in young girls who are not sexually active. Other than sexual abuse or sexually transmitted diseases, clinical reports have described non-sexual related causes such as Epstein-Barr virus infection, Behcet's syndrome and leukaemia.

The objective of this retrospective study was to review the common features of the young girls with vulval ulcerations, and to help guide physicians caring for girls with this unusual condition. A series of 10 premenarchal girls without evidence of sexual abuse or contact were identified. Data was abstracted from detailed histories, physical examinations, and laboratory investigations including age, menarche status, clothing, and undergarment styles, symptoms at the time of presentation, description of the ulcer, documented recurrences, history of oral aphthosis,

laboratory studies including serology and blood count, erythrocyte sedimentation rate, C-reactive protein, and biopsy information. Speculum exams were not performed and digital photographs were taken from the lesions after patient consent. Treatments were based on clinical judgment. All patients were followed until complete recovery of the vulvar ulcers and were encouraged to call with any recurrence of signs, symptoms or new illness.

Results showed that despite multiple evaluations, no patient had a specific medical cause identified to account for their vulvar ulcerations. None were diagnosed to have Behcet's syndrome. Seven had bilateral vulvar ulcerations, which the authors attributed to the practice of wearing tightly fitted polyester underwear frequently. No recurrences were documented in 6 months follow-up. Therefore, the author concluded that for non-sexually active girls presented with vulvar ulcer, besides thorough investigations for infections and Behcet's disease, the use of tight-fitting or irritative clothing should also be evaluated.

Psychiatric treatments in dermatology: an update

Sambhi R, Lepping P.
Clin Exp Dermatol 2010;35:120-5.

Dermatology outpatients were known to have a high prevalence of psychiatric disorders. The psychiatric symptoms in dermatology can originate as comorbid conditions from primary psychiatric disorders such as anxiety, depression, substance misuse and body dysmorphic disorder, or from a psychotic illness such as schizophrenia and delusional parasitosis. They often present to the dermatologist as dermatitis artefacta. Anxiety and depression may also be secondary to the distress of having a disfiguring, chronic, often relapsing and remitting diseases such as acne, eczema and psoriasis. Patients often experience a worsening of the skin condition when stressed. In some cases, the distress may even lead to suicidal attempt. However, it is sometimes difficult for the dermatologist to persuade the patient that they require psychiatric help, because of the stigma associated with mental illness and the need to consult a psychiatrist. Whether the patient would accept a referral for psychiatric or psychological

help largely depends on the patients' perception of their skin problems: purely as a physical disease or a combination of psychological and physical disease. As a result, dermatologist may need to consider the use of psychotropic drugs when patients refuse psychiatric referral.

This article provides a quick reference on the common psychiatric diagnoses that are relevant to the dermatologist, including anxiety, depression, obsessive compulsive disorders, delusional parasitosis and dermatitis artefacta. The common pharmacological treatments of the above mentioned conditions such as antidepressants, propranolol, hydroxyzine, pregabalin, etc; and their side effects were also summarized in comprehensive tables. However, when encountering patients presenting with severe psychiatric symptoms that markedly impair their quality of life or posing risk to themselves or others, the dermatologist must consider psychiatric referral.

Neonatal and early infantile cutaneous Langerhans cell histiocytosis: comparison of self-regressive and non-self-regressive forms

Battistella M, Freitag S, Teillac DH, Brousse N, de Prost Y, Bodemer C.
Arch Dermatol 2010;146:149-56.

Cutaneous Langerhans cell histiocytosis (LCH) in neonates and infants can present as various clinical morphologies sometimes mimic systemic infection and it has variable outcomes. This is a retrospective observational study aiming to compare the cutaneous self-regressive (SR) LCH and non-self-regressive (NSR) LCH with or without distant visceral involvement. A total of thirty-one patients diagnosed with cutaneous LCH in the first three months of life over a seventeen years period in a tertiary referral center were found. The initial histologic slides were reviewed and further immunohistochemical analyses were performed in eighteen patients.

The authors found that 21 patients had SR LCH and 10 patients had NSR LCH. The onset of lesion in SR LCH was significantly earlier than NSR LCH

in neonatal period and lesions that appeared at birth were almost always SR LCH. The number and type of cutaneous lesions were of no significant difference between 2 groups. Perineal lesions were significantly more common in NSR LCH than in SR LCH. Necrosis, solitary lesion and involvement of extremities can point the diagnosis towards SR LCH but larger cohort is needed to achieve statistical significance. The classic histopathological feature was no different in 2 groups. E-cadherin expression may be associated with good prognosis and limited disease in skin but not disease regression. Further study on frozen section will be required. The regulatory T-lymphocyte density was not predictive of disease regression. The study is limited by small sample size and larger study is needed to further confirm the findings for clinical application.

Occlusive therapy in atopic dermatitis: overview

Braham SJ, Pugashetti R, Koo J, Maibach HI. *J Dermatolog Treat* 2010;21:62-72.

This is a review on the current evidence for occlusive therapy in the treatment of atopic dermatitis. The authors found eighteen studies in PubMed and EMBASE databases from January 1966 to February 2009. Fourteen studies used wet-wrap therapy and four studies used dry occlusive therapy. Only six of the studies were randomized controlled trials. Five of the randomized control trials were using the wet-wrap therapy and the remaining one used dry occlusive therapy.

The authors found that all wet-wrap therapy studies showed benefits in moderate to severe or exacerbated atopic dermatitis. The dry occlusive therapy had conflicting results with one controlled study showing no benefit over conventional open topical steroid therapy and two prospective studies showing improvement. In mild-to-moderate atopic dermatitis, the occlusive therapy has not been well studied and results are conflicting. There were increased cutaneous bacterial counts or infections in all dry occlusive therapy studies and in four out of the fourteen studies using wet-wrap therapy. However, anti-staphylococcal therapy had conflicting results in improving the efficacy of

occlusive therapy except those who had obvious clinical infection. There were limited data showing a transient decrease in morning cortisol levels but laboratory adrenal suppression was rare. Strategies such as intermittent therapy, reduce potency of topical steroid used and once-daily treatment may help to limit the adrenal suppression side effect. Occlusive therapy with topical immunosuppressive agents such as tacrolimus or pimecrolimus had not been evaluated properly. The authors concluded that although there were variations in study protocols and the majority of studies were uncontrolled trials, the occlusive therapy provides an effective alternative or adjunct to the conventional topical steroid regimen for moderate-to-severe atopic dermatitis, acute exacerbation or refractory disease.

Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: Results of two placebo-controlled studies of daily application to the face and balding scalp for two 3-week cycles

Hanke CW, Beer KR, Stockfleth E, Wu J, Rosen T, Levy S. *J Am Acad Dermatol* 2010;62:573-81.

Imiquimod 5% cream is approved as a 16-week regimen for the treatment of actinic keratoses involving a 25-cm² area of skin. The authors evaluate imiquimod 2.5% and 3.75% creams for short-course treatment of the entire face and scalp. In two identical studies, adults with 5 to 20 lesions were randomized to placebo, or imiquimod 2.5% or 3.75% cream (1:1:1). Up to two packets (250 mg each) were applied per dose once daily for two 3-week treatment cycles, with a 3-week, no-treatment interval. Efficacy was assessed at 8 weeks post-treatment. The results showed that in all, 490 subjects were randomized to placebo, or imiquimod 2.5% or 3.75% cream. Median baseline lesion counts for the treatment groups were 9 to 10. Complete and partial clearance rates were 5.5% and 12.8% for placebo, 25.0% and 42.7% for imiquimod 2.5%, and 34.0% and 53.7% for imiquimod 3.75% ($P < 0.001$, each imiquimod vs placebo; $P = 0.034$, 3.75% vs 2.5% for partial clearance). Median reductions from

baseline in lesion count were 23.6%, 66.7%, and 80.0% for the placebo, imiquimod 2.5%, and imiquimod 3.75% groups, respectively ($P < 0.001$ each imiquimod vs placebo). There were few treatment-related discontinuations. Temporary treatment interruption (rest) rates were 0%, 17.1%, and 27.2% for the placebo, imiquimod 2.5%, and imiquimod 3.75%, respectively. The authors concluded that both imiquimod 2.5% and 3.75% creams were more effective than placebo and had an acceptable safety profile when administered daily as a 3-week on/off/on regimen. The study was limited by potential investigator and subject bias when erythematous local effects of imiquimod were encountered.

Low rates of clinical recurrence after biopsy of benign to moderately dysplastic melanocytic nevi

Goodson AG, Florell SR, Boucher KM, Grossman D. *J Am Acad Dermatol* 2010;62:591-6.

Little is known about the recurrence/persistence rates of dysplastic nevi (DN) after biopsy, and whether incompletely removed DN should be re-excised to prevent recurrence. The authors aimed to determine the recurrence rates of previously biopsied DN, and to assess whether biopsy method, margin involvement, congenital features, epidermal location, and degree of dysplasia are associated with recurrence. Patients having a history of a "nevus biopsy" at least 2 years earlier were assessed for clinical recurrence. Slides of original lesions were re-reviewed by a dermatopathologist. A total of 271 nevus biopsy sites were assessed in 115 patients. Of 195 DN with greater than 2 years of follow-up, 7 (3.6%) demonstrated recurrence on clinical examination. In all, 98 DN had a follow-up period of at least 4 years with no clinical recurrence. Of 61 benign nevus biopsy sites examined, clinical recurrence was observed in two (3.3%). For all nevi, recurrence was significantly associated with shave biopsy technique but not with nevus dysplasia or subtype, or the presence of positive margin or congenital features. They concluded that in this cohort, rates of clinical recurrence after biopsy of DN and benign nevi were extremely low. Re-excision of nevi, including mildly to moderately DN with a positive margin, may not be necessary.

This study was limited by the fact that most biopsies were performed in a pigmented lesion clinic at a single tertiary referral center and determinations of nevus recurrence were made on clinical rather than histologic grounds, and follow-up times were limited in some cases.

Prospective controlled clinical and histopathologic study of hidradenitis suppurativa treated with the long-pulsed neodymium:yttrium-aluminium-garnet laser

Mahmoud BH, Tierney E, Hexsel CL, Pui J, Ozog DM, Hamzavi IH.

J Am Acad Dermatol 2010;62:637-45.

Hidradenitis suppurativa (HS) is a chronic inflammatory disease involving the intertriginous areas. The authors conducted a clinical and histopathologic evaluation of the efficacy of long-pulsed neodymium:yttrium-aluminium-garnet laser treatment for HS. A prospective, randomized, right-left within-patient controlled trial for HS ($n = 22$) was performed. Four monthly laser sessions were performed. Disease activity was measured at baseline, and treatment response was assessed before each laser session and monthly for 2 months after the completion of laser treatment, using a modified scoring system based on Sartorius score. Histologic examination was performed at baseline, immediately after laser treatment, and at 1 and 4 weeks after treatment. A patient questionnaire was circulated on the last visit to assess patients' level of satisfaction. Results showed progressive improvement in disease activity, most significantly during the 4 months of treatment, which was maintained during the 2-month post-treatment follow-up period. Averaged over all anatomic sites, the percent improvement was 72.7% on the laser treated side, and 22.9% on the control side ($P < 0.05$). Histologic examination showed an initial acute neutrophilic infiltrate. Granulomatous inflammation was present on follow-up biopsy specimens 4 weeks later. An inflammatory infiltrate surrounded the hair shaft remnants, denoting destruction of hair follicles. The authors concluded that long-pulsed neodymium:yttrium-aluminium-garnet laser, together with topical benzoyl peroxide and clindamycin, is significantly more effective than

topical benzoyl peroxide and clindamycin alone for the treatment of HS. Preliminary review of histopathology suggests the mechanism of action is destruction of the hair follicle. The overall success of the treatment in both clearing pre-existing lesions and preventing new eruptions, coupled with high patient satisfaction, makes the neodymium:yttrium-aluminium-garnet laser a promising treatment advance for this highly disabling condition. The study was limited by its small sample size.

Prednisolone vs. ciclosporin for severe adult eczema. An investigator-initiated double-blind placebo-controlled multicentre trial

Schmitt J, Schakel K, Folster-Holst R, Bauer A, Oertel R, Augustin M, et al.
Br J Dermatol 2010;162:661-8.

This is a randomized control trial comparing the efficacy of prednisolone and ciclosporine for severe eczema. This study was conducted between February 2007 and November 2008 at the dermatological outpatient clinics of four university hospitals in Germany. Patients aged 18-55 years, who had eczema according to the U.K. Working Party diagnostic criteria, and had severe eczema as indicated by SCORAD score 40 or Dermatology Life Quality Index score 10, and eczema refractory to topical corticosteroids and topical calcineurin inhibitors, were included in the study.

Thirty-eight study subjects were randomly allocated to receive ciclosporine (daily dosage 2.7-4.0 mg/kg), given for 6 weeks or prednisolone (daily dosage 0.5-0.8 mg/kg) for 2 weeks. The measure of efficacy was stable remission which was defined as at least 50% improvement in the SCORAD index under active treatment and no flare within a 12-week follow-up. However, 15 out of the 38 randomized patients (39%) had to be withdrawn from the study within the follow-up period because of significant disease flares that were refractory to topical therapies. At the end of study period, stable remission was achieved in six of 17 patients (35%) treated with ciclosporine and in one of 21 patients (5%) receiving prednisolone. Eight of the nine responders to prednisolone (89%)

and five of the 11 responders to ciclosporine (45%) relapsed within follow-up. The authors thus suggested superiority of ciclosporine over prednisolone in severe eczema. This study is significantly limited by the small sample size and the high drop out rate.

Dermoscopic features of acral lentiginous melanoma in a large series of 110 cases in a white population

Phan A, Dalle S, Touzet S, Ronger-Savle S, Balme B, Thomas L.
Br J Dermatol 2010;162:765-71.

Acral lentiginous melanoma (ALM) is a rare but distinctive subtype of melanoma. The ABCDE rule is not good enough to detect suspicious cutaneous melanoma of ALM subtype. Dermoscopy will significantly improve the diagnostic accuracy in melanocytic lesions.

This is a retrospective study conducted in France to investigate all dermoscopic features in patients with ALM between 1996 and 2009, and to emphasize their diagnostic value in this subtype of melanoma. All dermoscopic photographs of ALM were collected retrospectively from the Melanoma register of the Department of Dermatology, Claude Bernard University Hospital in Lyons.

The dermoscopic patterns such as parallel-ridge pattern (PRP), irregular diffuse pigmentation (IDP), parallel-furrow pattern (PFP), lattice-like pattern (LLP), fibrillar pattern (FP), globular pattern (GP), acral reticular pattern, homogeneous pattern and globulostreak-like pattern were recorded in ALM of the palms and soles. For nail apparatus ALM, the author classified the dermoscopic patterns as follows: brown or greyish coloration, regular or irregular colour lines, linear microhaemorrhages and onychodystrophy.

One hundred and ten cases were included in this study, 55 (50%) were ALM of the soles, 11 (10%) were ALM of the palms and 44 (40%) were ALM of the nail apparatus. The mean Breslow thickness was 2.6 mm. The most common pattern of 66 ALM of the palms and soles was IDP (60%),

followed by PRP (53%). Among the 44 nail lesions, 29 (66%) presented as melanonychia striata longitudinalis. Nail plate dystrophy was present in 19 (43%) cases. The most prevalent feature of nail ALM was the irregular brown lines (70%). Thirty-seven cases (34%) of ALM were clinically amelanotic, 25 (68%) being fully unpigmented and 12 (33%) only partially unpigmented.

Dermoscopy could enable the detection of microscopic remnants of pigmentation in most cases.

The authors concluded that PRP and IDP in pigmented non-nail unit lesions are highly indicative of malignancy and their presence indicates the necessity for biopsy.

Answers to Dermato-venereological Quiz on pages 108-109

- 1) Subacute cutaneous lupus erythematosus (SCLE) of annular polycyclic type is the most likely diagnosis.
- 2) The differential diagnoses include tinea corporis, erythema annulare centrifugum, Jessner's lymphocytic infiltrate, polymorphic light eruption, granuloma annulare and urticarial vasculitis.
- 3) In the dermis, there is perivascular and periadnexal inflammatory cell infiltration (Figure 2). The inflammatory cells consist of small lymphocytes and few plasma cells (Figure 3). In the epidermis, there is lichenoid tissue reaction with vacuolar change, small lymphocytes infiltrate into basal layer of epidermis with 'necrotic' keratinocytes (arrow in Figure 4). Alcian blue stain shows increased stromal mucin. Direct immunofluorescence stain was positive for C3 and immunoglobulins at the dermal-epidermal junction.
- 4) SCLE may be associated with systemic illnesses, such as systemic lupus erythematosus (SLE) and Sjogren's syndrome. Half of the SCLE patients fulfill (at least 4 of 11) criteria to be classified as SLE, and 10% of SCLE patients have serious systemic involvement from SLE. The baby of an affected mother with anti-Ro antibodies may develop neonatal lupus including congenital heart block. This is due to maternal placental transfer of anti-Ro antibodies to baby before birth.
- 5) We need to exclude drug induced SCLE, e.g. hydrochlorothiazide and diltiazem. Therapeutic measures include sun avoidance, protective clothing, broad spectrum sunscreens, topical steroids or calcineurin inhibitors, and oral hydroxychloroquine. It is important to screen for associated systemic diseases and refer the patient to medical department if necessary.