Selected Abstracts of the First World Congress on Work-Related and Environmental Allergy (1st WOREAL)

and

Fourth International Symposium on Irritant Contact Dermatitis (4th ICD)

Abstracts

9–12 July 2003 Helsinki, Finland
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Prediction of Irritancy

**In vivo Irritation Models: Beyond Bioengineering Techniques – New Non-Invasive Approaches**

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Over the last 3 decades, functional studies on epidermal parameters have been performed using non-invasive instruments, based on biophysical measurements such as barrier function measuring trans-epidermal water loss, stratum corneum (SC) hydration and SC water-holding capacity, vascular parameters using laser Doppler, reflectance spectroscopy-based colour analysing instruments and ultrasound, and mechanical alteration of the skin in deeper compartments. Intrinsic and extrinsic skin alterations have been studied, e.g. allergic and irritant contact dermatitis, atopic dermatitis, psoriasis and ageing-related parameters, as well as in testing pharmaceutical and cosmetic compounds. Recent publications indicate a broadening range of studies regarding biochemical pathways in relation to functional biophysical parameters. Studies on micro-morphology and biochemistry require invasive biopsies, in vitro cell culture or animal models. Since new regulations prohibit the use of animal models in testing of cosmetic preparations and biopsies on human volunteers cannot be performed routinely, new techniques are needed in order to study biochemical pathways and cosmetic compounds. Results of non-invasive visualisation of ultrastructural morphology (electron microscopy) on tape stripplings have been published. A major focus has been the extra-cellular inter-corneocyte domains. Both lipid fractions and processing enzyme activities have been quantified after non-invasive removal of corneocytes with adhesion techniques. Inflammatory processes can be studied using absorbing tapes. There are emerging data on the antioxidant network of the SC using tape stripping. Proteins can be quantified on these tapes and thus the above-mentioned parameters might be normalised for the amount of removed SC. These new non-invasive techniques enable dermatology research to study biochemical pathways as well as cytokine cascades and correlate them with functional data acquired with biophysically based instruments.

**In vitro Irritancy Prediction Using a Three-Dimensional Culture Model**

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**Objective:** This study was undertaken to compare irritant potency for several cosmetic substances in vitro. **Methods:** Two non-commercial 3-dimensional models as well as monolayer culture models were used. MTT assay and histological observation were performed for comparison. We assessed ranking order and compared the results of the different models. **Results:** Although the general trend was similar, there were many differences between the different models. **Conclusion:** Caution should be exercised in the evaluation of the results. By briefly reviewing other authors’ recent results together, problems and limitations in this field can be discussed.

**Prediction of Subclinical Irritation**

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Bioengineering techniques have been proven to be helpful in monitoring changes in skin physiology and quantifying skin disease. Detection of subliminal or non-visual changes is a challenge in order to predict potentially pathological conditions such as irritation or pre-clinical dermatitis. Several techniques can be used depending on the mechanism eliciting irritant contact dermatitis. Laser Doppler velocimetry and evaporimetry are good discriminators between irritant and non-irritant substances, whereas corneometry and chromametry do not clearly distinguish between them. D-Squame, squamometry, microwave corneosurfametry and dansyl chloride extraction test have been reported to be capable of ranking surfactant irritancy. Stress tests can also be a good tool for investigating changes in the water-holding capacity of the stratum corneum directly linked to dehydration induced by subliminal chronic irritation.
The Glutathione Redox Ratio in Clinically Undamaged Skin May Predict the Duration of Treatment in Chronic Hand Dermatitis

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**Objective:** Chronic hand dermatitis, although restricted to a small area, causes oxidative stress in the whole skin, evidenced along with other changes by the decrease in reduced glutathione (GSH) and increase in its oxidized form (GSSG). We wondered if the duration of the treatment period necessary for improvement in patients could depend on the GSSG/GSH ratio in apparently healthy skin.

**Methods:** 12 outpatients (11 female, 1 male; age range 28–52 years) with exacerbated chronic hand dermatitis were observed and treated with topical glycocorticosteroids and emollients during a 2-month period. The level of GSH and GSSG in skin homogenates was measured before treatment in lesional and apparently healthy skin, and after treatment in lesional skin.

**Results:** After 2 months, dermatitis had improved entirely in 6 patients (group 1). The other 6 patients had a decreased eczema severity score, but had not totally improved (group 2). Statistical analysis showed that the GSSG/GSH ratio of unaffected skin differed significantly between the first and second groups (0.10 and 0.24, respectively, \(p < 0.02\)). At the same time, we could not find any statistical differences between GSSG/GSH ratios in lesional skin areas before and after local treatment. Further analysis showed that the mean duration of disease in the groups was also different (in group 1, it was 2.2 years, while in group 2, it was 6.1 years).

**Conclusions:** GSH, a crucial low-molecular-weight intracellular antioxidant, has been postulated to play an important role in the suppression of both irritant and allergic contact dermatitis. In long-standing hand dermatitis, slow normalization of the GSSG/GSH redox ratio may negatively influence the improvement process.

Identification of a Sensitive Skin Panel?

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The objective of this study was to identify a ‘sensitive’ panel by evaluating individual sensitivity to different chemicals using a range of test methods and examining different anatomical regions. Volunteers were recruited based on their sensitivity during previous studies. Their susceptibility to acute irritation, urticaria, stinging, itching, cooling and burning sensations was assessed using 0.1 and 0.3% sodium dodecyl sulphate, 0.3 and 0.6% Tego betain F50 and 0.1 and 0.2% benzalkonium chloride, 1 M benzoic acid and 125 mM trans-cinnamic acid, 10% lactic acid, 50% ethanol, 0.5% menthol and 0.1% capsaicin, respectively. Statistical evaluation indicated that the tests were not independent and showed that a significantly larger than anticipated proportion of panelists fell into the lowest (least sensitive) and highest (most sensitive) categories. In tests for acute irritancy, urticaria (trans-cinnamic acid only) and sensory perception (ethanol only), males tended to be more sensitive than females (\(p\) value <0.1). The results from the present study provide evidence which is consistent with the view that it is possible to identify, in the normal population, subjects who are more generally sensitive to a range of materials producing heightened non-immunologic skin reactions. However, relatively weak correlations were seen and the fact that the results applied mainly to males indicates that further work would be necessary to fully support the conclusions.

Prediction of Damaging Effects of Wash-Off Products on Human Skin Barrier Function

Hyldgaard, J.G., Halkier-Sørensen, L., Jensen, A.S.
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**Background:** From studies in the 1980s and 1990s, we learned that occlusive models do not predict effects experienced in real life with wash-off products. Field studies reflect real life situations, but are cumbersome, time consuming and expensive. **Objective:** To develop a new in vivo skin test method that imitates real life wet work conditions for wash-off products. **Methods:** The volar aspect of the elbow in human volunteers was used to evaluate the damaging effect on the skin barrier function of different wash-off products. Tests were performed with or without simultaneous application of skin care products. Skin physiological measurements, drop out time/number and skin scores were recorded for 12 days to evaluate the effect on human skin. Different statistical methods were applied for the evaluation of the results. **Results:** A number of products were tested and showed significant statistical differences. Some hygienic procedures were demonstrated to be well tolerated for frequent use. **Conclusions:** The elbow test gave reproducible and consistent results and made it possible to separate and select products with the potentially lowest damaging effects on the skin barrier.

Acquired Cutaneous Hyperirritability after Previous Hand Dermatitis

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**Objective:** Some patients with healed (occupational) dermatitis complain of experiencing ongoing increased skin sensitivity. However, in many of these cases, the clinician cannot identify any skin impairment. **Methods:** Recently, we have updated Burckhardt’s test by a well-tolerated modification [Swift dified alkaline resistance test (SMART)]. The SMART comprises a 0.5 M NaOH challenge at the volar forearm (FA) for only 2 \(\times\) 10 min with intermediate trans-epidermal water loss measurements and a clinical assessment. In a group of 572 patients with former occupational irritant hand eczema, the test was able to distinguish atopics from non-atopics with a specificity and sensitivity of 75%. With the aim of identifying acquired hyperirritability, the SMART was applied simultaneously to two different body areas in a comparative fashion: (1) one area which had previously been exposed to irritants at the workplace, i.e. back of hand (BOH), and (2) another which had not, i.e. FA. **Results:** In the controls (\(n = 31\)), there was reactivity in the FA in 12 persons, but there was no reactivity solely on the BOH. However, in the test group of 237 persons with former (healed) occupational dermatitis,
a subgroup of 23 (10%) was detected in whom the SMART was positive solely on the BOH; these patients claimed a remaining increased skin sensitivity. **Conclusions:** Comparing skin reactivity to the SMART in the FA and the BOH simultaneously (differential irritation test), we could confirm that in general, the BOH is relatively robust, even in individuals with sensitive skin. However, there is a minority of cases where the normal hierarchy of skin sensitivity is absent (isolated reactivity of the BOH); we claim that this a priori paradoxical constellation provides strong evidence for an acquired hyperirritability. Identifying this phenomenon is of major relevance (prognosis, claims).

**Early Upregulation of Chemokine Expression in Skin Injury following Tape Stripping**

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**Objective:** Chemokines are small proteins that mediate cellular trafficking through coupling to their G protein-coupled receptors. Chemokines are classified as CXC, CC, C and CX3C chemokines.

It has been shown recently that chemokines are important mediators of skin inflammation in both atopic dermatitis and allergic contact dermatitis [1]. As irritant dermatitis is an important occupational skin disease, we also wanted to study the role of chemokines in irritant contact dermatitis, using skin injury with tape stripping as the model. **Methods:** Naïve BALB/C mice were tape stripped with Tegaderm dressings 10 times. Groups of mice were sacrificed after 20 min and 2, 6 and 24 h. Expression of chemokines and their receptors was studied with competitive real-time PCR (TaqMan). **Results:** The expression of several chemokines was already upregulated from 20 min to 2 h when compared to baseline. These included CCL2 (MCP-1), CCL8 (MCP-2), CCL11 (eotaxin), CCL12 (MCP-5) and CCL17 (TARC). Conversely, CCL27 (CTACK) expression was already downregulated 20 min after tape stripping. **Conclusions:** Chemokines are important mediators involved in the early phase of irritant dermatitis caused by mechanical skin injury. Strategies to prevent chemokine ligand-receptor interactions can also provide treatment and prevention options for irritant contact dermatitis.

**Reference**

Barrier Creams and Moisturizers

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Contact dermatitis, and especially irritant contact dermatitis, is the most frequent manifestation of occupational skin disease. In Germany, the number of cases notified to the occupational health insurance companies has risen in recent decades and remains at a high level. Since the course of irritant dermatitis may be chronic, possibly leading to complications such as sensitization or disability, and since treatment is frequently of limited efficacy, prevention of this condition should have priority. Apart from total elimination of cutaneous exposure to hazardous substances, gloves and barrier creams are additional tools in an integrated concept of preventive measures [1]. The use of protective creams before work should be followed by appropriate cleansing and the use of barrier-regenerating skin care after work. While effective protective creams may prevent irritant contact dermatitis, there is also a risk that noxious products may enhance irritant contact dermatitis [2], for example by an increased penetration of specific irritants. It is therefore highly necessary to know which product is effective in which occupational setting before counselling workers on their use. For testing of the efficacy of protective creams, in vitro tests, animal models and human tests have been proposed. Regarding the latter, a repeated irritation test, repeated wash tests and percutaneous penetration tests have been described. Recently, minimum test standards for the assessment of protective (barrier) creams were proposed in a guideline of the German Society of Occupational Dermatology and the Society of Dermapharmacy. In addition to these minimum requirements, further tests were developed to substantiate claims such as efficacy against various types of irritants and efficacy of product combinations. It should be stressed, however, that the gold standard for efficacy assessment would be a randomized, controlled clinical prevention study in a risk population. Apart from the efficacy of a product, its cosmetic acceptability and practical application, aspects such as spreadability on the skin play an important role. A fluorescence-controlled application test allows the objective evaluation of these aspects [3].

References

Education Programs in the Prevention of Irritant Contact Dermatitis

Schwanitz, H.J., Klippel, U., Schlesinger, T., Wulffhorst, B., Schürer, N.

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(1) Primary prevention is directed at the avoidance of occupational skin diseases. Motivation and instructions from health educationalists concerning hands-on training in skin protection are most effective at that time point. (2) Secondary prevention aims at early recognition and intervention. Exact diagnosis and individualized glove recommendation are required. A model project of secondary individual prevention of hand dermatitis in geriatric nurses was conducted between 2000 and 2002. The interventional group comprised 135 individuals and the control group 107 motivated volunteers. Health educational measures included one-on-one consultations, skin protection seminars and employer consultation. After completion of the program, the interventional group displayed a higher usage of gloves (from 59 to 84%), while that of the control group remained unchanged (from 73 to 72%). After the program, 52% of volunteers reported better awareness of effective intervention for their skin diseases; i.e. they achieved a higher level of self-management. Severity of hand eczema improved significantly in the interventional group. Upon entry, 15% of volunteers exhibited no skin changes; after the program, 35% of volunteers presented with healthy skin. The number suffering moderate to severe hand eczema decreased from 57 to 6%. (3) Tertiary prevention tries to limit the sequelae of occupational skin diseases that have already occurred in an individual. Health education plays a significant role in the motivation that the disease must not be accepted as a given fate. Intervention by tertiary prevention was conducted in more than 1,000 inpatients. One year after this kind of intervention, two thirds of these fatal cases were still active in their profession with an improved clinical picture.
Causes of Occupational Irritant Contact Dermatitis – Finnish Statistics

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Objective: To present an overview of the causative agents of occupational irritant contact dermatitis (ICD) in Finland. Methods: The Finnish Institute of Occupational Health has compiled statistics on occupational skin diseases since 1975. The cases were classified according to the main diagnosis and the main cause. Results and Conclusions: 11,532 new cases of occupational dermatoses were reported during the 10-year observation period 1990–1999. Altogether, 3,667 cases (31%) were diagnosed as allergic contact dermatitis (ACD), 4,498 (39%) as ICD and 3,367 (29%) as other occupational dermatoses, including 633 unspecified contact dermatoses (either ACD or ICD). The incidence of occupational ICD was 20 new cases per 100,000 person years. The most common causes of all occupational dermatoses were detergents (13%), rubber and rubber chemicals (12%), plastic chemicals (9%), wet and dirty work (9%) and animal epithelia (7%). The most common causes of ICD were detergents (30.5%), wet work (12.2%), dirty work (7.9%), oils and lubricants, including metal-working fluids (7.2%), organic solvent mixtures (5.2%), handling of foodstuffs (4.4%), organic materials, e.g. animal-derived dust or substances, flours, grains and fodder, species of wood and plants (3.3%), mechanical friction of the skin (2.4%), cement, concrete (2.0%), sprays, fumes, dust and smoke (mixture), e.g. plastic, paint and sanding dust (1.9%), glues (1.7%), synthetic mineral fibres (MMVF) (1.2%), hairdressing chemicals (1.2%), warm moisture (1.1%), synthetic resins and plastics (0.9%), paints, varnishes and stains (0.7%), others (11.0%) and unknown factors (5.0%).

Causes and Prevention of Occupational Contact Dermatitis

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Occupational contact dermatitis (OCD) takes the first rank of all occupational diseases in many countries. The incidence rate is believed to be around 0.5–1.9 cases per 1,000 full-time workers per year. However, the true incidence of work-related hand eczema (mostly irritant hand eczema) is highly underreported. The development of OCD is determined by a combination of individual susceptibility (endogenous factors) and exposure characteristics (exogenous factors). Skin contact with irritants and/or allergens is a necessary condition of contact dermatitis and the probability and severity of a reaction depend on the type and intensity of exposure. Epidemiological studies play an important role in observing disease trends, analysing risk factors and monitoring the effect of preventive measures. OCD has become an issue of increasing importance worldwide, not only due to cost intensification for employers but also due to impairment of employees’ quality of life. This lecture summarizes some important causes of OCD in Europe, demonstrates possibilities of prevention and ends by highlighting important future health services and population research issues. The following questions will be discussed:
– How common is OCD in different industries and what is the extent of its underestimation?
– What kind of regulations are needed to prevent OCD?
– How should high-risk individuals (atopics) be dealt with?

Research into the causes and prevention of OCD using an epidemiological approach is still in its infancy, yet already there are some indications that OCD can be prevented effectively.

References

The Diagnosis and Treatment of Occupational Hand Eczema

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The pragmatic definition of occupational hand eczema is based on (1) identification of occupational hazardous skin exposure, (2) exposure of the patient to this factor and (3) a causal relationship demonstrated between exposure and the development of hand eczema. The establishment of a convincing relationship between occupational exposure and development of hand eczema may be time consuming because hand eczema is often of multifactorial origin with exogenous and endogenous factors involved, and a careful history, exposure analysis, clinical examination and allergological investigation are all necessary requirements for an optimal classification of each individual case. Irritant contact dermatitis on the hands is considered the most common type of occupational skin disease. Population-based epidemiological studies have reported the highest incidence rates in hairdressers, bakers and cooks. Wet work, detergents, disinfectants and acidic and alkaline chemicals are the main irritant etiologic factors. Symptomatic treatment with topical corticosteroids and skin care products is indicated together with instruction in preventive measures. The identification of allergens and irritants at the workplace and at home are decisive for treatment success, as well as for the possibility of giving appropriate information and education to the patient in order to avoid recurrences and to reduce the severity of the eczema. Patients who are diagnosed as reacting to relevant positive contact allergens show better improvement in both perceived eczema severity and quality of life score compared to patients with negative patch tests. Further, it must be emphasized that repetition of exposure history and repetition of information and patient education are important. Efficient educational programs need to be developed to reduce the risk of developing occupational dermatitis in hazardous occupations.

‘General Secondary Individual Prevention’ of Occupational Skin Disease: Prospective Intervention Study in Northwest Germany

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Objective: Work-related eczema, most often affecting the hands, was recently proved to be a prominent disorder predictive of unemployment. Since 2002, the Accident Insurance Fund for Health and Welfare Services offers their parties of all insured occupational groups a secondary individual prevention (ASIP) program to reverse early hand dermatitis and to prevent job loss. Methods: In 2002, 277 insured persons of 11 occupational groups from the region of Northwest Germany attended individualised skin protection seminars at our clinic and were followed up. In an uncontrolled prospective intervention study, they were reassessed and retrained 3 months after the seminar and interviewed by telephone 9 months later as to the course of their skin disease. Results: At the first follow-up, 167 participants (60%) were seen; median age was 39 years, median duration of employment 13 years and median duration of skin disease 3 years. Significant improvements were shown on our hand eczema scale (p = 0.003), the latter being significantly correlated with the participants’ self-assessment (p < 0.0001). Eight of the participants followed up (5%) had lost their job because of hand dermatitis. Conclusions: Our results suggest that ASIP can reduce clinical skin symptoms in affected workers of different occupational groups by increasing knowledge and prevention practices in the workplace. There is evidence that this exemplary concept of close cooperation between the workers’ compensation board, dermatologists, health-pedagogic teachers and company physicians should be applied generally to working populations affected by occupational skin disease.
Immediate hypersensitivity to natural rubber latex (NRL) has become increasingly common during the last 20 years and is currently one of the most frequently encountered occupational diseases among health care workers and others using protective gloves. Several groups at high risk of developing NRL allergy have been defined, and a large number of NRL allergens have been characterized at the molecular level. In addition to immediate type I allergy symptoms, more than half of NRL-allergic health care workers suffer from hand dermatitis. It has long been known that small-molecular-weight rubber chemicals can cause hand dermatitis, but it has been suggested recently that proteins eluting from NRL gloves may also play an important role in the development of hand dermatitis. However, the pathomechanisms of protein contact dermatitis are at present poorly understood. Moreover, it is not known by which mechanisms cutaneous route sensitization causes induction of NRL-specific IgE antibodies. A novel mouse model of NRL-induced protein contact dermatitis has recently been described. This model incorporates several features that are likely to be important in the pathogenesis of NRL hypersensitivity in humans. Repeated application of NRL proteins on tape stripped (slightly injured) mouse skin produced dermatitis manifested by epidermal and dermal thickening and characterized by the dermal accumulation of T cells, eosinophils and degranulated mast cells. The inflammatory cell infiltration to the skin correlated with an induction of proinflammatory and Th2 cytokines as well as chemokines. In addition, epicutaneous application of NRL proteins in the absence of adjuvant led to increased levels of total serum IgE and NRL-specific IgE as well. These results indicate that cutaneous route sensitization with NRL elicits a Th2-type systemic immune response and a local Th2-dominated skin inflammation. Epicutaneous sensitization to proteins eluting from NRL gloves may therefore play an important role in the development of hand dermatitis and NRL-specific IgE antibodies. This model of protein contact dermatitis can be utilized for studying the mechanisms of allergen-induced skin inflammation as well as for determination of threshold levels for sensitization to protein allergens via the cutaneous route. The contribution of injury and hydration to sensitization can also be systematically explored. Finally, the efficacy of novel topical and systemic therapies that might be predicted to have efficacy in humans can be carefully tested.

Allergy to natural rubber latex (NRL) proteins continues to be an important medical and occupational health problem. The World Health Organization/International Union of Immunological Societies Allergen Nomenclature Sub-Committee currently (March 2003) lists 13 NRL allergens (www.allergen.org). Which of these resist the harsh rubber manufacturing processes as immunologically active molecules and serve as allergenic stimuli is still insufficiently known. Genuine NRL allergy is directed against allergenic molecules present in manufactured products, but IgE class antibodies binding to various other rubber tree-derived proteins are commonly encountered and can complicate the diagnosis of NRL allergy. Dermal exposure via slightly damaged skin appears to be an important route of sensitisation. In this mode, hydrophilic proteins, such as Hev b 5 and Hev b 6, may play central roles, whereas in mucosal exposure during surgical operations, hydrophobic allergens, most notably Hev b 1 and Hev b 3, often elicit allergic immune responses. Which allergens can bind to glove powder and sensitize subjects via the respiratory tract is an important, yet unresolved question. Hev b 6.01 (prohevein) and its N-terminal hevein domain, Hev b 6.02, as well as Hev b 5 (acidic NRL protein), are the most important major allergens for adult patients, and, in particular, for people using gloves. These allergens are also the two most
abundant allergens in medical and household gloves. Hev b 1 (rubber elongation factor) and Hev b 3 (small rubber particle protein) are major allergens for children with spina bifida or other congenital anomalies requiring multiple surgical operations. Several NRL allergens have been categorised as minor allergens whose role could mainly be in commonly occurring allergen cross-reactions. The overall significance of Hev b 2 (beta-1,3-glucanase), Hev b 4 (microhelix component) and Hev b 7 (patatin homologue) as well as Hev b 13 (early nodulin-specific protein), is still controversial and needs further clarification. From the occupational safety point of view, no allergens should be detectable in NRL products. Since small amounts of proteins are, however, needed to maintain the proper tensile and barrier properties of NRL, the goal should be products in which the levels of allergenic components are as low as reasonably practicable. Recently, specific immunological methods to quantify clinically relevant NRL allergens have been developed, and such methods are currently under international evaluation. Eventually, these methods would enable the determination of meaningful safety limits. Finally, it is worth noting that numerous glove types with no detectable or very low allergen concentrations are already widely available. Health authorities in certain countries have arranged round-robin type tests and informed consumers about allergen levels in currently marketed medical gloves. This policy is believed to have a significant impact on glove purchasing decisions and thereby to improve the occupational safety of NRL-containing medical devices.

Problems of Latex Allergy in Clinical Praxis

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Allergy to natural rubber latex (latex) has become a well-understood entity during the last decade. However, the whole problem is not yet solved, and life-threatening reactions are still reported. For practical purposes, prevention of sensitization is crucial. When sensitization has occurred, accurate diagnosis is important in order to prevent symptoms from latex contacts. For prevention, the use of low-protein, non-powdered latex gloves has been widely adopted in health care. This has proved to be beneficial, although low protein content does not guarantee low allergenicity. Important latex allergens have small molecular weights, and even very small protein amounts may be enough for sensitization and elicitation of symptoms in sensitized persons. Estimation of the main allergens in latex products will be the future control of quality and safety. Preventive measurements outside of the health care field are still lacking; the allergenicity of consumer products is not known and has not been studied. Diagnosis of latex allergy is problematic. Skin prick testing and estimation of specific IgE antibodies only give information about sensitization to latex; symptoms are needed for proof of allergy. This may be self evident, but up to 30% of children with challenge-proven latex allergy did not remember having any symptoms from rubber products. The main problem in diagnosis today is the lack of standardized, high-allergenic challenge material. The allergenicity of gloves has decreased dramatically in recent years, and therefore special knowledge is needed to find a reliable glove for challenging to avoid false-negative results. At the moment, there are several different latex skin prick test materials (only one standardized) on the market outside the US. Estimation of specific IgE antibodies is widely used, but for both methods, the sensitivity and specificity values are unreliable, because they only can be estimated in correlation with a positive challenge test. Due to the diagnostic difficulties, different numbers exist for the prevalence of latex allergy in different populations.
Sensitive Skin Syndrome

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Sensitive skin syndrome (SSS) connotes different concepts to the dermatologist as it does to industry. To the latter, SSS denotes burn, sting, itch and discomfort. To the dermatologist and patient, SSS defines skin discomfort related to:

- irritant dermatitis syndrome, especially sensory irritation and non-erythematous irritation;
- allergic and photoallergic dermatitis;
- contact urticaria syndrome (CUS, NICU and ICU);
- chemical acne.

This presentation focuses on the epidemiology, etiology and physiology and pathophysiology of SSS.

Sensitive Skin Symptoms – Risk of Hand Eczema

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Objective: To evaluate questionnaire methods for estimating the risk of endogenous hand eczema (HE). Methods: Four questions for detecting sensitive skin symptoms are included in a standard questionnaire (Tuohilampi questionnaire) which has been used in HE surveys. The questions are: (1) Do you suffer from dry skin?; (2) Does your skin tend to itch when you sweat?; (3) Do you get a rash from jeans buttons, metal fasteners, costume jewelry (e.g. earrings) or other metal parts of clothes next to your skin? (excluding under rings), and (4) Do you feel itchy if you wear wool on your skin? Results: Answers to these questions correlated with reporting of HE. In a female population (dental nurses), itchiness when sweating correlated best with HE \( (p = 0.001) \), followed by a history of metal allergy \( (p = 0.001) \) and dry skin in general \( (p = 0.055) \), while itchiness when wearing wool did not correlate with HE. A linear correlation was detected between reporting of HE by forest industry workers (all men) and the number of sensitive skin symptoms. The prevalence of HE over 12 months was 6.6% among those with no symptoms of sensitive skin and 30.5% among those reporting 3–4 sensitive skin symptoms. In logistic modelling, sensitive skin symptoms proved to be at least as significant risk factors for reporting HE as a history of atopic dermatitis. The ability of the above questions to detect those who also report a history of atopic dermatitis was also studied among dental nurses. The highest sensitivity \( (0.82) \) was found for the question on dry skin, followed by that regarding itchiness when wearing wool \( (0.79) \). The highest specificity was detected for the question on itchiness when sweating \( (0.78) \). Conclusions: Questions used to assess sensitive skin symptoms are more straightforward than questions used to detect an atopic constitution. The correlation of reporting HE with sensitive skin parameters was better among male than female populations. Females more frequently reported their skin to be dry than males. It is possible that males pay less attention to skin dryness and only report it when it is distinct.
Allergens and Irritants in the Garden

Plant Allergens and Irritants
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A flower garden is full of allergens and irritants. The Asteraceae and Chicoraeae families contain hundreds of allergenic sesquiterpene lactones, *Tanacetum parthenium* (feverfew) being one of the most allergenic among them and *Sonchus arvensis* (field milk thistle) a newcomer on the list. Plant lactones can induce classical allergic contact dermatitis (ACD), erythema multiforme-like eruptions and aerogenic allergic dermatitis. A certain proportion of sesquiterpene lactone-allergic people become sensitive to ultraviolet light. The clinical picture and course of such dermatitis resemble that of polymorphous light eruption or chronic photosensitive dermatitis. Primin is one of the superallergens, a single application of which can sensitize a human. *Primula obconica* has been considered to be the only allergenic primula. A recent study from Great Britain showed that some other species of more than 400 primulas also contain primin and probably also other allergenic chemicals. Tuliposide A and B are well-known sensitizers in tulips; tuliposide A and tulipaline A in Alstromeria. In addition to tulips, other flower bulbs may also cause ACD or irritant contact dermatitis. Six years ago, *Pennisetum purpureum* and some other grasses were reported to cause ACD. Just recently, *Stellaria media* (common chickweed) and *Trifolium repens* (white clover) were added to the list of contact sensitizers, but the causative chemicals remain unknown.

Mosquito Bite Allergy
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Mosquitoes frequently cause harmful pruritic wheals and papules. While feeding on the blood, mosquitoes inject saliva into the skin. Most people become sensitised against salivary proteins after repeated bites. Pruritus is the main symptom in mosquito bite allergy. Peroral antihistamines have proven effective in treating patients with mosquito bite-associated pruritus or skin lesions.
Visual Scoring of Skin Irritation Reactions – What Are the Limits?
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We have previously reported that, with suitable training and experience, skin irritation reactions can be graded visually with a high degree of sensitivity and precision. The objective of the work presented here is to demonstrate the possibilities and limitations of the grading of skin irritation reactions by subjective visual assessment. In the present work, we recorded a wide range of relatively minor skin irritation reactions using a high-quality digital camera. The skin reactions recorded were then graded by independent observers according to their appearance on a computer monitor. (Note that in ‘real life’ testing, the skin is graded directly!) The results show that very subtle degrees of both erythema and skin dryness can be accurately described by trained skin graders in a reliable and reproducible manner. Examples of the grading scales and sensitivity of scoring will be shown. We conclude that visual scoring, when conducted well, represents a rapid and accurate method for the assessment of minor degrees of skin irritation. The present evidence, taken in combination with previously presented information on bio-engineering techniques, leads us to the conclusion that visual assessment is both an adequate and a robust technique, delivering information of the quality necessary for safety assessment of consumer products.

Endotoxin in Metal-Working Fluids Does Not Induce Irritant Contact Dermatitis
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Objective: Microbial contamination of water-based metal-working fluids (MWF) is minimized by the use of biocides. Eliminating living organisms does not necessarily prevent the contamination of MWF with cell constituents like endotoxins. To assess possible skin hazards of this contamination, the capacity of endotoxin in MWF to induce irritant contact dermatitis was studied. Methods: A high concentration of endotoxin (100 μg/ml) suspended in a common MWF as well as aqua was applied for 6 h on 4 consecutive days on sites of healthy skin as well as SLS-induced irritant contact dermatitis in 15 non-atopic and 15 atopic individuals. Skin reactions were monitored using a clinical score, laser blood flow monitor and determination of transepidermal water loss. As control for the penetration of a pro-inflammatory macromolecule into the skin, TNF-α (106 U/ml) was applied on days 1 and 2 at sites of NLS-induced irritant contact dermatitis. Statistical analysis was performed using the non-parametrical test of Wilcoxon for paired samples. Results: Neither in atopic nor non-atopic individuals was any significant influence of endotoxin on the skin parameters measured, nor did the clinical induction or maintenance of irritant contact dermatitis become apparent. Reconstitution of the skin following damage by SLS was delayed in test sites exposed to TNF-α but not endotoxin. Conclusions: Although endotoxin in MWF might be hazardous in the case of inhalation of aerosols, we found no evidence for any skin hazard arising from exposure of intact as well as damaged skin even to high amounts of endotoxin. In light of this, there seems to be no need to monitor endotoxin in MWF, nor to define a threshold.

Double-Blind Randomised Trial Evaluation of a New Product Containing Matrix Metalloprotease and Protein Kinase C Inhibitors in Cutaneous Contact Hypersensitivity
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Matrix metalloproteases (MMPs) and protein kinase C (PKC) are implicated in several skin pathologies, especially inflammatory cutaneous disorders such as psoriasis and contact hypersensitivity. Moreover, several molecules, among them MMPs and PKC, regulate the migration of skin dendritic cells, which are potent antigen-presenting cells implicated in the primary T cell-mediated immune response.

Skin (ISICD, Woreal)
response of the skin. We have previously shown that MMP and/or PKC inhibitors are able to modulate the migration of skin dendritic cells both in vitro and in vivo. Thus, the aim of this study was to evaluate the clinical efficiency of an innovative topical product containing both MMP and PKC inhibitors (verum) on cutaneous contact hypersensitivity (CHS). A double-blind randomised trial was conducted by 12 dermatologists on 50 selected volunteers with repeated nickel allergy due to buckles. The panelists had products applied to both ears (placebo or verum) twice a day for 7 days, and then buckles until CHS appeared (for at least 14 days, 8–12 h per day). An individual form had to be filled out by the panelist in order to assess the course and development of CHS. On day 14, a final examination was performed by the dermatologist. The first results showed that 75% of the panelists using the placebo developed CHS, while only 37% of the verum-treated panelists were sensitised. This trial demonstrates that topical application of both MMP and PKC inhibitor prior to nickel exposure is able to reduce the frequency of CHS in allergic patients by 50%.

**Irritant and Allergic Contact Dermatitis in Health Care Workers**

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**Objective:** Occupational skin diseases (OSDs) account for a large number of occupational diseases in Europe. Population-based epidemiological studies concerning certain occupations (e.g. health care workers), however, are missing. The aim of our study was to analyse the reports of OSD in health care workers (HCW) in the register of OSDs in Northern Bavaria and to assess the annual incidence in this occupational group in relationship to the total employed population in Northern Bavaria. Further, we investigated the spectrum of sensitizations with and without occupational relevance in this group.

**Methods:** A total of 5,285 cases of OSD were assessed prospectively and registered from 1990 to 1999. Data regarding total employment were provided by the German Federal Employment office. A total of 3,097 cases were confirmed as OSD in 24 occupational groups, of which 482 were confirmed in the group of HCW. The average annual incidence of OSD in this group was 7.3 per 10,000 workers. In 1990, the incidence of OSD in this occupational group was 11.4 and in 1999 5.0 per 10,000 workers. In 1990, the incidence of OSD in this occupational group was 11.4 and in 1999 5.0 per 10,000 workers. In 1990, the incidence of OSD in this occupational group was 11.4 and in 1999 5.0 per 10,000 workers.

**Results:** The average annual incidence of OSD in this group was 7.3 per 10,000 workers. In 1990, the incidence of OSD in this occupational group was 11.4 and in 1999 5.0 per 10,000 workers. In 1990, the incidence of OSD in this occupational group was 11.4 and in 1999 5.0 per 10,000 workers. In 1990, the incidence of OSD in this occupational group was 11.4 and in 1999 5.0 per 10,000 workers.

**Conclusions:** The results of this follow-up study show that the prognosis of OSD is fairly good. It is highly probable that the good results in these chronic cases is mainly due to the strategy that focuses on workplace intervention.

**Patch Testing with Methyldibromoglutaronitrile:**

A Multicentre Study within the EECDRG


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**Objective:** Contact allergy to and allergic contact dermatitis from methyldibromoglutaronitrile (MDBGN) have been frequently reported in the literature. As there has been no agreement on which MDBGN test preparation to use, a study was initiated to help determine the optimal patch test preparation for MDBGN. **Methods:** 2,661 consecutively patch-tested patients at 11 test clinics representing 9 European countries participated in the study. Petrolatum preparations with MDBGN at 1.0, 0.5, 0.3 and 0.1% were inserted in the standard series. **Results:** Contact allergy rates were noted in the range 4.4 to 1.0% following decreasing test concentrations. Reactions not fulfilling all criteria for classification as allergic reactions but which possibly represented weak allergic or irritant reactions were noted in the range 8.1 to 0.6% with decreasing concentrations. A significant number of
these reactors were allergic as they tested positively to higher concentrations. Morphologically irritant reactions were only noted for the highest concentrations. **Conclusions:** In summary, the contact allergy rates and frequencies of doubtful and irritant reactions vary with the patch test concentration of MDBGN. The final decision on the patch test concentration of MDBGN should not only rely on these factors but also include information on patch test concentrations required to diagnose individual cases with allergic contact dermatitis from MDBGN as well as ROAT results.

**Latex Allergy Awareness in a Glasgow Teaching Hospital**

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**Objectives:** In July 1999, a large city hospital published a latex allergy policy highlighting the increasing incidence of allergy among staff and patients and offering advice regarding its management. Circulation of the document to all hospital departments was followed by an audit of policy implementation to assess the impact of this information on clinical practice. **Methods:** The audit was conducted between March 2001 and July 2002, surveying 38 wards – 10 medical, 15 surgical and 4 ‘ward areas’ comprising 2 renal, 2 stroke, 3 rheumatology and 6 care of the elderly wards. Twenty-three senior and 65 staff nurses were interviewed, representing all 29 clinical areas. Ward stocks of available gloves and their usage was documented and resuscitation equipment checked. Interviewees were assessed on their awareness of the policy’s existence, content and risk management guidance, paying particular attention to recognition of latex in commonly used medical equipment and arrangements for obtaining latex-free alternatives, knowledge of skin care and availability of barrier cream at the ward level and perceived prevalence of latex allergy amongst immediate colleagues. **Results:** All specialties displayed an alarmingly limited ability to recognise latex-containing medical equipment and to source suitable alternatives. Almost all staff knew of access to barrier cream, but had little idea regarding general skin care. Latex gloves were widely stocked, sometimes to the exclusion of synthetic alternatives, but had little idea regarding general skin care. Latex gloves were suitable alternatives. Almost all staff knew of access to barrier cream, ability to recognise latex-containing medical equipment and to source colleagues. **Conclusions:** Despite the development and distribution of a latex allergy policy by a major teaching hospital, awareness, understanding and management of latex sensitivity is extremely poor. Its incidence continues to rise and action must be taken to ensure that all reasonable measures are adopted to minimise the risk both to latex-sensitive hospital personnel and also to patients.

**Skin Problems among Employees Included in the Danish Work Environment Cohort Study 2000**

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**Objective:** To study the occurrence of self-reported skin problems and occupational skin exposure among employees included in the Danish Work Environment Cohort Study 2000 (DWECS-2000). **Methods:** The DWECS-2000 included interviews with about 6,000 employees aged 18–59 years. The interview questionnaire included questions on skin problems within the last 3 months and the location of the skin problems. **Results:** Among 5,834 respondents who answered the questions on skin problems, 13% reported skin problems on the hands or forearms for some days or more within the last 3 months. Women reported skin problems more often than men (women 15%, men 10%). Skin problems were most frequent in the age groups below 40 years of age. 44% of respondents reported that skin problems occurred mostly in periods when they were at work. Occupational skin exposures (‘working hours with wet hands’, ‘skin contact with cleaning agents’, ‘skin contact with plastic or rubber gloves’) were in general more frequent among women than among men (e.g. ‘working with wet hands more than 1/4 of the working hours’: women 24%, men 17%). Among respondents reporting skin problems, this difference between women and men was smaller (i.e. ‘working with wet hands more than 1/4 of the working hours’ and ‘reporting skin problems on hands or forearms’: women 34%, men 31%). The same tendency was seen for ‘skin contact with cleaning agents’ and ‘skin contact with plastic or rubber gloves’. **Conclusions:** About half of the skin problems reported in a random sample of Danish employees were work-related. Furthermore, occupational skin exposures were related to higher frequencies of self-reported skin problems.

**Natural Rubber Latex Allergy in a Health Care Population in Wales**

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**Background:** The prevalence rate of type 1 (IgE-mediated) allergy to natural rubber latex (NRL) in health care workers has been reported as between 1 and 40%. These rates may vary due to the different populations studied and methodologies used for assessment and investigation of NRL allergy. Serological and skin prick tests may not correlate with clinical reactions to NRL, and false-negative and false-positive results can occur. The prevalence rate of type 1 NRL allergy in Wales is unknown, and therefore, a single NHS trust-based study was undertaken by three occupational health departments and one dermatology department (Singleton Hospital). **Objectives:** To investigate the rate of type 1 allergy to NRL in health care workers in a single NHS Trust in Wales. **Methods:** A response rate of 3,716 out of 5,548 employees (67%) was obtained with a latex allergy questionnaire administered by the occupational health departments. Type 1 NRL allergy was diagnosed by correlating clinical symptoms, skin prick testing and IgE RAST to latex in the dermatology department. **Results:** The period prevalence (1998–2001) for type 1 clinical latex allergy in health care workers was 25/4,439 (0.56%). Of the 25 positive health care workers, 18 (72%) were nurses. **Conclusion:** Despite the low prevalence rate of type 1 NRL allergy, the importance of clinically significant NRL allergy and the need to minimize risks should not be underestimated.
Epidemiology of Hand Eczema
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Good occupational skin disease (OSD) statistics exist in few countries. The coverage differs greatly depending on the notification system, legal concept of occupational disease and workers’ insurance coverage. According to some statistics, the top industries for OSD have been plywood/fiberboard work, machine operation/tool setting, floor laying/tiling, metal and plastic industry, chemical process work, foundry work, bricklaying, health care, food industry, cooking and catering, electronic assembling, printing and dairy farming. Questionnaires are often the only feasible method for collecting information on populations. The most common method used to diagnose hand eczema (HE) in questionnaire studies is the self-report (self-diagnosis: ‘Have you had …?’). In validations, clinical HE was diagnosed in 54–94% of those self-reporting HE/dermatitis in questionnaire studies. There has been more consistency in these figures within countries than between countries, which probably reflects the way the languages and terms used can screen for HE. The specificity of self-reporting of HE/dermatitis has been high in clinical validations (usually over 90%), while the sensitivity has been lower (less than 70%). The self-report is thus likely to underestimate the true prevalence of HE. The current reported prevalence of HE is at least 10% of workers in occupations with skin contact with allergens or irritants. This figure has been higher in most studies in high-risk occupations. According to epidemiological studies, environmental risk factors for HE include wet work or occlusion (glove use) for more than 2 h a day, skin contact with chemicals or oils, soaps or cleaners, animal and plant handling, and mechanical irritation. Endogenous risk factors include previous HE, previous or present widespread atopic dermatitis, history of dry, itchy skin, (history of) nickel allergy, history of (job-specific) allergy, female sex, and in several studies, also respiratory atopy. A proposed explanation of why women have more HE than men is the fact that they do more wet jobs at home and at work. However, endogenous causes have also been suggested for the sex difference by the results of a Swedish study showing that teenage girls have more HE than boys. A new standardized tool for HE surveys [Nordic Occupational Skin Questionnaire (NOSQ)-2002], compiled by a Nordic group of experts, is available in five languages at www.ami.dk/nosq. In addition to a questionnaire, it includes detailed information for conducting questionnaire surveys on HE and OSD.

Mechanisms of Irritant and Allergic Contact Dermatitis
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The pathophysiology of both irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD) have been well described at both the clinical and the microscopic level. However, at the level of cellular biology and biochemistry, matters become a little less clear. ACD is comparatively well understood; the early responses of keratinocytes, such as increases in cytokine expression and the associated changes in Langerhans cells, are well described. The processes of Langerhans cell migration, maturation and interaction with T lymphocytes are being increasingly better characterised. In sharp contrast, the processes by which substances give rise to ICD are poorly understood. The changes in keratinocyte activity triggered directly by irritants have been described, but other aspects, such as how, for example, surfactant interference with cellular membranes triggers cellular activation and release of cytokines, among other factors, are less well characterised. A similar contrast can be seen in the appreciation of how our understanding of allergen and irritant chemistry impacts upon these areas of science; again it is in the area of ACD where structure activity relationships are most developed. Set against this background, it is encouraging to see the new knowledge being generated with respect to both ICD and ACD, which contributes variously to our understanding of these endpoints and provides challenges for the future. These matters will be reviewed in the presentation.
Management of Work-Related Chronic Hand Dermatitis

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Objective: To review how best to manage work-related chronic hand dermatitis. Methods: The literature was scanned for guidance, and findings were assessed in the light of my own practice, as determined from the case records of the (very) few such patients whom I had followed up myself in recent years. Colleagues were subsequently informally consulted as to their own practice. Results: The literature that existed was somewhat scant, and light on scientific evidence. My own relatively conservative practice seemed at odds with the more aggressive options exhibited in many publications. Yet, when I asked my colleagues, their practice seemed closer to mine than to the impression given by much of the literature. It appeared that this was an area of clinical work where common sense, as recently recommended by an advocate of CRAP (Clinicians for the Restoration of Autonomous Practice), was a more realistic approach than evidence-based medicine. Conclusions: There may be a difference in emphasis between how dermatologists actually manage work-related chronic hand dermatitis and how we write about managing it. The first thing that most of us probably do is to ensure that we are not the ones doing the managing. When this fails, we tend to be more conservative than many publications might suggest. Some of our patients probably give up conventional therapies altogether and find their own, these remaining unacknowledged in the dermatological literature, unless they go wrong.
Legislation for the Prevention of Contact Dermatitis

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Objective: Legislation is an important tool in primary and secondary prevention of contact dermatitis. Examples will be given.

Methods and Results: The EU Directives on classification, packaging and labelling of dangerous substances and preparations cover chemicals intended for consumer and workplace use. The EU Nickel Directive limits nickel in posts used during epithelization after piercing, and in objects intended for direct and prolonged contact with the skin. The EU Cosmetics Directive covers cosmetics and hygiene products. It requires full ingredient identification by INCI names. Negative, restrictive and positive lists control cosmetic ingredients. A number of important skin sensitizers are restricted. National regulation in some countries limits chromate in cement. This approach has recently been decided on also by the EU. Conclusions: Some European regulations have already had a great impact on the prevention of contact dermatitis. Active participation of experts on contact dermatitis, including dermatologists, chemists, hygienists and toxicologists, is essential for the development of clinically relevant regulations. Scientific studies should be performed to evaluate the effects of legislation aiming at prevention of contact dermatitis.

Stripping, Vacuuming and Surrogate Skin – Measurement of Dust on Skin

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Objective: Skin exposure to airborne allergens and irritants may cause dermatitis. There is a lack of methods for assessment of skin exposure. We have developed techniques for this, based on surrogate skin (a patch sampler) and removal procedures (stripping and vacuuming). They make it possible to measure the mass of deposited dust on skin. Methods: The generation and deposition of dust onto the skin was performed in a whole-body exposure chamber, used also for studies on respiratory effects, or in a chamber for arms only. Forehead, shoulders or forearms were exposed. The patch (adhesive tape on an optical cover glass) was compared to tape stripping (Scotch Magic tape) using bakery dust. The suction sampler, a standard 25-mm filter cassette with a small metallic nozzle, was compared to stripping using inorganic and organic particles. The analytical procedures were optical microscopy, image analysis or X-ray diffraction. Results: Similar results were achieved with the different techniques. The comparison between the patch sampler and the stripping procedure indicated only a slight overestimation for the patch (approximately 20%). The comparison between the suction sampler and the stripping technique was good (the recovery efficiency of the sampler was almost 100%). No particle size dependence was observed. Conclusions: The three techniques are applicable for assessment of skin exposure to particles, as well as for dose-effect studies. The suction removal method will be further developed and applied in future workplace studies. The technique allows for dust sampling from larger areas of skin, and also for analysis of dust by a wide range of methods.

The Permeability of Surgical Gloves to Chemicals Commonly Used in Hospitals

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Objective: Many chemicals may permeate glove materials. The chemicals can cause adverse effects directly on the skin or systemically by permeating the skin. We studied whether surgical gloves provide protection against the chemicals commonly used in hospitals. Methods: The chemical permeation tests were carried out according to the American and European standard test methods, ASTM F739 and EN 374. The testing time was 4 h. We tested single-layered and double-layered natural rubber (NR) gloves and a brand of chloroprene rubber
gloves. Results: The gloves did not allow permeation of potassium hydroxide (45%), sodium hypochlorite (13%) or hydrogen peroxide (30%). Furthermore, neither glutaraldehyde, chlorhexidine digluconate nor iodine in the studied commercial disinfectant solutions exhibited permeation. Slight permeation of peracetic acid (0.35%) and acetic acid (4%) from a disinfectant agent through single-layered NR materials was observed. Clear evidence of formaldehyde permeation through single-layered NR gloves was detected, in which the ASTM breakthrough times were 17–67 min, but the permeation rates were not high enough for breakthrough to have occurred according to the EN standard. When tested with 70% isopropyl alcohol, the thin (0.22- to 0.28-mm) NR materials yielded breakthrough times of 4.6–9.1 min with both standards. For the thicker and double-layered NR gloves and the CR gloves, the EN breakthrough times were 21 to over 240 min, and the ASTM breakthrough times were 12–103 min.

Conclusions: Chemical permeation data are needed when selecting gloves for use against some hospital chemicals. CR and double-layered NR gloves provide better protection than single-layered ones.

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**Occupational Allergic Contact Dermatitis from Isocyanate Lacquer**

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Objective: During a short period of time, there was an outbreak of work-related skin lesions amongst workers at a company producing flooring laminate boards after the introduction of a water-repellent lacquer based on diphenylmethane-4,4'-diisocyanate (MDI). There were 20 machine operators working with the lacquer and 5 of them were referred to our department because they developed work-related skin lesions that were suspected to be caused by the lacquer. Methods: The 5 workers were patch tested with a standard series, an isocyanate series and work environmental products when indicated. Three of them were tested with the isocyanate-based lacquer. Results: In the 3 workers tested with the lacquer, contact allergy from this isocyanate product was established with concurrent reactions to 4,4'-diaminodiphenylmethane (MDA). One of the 3 also showed a simultaneous reaction to MDI, whilst 1 showed a positive reaction to dicyclohexylmethane-4,4'-diisocyanate. Of the 2 individuals not tested with the lacquer, 1 reacted to both MDI and MDA, whilst the other reacted to a soap used at work. In 3 of 4 cases, the isocyanate reactions appeared later than day 3. Conclusions: When attempting to diagnose contact allergy to isocyanates, it is desirable to also undertake a late reading, as positive reactions can appear late. Furthermore, MDA appears to be a good marker for isocyanate hypersensitivity.

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**European Surveillance System on Contact Allergies: A Scandinavian Perspective**

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Objective: The European Surveillance System on Contact Allergies (www.essca-dc.org) began operating in 2002, with the aim of monitoring time trends in contact allergy and identifying occupational subgroups at risk, based on routinely collected clinical patch test data. Methods: Patch test and anamnestic data routinely collected in the participating centres using various electronic data processing systems and data formats are transformed into a common standard format and, if necessary, mapped to standard catalogues like ISCO-88COM for occupations. Pooled analyses focus on (1) quality control, (2) variation between countries/centres and (3) other comparative and subgroup analyses. Results: By February 2003, data had successfully been integrated from various centres in Scandinavia and also from the UK, Netherlands, Switzerland, Austria and Germany. First descriptive data on contact allergy prevalence in the Scandinavian departments will be presented. Conclusion: The approach to integrating structurally heterogeneous data (QLK4-CT-2001-00343) has proven feasible and yielded first results.

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**Further Investigation of Elicitation Dose Responses for p-Phenylendiamine**

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It is widely understood that dose-response relationships exist for both the induction and the elicitation of allergic contact dermatitis. In the case of elicitation, we have shown that both the applied concentration and the duration of application have a major impact on the extent of the response elicited. However, none of these studies examined the relationship between a single application versus repeated application. The data presented address this specific question. Using groups of volunteers with an existing allergy to p-phenylendiamine (PPD), it was shown that whereas a single 5-min occluded application of 1% PPD in petrolatum caused reactions in only 2 of 19 volunteers, repeated application for 5 min daily caused 8 of 19 to respond. In parallel, evidence of the possible accumulation of PPD-related material in skin following repeated dosing has been obtained. Further investigation of the impact of repeated dosing showed an unexpected correlation between the elicitation response to, for example, a 20-min
single application and the same accumulated dose delivered by 4 once daily 5-min applications of PPD. Additional studies are under way which aim to provide clarification of time/dose/repetition parameters in the elicitation of PPD allergy. It is suggested that an understanding of these matters may also have some relevance in terms of the relative ability of chemicals to induce allergic contact dermatitis.

**Hypersensitivity to Hydrocortisone-21-Butyrate in Patients Allergic to Hydrocortisone-17-Butyrate**

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**Objective:** Hydrocortisone-17-butyrate in ethanol is used as a marker for corticosteroid contact allergy in patch test standard series. In water and ethanol, the corticosteroid degrades spontaneously to hydrocortisone-21-butyrate within weeks, which necessitates patch test solutions to be made up fresh every 4–6 weeks. If patients react to both substances similarly, there would be no need to make fresh test solutions. **Methods:** Eleven patients hypersensitive to hydrocortisone-17-butyrate were patch tested to serial dilutions of hydrocortisone-21-butyrate. **Results:** All 11 patients reacted to hydrocortisone-17-butyrate, whereas 8 reacted to hydrocortisone-21-butyrate. **Conclusions:** Although there was no statistical difference in the patch test results (positive or negative) between the two sensitizers ($p = 0.107$, Fisher’s exact test), the study indicates that up to 30% of hydrocortisone-17-butyrate-allergic patients may be missed if hydrocortisone-17-butyrate is entirely degraded. Therefore, the recommendation to make fresh test solutions should be followed, as long as we do not know the outcome of simultaneous testing of both esters in consecutively patch-tested dermatitis patients.

**Photoallergic Contact Dermatitis from Ketoprofen in Southern Sweden**

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**Objective:** In Sweden, ketoprofen has been available for topical application since 1995. Photoallergic contact dermatitis from ketoprofen has been reported for almost 20 years. Photoallergic contact dermatitis from ketoprofen-containing topical treatment usually includes severe eczematous reactions. Ketoprofen is an NSAID derived from propionic acid. Ketoprofen, fenofibrate and benzophenones are similar structurally. **Methods:** Photopatch testing and patch testing with two standard series, the ketoprofen-containing gels and their ingredients, fenofibrate and benzophenones, was performed. **Results:** During the previous year, 29 patients have been photopatch tested with ketoprofen with very strong photopatch test reactions. 22 patients also had positive reactions to fentichlor. 20 of these patients had also been photopatch tested with fenofibrate, and 13 of them had positive reactions. 5 out of 23 patients had positive reactions to benzophenone 3, and 5 patients also had positive reactions to benzophenone 10. 15 patients had positive reactions to balsam of Peru and 14 to fragrance mix. **Conclusion:** Ketoprofen is a strong photosensitiser.

**The Safety and Efficacy of Tacrolimus Ointment 0.1% in the Treatment of Nickel-Induced Allergic Contact Dermatitis**

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**Objective:** We sought to evaluate the efficacy of tacrolimus ointment 0.1% in the treatment of nickel-induced allergic contact dermatitis (ACD). **Methods:** This was a double-blind, vehicle-controlled, bilateral paired comparison study to assess the safety and efficacy of topical tacrolimus (Protopic®) ointment 0.1% in the treatment of ACD induced by nickel sulfate. Volunteers were individuals with known hypersensitivity to nickel. Reactivity to nickel was graded both as long as we do not know the outcome of simultaneous testing of both esters in consecutively patch-tested dermatitis patients.

**Allergic Contact Urticaria to Hexylene Glycol in Toiletries**

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**Case Report:** A 28-year-old female secretary with a negative background for atopy and other dermatoses complained of erythema, edema, pruritus and stinging, localized to the face, shortly after using disposable cleansing tissues, and spreading to the eyelid on the same side. This reaction had appeared on two former occasions under the same circumstances, increasing in severity. **Methods:** Analysis of the ingredients of the tissue, supplied by the manufacturer, showed the following: benzyl alcohol, dimethyl hydantoin and carbamates (Glidant plus), dl-alfa-tocopheryl acetate, aloe vera and castor oil. Prick tests were performed with all separate ingredients at the concentration used in the actual product, with histamine as positive control.
control and distilled water as negative control. Ten healthy volunteers participated as controls subjects. A tub test with the tissue was performed on the face and the antecubital fossae in the patient. **Results:** Of all the ingredients tested, only hexylene glycol produced a relevant erythema and wheal reaction, which in turn was negative in the 10 controls. A provocative rub test on the patient produced erythema, edema, pruritus and stinging on the face, which quickly spread to the eyelids and neck. A rub test on the antecubital fossae produced a similar reaction accompanied by vesicles. The reaction showed a maximum intensity at 20 min and lasted for almost 2 h, requiring systemic glucocorticosteroids to settle it. **Conclusions:** Allergic contact urticaria, an increasingly observed phenomenon, poses a challenge for both the clinician and the manufacturers of topical products. As demonstrated in this case, these sorts of aliphatic alcohols may produce urticarial reactions in some individuals and contribute to enlarge the list of identified urticaria-inducing substances. Declaration of cosmetic ingredients in México has proven enormously useful in the past 10 years, helping to diagnose and treat such cases.

**Performance of Questions Designed to Detect Subjects with Atopic Dermatitis in Questionnaire Studies**

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**Objective:** Atopic dermatitis is an important risk factor which needs to be measured in questionnaire studies on occupational skin diseases. The objective here is to compare the performance of different questions designed to detect subjects who have or have had atopic dermatitis. **Methods:** The Nordic Occupational Skin Questionnaire (NOSQ-2002) includes the single UK working party atopic dermatitis question, and in the Nordic translations, two additional Nordic atopic dermatitis questions. Questionnaires based on NOSQ-2002 have been used in three Danish intervention studies on prevention of work-related skin diseases in different occupations. **Results:** Preliminary results from the baseline surveys indicate that the single UK question on atopic dermatitis (A1: ‘Have you ever had an itchy rash that has been coming and going for at least 6 months, and at some time has affected skin creases?’) led to overreporting in populations with occupational skin exposure involving both hands and forearms. The number of respondents reporting atopic dermatitis according to the two Nordic questions is lower and seems to be more realistic (S5a: ‘Have you ever had eczema on the fronts of the elbows or behind the knees?’; S5b: ‘Have you ever had “childhood” eczema?’). **Conclusions:** Respondents with work-related eczema involving the forearms tended to answer positively to the single UK question on atopic dermatitis. Thus, this question seems to be less suitable for detecting atopic dermatitis in adult populations with work-related skin diseases involving the forearms.
Contact Urticaria Syndrome: 2003
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The contact urticaria syndrome, thought to be a rarity when described 25 years ago, is now a common diagnosis. This presentation will emphasize:
– updated classifications;
– algorithms for diagnosis;
– skin test versus RAST;
– new urticants;
– key to whom to test;
– relationship of urticaria to dermatitis.

What Is New in Work-Related Skin Diseases
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Occupational dermatoses are caused by infectious agents as well as physical and chemical factors. The individual physical and chemical factors may act alone, but often many potentially hazardous factors in combination cause the work-related skin disease. The physical factors remain the same, i.e. mechanical factors, temperature, humidity and radiation. On the other hand, new chemicals, of which some are irritants and/or sensitizers, are constantly being synthesized and introduced onto the market. Furthermore, well-known chemicals can be used for new applications, sometimes with work-related skin diseases as a consequence. In the lecture, examples of work-related skin diseases from preservatives, cutting fluids, plants, polymers such as isocyanates, epoxy resin systems and phenol-formaldehyde resins will be given.
ISICD

Blockade of Skin Dendritic Cell Migration by Topical Application of Matrix Metalloproteinase and Protein Kinase C Inhibitors

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Epidermal Langerhans cells and skin dendritic cells (DCs) are potent antigen-presenting cells in the induction of primary T cell-mediated immune responses in the skin. They capture foreign antigens and migrate to regional lymph nodes to carry and present these antigens to naive T cells. This mechanism is critical in the initiation of different cutaneous pathologies such as psoriasis, contact dermatitis or contact hypersensitivity. Several molecules regulate the migration of skin DCs, among which are matrix metalloproteinases (MMPs) and protein kinase C (PKC). The aim of this study was to evaluate the participation of MMPs and PKC in the in vivo migration of murine skin DCs, using topical inhibitors for MMPs and PKC. Mice’s ears were painted with FITC, and DC migration to the auricular lymph nodes was assessed 24 h later by flow cytometry quantification of FITC+ CD86+ and MHC class II highly positive cells. Topical application of MMP or PKC inhibitors on the skin once a day for 4 consecutive days induced a dose-dependent reduction in the number of FITC+ migrating DCs (around 30% inhibition with the optimal dose), compared to placebo application. When PKC and MMP inhibitors were mixed in the same ointment, the inhibitory effect was more pronounced (86% inhibition), suggesting a synergistic action. These data indicate that topical use of inhibitors of PKC plus MMPs could inhibit skin DC migration, which could have strong therapeutic implications in the treatment of skin inflammatory dermatoses.

Objective: In this investigation, the yearly incidence rates and causes of occupational skin diseases (OSDs) in the construction industry were analysed on the basis of our register in Northern Bavaria. Methods: From 1990 until 1999, all incidences of OSDs in the construction industry were recorded prospectively. This enables the calculation of incidence rates of OSDs in relation to the employed population in Northern Bavaria. Results: In the construction industry, a total of 335 OSDs were registered. These comprised 11.1% of all OSDs in the register. We classified them into four relevant groups: tile setters and terrazzo workers (incidence per 10,000 employees 19.9), painters (7.8), construction and cement workers (5.2) and wood processors (2.6). The overall incidence was 5.05 per 10,000 employees over 10 years, which is a little below average for the entire register (6.7). Of these, 42.4% were at least 40 years old. Allergic contact dermatitis (61.5%) occurred more often than irritative contact dermatitis (44.5%). Potassium dichromate caused roughly half of all occupational relevant sensitisation found in the construction industry (158 cases), followed by epoxy resin (41) and cobalt chloride (32). Conclusions: Within the construction industry, tile setters and terrazzo workers have a strikingly high incidence of OSDs. The results indicate that potassium dichromate is still the most important allergen in the construction industry of Northern Bavaria; there has been no significant decline during the 1990s. This contrasts with Scandinavian countries, where the prevalence of potassium dichromate sensitisation declined following the reduction of chromium VI levels resulting from the addition of ferrous sulphate.

Clinical Evaluation of a Cream Containing Matrix Metalloprotease and Protein Kinase C Inhibitors on Sensitive and Irritated Skin

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Matrix metalloproteases (MMPs) and protein kinase C (PKC) are implicated in several skin pathologies, especially inflammatory cutaneous disorders such as psoriasis and contact hypersensitivity. Moreover, several molecules regulate the migration of skin dendritic cells, which are potent antigen-presenting cells implicated in the primary T cell-mediated immune response of the skin, among which are MMPs and PKC. The aim of this study was to evaluate the clinical efficacy of an innovative topical product containing both MMP and PKC inhibitors on sensitive and irritated skin predisposed to allergy. 103 volunteers (mean age 39.7 years) were enrolled by 20 dermatologists. Among the panelists, 50 had sensitive skin and 53 irritated skin. The panelists applied the product twice a day for 1 month. Subjective and objective criteria were evaluated by the dermatologist at baseline and after 30 days. An autoevaluation was performed by the volunteers. Its tolerance was also evaluated. The results showed a clear improvement, of ~69 and ~82%, respectively, of the objective and subjective clinical features of sensitive and irritated skin (erythema,
dryness, desquamation, pruritus, stinging, burning). The autoevaluation by the panelists showed that the cream has an immediate and long-lasting effect (protective and apaising), and that it was able to improve the skin tolerance (66%). Moreover, the product was well tolerated and the cosmetic qualities were also delineated. In conclusion, this innovative cream containing an MMP and a PKC inhibitor has proven its efficacy in the management of sensitive and irritated skin.

**Results of a Standard Patch Test in Israeli Patients with Contact Dermatitis: A Review of 943 Patients between the Years 1999 and 2000**

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**Objective:** To evaluate the relative frequency of different allergens in Israeli patients with contact dermatitis. **Methods:** This study evaluated patch test results of patients referred to the contact dermatitis clinic, Rabin Medical Center, Israel, between January 1999 and December 2000. A total of 943 patients (59% females and 41% males; mean age 42 years, range 1–87 years) were patch tested to the European standard patch test series. **Results:** The most common allergens were nickel (17.4%), potassium dichromate (10.6%), fragrance mix (8.5%), cobalt (7.6%), balsam of Peru (6.6%) and kathon CG (4.6%). Women had a higher rate of positive reactions to nickel, cobalt and butyl phenyl formaldehyde, whereas men had a higher rate of positive reactions to balsam of Peru. Reactions to nickel were more prevalent in younger patients, whereas reactions to potassium dichromate, caine mix, black rubber mix, balsam of Peru and fragrance mix were more prevalent in older patients. All differences were statistically significant (p < 0.05). Multiple positive reactions to metals were demonstrated as well: to cobalt and nickel in 40 patients; to potassium dichromate and nickel in 28 patients, and to potassium dichromate and cobalt in 25 patients. **Conclusions:** In Israel, as in many other countries, nickel is the allergen that most frequently causes contact dermatitis. However, potassium dichromate is much more prevalent in Israel than in other countries (e.g. North America). This finding may reflect geographic differences in the prevalence of different allergens, and indicates the need for studies that focus on regionally prevalent allergens that are not included in standard patch tests.

**Working Environment and Occupational Dermatosis at Some Small and Medium Plating Factories in Vietnam**

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**Aim:** This study was carried out to evaluate the relationship between working environment and occupational skin diseases among subjects exposed to chromium. **Methods:** The research work included workplace monitoring and detection of work-related diseases in addition to paraclinical tests. A cross-section study was carried out in 290 chromium-exposed subjects and 260 nonexposed subjects at 10 small and medium plating factories in Vietnam. **Results:** The working environment was unsatisfactory; temperature and humidity were high, the concentration of chromic acid at different workplaces was 1.5–12.8 times higher than MAC and the concentration of chromic acid in the waste water was 26–48mg/l. This working environment caused hazards to the workers’ health. 290 exposed workers underwent a medical examination. The prevalence of throat diseases was 82.75%, while nasoseptal ulcers were present in 17.20%, skin disease in 62%, progressing or scarred dermal ulceration in 48.30%, contact dermatitis and eczema in 13.80% and prurigo in 27%. In 120 cases tested, patch testing was positive for potassium dichromate 0.25% by the International Contact Dermatitis Research Group method at a rate of 37.50%. 260 subjects were examined in the control group. The difference between rates of diseases was statistically significant (p < 0.001).

**Allergic Contact Dermatitis to Tego® and Isopropyl Alcohol**

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Antiseptic cotton wool composed of 30% alkylidiamoethyl glycine hydrochloride (Tego®) and 70% isopropyl alcohol is commonly used for disinfection in patients in Korea. Although contact allergy to Tego or isopropyl alcohol is not rarely encountered, contact allergy to both ingredients is uncommon. We report a case of contact allergy to both ingredients of common antiseptic cotton wool, i.e. Tego and isopropyl alcohol. A 36-year-old woman presented with pruritic erythematous papules and vesicles on the right forearm within 24 h after blood collection. We performed provocative use test on the normal opposite forearm with antiseptic cotton wool, and the same lesions developed after 24 h. The ingredients of the antiseptic cotton wool used were isopropyl alcohol and alkylidiamoethylglycine hydrochloride. After resolution of the lesions with topical and oral corticosteroids, the patient was patch tested with 1, 0.1, 0.01 and 0.001 dilutions of Tego and isopropyl alcohol, respectively. All of them showed a severe pruritic eczematous reaction with some vesicles after 48 h.

**Rehabilitation in Hairdressers with Skin Disease**

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**Background:** In Germany, about 1,600 hairdressers file claims of occupationally related skin disorders each year. A job-specific secondary prevention program was created to enable these hairdressers to stay in the job despite their skin problems. The effect of this prevention program on both the severity of skin disorders and the hairdressers’ behaviour regarding skin protection are evaluated in this presentation. **Methods:** Hairdressers who file claims due to skin disorders are eligible for the rehabilitation program. Individual behaviour regarding skin protection and care, as well as the severity of the
skin disorder, is assessed before the seminar, 3 months after the seminar (during an individual workplace consultation) and 9 months after the seminar. The available database covers hairdressers who completed the program between January 1998 and December 2002. **Results:** Since 1998, the year of the start of the program, 1,124 hairdressers completed the prevention program. Of these hairdressers, 65% had severe skin symptoms before entering the program. After completion of the program, the percentage of hairdressers with severe skin disorders dropped to 20%. The percentage of hairdressers who used appropriate gloves rose from 35% before entering the program to 95% after completion of the program. Less than 2% of the hairdressers who participated in the program had to change their profession because of occupationally related dermatitis in the years following completion of the program. **Conclusion:** Even though no appropriate control group is available, the data presented here seem to suggest that the job-specific secondary prevention program is an effective tool in helping hairdressers to stay in their profession despite occupationally related skin problems.

**Protein Kinase C and Matrix Metalloproteinase Inhibitors as Potential Modulators of Langerhans Cell Migration following Hapten-Induced Sensitization**

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Langerhans cell (LC) migration from the epidermis to draining lymph nodes is a critical first step for the sensitization as well as for the initiation of contact hypersensitivity. Among the intracellular mechanisms which mediate LC migration from the skin, proinflammatory cytokines, protein kinase C (PKC) and matrix metalloproteinase (MMP) activation seem to play a pivotal role. In the present work, we investigated the efficiency of different PKC inhibitors alone, or in association with an MMP inhibitor, in modulating the migration of activated LC. The migratory capacity of freshly isolated LC was assessed using a reconstituted basement membrane assay (Matrigel) mimicking the prerequisite passage through the dermal-epidermal junction on the way to lymph nodes. Suspensions highly enriched in LC were treated for 1 h with different concentrations of inhibitors of PKC and/or MMP before being exposed to a strong sensitizer, DNBS, and subjected to migration using modified Boyden chambers. Our results demonstrate that all the PKC inhibitors (with high or low specificity), as well as the MMP inhibitor, are per se potent modulators of activated LC migration. Moreover, these two kinds of compounds seem to act in an additive way. Indeed, in the presence of both inhibitors, the activated LC migration rate was comparable to that of nonactivated cells. Thus, PKC and MMP inhibitors can act as potentially important modulators of contact hypersensitivity.

**Occupational Skin Diseases of Health Care Workers in German Nursing Homes**

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**Background:** Claims of occupational skin disease were filed by 964 employees of nursing homes and day care centers for the elderly in the year 2000. At present, the occupational risks for skin diseases in this growing sector of the health service system are not well known. The database of occupational diseases (BK-DOC) of the statutory accident insurance of the health and welfare services was used to investigate the occupational causes of skin diseases in health care workers nursing the elderly. **Methods:** Every claim concerning a putative occupational disease is documented by the German statutory accident insurance. Documentation covers the occupation of the claimant, diagnosis and occupational causes of the disease. The database was analyzed for the years 1996 through 2000. **Results:** A total of 2,487 claims of skin disease were filed in the 5-year period by employees from nursing homes and day care centers for the elderly. In 59% of the claims, the skin disease was caused by occupational risk factors. 5% of the claimants had to change profession due to the disease. Wet work (51%) and working with disinfectants (55%) were the most common causes of dermatitis. The most frequent allergens were perfume mix (11%) and latex (8%). **Conclusions:** Prevention strategies should focus on wet work and disinfectants as the most important risk factors for skin disease in health care workers nursing the elderly. With respect to allergies, special emphasis should be placed on the reduction of perfume mix and latex in the workplace.

**Wet Cement Chemical Burns**

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**Aim:** To point out the danger of the caustic potential of wet cement and to warn those who work daily with this common and necessary construction material. **Methods:** A student with toxic ulceronecrotic dermatitis of both shins caused by kneeling for 3 h in wet cement was admitted to the Department of Dermatovenereology. Erythema, a burning sensation and pain had appeared. At first, the patient washed the affected area thoroughly with soap and water on his own. After admission, the initial treatment included antiseptic baths and dressings. The surgeon consulted disagreed with excision of the necrotic areas. Therefore, the wounds were debrided at our Department. The local therapy consisted of ointments with corticosteroid and antibiotics, hydrocolloid dressings and stimulants of epithelization. Antibiotics, analgetics and antipyretics were given systemically. **Results:** The hospital treatment of the skin of the left shin resulted in good reepithelization, while the right shin eschara was partially separated. The patient was advised to continue home care with fibrinolytic ointments. The wound healed with an atrophic hyperpigmented scar. **Conclusions:** Due to prolonged contact with wet cement, third-degree chemical...
burns developed on the skin of the shins of this patient. The patient was not informed about the caustic potential of wet cement at all. Deliverers and manufacturers should inform buyers and construction workers about the toxic effects of wet cement. They should place directions, warnings and first aid measures on all cement bags in accordance with classification, packing and labeling of dangerous substances.

Recovery from Sodium Lauryl Sulfate Irritation: Effect of Two Skin Care Oils Studied Comparing Various Techniques and Instruments
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Objective: The use of moisturizers and emollients after skin barrier damage has been shown to accelerate skin recovery, products with high lipid content being more effective. The effect of two commercial skin care oils on normal skin was studied using several instruments. Methods: After 24-hour patch tests with 0.5% sodium lauryl sulfate (SLS) in 18-mm Finn chambers on their arms, 12 healthy volunteers used two commercial skin care oils. Evaluations were made on days 0 (baseline), 2 (24 h after irritation) and 7 (after 5 days of treatment), visually and using measurement of transepidermal water loss (TEWL) with two instruments (Tewameter, Courage+Khazaka, and VapoMeter, Delfin Technologies), skin hydration with two instruments (Corneometer, Courage+Khazaka, and MoistureMeter, Delfin Technologies), skin erythema (DermaSpectrometer, Cortex) and blood flow (PIM II Laser Doppler Perfusion Imager, Perimed). Results: There was no measurable increase in skin hydration after a 5-day use of the oils. The two instruments used gave comparable results. Preuse of oils neither increased nor diminished the reaction to SLS. Both TEWL measurement instruments gave similar values at baseline. After SLS irritation, the VapoMeter showed slightly higher values than the Tewameter. MoistureMeter values showed a slightly larger variation in skin hydration compared to the Corneometer. Conclusions: Use of two non-occlusive skin care oils for 5 days on normal arm skin did not change skin hydration values, measured comparing two instruments. Nor did the use of the oils increase or decrease the SLS irritant reaction. The closed-chamber VapoMeter turned out to be a very quick, handy and reliable instrument for TEWL measurement.

Wetting Test in Irritant Contact Dermatitis
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Background: Irritant contact dermatitis is the most common occupational skin disease. It occurs as the result of one or more irritants. The most important endogeneous factors which predispose to irritant dermatitis are sensitive skin and atopy. Methods: To identify persons susceptible to irritant dermatitis, we investigated their irritability by the wetting test of Burckhardt and Schmid [1], applying sodium lauryl sulfate 1% and 5% aqua on the left forearm. Results:

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage positive on day 1</th>
<th>day 2</th>
<th>day 3</th>
<th>day 4</th>
<th>day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy persons (n = 40)</td>
<td>0</td>
<td>12</td>
<td>35</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Atopic hand dermatitis</td>
<td>12</td>
<td>38</td>
<td>25</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Flexural atopic dermatitis</td>
<td>18</td>
<td>50</td>
<td>24</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Irritant dermatitis (nurses) (n = 150)</td>
<td>15</td>
<td>46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apprentices (hairdressers) (n = 637)</td>
<td>7</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: The wetting test can be recommended to identify persons with sensitive skin and increased individual irritability to liquid irritants, i.e. predisposed to irritant contact dermatitis in wet work.
Prevalence of Allergic Contact Dermatitis from Cosmetics in Israel: A Questionnaire Study

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Objective: There is a constant rise in the prevalence of cosmetics-related contact dermatitis. Factors contributing to that rise are the wider use of cosmetics and routine use of patch tests. There are very few reports concerning the prevalence of rashes related to cosmetics among the general population. Methods: We tried to determine the prevalence of cosmetic allergy in Israel using a questionnaire study in a random sample of the adult population. We considered a true allergic response to be present only if a patch test was reported to be positive. The sample consisted of 360 females aged 15–89 years. Questions included a general health profile, family history of atopy, anatomical sites of rash, subjective aspects regarding the rash and habits of cosmetics consumption. Results: 11 out of the 360 females (3.1%) had true cosmetics-induced allergic contact dermatitis. There was a correlation between proven cosmetics allergy and subjective sensitivity to facial cream (p = 0.03). Conclusions: The prevalence rate of 3.1% found in this study is similar to the rate which has been described in the literature (approximately 2%). Significantly more patients than expected with proven allergy to cosmetics had subjective sensitivity to facial cream. This is probably due to the wide use of facial cream, the susceptibility of facial skin to insult and facial cream being a ‘leave-on’ product.

Can an Acute Irritation Test Predict the Outcome of a 3-Week Sodium Lauryl Sulfate Application?

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Objective: Little is known about the effectiveness of methods to test an individual's susceptibility to developing occupational contact dermatitis. For such tests, usually a brief application of sodium lauryl sulfate (SLS) or tape stripping is used. Although it is generally felt that repeated SLS exposure is preferable to a single application, there is little evidence to support this idea. Similarly, little is known regarding whether the outcome of an acute SLS test can predict the outcome of a repetitive test. Therefore, we studied the relationship between the skin reaction after a repetitive SLS test and two brief tests. Attention was given to the recovery rate, as this was suggested to be a reliable indicator of susceptibility. Methods: In 29 healthy volunteers, we measured transepidermal water loss and erythema after application of 0.03, 0.1 and 0.3% SLS for 6 hours, 3 days a week for 3 weeks. The data were compared to the effects after 0.1, 0.3 and 1.0% SLS for 24 h and to tape stripping for 10 and 15 times. Results: A poor correlation was found between the repetitive test and the brief SLS test or tape stripping when using the increase in transepidermal water loss (r = 0.04 resp. 0.25) or its recovery rate (r = −0.1 resp. 0.42). Conclusions: We hypothesize that in a repetitive test of sufficient duration, additional mechanisms are operating that are absent in a brief test, e.g. alteration of the thickness of the epidermis with a resulting change in the permeability of SLS. When such an effect differs between subjects, it might explain the lack of agreement between the acute and the repetitive test. For the moment, the standard brief test is likely unsuitable to assess an individual's susceptibility for occupational contact dermatitis.

Cytokine and Chemokine Receptor Expression by Keratinocytes in Normal Skin and Irritant Contact Dermatitis

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Objective: Cytokines and chemokines are known to play a pivotal role in the trafficking and activation of leukocytes in many inflammatory skin disorders, including irritant contact dermatitis. Their activities are mediated through a variety of receptors present on many cell types, including epidermal keratinocytes. Because of the importance of keratinocytes in the initiation and development of irritant contact dermatitis, we undertook a study to evaluate the profile of receptor expression by these cells under normal conditions and in experimentally induced irritant reactions. Methods: Healthy, nonatopic volunteers were patch tested with dithranol (0.2%) and sodium lauryl sulphate (5%), and biopsied at 1, 6, 48 and 96 h. Normal skin and vehicle control biopsies were also taken (n = 8 for all). Frozen sections were then immunolabelled with antibodies against the following receptors: IL-1RI, IL-1RII, TNF-RI, TNF-RII, CCR1, CCR2, CCR3, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, CXCR1, CXCR2, CXCR3, CXCR4, CXCR5, CXCR6 and CX3CR1. An avidin-biotin peroxidase detection system was employed for antibody localisation. Results: On microscopic examination, it was found that, at this level of methodological sensitivity, keratinocytes in normal skin expressed the following: IL-1RII, TNF-RI, CCR5, CCR6, CCR8, CCR10, CXCR2, CXCR3, CXCR4 and CX3CR1. The distribution and intensity of staining within the epidermis varied considerably between these different receptors. In the reactions to the two irritants, no significant changes were apparent at the early time periods. After 48 and 96 h, however, some samples showed changes in the expression of several receptors. Enhanced expression of IL-1RII, CXCR3 and CXCR4 occurred, with a reduction in CCR6 immunoreactivity. Conclusion: The results indicate that there is a differential modulation of receptor expression by keratinocytes in evolving acute irritant reactions, perhaps reflecting varying kinetics in the production of the relevant cytokines.
WOREAL – Skin

Formaldehyde-Negative Allergic Contact Dermatitis from Melamine Formaldehyde Resin

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Objective: Contact allergy to melamine formaldehyde resin is often combined with formaldehyde allergy. Besides textile finishes, allergic contact dermatitis from melamine formaldehyde resin has been described in composite production and in an orthopaedic plaster technician. Method: We searched for patients with a positive patch test reaction to melamine formaldehyde resin in our files. Results: We describe three cases of formaldehyde-negative allergic contact dermatitis from melamine formaldehyde resin. One of the patients worked in the plywood industry, one in the production of melamine laminated board and one in a laboratory. All these patients were also exposed to phenol formaldehyde resin, and two of them were sensitised to it. One of the patients had firstly a false-negative patch test result with 19-month-old test substance of melamine formaldehyde resin. He later reacted with a strong allergic reaction to fresh test substance. Between 1991 and 2001 at the Finnish Institute of Occupational Health, there were 15 patients with concomitant allergic reactions to melamine formaldehyde resin and formaldehyde. They had been exposed to formaldehyde or its liberators in cosmetics, liquid soaps, detergents, photographic developers, freezing liquids, furs and topical medicaments, or to textile finishes in working clothes or other textiles. Conclusions: To our knowledge, this is the first report of allergic contact dermatitis from melamine formaldehyde resin in the plywood industry. Melamine formaldehyde resin is considered to be an infrequent sensitizer. This may be due to the low level of exposure. Degradation of melamine formaldehyde resin in the test substance may lead to false-negative test results.

Classification of Skin Sensitization Potency Using the Local Lymph Node Assay

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It has long been appreciated that chemicals which possess the potential to cause skin sensitization (allergic contact dermatitis) vary widely in their relative potency. However, until recently, predictive test methods have not been well suited to measurement of this parameter. The local lymph node assay has been shown to provide a clinically relevant indication of the relative potency of skin sensitisers via the estimated concentration required to produce a 3-fold stimulation of proliferation in draining lymph nodes (EC3; the threshold for identification of a chemical as a sensitizer). In the present investigations, we examined the utility of a simple grading scheme for skin sensitisers based on the order of magnitude of differences in EC3 values. Fifty chemicals were classified as extreme (EC3 <0.1%), strong (EC3 <1.0%), moderate (EC3 <10%), weak (EC3 ≤100%) or nonsensitizing (i.e. the threshold for classification as a skin sensitizer was not reached). It is suggested that this simple grading scheme provides a useful foundation on which to develop regulatory risk assessment/management strategies.

Two Occupational Allergic Contact Dermatitis Case Studies in an Engine Cylinder Factory

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Objective: To report on occupational ACD in two workers employed in an engine cylinder factory. The first one, Marco T., from the core department of the workshop, made engine cylinder cores with polyurethane resins and suffered from eczema of the hands, blepharitis and conjunctivitis. The other, Massimiliano G., from the finishing department of the workshop, polished the nickel-coated inner surface of alloy cylinders with a lapping machine and emulsion oil. Methods: The first patient was submitted to the following tests: ECG, spirometry, emogasanalysis, X-ray of the thorax, ophthalmologic examination, immunodosage of total IgE and atopy-specific IgE, p.t. with standard S. and additional S., i.e. formaldehyde r., isocyanates r., foundries, palpebral and with core fragments and relevant surrnant after its incubation in 20% acetone, in which methylene diphenyl diisocyanate (MDI) has been found through the use of the OSHA 47 method. The second patient was submitted to the following tests: p.t. with standard S. and additional S., i.e. emulsion oils, oils supplied by the patient as such (before, during and after use). In addition, the oils were tested for quali-quantitative nickel content through spot tests and atomic absorption. Results: The first patient was found to be sensitive to MDI (1%) and diaminodiphenyl methane (0.5%), as well as surrnant containing MDI. Even though the case history revealed no reactions to nickel sulphate (5%), the second patient exhibited a positive reaction to oil as such, during and after use. Conclusion: The diagnosis for the second patient was occupational ACD of the hands caused by nickel and emulsion oils.
**Nordic Occupational Skin Questionnaire: A Tool for Surveying Work-Related Skin Diseases**


National Institute of Occupational Health, Copenhagen, Denmark; Department of Dermatology, North Karelia Central Hospital, Joensuu, Finland; National Institute of Working Life, Stockholm, Sweden; Finnish Institute of Occupational Health, Helsinki, Finland; Occupational and Environmental Dermatology, Stockholm County Council, Stockholm, Sweden; Department of Dermatology, University Hospital, Malmö, Sweden; Department of Dermatology, Landspitali, University Hospital, Reykjavik, Iceland

**Objective:** Occupational skin diseases are among the most frequent occupational diseases in industrialized countries. Questionnaire tools for surveying occupational skin diseases and exposure are needed for comparable epidemiological research, workplace assessments and evaluation of workplace interventions. **Method:** The Nordic Occupational Skin Questionnaire Group supported by the Nordic Council of Ministers has developed a standardized questionnaire tool for surveys on work-related skin diseases and skin exposure to environmental factors. **Results:** The Nordic Occupational Skin Questionnaire (NOSQ-2000) includes two questionnaires designed for separate purposes. NOSQ-2000/long is an in-depth survey tool for research purposes. NOSQ-2000/short is a 4-page questionnaire for screening skin problems at workplaces (e.g. by occupational health services). The questionnaire covers occupational history, atopic symptoms, self-reported hand or forearm eczema, exacerbating factors, consequences and impact on life of dermatoses, self-reported contact urticaria on hands or forearms, skin symptoms, skin tests, exposure and protective glove use. For the time being, NOSQ-2002 is available in English, Danish, Swedish, Finnish and Icelandic. Further translations are welcomed. **Conclusions:** The NOSQ-2002 questionnaire files can be downloaded from www.ami.dk/NOSQ. A link to the Nordic Council of Ministers and download of the report in PDF format is included.

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**EPOX 2002: A Study on Contact Allergy due to Epoxy Resin Components**

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**Background:** Epoxy resin systems (ES) are widely used, e.g. in adhesives, in the construction and metal industry, in the painting and varnishing trade, in the plastics industry and in the electrical industry. Sensitizing components of ES are predominantly resins based on diglycidyl ether of bisphenol A or bisphenol F (DGEBA, DGEBF), hardeners and reactive diluents. Only a few of the substances used nowadays in ES are commercially available as patch test substances. Therefore, many contact allergies to components of ES probably remain undetected. **Objective:** To compile the most frequently used ES components, to prepare patch test substances and to test these in exposed patients with contact dermatitis. **Method:** A multicenter study within the German Contact Dermatitis Research Group (DKG) and the Information Network of Departments of Dermatology (IVDK). **Results:** When the first 23 patients were tested with 11 ES components commercially available as patch test substances and 16 newly prepared test preparations of ES components, positive reactions were most frequently observed to the following: DGEBA resin (16 patients), DGEBF resin (13), 1,6-hexanediol diglycidyl ether (7), p-tert. butylphenyl glycidyl ether (5), m-xylidine diamine (5), 1,4-butanediol diglycidylether (4) and phenyl glycidyl ether (4). This underlines the importance of patch testing more ES components than currently commercially available. Latest results will be presented at the congress. **Conclusion:** By identifying ES components which most frequently cause allergic reactions, preventive measures can be focussed.

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**Patch Testing with a New Metalworking Fluid Series**

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**Background:** Water-based metalworking fluids (MWF) can cause irritant and allergic contact dermatitis. MWF consist of basic oils, emulsifiers, antirust agents, antitrust additives, preservatives and other additives, e.g. extreme-pressure additives. Recently, the German Contact Dermatitis Research Group (DKG) updated respective patch test series. However, the sensitizing properties of many MWF components are not yet studied adequately. **Objective:** To assess the frequency of contact allergy to MWF components not tested routinely. **Method:** We selected 13 frequently used MWF components for patch testing in patients exposed to MWF suffering from work-related hand eczema in five centers of the DKG and the Information Network of Departments of Dermatology (IVDK). **Results:** 233 patients were tested. 5 patients showed an allergic reaction to diglycolamine. Only one of these also reacted to monoethanolamine and diethanolamine. Further allergic reactions were observed with 2-amino-2-ethyl-1,3-propanediol and methylidithanolamine (1 patient each). No allergic reactions were seen to aminobutanol, oleic acid, isodecanoic acid, aminomethylpropanol, aminopropanol, hexyldecanol, dihydroxydi-oxahexane, hydroxyethylglycidic acid, imidazoline, methyl-β-benzotriazole and iodopropynyl butylcarbamate. **Conclusions:** Diglycolamine seems to be an important allergen in MWF. Studies of this kind may further promote the diagnostics of contact allergy due to MWF.
**Occupational IgE-Mediated Spider Allergy: A Case Report**

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¹Department of Dermatology, Tampere University Hospital, Tampere, ²Helsinki University Hospital, Helsinki, Finland

**Case Report:** A 45-year-old male a pig farmer had suffered for several months from dermatitis on the hands, face and neck. A flare-up of dermatitis occurred every time he worked with the pigs, and healing was evident when he was on holidays. He did not suffer from any work-related respiratory symptoms and there was no history of any atopic diseases. The patient was suspected to have an occupational dermatitis and he was admitted to our department for more detailed allergological examinations. **Results:** Patch tests for extended European standard, cosmetic and rubber series as well as for different swine food and food additives, swine hair and dander were totally negative. The same was true for IgE antibody tests (Cap FEIA, Pharmacia) against cereals, house dust and storage mites and for skin prick tests against pollens, animal dander, mites, moulds and swine and swine food. The patient also suspected spiders, the number of which had recently increased in the swine house, as a cause of his dermatitis. Thereafter, skin prick tests were performed with adult spiders and spider net collected from the swine house. The results were clearly positive: 8- to 11-mm-diameter wheals to spiders, 5-mm-diameter wheal to spider net and 6-mm wheal to 10 mg/ml of histamine. An open application test with crushed spider and spider net was also positive. An immunospot assay demonstrated IgE antibodies to spider in the patient but not in the sera from other farmers. A controlled exposure in the swine house produced flare-up of the dermatitis within 1–2 days without any previous or present type I urticarial or respiratory symptoms. **Conclusions:** To our knowledge, the present case is the first reported occupational IgE-mediated allergy to a common house spider. The clinical picture was exceptional; there were no type I urticarial or respiratory symptoms but a dermatitis occurring on the open areas of the skin. This could well be protein contact dermatitis caused by airborne spider allergens.

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**Two Cases of Occupational Allergic Contact Dermatitis from a Cycloaliphatic Epoxy Resin in a Neat Oil**

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**Objective:** Two metal workers developed allergic contact dermatitis on the hands and lower arms from a neat oil metalworking fluid. Identification of the sensitizing substance in the oil was attempted in a series of patients. **Method:** Patch tests were performed with the European standard series, fractions containing the ingredients of the oil and a series of epoxy resins. **Results:** Patch testing revealed that the relevant contact allergen was a cycloaliphatic epoxy resin, 1,2-cyclohexanedicarboxylic acid, bis(oxiranylmethyl) ester, which is added to the oil as a stabilizer. None of the patients had positive reactions to the bisphenol A-based epoxy resin in the standard series. One of the patients also reacted to the reactive diluent phenyl glycidyl ether. Four of 5 patients who tested allergic to cycloaliphatic epoxy resin at our department also reacted to phenyl glycidyl ether. This possibly indicates cross-reactivity between the cycloaliphatic epoxy resin and the reactive diluent. **Conclusions:** Positive reactions to a cycloaliphatic epoxy resin were seen, while neither of the case patients had reactions to the bisphenol A-based epoxy resin in the standard series. This shows that it is important to supplement standard patch testing with relevant epoxy resins to which the patient has been exposed. These cases also emphasize that well-known contact allergens may show up from unexpected sources of exposure. Moreover, it can be a long-lasting, laborious process to detect an occupational contact allergen, and cooperation from the manufacturer of the sensitizing product is essential.

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**Skin Diseases and Allergy Risks in Paper Production: A Clinical Study**

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**Objective:** To obtain information on skin diseases and allergy risks in mechanical pulp production using chlorine-free bleaching methods. **Methods:** The study group consisted of 119 workers exposed to mechanical pulp or wood extracts and 105 nonexposed workers. Wood extracts were isolated from samples taken during different pulping processes. The test substances made of the extracts were first calibrated by patch testing the patients at the Finnish Institute of Occupational Health. A test concentration of 3.2% in petrolatum was chosen for patch testing with the extracts. **Results:** The extractable substance concentrations were 1.1–3.3% in wood chips, 0.5–1.1% in mechanical TMP pulp, 0.4% in chemothermomechanical CTMP pulp, 0.04–0.2% in chlorine-free bleached TCF pulp and about 0.2% in paper manufactured from recycled fibers. No cases of occupational skin diseases were detected, but one worker in the exposed group had contact allergy to mercaptobenzothiazole, possibly due to occupational exposure to pulp. Those who had contact allergy to colophony also had positive patch test reactions to the patch test substances prepared from extracted wood chips, mechanical pulp, chemothermomechanical pulp or paper made of recycled fibers. This study showed that colophony allergens in spruce and pine wood are still present in paper manufactured from recycled fibers. **Conclusion:** The paper mill workers who were exposed to pulping processes and chlorine-free bleaching methods did not have more contact allergies than the nonexposed workers.
Exposure of Cleaners to Alkoxyalcohols in Simultaneous Exposure to Different Solvents
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Objective: To analyse exposure of cleaners to alkoxyalcohols and to develop assessment of their exposure during floor waxing.

Methods: Nineteen cleaners participated in this study, and their inhalation, dermal and total exposure was assessed. Inhalation exposure was measured from the cleaners’ breathing zone and dermal exposure was estimated by hand wash samples. The total exposure was measured by urine analysis of 1-alkoxy-2-propanols, 2-(2-alkoxyethoxy)ethanol compared to that of a single compound. Results: Inhalation exposure of cleaners to alkoxyalcohols was low, and hand wash samples contained similar compounds as detected from air, except 1-methoxy-2-propanol. The urinary 2-(2-alkoxyethoxy)acetic acid concentrations were higher than expected according to the air samples. The slight increase in the rate of penetration through the artificial membrane was established in simultaneous exposure to 1-methoxy-2-propanol and 2-(2-butoxyethoxy)ethanol compared to that of a single compound. Conclusions: Inhalation exposure seems to underestimate the total exposure to alkoxyalcohols. One explanation is the strain of the work, which increased the uptake of alkoxyalcohols up to 2- to 6-fold compared to light work. The highest measured concentrations of 2-(2-methoxyethoxy)acetic acid were significant, because it is proved to be harmful for unborn children (category 3). Biomonitoring seems to give more reliable estimates of total exposure than air monitoring, although the inhalation was the major exposure route.

Prevention of Nickel Allergy: The EU Nickel Directive
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Objective: Nickel is the most frequent cause of contact allergy, affecting 10–15% of women and 2–5% of men. 30–40% of nickel-sensitive people develop hand eczema. The Nickel Directive entered into full force in 2001 to prevent sensitization and elicitation of contact dermatitis. Methods: Nickel is limited (1) in posts used during epithelization after piercing, (2) in objects intended for direct and prolonged contact with the skin and (3) coated items under (2) must fulfill the criteria after ‘two years of normal use’. Three reference test methods (CEN standards) for showing compliance were developed by CEN/TC 283/WG 4, under a European Commission mandate. The screening test for nickel release (dimethylglyoxime test) has been made more sensitive and specific. It may be used as a guide for nickel release. Results: Since 1989, Denmark has limited nickel release as part 2 of the Directive. Reduced sensitization to nickel has been recorded among dermatitis patients, interpreted to be a result of the Danish regulation. In Sweden, the market has started adaptation to the Nickel Directive part 2 as shown by studies of nickel release from items on the market. Conclusions: Prevention of nickel allergy is of great concern. The Nickel Directive limits nickel in items known to be the most important causes of sensitization. Limitation of nickel release has already been shown to have an impact. Nickel allergy will hopefully be much reduced in the future, provided that the market adapts to the requirements of the Nickel Directive. Further information, for increased understanding of the problem and effective control, will be needed.

Methods for Analysis of Allergens: A European Standardisation Project
Lidén, C.
Department of Occupational and Environmental Dermatology, Stockholm County Council and Karolinska Institutet, Stockholm, Sweden, convener of CEN/BT/WG 132

Objective: Several contact allergens that cause dermatitis, and some respiratory allergens that cause asthma and rhinitis, are chemical substances present in materials and products. The EU and national authorities try to prevent the problem to a certain extent by regulations concerning limitations in use and by labelling. Analytical methods are lacking for control of compliance with many of the regulations. The aim of the European standardisation project...
CEN BT/WG 132, ‘Methods for analysis of allergens’, was to examine the need to develop standards for analytical methods applicable to known allergens in materials and products in both working and private life. **Methods and Results:** CEN BT/WG 132 started its work in 2001 and delivered its final report in 2003. The following aspects were examined for 69 selected allergens (metals, plastics and rubber chemicals, preservatives and dyes, perfumes and colophony): prevalence of allergy and major causes; current and planned regulations; available analytical methods and their clinical relevance; and possibilities for standardisation and for prevention by regulation. **Conclusions:** CEN BT/WG 132 has proposed that a new CEN/TC is created. Work items have been proposed for 56 allergens where there is a strong need for development of standardised analytical methods. Such CEN standards would support European legislation aiming at the prevention of allergy.

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**Use of Teledermatology in Diagnosis of Allergic Contact Dermatitis**

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**Objective:** Occupational skin morbidity in Russia is significantly lower than in European countries. One of the principal reasons for this might be the low availability of occupational dermatology services in most of distant regions of Russia. To provide better services for such regions, a system for teledermatological diagnosis of occupational dermatoses was developed and implemented in the Nizhny Novgorod Research Institute for Hygiene and Occupational Pathology (http://webcenter.ru/~ip2). The task of this investigation was to assess the efficacy of the system, and to reveal its benefits and possible drawbacks. **Methods:** Digital images of skin lesions of 30 workers and 144 allergic skin test images (skin tests were performed using Finn chambers) were sent to a distant consultant in Moscow via e-mail. The diagnostic accuracy of store-and-forward teledermatological consultations was evaluated by comparison of in-person and distant diagnoses. The results of distant and in-person assessments of skin tests were also compared. **Results:** There was 77% concordance between distant and in-person diagnoses of skin lesions (mistakes were made mainly in cases of mycological and oncological pathology). The concordance in skin test assessment was 81%. Communication costs were low – less than 0.20 USD per consultation – so the use of the system would be affordable for most Russian regions. **Conclusions:** Store-and-forward teledermatological consultations are very promising for the regions where direct consultation of an occupational dermatologist is not available. The diagnostic accuracy of the method is high enough. Some elaborate technical requirements for digital cameras should be observed to make teledermatological consultations more effective.

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**Work-Related Skin and Respiratory Symptoms among Finnish Machinists: Results of a Computer-Assisted Telephone Interview**


1Department of Occupational Medicine, Helsinki, 2Department of Epidemiology and Biostatistics, Helsinki, 3Department of Research and Development in Occupational Health Services, Kuopio, Finnish Institute of Occupational Health, 4North Karelia Central Hospital, Joensuu, 5Helsinki University Central Hospital, Jorvi Hospital, Espoo, Finland

**Objective:** To obtain information on the chemical exposure and the prevalence of skin and respiratory symptoms among machinists in southern Finland. This epidemiological survey is part of a research project aiming to improve working conditions in machine shops. **Methods:** A cross-sectional study was carried out on a population of machinists (n = 961) selected based on the membership catalogue of the federation of metal industries, as well as the employers’ information on metal working personnel. Skin and respiratory symptoms, atopy, living habits, work history and methods, as well as exposure at work were investigated. **Results:** 757 (79%) of the interviewees had worked as machinists or machine servicemen during the last 12 months. 263 (35%) of them reported work-related symptoms: 13% reported hand or arm dermatitis, 15% reported rhinitis, 10% reported eye symptoms, 8% reported phlegm production, 8% reported cough, 5% reported pharyngeal symptoms, 2% reported dyspnea and 2% reported wheezing. 86% were exposed to metalworking fluids almost daily, and 92% used protective gloves at work. **Conclusions:** This study shows that work-related skin and respiratory symptoms are common among machinists in Finland. The workers suspected of having an occupational disease, the working conditions and metalworking fluids are being investigated in more detail.

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**Occupational Immediate Hypersensitivity to Yucca (Yucca elephantipes) and Weeping Fig (Ficus benjamina)**

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Department of Dermatology, Odense University Hospital, University of Southern Denmark, Odense, Denmark

**Objective:** Type I allergy from ornamental green indoor plants is not often suspected and rarely reported. We present the results of testing for type I allergy in a nonatopic female plant keeper with work-related skin and mucosal symptoms. Furthermore, she described oral allergy symptoms after ingestion of, for example, avocado, banana and kiwi. **Method:** Type I sensitization was evaluated by skin prick test (SPT) and histamine release tests. **Results:** SPT and histamine release tests were positive for both yucca (Yucca elephantipes) and weeping fig (Ficus benjamina), whereas SPT to 10 common inhalant allergens, latex 10 HEP and various fresh food items including kiwi and banana were negative. **Conclusions:** The results confirm the risk associated with the continuous handling of large, green, dusty plants as in the job of indoor plant keepers. Type I allergy from another yucca species has been reported before, but this is the first case of allergy from Y. elephantipes, which belongs to another plant family than weeping fig. Sensitization to...
the latter may be relevant for the oral allergy symptoms in this patient. The results emphasize the importance of testing with nonflowering green plants, the risk of sensitization even in nonatopics and the possibly underestimated allergenic potential of the common yucca plants.

**Decrease in the Number of Occupational Cases and Sensitization Rate to Latex in Finland**

Reunala, T., Koskinen, A., Alenius, H., Alanko, K., Palosuo, T., Turjanmaa, K.

*Department of Dermatology, Tampere University Hospital, Institute, Helsinki, Finland*

**Background:** Latex allergy has been one of the most frequently encountered occupational diseases among health care and other workers using gloves manufactured from natural rubber latex. Atopy and hand dermatitis are the risk factors. The allergen content of the gloves can be measured, and our national strategy has been to withdraw highly allergenic medical gloves from the market. **Methods:** Occupational cases of latex allergy were analysed from the Finnish Register of Occupational Diseases. The sensitization rate to latex was analysed from a large number of patients skin prick tested with common inhalant and latex allergens (Stallergenes, France). Glove allergen content measurements were performed with an IgE ELISA [1]. **Results:** In 1994, 30% of the marketed latex gloves used in health care were highly allergenic, whereas in 2001, the frequency was only 6%. A parallel decrease was seen in the number of notified latex-allergic occupational cases from the health care field. From 1992 to 1996, there were 169, and from 1997 to 2001, only 98 latex-allergic physicians and nurses. A total of 5,831 adult patients suspected to have type I allergy were screened for latex allergy, and the prevalence of positive skin prick test to latex decreased from 2% from 1995 to 1998 to 1.5% from 1999 to 2002. **Conclusions:** This study shows that the strategy of withdrawing highly allergenic latex gloves from the health care field is efficient by decreasing occupational latex allergy. The present results also suggest that the sensitization rate among the atopic patient population is decreasing in parallel.

**Reference**


**Skin Diseases and Allergy Risks in Paper Production: A Questionnaire Survey**


*North Karelia Central Hospital, Joensuu, bFinnish Institute of Occupational Health, Helsinki, cStora Enso Oyj, Imatra, dOy Keskuslaboratorio – Centrallaboratorium Ab (KCL), Espoo, Finland*

**Objective:** The aim of this survey was to chart whether the reporting of hand dermatitis is more frequent among those exposed to mechanically produced wood pulp compared to those not exposed. **Methods:** The study was a questionnaire survey amongst workers in five paper mills. The questionnaire was returned by 114 of 125 exposed and 104 of 125 nonexposed workers. **Results:** Half of the respondents reported a history of atopic symptoms, with no difference between the exposed and the nonexposed workers. 37% of the respondents reported having had dermatitis on their hands or forearms within the past 12 months. There were no statistical differences in the reporting between the exposed and nonexposed workers, nor between the men and women. Dermatitis on the hands or forearms was reported significantly more often by those who also had a history of atopic dermatitis or sensitive skin. One out of four with a history of dermatitis within the past 12 months felt that occupational factors aggravated the dermatitis. Almost half of the aggravating factors were linked to the pulping process (pulp, chemicals). **Conclusions:** Dry or sensitive skin was the most commonly reported causative factor for hand dermatitis. In logistic regression with a multivariate model, the most significant risk factors for hand/forearm dermatitis were symptoms of sensitive skin (symptoms of metal allergy, dry skin, itch when sweating and itch from wool) and age between 36 and 45 years.

**Testing with Fine Fragrances: Comparison with Fragrance Mix, Balsam of Peru and the Fragrance Series**

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**Objective:** The aims of this study were to study patch test reactions to fine fragrances and compare the reactions to those with fragrance mix, balsam of Peru and the fragrance series. **Methods:** 641 consecutive eczema patients were tested with the European standard patch series and with two selected fine fragrances. Those who were positive to one of the fine fragrances or to fragrance mix or balsam of Peru were also positive with the fragrance series. **Results:** 95 patients (14.8%) were found to have a positive patch test reaction to one of the fragrance allergens; 41 of these (6.4%) had positive results to fine fragrance No. 1 and 29 (4.5%) to No. 2; 9 (9.5%) had positive results to fine fragrances and compare the reactions to those with fragrance mix, balsam of Peru and the fragrance series. **Conclusions:** Tests with fine fragrances can add to our evaluation of fragrance-sensitive patients.

**Contact Allergy in Construction Workers: Results of a Multifactorial Analysis**

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**Objective:** To quantify the risk of contact allergy (CA) to important ‘ubiquitous’ allergens associated with certain occupations,
in particular the construction industry, and to identify possible time trends, controlling for potential confounding variables. **Methods:** Bivariate and multifactorial Poisson regression analysis of standardised anamnestic and patch test data, comprising 82,561 patients assessed in the 33 German and Austrian contact dermatitis units of the Information Network of Departments of Dermatology (IVDK) between 1992 and 2000. **Results:** CA to five of the 18 (groups of) allergens considered here was observed significantly more often in construction workers: dichromate, epoxy resin (BADGE), cobalt, thiurams and N-isopropyl-p-phenylenediamine (IPPD). Multifactorial analysis confirmed an increased risk of CA to these allergens in construction workers compared to other occupations. **Conclusions:** Dichromate is still an eminent allergen in construction workers; as yet, there is only weak evidence of a decrease in Germany. Therefore, the addition of ferrous sulphate to cement, which has been a successful intervention in other countries, should be further promoted. While CA to other allergens like cobalt, thiurams and epoxy resin is less frequent, estimates of the relative risk are about as high, rendering these targets of prevention, e.g. by use of protective gloves with minimal intrinsic CA risk.

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**Intestinal Microflora in Children with Atopic Dermatitis**

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**Objective:** To determine the age-dependent intestinal microbiocenosis in children with atopic dermatitis. **Method:** Clinical and laboratory investigations in 24 children under 1 year of age and in 36 older children suffering from atopic dermatitis (AD). **Results:** Second-degree dysbacteriosis was revealed in 50% of AD children. Intestinal dysbiotic disorders were more frequently observed in the advanced forms of AD. A distinctive feature of the intestinal microbial landscape in AD patients was a deficiency of *Bifidobacteria*. Inhibition of the basic components of protective microflora led to an imbalance of the microecological system towards an increase in aerobic associations and conditionally pathogenic microorganisms in the colon, namely the persistent bacteria vegetans of *Proteus* and *Klebsiella* classes. Erosive changes in the gastric mucous membrane were revealed in 16.67% of children. The children with erosive changes had the advanced and severe form of AD. Furthermore, *Staphylococcus aureus* were detected in microbiological exams of excrement and scrapes from the skin surface. Factors that aggravated the degree of dysbacteriosis were the following: irrational previous antibiotic therapy in 52.09%, seeding of *S. aureus* from breast milk in 66.67%, chronic infection foci in 23.78% and hypochromic anemias in 27.79% of cases. **Conclusions:** This study of intestinal microflora in AD children allowed us to determine a significant decrease in *Bifidobacteria* in the majority of them. This fact is especially important for the development of therapeutic approaches, as the Bifidoflora substantially influences the microbiocenosis as a whole.

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**Sensitization to Epoxy Resin Systems in Special Floor Layers**

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**Objective:** To review the clinical data relating to sensitization to epoxy resin systems in special floor layers over the years. **Method:** We studied the clinical data of all construction workers with sensitization to epoxy resin systems seen in the above-mentioned institutions between 1989 and 2003. **Results:** A total of 40 patients were seen. Ages ranged from 21 to 65 years (mean 38.7 years); 28 patients were younger than 40 years. The localization of the lesions was predominantly on the hands, face, eyelids and forearms. The time between the start of contact with resins and the onset of the lesions was less than 3 months in 67% of the patients. Most patients sought medical help from days to a few months after onset. All patients were strongly positive on patch testing to epoxy resin and/or to one of the components of the epoxy resin series, whereas only 7 were positive to dichromate. The special floor layers usually had an exclusive dedication to this type of work, which was mostly temporary, itinerant, better paid and with scanty preemployment advice and use of protective measures. **Conclusions:** Sensitization to epoxy resin systems in special floor layers is an actual and distinct clinical entity among construction workers, characterized by a special pattern of work, young age and relatively rapid development of characteristic clinical features with frequent involvement of the face, with a different pattern on patch testing.

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**Partnership Makes Scents**

*Vey, M.*

International Fragrance Association, Brussels, Belgium

The topic of this presentation is the timely supply of fragrance information to dermatologists. The poster describes a process that should assist dermatologists in identifying and tracing information about ingredients contained in fragranced cosmetic products in case the fragrance (a fragrance ingredient) is a suspected cause of a skin reaction.

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**Wheal-and-Flare Reactions Induced by Histamine and Type I Allergens: Comparative Time Courses of Blood Flow and Itch**

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**Objective:** Itch is arguably one of the most distressing aspects of allergic reactions. Yet despite its clinical significance, it remains one of the most poorly understood and poorly controlled sensations of the skin. As a prelude to investigations involving itch-related brain activation, we set out to establish an experimental model suitable for the elicitation of itch in volunteers undergoing simultaneous functional...
magnetic resonance imaging. The skin prick test routinely used for type I allergy testing was the obvious choice, given its simplicity, and a study was therefore conducted to characterize and optimize the procedure. **Methods:** Cohorts of atopic and nonatopic individuals (n = 14 for both) underwent standardized prick testing with histamine, saline control and the relevant type I allergen (atopics only). Skin blood flow was measured continuously by laser Doppler flowmetry over a 20-min period, with the volunteers’ concurrent perception of itch intensity being recorded using an electronic visual analogue scale (0–10). **Results:** Analysis of the data revealed significant differences between the responses to histamine and allergen in atopic subjects. Histamine induced a more rapid increase in blood flow, which occurred in parallel with the onset of itch. However, the magnitudes of both blood flow increase and itch intensity were significantly greater following allergen administration and, unlike the histamine changes, were sustained at their maximum levels throughout the 20-min assessment period. Atopics and nonatopics exhibited similar responses to histamine. **Conclusions:** The study showed that the prick testing of atopic individuals with their appropriate type I allergen provides a better paradigm for the sensation of itch than histamine alone. The results also lend support to the view that histamine is only one of a number of mediators responsible for the allergen-induced wheal-and-flare response.

### Abstracts

**Clinical and Allergological Biomonitoring of Occupational Hypersensitivity to Platinum Group Elements**

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**Objective:** Exposure to platinum group elements (PGEs; Pt, Pd, Ir, Rh) may cause acute toxicity or hypersensitivity with respiratory symptoms, urticaria and, less frequently, contact dermatitis. These effects depend on both the intensity of the exposure and on the chemical forms of the metals. Currently, the most common occupational exposure to soluble Pt compounds is in Pt refining and catalyst manufacture. The aim of this study was to determine PGE levels in the air and in biological samples of employees working in the assembly of catalysts and recycling metals, the incidence and the medical clinical characteristics of allergy to Pt salts and the role of environmental exposure in the onset of allergy. **Methods:** The study was performed in a catalyst plant. 123 subjects variably exposed to PGEs were informed about the purpose of this study and gave their consent. The examination consisted of a work exposure and medical questionnaire, physical examination, skin prick test to Pt salts and other aeroallergens and patch tests to Pt salts. Airborne PGEs were collected by personal and area samples. Biological samples (serum, urine and hair) were also collected. An analytical procedure based on sector field inductively coupled plasma mass spectrometry for the analysis of airborne filter, blood, serum and air was used. Statistical evaluation was conducted. **Results:** Positive prick test reactions to Pt salts were found in 14 workers (17.2%); 4 of these 14 had simultaneous positive reactions to Pt, Rh and Ir. Two of these 14 had a positive prick test reaction to Pt and Pd. **Conclusion:** The preliminary results of the investigation clearly indicate that Pt salts represent important allergens in catalyst production plants, and the sensitization and clinical manifestations were associated with a high level of exposure.

**Yeast Infections and IgE-Mediated Sensitization to Yeast and Actinobacteria in a Moisture-Damaged Food Store**

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**Objective:** A cluster of yeast infections and IgE-mediated sensitization to yeast and actinobacteria in workers in a water-damaged food store is described. **Methods:** A symptom questionnaire was sent to all workers of the case building and matched reference persons. Moisture and associated microbial growth were measured. A mucosal swab sample from the throat was examined. Microbe-specific IgG and IgE antibodies were determined. The subpopulations and activation of lymphocytes were analyzed with flow cytometry. **Results:** Severe moisture damage, including leaking roof and soil moisture in the basement floor, was found. High concentrations of potentially toxin-producing microbes were detected in material samples (e.g. *Stachybotrys chartarum*, *Aspergillus niger*, *Aspergillus versicolor*, *Acremonium*, *Trichoderma*, and actinobacteria), together with common moisture indicative and allergenic fungi and yeast. All employees (n = 14) complained of work-related symptoms, almost all suffered from common respiratory infections and 13 workers had yeast growth in the swab sample from the throat. Five out of 14 workers had IgE antibodies to *Streptomyces albus*, 4 to *Candida albicans*, 2 to *Geotrichum candidum* and 2 to *Rhodotorula glutinis*. Flow cytometric analysis of blood lymphocytes showed altered immunoreactivation and CD4 to CD8 ratio compared with matched controls from a non-damaged food store. **Conclusions:** Long-term exposure to potentially toxin-producing moisture indicative microbes may lead to an altered immune response and infection with *C. albicans* yeast. Yeast infections were associated with IgE-mediated sensitization to yeast.

**Mite Exposure and Allergy in Food Stores and Restaurants**

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**Objective:** The objective of this study was to estimate the mite exposure and related health effects in food stores, restaurants and one bakery. **Methods:** The concentrations of storage and house dust mites were measured in dust samples. Health data were collected with a questionnaire. IgE-mediated allergy to storage and house dust mites was measured with skin prick tests and IgE antibodies in serum samples. Altogether, 290 workers in eight work places participated in
the study. **Results:** Storage mites were found in all workplaces. The concentrations of storage mites were high in food stores and low in restaurants and in the bakery. Concentrations of storage mites were highest in old and moisture-damaged buildings. The workers had a high prevalence of respiratory symptoms and high occurrence of common respiratory infections compared with the general population. The most common symptoms were rhinitis, skin irritation, cough, eye irritation, throat symptoms and hoarseness. Asthma was as common as in the general population (5.8%), and 30% reported allergic rhinitis diagnosed by a physician. In skin prick tests, 8% of the workers showed a positive reaction (diameter of the weal >3 mm) to at least one mite allergen. Positive skin tests were more often found to storage mites than house dust mites. **Conclusions:** Storage mites are commonly found in workplaces where food is handled. Allergy to storage mites is frequently found among such workers. Mite allergy is associated with a high occurrence of respiratory symptoms.

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**Specific IgE in Children Living in Regions with Different Levels of Air Pollution**

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**Objective:** Study of specific IgE synthesis in children with atopy living in regions with different levels of air pollution (region A: oil mining region; region B: city with large petrochemical complex; region C: agricultural region; region D: city with numerous industries of different profiles). **Methods:** Specific IgE levels were examined in serum of 85 children from 1 to 15 years old, including 22 in region A, 24 in region B, 16 in region C and 23 in region D. All groups were identical according to sex, age and correlation of atopy (atopic dermatitis and bronchial asthma). Chemiluminescence analyzer MAST CLA-1 and allergens of the ‘Medland System’ were used for analysis. Hygienic examination of air pollution was performed at the same time. **Results:** Sensitization to food allergens was the same in all groups. Specific IgE to house dust was found in 72.7% of the children in region A, 54.2% in region B, 68.8% in region C and 56.5% in region D. 50.1% of the children in region C were sensitized to *M. pteronyssinus* and *M. farinae*. High levels of specific IgE to epidermal allergens were more frequently found in children from region A (63.6% to cat, 59.1% to dog). The level of specific IgE to tree pollen allergens in children from region C was 18.8%, which was less than in regions A (50.0%), B (25.0%) and D (47.2%). There was not much difference in sensitization to cereal pollen (region A, 36.3%; region B, 29.2%; region C, 31.3%; region D, 26.1%). Sensitization to allergens of weed pollen (*Atriplex*, *Sagebrinel*) was as high as in region B. 6.3% of children in region C were found to have sensitization to fungal allergens. The same index in other groups was 4.5–6 times higher (region A, 36.4%; region B, 29.2%; region D, 30.4%). At the same time, in region D, there was a very high level of specific IgE to allergens of *Penicillium* (13.0%). **Conclusions:** Sensitization to food allergens did not differ in children with atopy living in regions with different levels of industry. The frequency of specific IgE to allergens of dust mites was twice as high in children from an agricultural region (D) than in other regions. Specific IgE to moulds in children with atopy was more frequently detected in industrial regions (A, B, D) than in children from the rural area.

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**Significant Decrease in Latex Allergens**

**Hev b 1, 3, 5 and 6.02 in Medical Gloves Marketed in Finland between 1995 and 2001**

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**Objective:** Latex allergy continues to be an important occupational health problem. Methods that can reliably measure specific allergens in gloves and other latex devices, instead of nonspecific total protein, are needed. **Methods:** A new immunoassay, making use of monoclonal antibodies and recombinant allergens, was used to quantify the clinically relevant latex allergens *Hev b* 6.02, 5, 3 and 1, all known to retain their IgE-binding ability during rubber manufacturing. The Finnish National Agency of Medicines has arranged nationwide market surveys of medical gloves on a biennial basis. We report here the results for the new latex allergen-specific assay in surveys in 1995 (22 gloves) and 2001 (71 gloves). **Results:** In 1995, *Hev b 6.02* was detected in 73%, *Hev b 5* in 73%, *Hev b 3* in 45% and *Hev b 1* in 14% of medical gloves. In 2001, *Hev b 6.02* was detected in 53%, *Hev b 5* in 24%, *Hev b 3* in 22% and *Hev b 1* in 0% of medical gloves. When the sum of the four allergens in gloves exceeded 1 μg/g, most latex-allergic patients showed positive skin prick test reactions to extracts of such gloves. In 1995, 41% of the gloves revealed more than 1 μg/g latex allergens, while in 2001, only 14% exceeded this value. **Conclusions:** A marked decrease in the concentrations of four clinically relevant latex allergens in medical gloves was noted between the years 1995 and 2001. Quantifying selected latex allergens in manufactured products offers the means to reliably monitor their allergen content. This methodology could eventually be used to assess and set up meaningful safety limits for latex devices.

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**Measurement of Thioglycolates in Hairdressing**

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Thioglycolate (TG) and related compounds are known to cause occupational dermatoses and probably contribute to asthma in hairdressers. Few studies on the TG exposure of hairdressers have been performed due to difficulties with sampling and analysis. The purpose of this study was to develop a method to evaluate the TG concentration during the preparation of permanents. The TG solution was atomized with a Liu-Lee type aerosol generator to submicron-sized particles and sampled on a filter. Six different filter and extraction combinations were tested. The storage life of reagents and samples was investigated. The HPLC-iontrap-API-detector system was used for analysis, being a fast and specific instrumentation. The analysis conditions were optimized in relation to acetonitrile concentration, pH and column. The test chamber aerosols were characterized with a scanning electron microscope. During analysis, TG was found to convert into dithioglycolic acid. Due to oxidation, TG recovery was only 25%, while recovery of the acid component...
was 180%. Oxidation was reduced in cold storage (−20°C). The correlation coefficients were excellent for calibration curves but recovery was usually poor. The best filter and extraction solution combination was the glass fiber filter and diethylether. Cellulose acetate filters yielded only 40% of glass fiber filter recovery. The protein components of commercial cold permanent lotions were stripped in the prepurification procedure. The determination limit (DL) of TG was 0.7 ng/μl in HPLC, giving a DL of 0.7 mg/m³ for airborne aerosol concentrations. The other thioglycol compounds used in hairdressing had higher DL values. The method is suitable for product analysis and long-term monitoring in hairdressing salons. Measuring short-term exposure during the preparation of permanents would require a lower DL. The results were promising, but further development is still needed to reduce the DL and to enhance the stability of TG during sampling and analysis.

**Abstracts**

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**Allergic and Toxic Airborne Particulate Matter in Minsk**

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A complex study of the allergic and toxic aerosol particles in Minsk city was carried out for ecological monitoring. Pollen, spores and industrial particulate matter (PM) were the main objects. Two methodological approaches were used: (a) single-particle study, and (b) common analysis of massive samples (mould colonies, pollen of blossoming plants and industrial filter cakes). SEM, microprobe, X-ray fluorescence, X-ray diffraction and particle size laser analysis were used. Seasonal pollination calendars (2000–2002) were compiled. During the Pinus and Picea pollination peak, a small percentage of pollen grains with morphological deviations were observed. After mass pollination is finished, the destroyed pollen grains with adhered fungal spores and inorganic PM were recorded. Therefore, the complex pollen-spore-inorganic PM particles was the specific object of investigation in Minsk city aerosols. The allergic spores Deuteromycetes were observed during the summer period, and in August and September, the allergic or toxic spores of smuts and rust were plentiful. Spore identification is a difficult task because of their morphological modification. The method of spore identification may be developed on the basis of SEM morphological analysis. Industrial PM mostly have spherical forms and may be recognized by their crystalline surfaces. Their chemical compositions were defined by microprobe analysis. Particles of iron (Fe 100%), copper-zinc alloys (Cu 85%, Zn 15%) and iron with a copper-zinc admixture (Fe 99%, Cu 1%, Zn 0.1%) were observed. A great variety of allergic and toxic aerosol particles was identified in the Minsk city area. Pollen, spores and industrial PM are the common objects of interest. Spores, some industrial PM, drop pollutant and other objects have to be studied in a more detailed manner to evaluate their allergic characteristics.

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**Molecular Mechanism of the Allergic Action of Epoxides**

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Epoxides are the most well-known and widespread classes of reactive substances. They contain an epoxy group that reacts with tissue and serum proteins of human organisms. As a result of this interaction, the protein molecule structure can be modified. This process creates the prerequisites for allergy development. We have made an attempt to investigate the initial stage of epoxide interaction with human serum albumin (HSA) by one of the quantum chemistry methods. Six amino acid residues were isolated from an HSA molecule for construction of a quantum chemical model based on the X-ray crystal analysis data. They were amino acid residues Arg 257, Arg 222, Lys 119, His 242, Arg 218 and Lys 195, forming the so-called main ‘linkage center – hole’ of the HSA molecule. Ethylene oxide, the simplest representative of the epoxide class, was chosen as a substance reacting with HSA. The electrostatic potential (ESP) of the HSA active center was calculated based on the quantum chemical estimation. The ESP maximal value is observed in the nitrogen atom region of the amino acid residuum Lys 195, and it is equal to +468 kJ/mol. The range of the ESP minimum value is localized above a plane of the so-called ‘guanidine key’ Arg 257, and it is equal to −419 kJ/mol. The same quantum chemical estimation was carried out for the ethylene oxide molecule. The ESP allocation minimum value in a plane of the epoxy cycle near the oxygen atom equaled −209 kJ/mol; both maximums near hydrogen atoms symmetrically equaled +159 kJ/mol. A so-called two-centered complex is formed when the ethylene oxide molecule gets into the HSA linkage center. It is formed on the one hand by a hydrogen bond between the oxygen atom of the ethylene oxide molecule and the hydrogen atom of the polar group Lys 195 and on the other hand by a hydrogen bond between the guanidine key Arg 257 proteoaccepter center and one of the hydrogen atoms of ethylene oxide. In our opinion, this interaction is the primary mechanism of formation of complex antigen following allergic responses.

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**Respiratory Complaints and Sensitization to Rennet Powder and Fluid Rennet**

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Enzymes are potential allergens. Proteolytic enzymes are the active component in rennet, which is produced as a solution and recently also as a powder. In a rennet-producing plant, employees had rhinitis and/or cough at work. The purpose of this investigation was to find out if these complaints were irritative or allergic. A skin prick test (SPT) with standard allergens and 5 different rennets were performed on 35 of the 38 employees. 12 had respiratory complaints. The tested rennets were traditional rennet from bovine stomachs with pepsin and chymosin in two different concentrations, 2 types of biotechnological rennet with aspartic protease as the active component and a chymosin product, produced in a GMO-like process. An identical SPT was performed in 9 controls (physicians). 14 of the
35 employees had a positive SPT to 1 or more rennets, 2 only to standard allergens and 4 to both. The sensitization rate was higher among those who had close contact with rennet powder than among those who predominantly had contact with fluid rennet. One rennet type was not produced as a powder and had the lowest sensitization rate. 6 of 14 employees with positive SPT to rennet had respiratory complaints at work; the other 6 with complaints had a negative SPT. 9 subjects reported allergic symptoms to something other than rennet. 3 of those were sensitized to rennet (33%). Of the remaining 26 with no other allergic symptoms, a positive SPT to rennet was found in 9 cases (42%). None of the controls reacted to rennet, but 2 reacted to standard allergens. Rennet powder appears to have a greater allergenic potential than fluid rennet, which could explain why rennet allergies have not been reported more often in the past. Allergy can explain all respiratory complaints. Irritation from proteolytic activity seems to play a role as well. Our findings suggest that a pre-existing allergy had no relation to the development of a work-related rennet allergy.

**Studies of Work-Related Respiratory Morbidity among Employees of a Cement Industry in Shiraz, Iran**

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Portland cement is made from hydrated calcium silicates, aluminium oxide, magnesium oxide, iron oxide, calcium sulphate, clay, shale and sand. The mixture is crushed and calcinated at high temperatures with the addition of gypsum. Cement finds numerous uses in road and building construction. Pathological conditions encountered in the cement industry include diseases of the respiratory tract, digestive disorders, skin diseases, rheumatic and nervous conditions and hearing and visual disorders. Although the main hazard in cement processing is dust, and respiratory tract diseases are the most important group of occupational diseases in this industry, evidence for associations between exposure to cement dust and either respiratory symptoms or functional impairment has not been so conclusive. Additionally, the potential adverse health effects of Portland cement have not been extensively studied. Therefore, this study was undertaken to evaluate more thoroughly the effects on the respiratory system of occupational exposure to cement dust. The study population consisted of a group of 88 randomly selected male workers with current occupational exposure to cement dust and 80 healthy male office workers without present or past exposure to dust, who served as the control group. The average (mean ± SD) age, weight, height and duration of exposure to dust for the exposed group were 44.3 ± 7.9 years, 73.8 ± 10.7 kg, 170.8 ± 7.2 cm and 18.8 ± 7 years, respectively. The corresponding values for the control group were 41.7 ± 5.8 years, 76.4 ± 11.6 kg, and 172.5 ± 7.8 cm respectively. There was no statistically significant difference between any of these means (except, of course, for duration of exposure to dust). Subjects were interviewed and respiratory symptom questionnaires, as suggested by the American Thoracic Society (1978), were completed for all of them. They were classified as smokers and non-smokers and underwent chest X-ray and lung function tests according to the guidelines of the American Thoracic Society (1979). Furthermore, using standard methods, personal dust monitoring for airborne inhalable and respirable dust was carried out at nine different worksites. Moreover, X-ray diffraction and X-ray fluorescence were performed to determine the silica phases and the SiO₂ contents of the dust samples. X-ray diffraction and X-ray fluorescence revealed that the crystalline silica phase of the sample was quartz and the sample contained 26.9% SiO₂. Similarly, levels of exposure to inhalable and respirable cement dust were estimated to be 53.4 ± 42.6 and 26 ± 14.2 mg/m³, respectively (mean ± SD). These values exceeded the current standard of 10 mg/m³ for inhalable and 3 mg/m³ for respirable dust. Exposed workers, regardless of their smoking habits, had higher prevalences of regular cough (31.8%), phlegm (26.1%), wheezing (28.4%) and shortness of breath (17%). The corresponding values for the control group were 20, 15, 5 and 5%, respectively. These differences were statistically significant (p < 0.05). These symptoms were more frequent among the smokers for both groups. Chest radiograms of exposed workers showed emphysematous changes (15.9%), old calcified granulomas (5.7%), emphysematous changes associated with inflammatory processes (4.5%), evidence of chronic inflammatory processes (4.5%), focal calcification of the lungs (4.5%) and infiltrative changes (2.3%). However, no significant changes were noted in the radiograms of the control group. Similarly, the results of spirometry demonstrated a statistically significant reduction in lung function parameters, i.e. vital capacity (p = 0.002), forced vital capacity (p = 0.0006), forced expiratory volume in the first second (p = 0.0006), forced expiratory flow between 25 and 75% of the forced vital capacity (p = 0.0003) and peak expiratory flow (p = 0.01), in exposed workers when compared with controls. In conclusion, our data provide corroborative evidence to further substantiate the contention that exposure to cement dust is associated with respiratory symptoms and functional impairment.

**Respiratory Symptoms and Ventilatory Disorders among a Group of Rubber Workers in Shiraz, Iran**

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Talc, a hydrated magnesium silicate, is one of the most important hazards in the rubber industry, and occupational exposure to it has been associated with chronic respiratory diseases and ventilatory disorders. The purpose of this study was to determine the prevalence of respiratory symptoms and/or ventilatory impairment among a group of rubber workers with current occupational exposure to talc dust. Standard respiratory symptom questionnaires as well as pulmonary function tests were administered to a group of 105 randomly selected male rubber workers. Additionally, 75 subjects underwent chest radiography. Moreover, environmental monitoring, measurement and analysis of atmospheric inhalable and respirable dust were performed at the site. The length of exposure to talc dust (mean ± SD) was 16.8 ± 6.5 years. Analysis of the dust showed that it contained about
55% crystalline silica (quartz, SiO₂). Additionally, the concentrations of inhalable and respirable dust were calculated to be 37.5 ± 22.8 and 17.8 ± 7.8 mg/m³ (mean ± SD), respectively, which are far beyond the current standard of 0.3 mg/m³ for inhalable and 0.1 mg/m³ for respirable fractions. The prevalence of abnormal clinical symptoms including, cough, phlegm, wheezing and dyspnea were found to be 71.4, 69.5, 68.6 and 73.3%, respectively. These symptoms were more frequent among workers with more than 10 years of exposure. Chest radiograms of the subjects showed abnormalities in about 11%, including emphysematous and infiltrative changes, pleural thickening and density in the right superhilar area. Respiratory parameters of the workers were found to be significantly different from the standard reference values. Therefore, it is concluded that exposure to talc dust is associated with impaired lung function and abnormal symptoms.