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E.		Frenk
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Cellular Sensitivity to Oxidative Stress in the Photosensitivity Dermatitis/Actinic Reticuloid Syndrome

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Using cultured human fibroblasts, we confirm a slight UVA sensitivity in cells from patients with the photosensitivity dermatitis/actinic reticuloid syndrome (PD/AR) and demonstrate for the first time that cell lines from these patients are markedly sensitive to hydrogen peroxide. Heme oxygenase (HO-1) is an oxidant-inducible stress gene which now appears to play an important role in cellular defense against oxidative stress. However, hydrogen peroxide induces

accumulation of HO-1 mRNA to a similar maximum level (4 h after induction) and to a similar enhancement over basal mRNA levels in both normal and PD/AR cell strains. The observed sensitivity of PD/AR cell lines to both UVA radiation and hydrogen peroxide supports the hypothesis that such cells are defective in cellular defense against oxidative stress. Furthermore, the results with an oxidant-inducible stress gene suggest that the defect lies at a late step in damage processing rather than an early step involving quenching of radiation-generated active intermediates.

Glutathione-Related Antioxidant Defenses Are Increased in Melanin-Containing Melanoma Cells

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Glutathione plays a pivotal role in the maintenance of the intra-cellular redox balance and may affect the therapeutic response of tumor cells. Its possible implication in melanogenesis led us to investigate the relationship between GSH expression and melanin synthetic activity in human melanoma cells. Amelanotic and melanotic cell lines were maintained in Minimum Essential Medium supplemented with nonessential amino acids and 5% FCS. Melanin was characterized by electron microscopy and determined by spectrophotometry. The levels of GSH, dopa oxidase, glutathione reductase (GR) and glutathione peroxidase (GPO) were assessed by standard kinetic methods. Melanotic melanoma cells showed high levels of GSH and GR compared to amelanotic melanoma cells and normal human fibroblasts. While GPO was increased in the most pigmented cell lines, enzymatic systems involved in detoxification of superoxide radicals (superoxide dismutase) and H₂O₂ (catalase) did not show any relationship with the melanin content. Melanoma cells are likely to be submitted to an intense oxidative stress during melanin synthesis. The high levels of GSH and GSH-dependent enzymes in melanotic melanoma cells could represent a defense mechanism against the oxidative activity developed in melanogenesis.

Skin Infection with Atypical Mycobacteria

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Dermatologists are confronted with skin infections caused by atypical or better, nontuberculous mycobacteria. These organisms are widespread in nature. Patients with AIDS or taking immunosuppressive drugs are most at risk. Skin symptoms may include papules and nodules. The histopathology is not specific, but tuberculoid granulomas can be found. Treatment is difficult, because the organisms can resist antituberculous and antibiotic medications. Based on case reports, we will discuss diagnostic and therapeutic measures.

Contact Sensitization to Corticosteroids in Switzerland: A Multicenter Study of the Swiss Contact Dermatitis Research Group

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In the last years increasing prevalence of contact sensitization to corticosteroids has been reported. To address this problem, the Swiss Contact Dermatitis Research Group conducted a study from November 1, 1991, to October 30, 1992, with the participation of the five university clinics, the city clinic of Zurich and 11 dermatologists in private practice. As screening substances, tixocortol pivalate and budesonide (both 1% in PET) as well as hydrocortisone alcohol and hydrocortisone-17-butyrate (1.5 and 1%, respectively, in alcohol) were used.

Readings were taken after 48 and 72 h according to the guidelines of the ICDRG. When a positive test was observed, a steroid series (12 steroids) was tested and a user test was performed. A total of 3,016 patients (60% women) were tested. The mean age was 42 years (range 6-96). 54% of the male and 37% of the female patients were negative in the standard test series. The prevalence of contact sensitization to nickel (men: 7.2%, women: 31.4%), formaldehyde (men: 3.5%, women: 4.9%) and Kathon CG (men: 3%, women: 4.9%) was in the range of earlier studies. In 65 patients (26 men, 2.2%; 39 women, 2.1%) 106, positive patch tests to one or several corticosteroids were found (tixocortol pivalate 31, budesonide 30, hydrocortisone-17-butyrate 29 and hydrocortisone alcohol 16). Due to different test populations (patient number and selection) a considerable variation in the prevalence (0-5.6%) was observed. According to this study, the prevalence of contact sensitization to corticosteroids is rather high (mean 2%) in Switzerland. Therefore, the introduction of corticosteroids into the standard series should be considered. However, a screening substance that reliably detects the majority of corticosteroid-sensitive patients has not been identified yet, and the optimal test concentrations and vehicles of corticosteroids have not been established so far.

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Treatment of Basal Cell Carcinoma with Intralesional Interferon-Alpha

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Recent studies have provided evidence that intralesional interferon-alpha-2b (IFN- α 2b) is an effective treatment for basal cell carcinoma (BCC). Twenty-two patients (18 men and 4 women) ranging in age from 27 to 70 years, each with biopsy-proved BCC, were treated with intralesional injections of IFN- α 2b three times a week for 3 weeks. The dose per injection was 1.5×10^6 IU (total dose 13.5×10^6 IU) if the lesion was less than 2 cm in diameter (17 patients) and 3.0×10^6 IU between 2.0 and 3.0 cm (5 patients). The efficacy of the treatment was determined by examination of biopsy specimens at 4 weeks (10 patients) and 8 weeks (12 patients) after completion of therapy. Nineteen of 22 patients responded to the treatment with no histological evidence of tumor present on rebiopsy. A dense mononuclear cell infiltrate and numerous ectatic blood vessels were present in the dermis at the sites of previous BCC. In 2 patients small epidermoid cysts were noted in the dermis. Immunohistologically, the dermal infiltrate consisted of CD3+, HLA-DR+ lymphocytes with a predominance of CD4+ T cells. The dermal infiltrate showed an intense expression of lymphocyte function-associated antigen (LFA-1). The intercellular adhesion molecule type 1 (ICAM-1) was focally expressed on the tumor cells. Our findings suggest that IFN- α 2b acts on BCC cells by enhancement of cell-mediated immune responses.

Human Scalp Hair Follicle Development from Birth to Adulthood

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The scalp is often used as donor site for split-thickness skin grafts in children. Alopecia at the donor site was reported with variable incidence and might be caused by grafts harvested below the follicular stem cells. The bulge, the putative site of follicular stem cells, is poorly studied. We therefore decided to investigate the development of the infundibulum, the bulge, Adamson's fringe, the B-fringe, and the matrix which houses the proliferating cells of the anagen follicle.

The mean depths of these 5 follicular compartments were measured in parietal scalp of 100 patients aged from 2 weeks to 21 years. The thickness of the epidermis and dermis also were assessed. To analyze the correlation with age, their regression on age (y in years) was calculated. For the bulge it was $b [\mu\text{m}] = 30.8 y + 683.3$ ($r = 0.73$; $\text{SEM} = 145.5$), and for the matrix it was $m [\mu\text{m}] = 90.4 y + 1616.2$ ($r = 0.76$, $\text{SEM} = 406.5$). p for the null hypothesis was < 0.0001 . The growth of the inferior portion below the bulge was not parallel but proportional to that of the superior portion. The relative position of the bulge in the dermis was stable, whereas the inferior portion advanced progressively to deeper positions in the subcutis. This finding is another proof for the postulated privileged localization of the bulge and thus is a further argument in favor of the bulge as putative site of follicular stem cells. This study provides age-adjusted guidelines for surgeons on safe harvesting of scalp grafts. Up to the age of 5 years, only skin grafts of maximal 300 μm thickness should be harvested to avoid amputation of putative follicular stem cells in the bulge. This recommendation takes into account the differences in the thickness of harvested grafts due to unequal dermatome pressure by the surgeon. We found that the true thickness of skin grafts varied between 38 and 192% of the intended value, as controlled in a series of 23 grafts.

Infantile and Progressive Papular Mucinosi

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Switzerland

A 6-year-old boy was first seen in our clinic with several flesh-colored papules arranged in rows on the lower part of the back, on the abdomen and the posterior part of the legs; they had enlarged progressively since the age of 3 months. The clinical aspect is similar to mucopolysaccharidosis. Otherwise the physical exam was normal. His father seemed to have presented the same type of lesions when he was young. The biopsy (hematoxylin-eosin) showed an edematous dermis with splitting collagen bundles. Colloidal iron stain revealed wispy mucin-like material in the dermis. The substance was also Alcian blue positive and showed metachromasy with toluidine blue; toluidine blue is almost completely removed with hyaluronidase. The hyaluronidase test is specific for mucinosis because of large amounts of hyaluronic acid in mucin. Because this type of mucinosis is unusual and because of the family history, we made exams to exclude mucopolysaccharidosis definitively. Research of urinary glycosaminoglycans was negative and lysosomal enzymatic activity in cultured skin fibroblasts was normal. To our knowledge, this is the first reported case of this type of dermal mucinosis.

Cutaneous Lymphadenoma – A Variant of Trichoblastoma

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Cutaneous lymphadenoma is a rare neoplasm of which only 27 cases are reported. It consists of neoplastic lobules within the dermis and is composed of epithelial cells which are intermingled with lymphocytes. The nature of cutaneous lymphadenoma is controversial; on morphological grounds it has been proposed to show a sweat gland differentiation, while it has also been presumed to show a folliculo-sebaceous differentiation with accentuation either on the sebaceous or the follicular component. We have investigated by immuno-histochemistry the expression of keratins in 4 cases using monoclonal antibodies against the keratins K1, K7, K8, K10, K18, K19, K20 and K15/10/14.

In our study, cutaneous lymphadenomas are characterized by a constant expression of keratins K1/5/10/14 in the peripheral and most of the central cells of the neoplastic lobules. Similarly, a strong immuno-noreactivity for keratin K19 is noticed in the peripheral and most of the central cells. Those central cells which are negative for keratins are of lymphocytic lineage, as evidenced by a positive staining with UHCL1. No immunoreactivity for keratins K7, K8, K18 or K20 is detected in our tumors. Keratins K1 and K10 are found only in those parts of the tumors which are connected to infundibula.

The strong staining of peripheral and central cells with keratin K19 is not compatible with a sebaceous differentiation, since sebaceous glands and ducts lack K19 expression. Also, putative sweat gland differentiation is not corroborated by our findings which show the absence of keratins characteristic of glandular epithelia, while K19 is expressed in peripheral cells. In sweat ducts K19 is expressed only in luminal cells. Our results show a keratin pattern which is compatible with a follicular differentiation and which, particularly, is similar to that of trichoblastomas. Therefore, on the basis of these keratin immunohistochemical results and of morphological similarities, we believe cutaneous lymphadenoma to be a variant of trichoblastoma.

Evaluation of Skin Care Products for Their Barrier-Regenerating Efficacy

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Occupational skin protection may be divided into pre-exposure protection by barrier creams, removal of irritants by cleansing agents and enhancement of barrier function regeneration by emollients or moisturizers. As first steps on the way to objective tests for barrier regeneration enhancers, we developed two test models using bioengineering technology that allow the evaluation of the effects of a base preparation on barrier recovery following acute irritant dermatitis and protection from cumulative damage leading to cumulative irritant dermatitis. In the first testing method, we induce subclinical irritant dermatitis on the forearm of volunteers by the application of 0.5% sodium lauryl sulfate (STS) for 24 h. For two days after the irritation, we apply the test products on the irritated spots. On day 4, we irritate the treated and control areas again by the application of 0.5% SLS for 24 h. On day 5, we take the visual scores and measure transepidermal water loss (TEWL). The reduction of TEWL increase in treated areas is used as an indicator of the regenerating activity. In our second testing method, we induce cumulative irritant dermatitis by daily short-term application of SLS and toluol for 9 days. After the daily challenges, we apply the test products on the irritated areas. Cumulative irritation is documented by visual score, TEWL, skin moisture and skin color reflection. Again, the reduction of irritation on treated areas is used as an indicator of the regenerating activity of the tested products.

Although our testing methods need further optimization and standardization and although the correlation between the test results and clinical efficacy at the workplace needs to be demonstrated, we believe that a standardized testing method for the determination of a 'skin regeneration factor' in analogy to the sun protection factor will be possible.

Improvement in the Treatment of Chronic and Subacute Cutaneous Lupus erythematosus by the Association of Two Antimalarial Drugs: Chloroquine and Quinacrine

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Antimalarials have proved of value for the treatment of chronic and subacute cutaneous lupus erythematosus (LE). However, some patients show either no or minor improvement on antimalarial mono-therapy. In these cases, the association of chloroquine and quinacrine (C-Q) may be useful, but this remains controversial. To study this question, we treated 15 patients (10 with chronic LE and 5 with sub-acute cutaneous LE) who had poorly responded to chloroquine or hydroxychloroquine with C-Q. At the usual therapeutic dose, hydroxychloroquine had proven unsuccessful in 8 of 10 cases and chloroquine in 4 of 5 cases. All the 15 patients were treated afterwards with C-Q. The initial dose usually was: chloroquine 100 mg 3 ×/day and quinacrine 65 mg 3×/day. The skin lesions improved significantly or cleared totally in 5 out of the 10 patients with chronic LE and in all the 5 patients with subacute cutaneous LE. The mean duration of C-Q treatment was 15 months, ranging from 1 month to 4 years. The overall drug tolerance was good. A few patients observed mild and dose-dependent side effects as nausea, dizziness and photophobia. One patient showed electroretinographic abnormalities and had to be withdrawn from treatment. The jaundice-like discoloration of the skin and sclera was an expected hallmark of quinacrine. Our observations suggest that the C-Q may sometimes be superior to the usual antimalarial monotherapy. If chloroquine or hydroxychloroquine failed to control chronic or subacute cutaneous LE, C-Q is worth trying.

Clinical Spectrum of Lymphadenosis cutis benigna

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We report the clinical findings of 41 patients with lymphadenosis cutis benigna Bäfverstedt (LACB) by a retrospective analysis of the files from the Department of Dermatology, University of Basel. Inclusion criteria were the typical clinic, suitable histology and immunohistochemistry, reactive serology for *Borrelia burgdorferi* and clearance of the antibiotic treatment. Of the 41 patients 17 (42%) were female and 24 (58%) were male. The average age was 42 years (women 49, men 38 years). Most patients were aged between 40 and 50 years. A peak incidence was found in 1987, with 11 cases (27%) of LACB. Latency from clinical detection to the first consultation was 1 week to 7 years. In 57% the time lag was less than 10 months, in 76% less than 21 months. Twenty-nine patients (72%) showed the solitary type of LACB, 4 (10%) had a solitary aggregated variant, 4 (10%) had an infiltrative and 3 (8%) a disseminated papulonodular type. Predilection sites of the solitary variant and the aggregated type were the ear and earlobe

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with 7/33 (21%), the face was affected in 18%, the leg including the foot in 15% and the arm was affected in 12%. The areola mammae, neck and genitals were affected in 9% each. Serology with IFAT showed IgM fraction in 2/32 patients (6%) (IgM titer $\leq 1:64$), in 16/32 (50%) elevated IgG titers were found.

Pathogenesis of Epidermolytic Hyperkeratosis

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Bullous congenital ichthyosiform erythroderma (BCIE; epidermolytic hyperkeratosis) is an autosomal dominant disorder of keratinization. During the first years of life, erythema and disseminated formation of blisters due to continuous suprabasal lysis of keratinocytes dominate the clinical pictures. Later on, erythroderma and bullous formation cease and are replaced by

hyperkeratotic hystrix-like lesions, predominantly on the trunk, the joints and more rarely on palmo-plantar areas. Histologically, BCIE is characterized by an acanthokeratolysis (epidermolytic hyperkeratosis) and ultrastructurally by perinuclear clumped bundles of tonofibrils in the spinous layers. Recently, we have identified mutations of the suprabasally expressed keratins K1 and K10 as the cause of BCIE [Science 1992;257: 1128-1130]. One family showed an A→K mutation of the helix termination peptide of K1, another family an L→S mutation in the helix initiation peptide of K10. Several families revealed R→H mutations in the helix initiation peptide of K10 indicating a hot spot of mutations. The helix initiation peptide and the helix termination peptide are highly conserved domains of keratin intermediate filaments. The high conservation implies a crucial functional importance of these sequences. Structure analysis of the mutations identified indicated a pathological lateral and longitudinal polymerisation of keratin intermediate filaments K1 and K10 during intact formation of heterodimers. These data stress the crucial physical functions of intact keratins for the physical integrity of keratinocytes.

'matosis of childhood' is still used. Most of these cases have been thought to be linear IgA disease. We report on a 7-year-old boy suffering from childhood acquired epidermolysis bullosa, presenting with extensive lesions of the mucous membranes as well as disseminated, in part herpetiform vesicles and bullae on plaques of cutaneous erythema, slight scarring and milia. Direct immunofluorescence staining showed linear deposits of IgG and C3 at the epidermal basement membrane, and circulating autoantibodies (titre 1:128-1:256) reacted with the blister floor of NaCl-split skin and specifically with the anchoring fibril collagen VII as demonstrated by immunoblotting. This case demonstrates that specific classification using modern immunological techniques is indispensable, also in childhood autoimmune bullous diseases, as the exact diagnosis has a great impact on the therapeutic strategy.

Spider Hairs (Pili aranei) – A New Entity

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We present a new hair disorder characterized by unusual knotting of body hairs which may occur as an acquired or possibly inherited variant. We analyze the clinical features and report the changes found under the light microscope and scanning electron microscope (SEM) in this entity. We observed two unrelated adults with localized acquired extreme knotting of body hairs and a newborn with a familial type of the same hair disorder. In the two adults, knotting of body hairs occurred in areas where rubbing was frequent. In the familial type with possibly an autosomal dominant inheritance pattern, no mechanical explanation could be found. History revealed that the father, a paternal aunt and her son and a paternal cousin exhibited identical lesions at the same site at birth. In all affected family members, the lesions disappeared during the first months of life. Light microscopy confirmed the clinical impression of a large knot and SEM exhibited knotting of at least 20 hairs. No underlying skin disease or deeper process was found. According to the clinical appearance and the results of the SEM that shows multiple hairs with knotting and sticking of multiple hairs originating from different follicles, we suggest the term 'spider hairs' or 'pili aranei'.

Autoimmune Bullous Diseases of Childhood: A Case of Epidermolysis bullosa acquisita

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Autoimmune bullous diseases mainly occur in adults. Based on today's classification criteria, more and more cases of mixed bullous diseases are reported. In the rare cases of autoimmune bullous diseases of childhood, however, the old term 'benign chronic bullous der-

Confirmation of Oral Hairy Leukoplakia by Ultrastructural Examination of Lingual Exfoliative Cytological Specimens

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Oral hairy leukoplakia (OHL) is one of the most common oral manifestations of human immunodeficiency virus (HIV) infection. In addition, OHL in HIV-negative patients has been observed

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repeatedly. OHL is regarded as a specific manifestation of Epstein-Barr virus which belongs to the herpes family. Although the clinical appearance of OHL is characteristic, several entities of oral diseases may clinically mimic OHL. The differential diagnosis includes candidiasis, lichen planus, graft-versus-host disease, idiopathic leukoplakia, white sponge nevus, leukokeratosis nicotinic, geographic tongue, marked edema, occlusal trauma, and chronic tongue chewing. In doubtful cases or in children where OHL is very rare, diagnosis has to be confirmed by further tests. Biopsy, however, is invasive and not feasible, especially in children. Detection of herpes-type viruses by electron microscopy in keratinocytes from clinically suspected OHL provides an objective diagnosis. We performed a smear of exfoliated cells from 8 patients with lesions suspicious for OHL. Seven of them were infected by HIV and one patient had marked immunosuppression because of aggressive ulcerative colitis. In 6 of these patients herpes-type virus could be documented which confirmed the clinical diagnosis of OHL. One of the patients was an 11-year-old child with HIV infection. This is the 5th child with OHL described so far. We conclude that ultrastructural examination of lingual exfoliative cytological specimens is a noninvasive and painless method to confirm the clinical diagnosis of OHL.

Pastes: What Is in Them? How Do they Work?

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Pastes are semi-solid stiff preparations containing a high proportion of finely powdered material. Powders such as zinc oxide, titanium dioxide, starch, kaolin, talc, etc. are incorporated in high concentrations of up to 50% into a preferably lipophilic, greasy vehicle. A clinically distinctive feature which is generally attributed to pastes is the quality to absorb exudates by nature of the powder or other absorptive components. Reviewing the Swiss and other pharmacopoeias, serious doubts arise concerning the various formulas of pastes and their absorptive features: e.g., the pasta zinci of the Swiss pharmacopoeia is composed of petrolatum, zinc oxide and starch. Petrolatum, a highly lipophilic vehicle nonmiscible with water surrounds the powder, preventing any absorption of water or exudates. The goal of our investigation was to develop an experimental setting to characterize the clinically important absorptive feature of powders and pastes. First, the absorptive features of titanium dioxide, zinc oxide, kaolin and corn starch powder of pharmacopoeia quality were determined. Zinc oxide and kaolin powder showed the highest absorption of 1,000 mg water/g powder (100%). The water absorption of corn starch and titan

dioxide was 700 and 450 mg/g powder, respectively. Second, the absorptive features of a series of paste formulations were studied in a new experimental setting. The data from these experiments show that two-phase pastes consisting of two nonmiscible components, one (the dispersed or inner phase; powder) being suspended in the other (the continuous or outer phase; lipophilic vehicle), have no absorptive features. In contrast, three-phase pastes consisting of a hydrophilic two-phase emulsion with high concentrations of incorporated powder (cream pastes) show considerable water uptake. Depending on the formula of the cream pastes, the water uptake varied between 45 and 450 mg/g

paste. We conclude that the classical two-phase pastes, such as pasta zinci, have no absorptive features. On the contrary, these formulations are highly occlusive. Therefore lipophilic pastes are only indicated when protection of intact skin against aggressive body exudates and humidity is required. The three-phase pastes or cream pastes show considerable water uptake and fulfil common expectations of pastes to dry the skin. A simple experimental setting to study the water uptake allows distinction between different paste formulas.

Atopic Dermatitis: Cytokine Profiles in Lesional Skin and Peripheral Blood Revealed High Levels of IL-4 in the Extrinsic Form Only

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In previous studies we were able to demonstrate that serum parameters like sIL-2R, ECP and sCD14 correlate with the activity and the course of atopic dermatitis (AD). In the present study, we analyzed peripheral blood lymphocyte subpopulations and their activation state in patients with extrinsic and intrinsic atopic dermatitis (n = 33), psoriasis (n = 6) and normal controls (n = 13). Characteristics of the extrinsic type of AD (EAD) were IgE levels above 200 U/ml, a positive Phadiatop, positive radioallergosorbent tests (RAST) as well as positive immediate type skin tests and a positive family or patient history of allergic diseases. AD patients were termed intrinsic (IAD) when they had low levels of total IgE (< 200 U/ml) and neither IgE antibodies nor immediate type skin reactions to a routine panel of aero- and food allergens as well as a negative family or patient history of allergic diseases. Compared to normal controls and patients with psoriasis, all AD patients showed characteristic eosinophilia. Increased numbers of CD4⁺ T cells with increased expression of IL-2R and HLA-DR were noted in all AD and psoriasis patients when compared to normal individuals. To further characterize the pathogenic mechanisms which lead to the different types of AD, we measured cytokine profiles (IL-4, IL-5, IL-2 and IFN- γ) in peripheral blood (24 h unstimulated T cell supernatants) and in skin biopsies from patients with EAD (n = 19) and patients with IAD (n = 14) compared to psoriasis and normal controls. In peripheral blood and lesional skin, high levels of IL-4 were found in extrinsic AD only, whereas in intrinsic and extrinsic AD, significantly elevated levels of IL-5 could be shown. In addition, patients with intrinsic AD showed elevated levels of IFN- γ in peripheral blood. By calculating the IL-4/IFN- γ ratio we were able to demonstrate a significantly higher ratio again in EAD only. Whereas IgE-mediated mechanisms seem to play an important role in extrinsic AD, the results of our study suggest that the inflammatory response in intrinsic AD may occur independently of the presence or absence of IgE, driven by chronic cell-mediated mechanisms on the basis of a distinct cytokine pattern.

Clinical Spectrum of Acrokeratosis paraneoplastica (Bazex Syndrome)

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We describe 4 patients with acrokeratosis paraneoplastica (Bazex syndrome) who document the characteristic evolution of this specific cutaneous marker of an underlying malignant tumor. The syndrome occurs in three stages. First, the eruption is confined to the fingers and toes. Often it is accompanied by painful eruptions in the paronychia areas. In addition, psoriasis-like lesions occur on the nose and the outer rim of the ears. The nail changes range from scaling and grooving to severe onycholysis with complete destruction of the nail plate. In the second stage, the eruption is more extensive and the erythematous and scaly lesions involve the whole palms and soles, resulting in marked keratoderma. The primary and/or metastatic neoplasm is now producing local signs and symptoms. Without treatment of the underlying malignancy, the disease progresses to the third stage. The eruption is now more extensive and affects the proximal extremities as well as further parts of the body. The subtotal erythrodermia of one of our patients is a very rare variant of stage III. The primary tumor is often a squamous cell carcinoma of the upper aerodigestive tract. Most often males aged over 40 years are affected. Treatment has to be directed against the underlying tumor. Adjuvant topical treatment includes steroids and keratolytics. In addition, systemic treatment with etretinate may be helpful. Although acrokeratosis paraneoplastica (Bazex syndrome) is rare, recognition of the cutaneous clinical findings may lead to diagnosis of underlying malignancy.

UVA-Irradiation-Induced Membrane Damage in Human Skin Fibroblasts Revealing a Resistance Limited to Foreskin Fibroblasts

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UVA-irradiation-induced membrane damage was assessed in human skin fibroblasts in order to establish a group of normal controls for comparison against photosensitive disease states. Membrane damage was determined by a sensitive enzyme-release assay of lactate dehydrogenase (LDH). LDH release was measured in 7 skin fibroblast cell lines derived from non-exposed skin of individuals ranging from 1 to 69 years of age (A lines) and in 6 fibroblast cell lines derived from human foreskin (B lines) following various influences of UVA irradiation (330-450 nm). The release of LDH from all A lines tested was linear as a function of UVA fluence with maximum levels up to 18.4-fold over spontaneous LDH release at the highest fluence of UVA employed (1×10^6 J/m²). Variability of LDH release among cells from different people was broad with maximum levels ranging from 6.9- to 18.4-fold. The results from 6 fibroblast cell lines derived from human foreskin B lines, where minimal levels of membrane damage were detected with the LDH release assay, contrasted with these results. Even though foreskin tissue is an easy and frequently used source of 'normal' control cell cultures, one has to be aware that cells derived from this tissue have been found to be rather resistant to certain forms of oxidizing stress such as UVA irradiation and should perhaps not be used as controls in comparison with disease states.

Comparative Study of Contracted Lattices and Stretched Lattices using Light and Transmission Electron Microscopy

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Collagen gel cultures containing human fibroblasts have been observed to undergo rapid contraction. If contraction is prevented, the lattice becomes stretched and very thin. We have used light microscopy (on semithin sections stained with toluidine blue) and transmission electron microscopy (TEM) (on ultrathin sections contrasted with uranyl acetate and lead citrate) to study cellular and intercellular changes induced by this mechanical stress. The mechanical inhibition of retraction induced a bipolarisation of fibroblasts along the axis of tensile force, a decrease in the density of the collagen fibers and their parallel orientation to the lattice surface. When compared with contracted lattices by TEM, the fibroblasts of the stretched lattices had prominent nucleoli, while the RER was distended and more developed. This is all consistent with an increased synthetic activity. The fibroblasts also had a lot of cytoskeletal elements and electron-dense plaques within the membrane. Coated pits and vesicles were found in cell-to-cell and cell-to-collagen interactions. This in vitro model of dermal equivalent which mimics the in situ dermal tension offers a promising culture system to study the influence of mechanical forces on cellular function.

Lipid Profiles in Patients Treated with Retinoids: Influence of Apolipoprotein E Polymorphism C. Mainetti¹, R.W. James², M. Harms², D. Pometta³,

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Retinoid therapy is known to induce undesirable changes in plasma lipid levels, interference in lipoprotein catabolism being evoked as one cause. Apolipoprotein (apo) E, which is a key protein in the metabolism and elimination of plasma lipoproteins, is genetically determined and polymorphic. Three common alleles code for 3 apo E isoforms: the normal form (E3) and two mutant forms, E4 and E2 (14 and 8% of the population), which pathologically influence plasma cholesterol and triglycerides. Apo E polymorphism may be a major determinant in the interindividual susceptibility to coronary artery disease. Possible interactions between retinoid therapy and apo E polymorphism were investigated in 145 patients undergoing either isotretinoin (n = 98) or acitretin (n = 47) treatment. We have found the same results as in the literature: significant increases in cholesterol, triglycerides and apo B, and decreases in HDL-cholesterol were observed. New observations in our study: when analyzed as a function of apo E phenotype, greater increases in cholesterol were associated

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with the E4 (+0.40 mmol/l) and E2 (+0.46 mmol/l) isoforms, as compared to the E3 isoform (+0.26 mmol/l). Apo E polymorphism also influenced triglycerides but had a less consistent influence on HDL-cholesterol concentrations.

The results suggest that apo E polymorphism may modulate retinoid-induced alterations in plasma lipid levels. A greater increase in cholesterol levels associated with mutant isoforms was noted when isotretinoin- and acitretin-treated patients were analyzed individually. The apo E4 isoform may induce unacceptable increases of plasma cholesterol, particularly in older patients on retinoid therapy.

Diagnostic Screening of Systemic Amyloidosis by Abdominal Fat Aspiration: An Analysis of 100 Cases

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Congo red staining of abdominal fat aspirates was used as a screening procedure for systemic amyloidosis in 100 consecutive patients; 9 out of 108 samples were positive for amyloid, 94 were negative and 5 samples were inadequate for examination. To evaluate the reliability of this method, we reviewed the clinical records of these patients. The screening for amyloidosis was performed for the following reasons: 49 patients had predisposing disease for secondary amyloidosis, 18 had multiple myeloma, 12 were investigated for neuropathy and 13 for cardiomyopathy, 6 presented bullous and/or purpuric cutaneous eruptions and in 2 patients amyloid deposits were demonstrated in another organ biopsy. All 9 patients with positive fat samples had a clinical course suggestive of amyloid disease; biopsy of another organ and/or autopsy confirmed the diagnosis of systemic amyloidosis in 5 cases (2 AA amyloidosis, 2 AL amyloidosis and 1 hereditary type 1 amyloidosis). No false-positive results were obtained. Eighty-nine patients had 1 or 2 negative fat aspirates; in 21 cases, another biopsy site disclosed a negative result for amyloid. Two patients had proved AL amyloidosis demonstrated on hepatic and medullary biopsies and on autopsy, respectively.

In our series, amyloid deposits were demonstrated in 82% (9/11) of systemic amyloidosis.

Abdominal fat aspiration is a simple and sensitive screening method for AA and AL systemic amyloidosis; a positive result has a high predictive value.

Influence of UVA on the Shedding of Soluble ICAM-1 (sICAM-1) Molecules from HaCaT Cells
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The expression of intercellular adhesion molecule-1 (ICAM-1) on keratinocytes is a crucial point in cutaneous inflammation by mediating the contact to mononuclear cells. Soluble ICAM-1 molecules

have been shown to inhibit cellular interactions. Since UV light is capable of inducing cutaneous inflammation, but is also used to treat various inflammatory skin diseases, we studied the impact of UVA on ICAM-1 shedding in a keratinocyte cell line. HaCaT cells, kindly provided by Dr. N. Fusenig, were cultivated in DMEM without antibiotics in 10% CO₂ at 37 °C and stimulated for 24 h with rhIFN- γ (200 U/ ml). Duplicates were then irradiated with 0.1 or 1 J/cm² of UVA or exposed to the heat of the UV lamps by covering the plates with aluminium foil and then further incubated for 4, 8, 24 and 48 h. At these time points, sICAM-1 was determined by an ELISA technique in cell-free medium. Results were expressed as nanograms sICAM-1 per 10 μ g of DNA. Incubation with IFN- γ resulted in a steadily raising release of sICAM-1 into the cell-free medium. At 24 h we found 6.48 ng of sICAM-1 per 10 μ g DNA from unirradiated cells and in supernatants of cells irradiated with 0.1 or 1 J/cm², 2.13 and 1.91 ng/10 μ g DNA, respectively. Both 0.1 and 1 J/cm² irradiated cells showed a delayed increase of sICAM-1 shedding from approximately 1 to 2 ng/ 10 μ g DNA up to 24 h and then a sharp increase from 1.91 to 6.04 was observed in cells irradiated with 0.1 J/cm² until 48 h. Our results demonstrate an inhibitory effect on sICAM-1 release in HaCaT cells pre-treated with IFN- γ in the first 24 h after irradiation. UV light is known to increase ICAM-1 transcription. Our data suggest that UV irradiation is able to regulate ICAM-1 expression and shedding also at a posttranscriptional level.

Diagnosis of Chlamydia trachomatis by PCR -Comparison to Culture and DNA Hybridization

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Chlamydia trachomatis infection is the most frequent infection among sexually transmitted disease in the western hemisphere (approximately 3 times more frequently than *N. gonorrhoeae*). Therefore, a reliable diagnostic method is of great importance. The culturing of *C. trachomatis* on cell cultures, like McCoy cells is still the gold standard for the detection of this infection. Faster and simpler methods, like enzyme immunoassays, direct immunofluorescence and DNA hybridization, are less sensitive. In the last few years, the use of polymerase chain reaction (PCR) has been proposed by various authors as a new extremely sensitive method for this purpose. In October 1992, 2 commercially available PCR kits have been introduced (Amplicor from Roche Diagnostic Systems), one for the detection of *C. trachomatis* in cervical and female urethral specimens and one for its detection in male urine. The urine kit has been introduced in our laboratory in August 1992. Until now, 283 urinary specimens have been diagnosed and 45 (15.9%) have been found positive with the PCR method. This method was found to be more sensitive than the culture method. Seven cases were negative in the culture and positive with the PCR method. Most of them proved to be treated patients, whereas in one case a partner of a positive patient was diagnosed. It takes at least 3 weeks after beginning of treatment until the PCR test becomes negative. Furthermore, culture-positive women investigated so far were positive with the urine PCR as well.

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Data Base of Topical Drugs for Swiss Dermatologists

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In order to diagnose, treat and prevent contact dermatitis to topical drugs, it is important to have access to their complete and detailed composition. However, the present laws do not impose the declaration of all components of topical preparations that are commercialized in Switzerland. To close this gap and prevent noncoordinated collection of information from the producers, it has been decided with the support of the Swiss Contact Dermatitis Research Group (SCDRG) to establish a data base (DB) for Swiss Dermatologists. A computer program has been created to fulfil this task. It has been designed in such a way that it allows easy updating.

The large majority of producers that were approached have voluntarily disclosed the composition of their products. To preserve the confidentiality of this information, the access to the data will be restricted to Swiss dermatologists who have given their written consent to respect the confidentiality of the information to receive. Until now, information on over 500 products has been entered into the data base. In order to reach the needs of the practitioner, a printed alphabetical file will be made available. This file will be issued in 1994 once it has been tested by the members of the SCDRG. A software version will ultimately be developed. Future

extension of the DB to certain categories of OTC preparations and cosmetics will depend on the acceptance by the users.

4patients. The main benefit is the reduction (50%) of itch, most likely due to the association of H1 and H2 receptor antagonists given during the trial. No major side effects were observed.

Treatment of Warts using the 'Bleo-Prick' Technique without Anesthesia

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Intralesionally injected bleomycin is efficient in the treatment of up to 99% of warts. Recently, a novel prick technique using a bifurcated vaccination needle to introduce bleomycin into warts after local anesthesia was claimed to yield excellent results and to allow sensing of the epidermal base of the warts by the operator [Shelley and Shelley, Arch Dermatol 1991; 234-236]. Thus, the present study was designed to evaluate the reproducibility of their excellent results without anesthesia. Forty-two immunocompetent individuals were treated one to three times for a total of 315 warts (60% plantar mosaic, 28% plantar endophytic, 10% vulgar and 2% periungual warts). Elimination as defined as a 3-month recurrence-free interval was observed in 74% overall, i.e. 84% of plantar mosaic, 57% of plantar endophytic, 68% of vulgar and 67% of periungual warts. The technique is simple, precise, and the side effects are minimal. The main inconvenience is the failure to sense the base of the warts which might in part explain our less good results without anesthesia (74 versus 92%). The best indication for the 'bleo-prick' technique without anesthesia are mosaic warts.

Gold Salts in the Treatment of Atopic Dermatitis

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Gold compounds are extensively used as therapeutic agents in the treatment of rheumatoid arthritis. Auranofin has anti-inflammatory, specific immunomodulatory and antibacterial properties. Since auranofin may act at several levels of the inflammatory and immune response with fewer and milder side effects than classical gold salts, it might be useful in the treatment of atopic dermatitis (AD), a disease with immunologic abnormalities including deficient regulation of IgE synthesis, disturbed T cell function and altered pharmacological reactivity and releasability of vasoactive mediators. Four patients with severe AD were treated during a 6-month period with a triple association consisting in auranofin (Ridaura®) 6 mg/d, astemizole (Hisma-nal®) 10 mg/d and ranitidine (Zantic®) 300 mg/d. Patients were allowed to continue using topical steroid treatment, but no other changes were made. The response to the treatment was evaluated by a clinical scoring system. The clinical benefits of auranofin (reduction of the topographical and lesional score) after 6 months are minimal. No patients described an improvement of their AD, none could omit or significantly reduce topical corticosteroid treatment. Important fluctuation in the disease activity occurred during the treatment in 3 out of Chronic Urticaria and Quincke Edema of 8 Years' Duration due to Strongyloidosis

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Strongyloidosis, mostly caused by *S. stercoralis*, produces different skin manifestations, which can be very unspecific and therefore difficult to diagnose.

We describe the case of a 57-year-old manual worker, who suffered from paroxysmal episodes of urticaria after a long stay in Brazil 8 years ago: He also complained of Quincke edema of the

lips and rapidly moving 'welts' on the skin of the trunk, disappearing after a few hours. Corticosteroids and antihistaminics gave some improvement, but without lasting benefit. Persistent high total IgE and eosinophilia led to an allergological investigation -which was completely negative. But a positive culture of *S. stercoralis* in the feces and a highly specific IgE against *Strongyloides* (3.2 with ELISA) led to the diagnosis of strongyloidosis. After a treatment with albendazol (Zentel®) with 11 mg/kg BW for 10 days, the urticaria disappeared in 4 months. Eosinophilia normalized within 3 months, while total and specific IgE took 12 months to reach normal values. Besides bowel disease and diarrhea, urticaria represents a typical symptom of chronic strongyloidosis. Very often, a marked eosinophilia and high levels of total IgE are
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found. The described 'welts' might be a larva currens – a phenomenon highly specific of strongyloidosis, which lasts only a few hours. It has to be differentiated from a larva migrans, which is usually visible for a few days and caused by other parasites than *Strongyloides*. Itching dermatitis at the moment of skin penetration is another cutaneous sign, as well as anal pruritus at the end of an intestinal cycle. In cases of immunodeficiency, life-threatening disseminated strongyloidosis can occur with periumbilical, petechial efflorescences as visible signs. In our case, the repeated use of corticosteroids might have aggravated the symptoms of strongyloidosis. Coexistence of Disseminated Superficial Actinic Porokeratosis and Zosteriform Porokeratosis
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Porokeratosis is a chronic disorder of keratinization characterized by annular, circinate or gyrate plaques with an elevated hyperkeratotic border, histologically corresponding to the cornoid lamella. Clonal chromosome abnormalities seem to be responsible for the disorder of keratinization. Porokeratosis can be classified into the following types: (1) Mibelli (plaque-type or superficial disseminated eruptive form); (2) disseminated superficial actinic; (3) linear; (4) palmaris et plantaris disseminata; (5) punctata palmaris et plantaris; (6) gigantic.

The coexistence of disseminated superficial actinic porokeratosis and linear porokeratosis is rare. A description of the most frequent variations of porokeratosis is presented. And a 75-year-old woman affected with a rare linear porokeratosis – a zosteriform porokeratosis – and at the same time with a disseminated superficial actinic porokeratosis is reported.

Different treatments have been reported: keratolytics, vitamin A acid, 5-fluorouracil, cryotherapy, electrocoagulation, laser therapy and systemic retinoids.

better therapeutic results and to cause less complications. Patients⁵ who had earlier been treated with the argon laser report unanimously less pain with the dye laser treatment. This allowed us to treat children as well. The Hexascan system proved very useful for the treatment of larger surfaces.

Evaluation of Barrier Creams: An in vitro Technique for Human Skin

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An in vitro method was developed to measure the effectiveness of barrier creams against three dyes (eosin, methyl-violet and oil red O) with different octanol/water partition coefficients (0.19, 29.8 and 165, respectively) in human skin. Some galenic properties (water washability, water content and viscosity) of the products were also evaluated to try to understand the mechanisms of such a protection. The barrier creams were assayed by measurements of the dyes in the epidermis of protected skin samples after an application time of 30 min. Whereas some products showed a

degree of protection, as claimed on the packaging, we demonstrated disagreement with the manufacturer's information in several cases. Petrolatum was found as having the best protection of all tested products in our in vitro model. There was no correlation between the galenic parameters of the assayed products and the level of protection, indicating that neither the water content nor the consistence of the formulations influenced the protective effectiveness. In conclusion, knowing the possible skin effects of some irritants and the protection limits of some of the formulations on the market, our results stress that barrier creams should be used with caution.

Continuous Wave Tunable Dye Laser with Hexascan in Dermatology: Experience with 304 Treated Patients

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This is a report on our experience with the dye laser during the first 15 months on 304 treated patients. 197 were female and 107 male, the ages ranged from 6 to 71 years. Port wine stain was the most frequent diagnosis with 30.3%, followed by telangiectasias in 27.6%, spider nevi in 21.1%, capillary or senile angiomas in 9.8%, and other diagnoses in 11.2%. The most often treated localization were the cheeks. The wave length of 585 nm proved to be better than 577 nm. The power range was between 1.0 and 1.8 W, pulse durations between 80 and 200 ms (energy fluence 10-32 J/cm²) with a medium of 3.2 treatment sessions per patient. The response rate was excellent in 24.8%, good in 49.3%, fair in 20.5% and poor in 5.4%. Secondary effects were mostly hypopigmentation (12.4%), seldom hyperpigmentation (2.8%), and scars (1.9%). These results show that the dye laser seems to yield

Topical Hemotherapy: A Treatment for Chronic Wounds?

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Growth factors present in the plasma or produced by blood cells should favor wound healing. In order to test the potential of blood for the treatment of chronic wounds, we have treated chronic leg ulcers by 'topical hemotherapy' (THT) in 16 patients (venous insufficiency ulcers: 6; posttraumatic ulcers: 4; arterial ulcers: 2; postcellulitis ulcer: 1; 'malum perforans plantaris': 3). THT consists in applying the patient's own, heparinized blood (volume mean = 3.2 ml; range: 0.25-13.4 ml) onto the ulcer. The wound is immediately covered by an occlusive hydrocolloidal dressing that stops the blood from oozing out and keeps a wet environment, thus preventing protein degradation. The procedure is applied every second day.

Before the treatment, the granulation tissue represented 25% of the surface of the bottom of the wound on average. After the first THT, part of the fibrinonecrotic material could be removed from all the wounds. After a mean of 9 THT applications (range: 3-18), granulation tissue covered up 65% of the total surface of the ulcer on average (range: 5-100%). At that time, an autologous skin graft could be

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done in 11 patients; the graft was successful in the 80% of the cases and we obtained complete healing in 83% of the cases after a mean of 21 days (range: 15-30 days). We have seen neither local or systemic toxic effects, nor superinfection. THT seems to accelerate the development of

granulation tissue. Growth factors and proteases produced by the blood cells could have a relevant role in this process.

Pili torti et canaliculi in Ectodermal Dysplasia

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Uncombable hair is a heterogeneous symptom with a partially genetic background. In order to make an exact diagnosis, it is mandatory to recognize associated abnormalities, to do pedigree analyses and scanning electron microscopic studies of the hair. In a case of Rüdiger syndrome (ectodermal dysplasia, ectrodactyly, cleft lip/ palate), and in a patient with familial trichodonto-onychial ectodermal dysplasia with syndactyly scanning electron microscopy demonstrated pili torti et canaliculi, helicotrichia and cuticular dystrophy. Congenital pili torti et canaliculi must be differentiated from classic pili torti and from 'cheveux incoiffables' (pili trianguli et canaliculi), inasmuch as they may present in hypotrichosis congenita hereditaria of Marie-Unna, or as part of a complex ectodermal dysplasia syndrome with clefting of the lip/palate and/or limb defects. It is noteworthy that some of those patients show a dysmorphic facies and an atopic constitution in addition to the aforementioned abnormalities. Possible relations of these syndromes with each other, with special respect to the Rapp-Hodgkin (ectodermal dysplasia, midfacial hypoplasia, cleft lip/ palate) and to the Hay-Wells (ankyloblepharon, ectodermal dysplasia, cleft lip/palate) syndromes, are discussed.

Prevalence of Atopy and Atopic Diseases in the Adult Population of Switzerland (Sapaldia Study)

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The Swiss Sapaldia study is a multicenter cross-sectional study initiated in 1991 to evaluate the relationship between environmental exposure and respiratory symptoms and diseases in a random population sample of eight areas in Switzerland with distinctive environmental characteristics. We present here prevalence data of 8,357 adults (18-60 years) who completed a standardized questionnaire, for whom allergy skin prick tests (SPT) to eight inhalative allergens (performed with Phazet) and in vitro allergy screen test (Phadiatop, CAP FEIA system) were obtained.

Results. On the basis of a positive Phadiatop and/or a positive skin prick test (wheal ≥ 3 mm) to any of the 8 seasonal or perennial aller-

gens, 32.3% (men 35.7%, women 28.8%; $p < 0.001$) were considered as atopic. 13.6% (men 14.5%, women 12.7%; $p < 0.05$) suffered from allergic rhinitis (including hay fever), 12.3% (men 12.9%, women 11.6%; n.s.) from hay fever (seasonal symptoms). Atopic asthma was diagnosed in 4.4% (men 4.9%, women 4.0%; n.s.). 13.8% of the atopic patients (men 12.3%, women 15.3%; $p < 0.001$) had eczema or skin problems. Taken together, 21.8% (men 22.2%, women 21.46%; n.s.) of the population suffers or suffered from an atopic disease. 3.7% (men 2.7%, women 4.6%; $p < 0.001$) experienced generalized reactions after insect stings.

Conclusions. These data, combining questionnaire answers and data from SPT and PH, confirm the high prevalence of atopy (about 30%) and atopic diseases (about 20%) in an industrialized country. Two-thirds of the atopic persons also developed an atopic disease.

Unusual Skin Test Reaction to Molybdenum -Hypersensitivity to Molybdenum as a Possible Trigger of Systemic Lupus erythematosus?

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A 24-year-old female patient had developed remittent fever up to 39.5 °C, arthralgia and oral ulcerations after the implantation of 2 metal plates for posterior fusion of the segments C6-Th₁. After a diagnostic medical work-up with negative results, the metal implant was suspected to be responsible for the symptoms and the patient was referred for skin testing. Scratch testing with the metal alloy and molybdenum was negative after 15 min, but showed an erythematous and infiltrated reaction after 6 h followed by an erosion. Patch testing resulted in an erythematous infiltration after 48 h that progressed to an erosion. Patch testing with the other components of the alloy was negative. Six control patients showed no skin reaction to molybdenum. Histologic examination of the positive patch test reaction showed parakeratosis, acanthosis and a lymphohistiocytic dermal infiltrate. A lymphocyte transformation test resulted in an increased reaction to molybdenum. After removal of the metal plates, a striking remission of the symptoms could be observed. However, there was a new flare up after the second skin test, and following dental treatment with a molybdenum-containing drill. Two months later, the patient showed a progression of the disease without obvious exposure to molybdenum. She developed not only high fever, arthralgia, oral ulcerations and alopecia, but also pathologic laboratory results (pancytopenia, hypocomplementemia, increased anti-Ro/SS-A, anti-La/SS-B, anti-Sm and anti-RNP). Therefore the diagnosis of systemic lupus erythematosus was established and treatment with immunosuppressive agents was initiated. The coincidence with the implantation of the metal plates, the impressive – but only transient – remission after the removal of the implant, the skin test reaction and the lymphocyte transformation test indicate that an unusual delayed type hypersensitivity to molybdenum may have been a triggering factor for the onset of systemic lupus erythematosus.