Current Best Evidence

Current best evidence from dermatology literature

Jang N, Fischer G. Treatment of erosive vulvovaginal lichen planus with methotrexate. Australas J Dermatol 2008; 49 (4): 216-219.

Authors report the successful treatment of severe long-standing erosive vulvovaginal lichen planus in four adult female patients using 2.5–7.5 mg of oral methotrexate once weekly in conjunction with topical clobetasol dipropionate 0.05% ointment and tacrolimus 0.03–0.10% ointment. All cases experienced improvement in symptoms and healing of lesions within 4–8 weeks. Methotrexate was well tolerated and no adverse events have been observed in any of the patients at follow up 4–6 months later.

Comments: Erosive genital LP poses a particular therapeutic challenge because, in contrast to cutaneous lesions, it is usually resistant to topical treatment and typically runs a chronic course with most patients requiring long-term maintenance treatment. Systemic therapy should only be considered when topical therapy does not achieve adequate improvement. Although systemic corticosteroid therapy is effective against erosive vulvovaginal LP it is an unacceptable long-term treatment when any other alternatives exist. Other systemic treatments that have been tried with variable results include griseofulvin, dapsone, hydroxychloroquine, oral retinoids, azathioprine, minocycline combined with nicotinamide, cyclosporin and thalidomide. There have been few reports regarding the effectiveness of methotrexate alone or in conjunction with topical agents. This report supports low-dose oral methotrexate, supplemented with local use of an ultrapotent corticosteroid and topical tacrolimus, as an effective and emerging treatment in severe erosive vulvovaginal LP. Authors propose that methotrexate should be considered in the treatment of this chronic and debilitating disease when the response to topical treatments is inadequate.

Ivanov OL, Lvov AN, Michenko AV, Künzel J, Mayser P , Gieler U. Autoerythrocyte sensitization syndrome (Gardner–Diamond syndrome): review of the literature. J Eur Acad Dermatol Venereol 2009; 23 (5): 499-504.

This article review the literature concerning psychogenic purpura. The diagnosis is usually based on typical anamnestic data, clinical presentation (painful inflammatory skin lesions, which progressed to ecchymoses during the next 24 h) and positive diagnostic tests with intracutaneous injections of 80% solution of washed autologous erythrocytes. No pathological findings of blood coagulation parameters are usually detected. Histopathological evaluations of lesional biopsies revealed non-specific changes. Taking into account the high frequency of psychic disorders and stress dependence of skin symptoms, therapy with psychotropic drugs (according to indications) and psychotherapy are pathogenetically grounded methods of treatment in psychogenic purpura, and should be provided together with symptomatic therapy.

Comments: Gardner–Diamond syndrome (GDS; also called autoerythrocyte sensitization syndrome, autoerythrocyte sensitization syndrome, painful bruising syndrome, painful blue spots) is an autoimmune vasculopathy with sensitization to a component of erythrocyte stroma, phosphatidylserine. In most cases, the disease develops after psychic stress and is characterized by induced/spontaneous development of painful oedematous infiltrated skin lesions (isolated or multiple), progressing to ecchymoses during the next 24 h. Although the lower limbs, especially on their ventral surfaces, and the trunk are the most often reported localizations of these lesions, they can appear on any other skin area, including the face. Also, several areas may be involved at the same time. The development of skin changes can be accompanied by several systemic disorders. Sometimes, the appearance of new skin lesions is associated with fever, arthralgias, myalgias, headaches and dizziness. More than half of patients with GDS

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report about different gastrointestinal symptoms (epigastric pain, gastrointestinal haemorrhages, nausea, vomiting, diarrhea), which develop simultaneously with skin lesions. A reliable diagnostic test for GDS consists of an intracutaneous injection of 1 mL 80% suspension of washed erythrocytes obtained by the patient. The test is positive, if the typical GDS inflammatory lesion develops within 24 h, then gradually progressing into ecchymosis. The test should be made on the inaccessible for patient's hands skin areas.

Clinical and laboratory characteristics of patients with Gardner–Diamond syndrome are:

- Patients are mainly women
- Typical anamnesis (psychical stress and/or physical trauma, preceding of the disease onset)
- Typical eruptions: oedematous erythema evolving to the painful ecchymoses during 24 h
- General symptoms (fever, arthralgia, etc.) are not obligatory
- Frequent association with mental disorders
- Positive intracutaneous test with autoerythtrocytes
- Coagulogramm is normal
- Pathohistological findings are not specific.

No method of treatment is sufficiently effective in this disease. Taking into account the high frequency of psychic disorders and stress dependence of skin symptoms, therapy with psychotropic drugs (according to indications) and psychotherapy are pathogenetically grounded methods of treatment in psychogenic purpura. Timely made diagnosis will help to avoid excessive and sometimes aggressive treatment.

Witt CM, Lüdtke R, Willich SN. Homeopathic treatment of patients with psoriasis: A prospective observational study with 2 years follow-up. J Eur Acad Dermatol Venereol 2009; 23 (5): 538-543.

A prospective multicentre observational study was done to evaluate details and effects of homeopathic treatment in patients with psoriasis in usual medical care. Primary care patients were evaluated over 2 years using standardized questionnaires, recording diagnosis and complaints severity, health-related quality of life (QoL), medical history, consultations, all treatments, and use of other health services. Forty-five physicians treated 82 adults, 51.2% women, aged 41.6 ± 12.2 (mean ± SD) years. Patients had psoriasis for 14.7 ± 11.9 years; 96.3% had been treated before. Initial case taking took 127 ± 47 min. The 7.4 ± 7.4 subsequent consultations (duration: 19.4 ± 10.5 min) cumulated to 169.0 ± 138.8 min. Patients received 6.0 ± 4.9 homeopathic prescriptions. Diagnoses and complaints severity improved markedly with large effect sizes (Cohen's d= 1.02–2.09). In addition, QoL improved (SF-36 physical component score d = 0.26, mental component score d = 0.49), while conventional treatment and health service use were considerably reduced. Authors conclude that under classical homeopathic treatment, patients with psoriasis improved in symptoms and QoL.

Comments: Homeopathy is practiced in many regions of the world including India, especially in high-income countries where it ranks the most popular among traditional, complementary, or alternative medicines. According to its 'rule of similarity', patients are treated with a remedy that in a healthy proband has caused similar symptoms. A diagnosis can be treated with different remedies in different patients ('individualization'), depending on varying side symptoms. Homeopathic drugs ('remedies') are produced by alternating steps of diluting and agitating a starting substance; the resulting 'potencies' quickly reach dilutions beyond Avogadro's number. Such 'high potencies' are often prescribed; their effects constitute a subject of scientific controversy. Meta-analyses of placebo-controlled studies have shown inconsistent results. Hence to establish data on use and effects of homeopathy under conditions of usual care, authors investigated 3981 patients in a prospective observational study. This above paper presents the subgroup of 82 adults consulting a homeopathic physician because of psoriasis. Assessments of disease severity and health-related QoL consistently showed substantial improvements, although the disease was long-standing, chronic and conventionally pretreated. Similarly, all accompanying diseases (almost all chronic) were markedly ameliorated. The major improvements were seen within the first 3 months of homeopathic treatment, after 12 months ratings were less than half of baseline and continued to improve. Accordingly, QoL increased, and uses of health care services or conventional medication decreased markedly.

Lehman JS, Camilleri MJ, Gibson LE. Epidermolysis bullosa acquisita: Concise review and practical considerations. Int J Dermatol 2009; 48 (3): 227-236.

Epidermolysis bullosa acquisita (EBA) is a cutaneous subepidermal autoimmune blistering disorder (CSEAIBD) that results from the effects of

IgG autoantibodies directed against the 145-kDa noncollagenous amino-terminal (NC-1) domain of collagen VII, a major component of anchoring fibrils. Clinical, histopathologic, and immunopathologic, diagnostic criteria for epidermolysis bullosa acquisita include:

- Bullous disorder arising in adulthood or, less commonly, childhood
- Absence of family history of blistering diseases
- Spontaneous or post-traumatic bullae resembling hereditary dystrophic EB
- Exclusion of other bullous diseases
- Subepidermal blister on histology
- Deposition of IgG at dermal–epidermal junction (DEJ)
- IgG deposits localized to the lower lamina densa or sublamina densa of the DEJ

A diverse collection of conditions may mimic epidermolysis bullosa acquisita clinically and histologically. In recent decades, advanced laboratory tests, including immunofluorescence, molecular techniques including immunoblotting (collagen VII/laminin-332/collagen IV/p105/p200 antibodies), laser scanning confocal microscopy, immunoelectron microscopy, and determination of anticollagen VII antibody titers by ELISA offers information that may help to guide disease management.

EBA often is refractory to the conventional treatment approach of high-dose corticosteroids and corticosteroid-sparing agents. Difficulty in selecting optimal treatments for patients with EBA is compounded by the absence of published randomized, controlled therapeutic trials. A literature review of previously reported cases of EBA treated with cyclosporine, colchicine, extracorporeal photochemotherapy, and intravenous immunoglobulin (IVIg) found favorable responses with each treatment. Hence, the authors assert that conventional therapy with prolonged, high-dose corticosteroids subjects patients to significant risk without consistent benefit. Therefore, they proposed that colchicine or IVIg be considered as first-line treatments in mild or advanced cases, respectively.

Guevara-Gutierrez E, Uribe-Jimenez E, Diaz-Canchola M, Tlacuilo-Parra A. Acute generalized exanthematous pustulosis: report of 12 cases and literature review Int J Dermatol 2009; 48 (3): 253–258.

Acute generalized exanthematous pustulosis is an acute pustular eruption occurring after infection and/or drug ingestion, with spontaneous cure after a single eruption. This study aims to communicate a series of cases of acute generalized exanthematous pustulosis. A retrospective analysis was performed by authors on cases of acute generalized exanthematous pustulosis, observed between 1993 and 2006 at the Dermatology Department, Hospital General de Occidente, Jalisco, Mexico. Twelve patients were included, with a predominance of male patients and a mean age of 28 years. The most common cause was drugs, detected in 83% of cases, and most of these were a result of anticonvulsants and antimicrobials. The most frequent symptoms were itching, present in all cases, and fever, present in 92% of cases. Authors conclude that acute generalized exanthematous pustulosis should be considered a distinct clinical and histopathologic entity. Because of its self-resolving character, early recognition can help to avoid unnecessary diagnostic studies and treatments.

Comments: Acute generalized exanthematous pustulosis (AGEP) is a rare skin eruption, associated principally with drugs, acute viral infections, and mercury. Over time, cases with similar clinical characteristics have been described using different names, such as generalized toxic pustuloderma, blistering drug eruptions, and generalized pustular dermatosis. AGEP is considered to be a clinical and histologic entity with distinctive characteristics: an abrupt and sudden onset marked by edematous erythema or scarlatinoid exanthema, which is quickly covered with numerous small pustules (< 5 mm), mainly nonfollicular and superficial (intraepidermal or subcorneal), together with the presence of a fever greater than 38 °C and peripheral neutrophilia. The symptoms (both pustules and fever) resolve spontaneously within 2 weeks, and residual shedding is observed. A spontaneous resolution occurs shortly after the start of symptoms, and is usually limited to a single episode. These findings allow AGEP to be distinguished from other entities, principally from anticonvulsive hypersensitivity syndrome and pustular psoriasis. The difference from the latter condition lies principally in the fact that, in most cases, AGEP is induced by drugs and has a more acute course and a rapid spontaneous resolution. Less commonly, AGEP needs to be differentiated from other entities, such as Sweet's syndrome, subcorneal pustulosis, erythema multiforme, and toxic epidermal necrolysis.

Thyssen JP, Menné T, Linneberg A, Johansen JD. Contact sensitization to fragrances in the general population: a Koch's approach may reveal the burden of disease. Br J Dermatol 2009; 160 (4): 729-735.

Contact sensitization to fragrance mix (FM) I and Myroxylon pereirae (MP) is common among European patients with dermatitis. Recently, FM II was included in the European baseline series as an additional marker of fragrance sensitization. A systematic review of the literature was carried out by searching Pubmed-Medline, Biosis and contact dermatitis textbooks.This paper reviews literature with the aim to assess the prevalence of fragrance sensitization in the general population, and to suggest how future population-based studies and questionnaires should be constructed, better to assess the prevalence and burden of fragrance sensitization. This is of relevance as it is often difficult to establish causality in biological systems. Nineteen studies were identified, of which 13 were performed among adults. Sample sizes varied between 82 and 2545 tested subjects, and 11 648 subjects were tested in total. The median prevalence of FM and MP sensitization among adults was 2·3% (women, 1·7%; men, 1·3%) and 1·1% (women, 1·4%; men, 0%), respectively. Authors conclude that based on the reliability of patch test data from the general population and exposure data obtained from patients with dermatitis, the prevalence and burden of fragrance sensitization in the general population is significant.

Comments: Contact sensitization to fragrance mix (FM) I and Myroxylon pereirae (MP; balsam of Peru) is common among European patients with dermatitis. Recently, FM II was included in the European baseline series as an additional marker of fragrance sensitization. This literature review aims to assess the prevalence of fragrance sensitization in the general population and to suggest how future population-based studies and questionnaires should be constructed, better to assess the prevalence and burden of fragrance sensitization. This is of relevance as it is often difficult to establish causality in biological systems. In the 19th century, the German physician Robert Koch developed his renowned postulates as general guidelines to identify and establish the cause of an infectious disease. Koch's postulates state: (i) the organism must be found in all animals with the disease, but not in healthy animals; (ii) the organism must be isolated from a diseased animal and grown in pure culture; (iii) the cultured organism should cause disease when introduced into a healthy animal; and (iv) the organism must be re-isolated from the experimentally infected animal. A Koch's approach may be helpful to assess the relevance and burden of prevalent contact allergies in the general population. By using such logical thinking, valuable information may be offered to dermatologists, industries and policy makers regarding the risk of fragrance exposure.

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