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ESCD Abstracts 2004

Wednesday, 09 June 2004
11:00–16:30

PCS

Risk assessment of contact allergy

Chairs: David A Basketter, UK & Torkil Menné, Denmark

PCS.01

Risk assessment: a brief history for ACD

Winfried Steiling
EUROTOX Certified Toxicologist, Henkel KGaA, Düsseldorf, Germany

Risk assessments of chemicals are key issues in our live.

Prior to industrialisation, risk assessments based on individual experience, for the allergic contact dermatitis (ACD) for instance, after contact with allergic plants affecting the skin exposed. Today, the risk to get an ADC becomes more and more important, because of increasing contact to new chemicals because of frequent contact with consumer products. Therefore sufficient test systems are required, appropriate to estimate the sensitisation potential of individual chemicals. To be able to predict weak sensitisers, adjuvants were simultaneously injected to test animals to booster their allergic reactions. One of the most well known test method, is the maximisation test in guinea pigs according to Magnusson and Kligman. Regulatory authorities have required this method for chemical classification, as well as for estimating the risk to get sensitised when dermaly exposed.

Beside the advantages of these guinea pig studies, the limitations became prominent not only in respect to ethical aspects, but also because of the lack to quantify the sensitisation potency of chemicals. To be able to perform accurate, realistic risk assessments, the knowledge of potency is becoming mandatory, especially when sensitive test methods are used. Based on the possibility to measure the biological response during induction of sensitisation, the local lymph node assay (LLNA) gets popular. Today, this test is officially accepted by regulators to give information on skin sensitisation potential. With the quantitative approach on potency, risk assessment of ACD will become much more reliable and useful for Men.

PCS.02

Risk assessment in practice – clinical problems in ACD. Consumer perspectives

Ian R White
St John's Institute of Dermatology, St Thomas' Hospital, London, UK

That a cosmetic product must not cause *damage* to human health is enshrined in European legislation. Within the EU, the Scientific Committee for Cosmetic and Non-food Products (SCC NFP) of the Directorate General for Consumer Safety & Health Protection provides independent risk assessments of certain cosmetic ingredients. The evaluations depend largely on the completeness of dossiers submitted by industry. Requirements for submissions are published by the SCC NFP http://europa.eu.int/comm/health/ph_risk/committees/sccp/documents/out242_en.pdf) and cutaneous toxicology, including contact allergy, is only a part of the overall assessment.

Opinions adopted by the SCC NFP are published in full (http://europa.eu.int/comm/health/ph_risk/committees/sccp/sccp_opinions_en.htm), presented to the Directorate General responsible for the legislation (Enterprise), who are risk managers, and discussed with Member States before the recommendations are included in the annexes of the Cosmetics Directive, if appropriate.

The Cosmetics Directive (http://pharmacos.eudra.org/F3/cosmetic/pdf/vol_1en.pdf) contains positive lists of certain ingredient types (including preservatives, UV filters) and only those substances listed may be used. Annex 3 lists substances that may be used under certain conditions (concentration, exposure sites, warnings, age).

Increasingly, revision of assessments of risks related to contact allergy have been brought about by epidemiological and robust clinical data (elicitation studies) submitted by dermatologists. As illustrated with the examples of methyldibromo glutaronitrile and Lyral®, rapid responses to protect the consumer are possible when the Commission is provided with appropriate information. Similar examples illustrate failures to predict risks for the induction of contact

allergy before the consumer was excessively exposed.

In contrast to the above, some permanent hair dye chemicals (for which there is, as yet, no positive list) are important and potent allergens and are permitted only because of the absence of acceptable alternatives and social need. Warnings and recommendations for testing before use have not been validated despite the long history of complaints. The 'damage' experienced by the consumer with an adverse reaction to a hair dye must be balanced against their possible carcinogenic potential.

The consumer expects products to be safe. Why do risk assessments fail?

PCS.03

Risk assessment in practice – clinical problems in ACD. Occupational perspectives

Marlene Isaksson
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This lecture will focus on consequences for the affected labour force following contact with well-known allergens in new technical applications, or when the risk assessment of chemicals has been done by persons without sufficient knowledge of factors significant for the induction and elicitation of contact allergy and allergic contact dermatitis. When chemicals with noxious characteristics to both the airways and the skin are handled, the focus is by far and foremost on protection of the airways. However, one must consider the difference of dose needed for airway diseases compared to skin diseases with regard to allergic contact dermatitis. For contact allergy, it is not the total dose that is the culprit but the dose/unit area, i.e. a high concentration of a chemical on a limited skin area may be deleterious. This implies that contamination outside the working operation (e.g. on handles and doors) may lead to sensitisation and allergic contact dermatitis.

Examples will be given from the dental profession ((meth)acrylates), the manufacture of resol resins based on phenol and formaldehyde in the production of laminate, and from manual labour including contact with isocyanates and epoxy resins in the manufacture of water-repelling surfaces on floor boards and in the production of wings for wind mills, respectively.

PCS.04

Establishment of safe exposure limits for the induction of allergy. Theory

G Frank Gerberick[1], P McNamee[1], PS Kern[1], CA Ryan[1]. DA Basketter[2]
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For new chemicals introduced into the workplace or marketplace, and which come into contact with the skin, it is necessary, to conduct a thorough skin safety testing and risk assessment program to be certain that the exposures will be well tolerated. One vital risk assessment process involves the determination of allergic skin reactions, referred to as skin sensitization, the clinical manifestation of which is allergic contact dermatitis. The process by which low molecular weight chemicals induce and elicit skin sensitization is dependent on many factors including the ability of the chemical to penetrate the skin, react with protein, and trigger a cell-mediated immune response. Based on our chemical, cellular and molecular understanding of allergic contact dermatitis, it is possible to carry out a quantitative risk assessment. It has been well known for years that chemical allergens display dose-response characteristics regardless of whether the sensitization is induced in an experimental system or in humans. Moreover, it is well known that the critical exposure determinant for evaluating skin sensitization risk is dose per unit area of skin exposed. The skin sensitization testing and risk assessment process for new ingredients and consumer products generally follows a step-wise approach that may involve structure-activity evaluations, analytical assessments, preclinical skin sensitization testing (e.g., the mouse local lymph node assay), confirmatory clinical testing (e.g., the human repeat insult patch test), and benchmarking of resulting data against similar ingredients and product types. Essential elements for conducting a sound risk assessment involve the development of an understanding of the sensitization potential of the contact allergen and the likely dose, nature, extent and duration of exposure. With an understanding of the exposure and potency of the chemical one can assess whether the chemical, under the specific conditions of exposure, ould pose an acceptable or unacceptable risk of induction of skin sensitization. As with any test method or risk assessment approach, it is critical to understand the strengths and limitations so that one can conduct the best assessment possible and assure the skin safety of the chemical under evaluation.

PCS.05

Establishment of safe exposure limits for the induction of allergy. Practical examples

Torkil Menné
Department of Dermatology, University of Copenhagen, Gentofte Hospital.

The WHO criteria for drug allergy can be adapted as guidelines for primary sensitisation from consumer products or occupational exposures. In case a person with a formerly healthy skin, develops allergic contact dermatitis after a specific exposure (a product or occupational exposure) has a positive patch test to specific chemical present in the product and ideally a positive either patch test or use test to the product during re-exposure primary sensitisation is likely.

Allergic contact sensitisation is a unique toxicological event (e.g. compared to cancer) as there is a direct (time and skin area) correlation between exposure and disease and the basic damage on the individual can be identified by the diagnostic patch test. Primary sensitisation may occur after single exposure to potent allergens, experimental from DNCB, in the US poison ivy, occupational accidental exposure to isothiazolones (in%) or from hair dying with PPD and its derivatives as a flare-up reaction occurring 1–2 weeks after the original exposure.

The ongoing epidemic caused by methyldibromo glutaronitrile (MDGN) provides unique options for studying primary sensitisation from consumer products as the clinical reactions are often very severe and patch test reaction with the products often exceeds the strength of the standard patch test response. Chemical analysis of the products involved uniformly illustrates the presence of MDGN within the legal permitted concentration. At the start of the epidemic, primary sensitisation was mostly seen from leave on products. After EU actions in 2002 against the use of MDGN in leave on products primary sensitisation from this preservative is now caused by wash off products. This observation is significant as it underscores the effect of specific exposures for primary sensitisation from consumer products but also the fact that primary sensitisation from a moderate to strong hapten is possible from wash off products. The MDGN story has illustrated that human data are pivotal for the current risk assessment – risk management. No new chemical should be permanently permitted in consumer products before significant post marketing data, collected after stringent criteria, are public available and scrutinised by an independent scientific committee.

Human sensitisation data has successfully been used to introduce regulation of nickel exposure from consumer items. The year 2000 EU regulation has been in use in Denmark for more than 10 years. A significant decline in both induction and elicitation of dermatitis from nickel releasing items has been observed. Health economists have calculated that the direct savings from the regulation amount to 1.2 bill Euro over a 20-year period in a population of 5.2. mio individuals.

Translated to the whole EU-region substantial gains can be achieved by improving the contact allergy risk assessment – risk management process.

PCS.06

Establishment of safe exposure limits for the elicitation of allergy – fragrances

Jeanne Duus Johansen
National Allergy Research Centre, Department of Dermatology, Gentofte Hospital, University of Copenhagen, Denmark

Safe exposure limits for the elicitation of fragrance contact allergy have been a subject of research in several EU-funded studies, against the background of high frequencies of contact allergy to certain fragrance ingredients. Elicitation studies can be easily performed in already sensitised individuals, they bear no ethical problems and by using simulated realistic exposures, safe thresholds relevant for exposure can be determined. The challenge in establishing safe thresholds for fragrance ingredients is the many different applications and thus potential exposures to fragrances. Deodorant exposures have been regarded a worst case assumption model for safety assessment and the fragrance ingredients: isoeugenol, hydroxycitronellal and cinnamic aldehyde, have been studied, showing that current exposure to these ingredients in some deodorants exceeds the safe limits for elicitation. Recent investigations show that the impact of fragrance allergy on hand eczema may need to be looked at a different angle, as it appears that it is more the combined exposures to several allergens and irritants that matters than the action of a single ingredient. At the moment, studies are being performed to elucidate whether dose-response patch test data can be used more systematically as the basis of safety assessments. This will make studies even easier and it will be possible to provide data on more allergens than at the present time.

PCS.07

Establishment of safe exposure limits for the elicitation of allergy – hair dyes

David A Basketter
SEAC, Unilever Colworth, Sharnbrook, Bedford, UK

It is well known that a subtle balance exists between consumer desire to use hair dyes of various kinds and the sensitizing effects of particular dye ingredients. Of these, p-phenylenediamine (PPD) is the mostly commonly reported contact allergen and which serves as a general model for hair dye allergy. PPD is reported as a strong sensitizer in all predictive tests; it is fairly commonly identified as a contact allergen in diagnostic patch testing, with relevance to hair dye ACD being about 50%. Whilst it may not be possible always to eliminate, or even greatly reduce, the extent to which sensitisation is induced, a final opportunity for limiting the degree of ACD occurs at the elicitation phase. Here, ensuring the extent of skin exposure is below the level at which all except the most strongly sensitized will react can provide clear consumer benefits. To achieve this aim, it is necessary to ensure a full appreciation of the variables impacting the elicitation of ACD exist. To this end, series of investigations of the elicitation of p-phenylenediamine (PPD) sensitization has been conducted. In particular, the impact of duration and frequency of exposure on elicitation has been studied. Using groups of PPD sensitized volunteers, in patch tests and repeated open application tests, we have shown that exposures of only a few minutes are often without consequence in such individuals, except where the exposure is often repeated and/or the individual is highly allergic. With volunteers who were 1+ or 2+ positive to the diagnostic patch test, and where exposure to PPD was at 0.5%–1.0% in a short contact rinse-off hair colouring product, no scalp reactions were experienced. It is our view that the establishment of safe exposure limits to contact allergens should be based wherever possible on a detailed assessment of the risk to sensitized humans.

PCS.08

Risk assessment versus risk management – is there a role for legislation? Yes

Elisabet Berggren
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Classification and labeling of substances and preparations within the EU is made in accordance with the criteria as written out in Directive 67/548/EEC ('the substances directive') and Directive 1999/45/EC ('the preparation directive' setting general concentration limits for preparations containing substances classified under 67/548). The basis for the criteria concerning hazard for skin sensitisation is based on practical experience showing that the substance or preparation is capable to induce a sensitization by skin contact in a substantial number of persons (appropriate patch testing or epidemiological data); or where positive tests from appropriate animal testing are available. Recently at the EU level and currently continued at the OECD, there is an expert discussion on the appropriateness to make potency considerations of skin sensitisers. The experts evaluate the possibility to set specific concentration limits for induction skin sensitisers contained in preparations. These limits would then give the possibility to classify such preparations better mirroring the reality than the current general limits given in the preparations directive. The first measure to prevent the hazard when a chemical or preparation fulfills the criteria to be classified as a skin sensitiser, is through the labeling indicating the standardized risk phrase: 'May cause sensitization by skin contact', which also must be followed with an adequate safety advice. The classification of a substance has further consequences in other legal instruments on EU level leading to additional risk management measures.

PCS.09

Risk assessment versus risk management – is there a role for legislation? No

Charles Laroche
France

Abstract not available at the time of printing.

Thursday, 10 June 2004
09:10–10:00

KL01

Keynote Lecture

Chair: Torkil Menné

Mouse models of skin autoimmunity and peripheral tolerance

Stephen I Katz
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To understand the mechanisms involved in immunological tolerance to skin-associated proteins, we have developed trangenic (Tg) mice that express a model self antigen, membrane-bound

chicken ovalbumin (OVA), under the control of a keratin 14 (K14) promoter. We have characterized these mice and have shown that their skin serves as an excellent target for CD8+ T cells from OVA-specific T cell receptor Tg (OT-I) mice. When the K14 OVA transgenic mice are crossed with the OT-I mice they no longer serve as targets for the OT-I CD8+ T cells from the OT-I mice. This paradox is due to peripheral tolerance that is exhibited by the double Tg mice. I will discuss these two models and describe studies that are attempting to determine the mechanism of this peripheral tolerance.

Thursday, 10 June 2004
10:30–11:55

FS01

Textile dermatitis & PPD

Chairs: Francisco Brandão, Portugal & Stefania Seidenari, Italy

FS01.1

The use of azo dyes in the European Union – legislation review

Angelo Azenha
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The aim of this paper is to review the European legislation concerning the use of textile dyes.

It is known that different dyes of different classes can be sensitizing and cause allergic contact dermatitis for both textile workers and consumers.

The European Union has created restraining directives regarding the manufacture and distribution of potentially dangerous products, such as aromatic amines. A specific scientific committee of EU stated that the carcinogenic capacity of some azo dyes is related to chemical releasing of aromatic amines (groups MAK III; A1; A2).

In this paper, focus will be centred on the latest European Union Directives in this matter and the prohibition of some azo dyes in textile industry.

FS01.2

Contact dermatitis to disperse blue 106 in Portugal

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Disperse blue 106 is one of the most important allergenic textile dyes. We reviewed all the patients that proved to be allergic to this dye, in 10 contact clinics, in Portugal, from 01/2000 to 06/2003. In the first 2 years disperse blue 106 was only tested in suspected cases, while in 2002/2003 it was routinely tested in our standard series. A total of 8957 patients (2797M + 6160F) were tested; fifty five patients (17M + 38F) (0.6%) were allergic to the dye, with a significant difference in incidence between the 2 periods (0.2 to 0.9%); a current relevance was found in 38 (69%) patients. In 5 patients the dermatitis was considered occupational. The main localizations were the axillae (25p), the antecubital fossae and the face (13p each), the neck (11p), the feet (8p), the hands and then trunk (7p each). Thirty six out of 44 patients (80%) that were tested with disperse blue 124 were allergic to this dye. Simultaneous reactions to PPDA and to fragrance mix were observed in 12 and 11 patients, respectively. Allergy to other dyes was found in 15 patients. Blouses and skirts were the main offending garments that induced contact allergy. Although both disperse blue 106 and 124 have been reported as frequent sensitizers, it proved not to be such an important allergen in Portugal. However, if tested routinely it can pick up some unexpected relevant allergic patients.

FS01.3

Disperse (yes), orange (yes), 3 (no): what do we test in textile dye dermatitis?

Christophe J Le Coz[1], G Jelen[2], A Goossens[3], M Vigan[4], G Ducombs[5], A Bircher[6], F Giordano-Labadie[7], A Pons-Guiraud[8], Milpied-Homsi[9], M Castelain[10], D Tennstedt[11], J-L Bourrain[12], G Bernard[13], GERDA France
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[4]Unité de Dermato-Allergologie, Besançon, France
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Introduction: Patients sensitized to para-phenylenediamine (PPD) have a high degree of patch test reactivity to Disperse Orange 3 (DO3), and a lesser one to Disperse Red 1 and Red 17. Two successive patients positive to PPD, Disperse Red 1 and 17, negative to DO3 were real eye-openers for our considerations about purity of our current allergen DO3.
Materials and methods: We realized comparative thin-layer chromatography (TLC), with DO3 from Chemotechnique® (DO3-Chem) and Trolab® (both extracted from petrolatum), and "pure" DO3 from two chemical providers. TLC clearly indicated that DO3-Chem was not DO3. HPLC analysis with pure DO3 from Chemotechnique® and comparison of structures by NMR with samples of DO3, revealed that DO3-Chem was Disperse Orange 31 (DO31). In addition, signals through the GERDA network allowed the collection of test materials and observations. Among other members, only 2 used DO3-Chem (from 2 different batches) that was DO31 too, according to TLC Results: According to their data, they observed no or a lower reactivity to DO3 than expected (4 patients DO3-Chem + among 23 PPD+ e.g.). Finally, the error was proved to be due to the provider of the dye to Chemotechnique®, who likely deleted the 1 of Disperse Orange 31 on his packaging.
Discussion: Chemical structure of DO31 indicates a possible in vivo hydrolysis into nitroaniline and a second compound, a substituted PPD derivative that clearly does not frequently react in PPD positive patients. Like drugs, patch tests are submitted to post-commercialization controls. In addition to allergens providers who should enhance their quality controls, dermato-allergologists have to be vigilant, and must active networks when they observe a rare bird.

FS01.4

Hailey Hailey disease – a significant hazard to consider when patch testing

S Walker, Jason Williams, J O'Driscoll, M Beck Dermatology Centre, University of Manchester, Manchester, UK

A 42 year old man was referred to the Contact Dermatitis Investigation Unit because of a 12 month history of an inflammatory eruption affecting his neck. He was patch tested to our standard series, textile series and his own medicaments. At the 48 hour reading the patches were removed and there were large areas of unusual painful superficial erosions where the patch test tape – Scanporä had been in contact with the skin. This appearance was difficult to explain. He denied interfering with the patches. The erosions were dressed with non-adherent dressings held in place by a different tape-Microporeä. At the 96 hour reading these dressings were removed and in the areas under the Microporeä tape there were further erosions around the edge and also some thin walled vesicles and small bullae. There were ++ allergic reactions to sodium metabisulphite, disperse blue 35, 124 and 106 all of which were felt to be relevant as he had used Trimovateâ cream and regularly wore dark nylon clothing when refereeing lacrosse matches. A biopsy was taken for histology and immunofluorescence from an area of blistering. This demonstrated suprabasal acantholysis with vesicle formation. There were occasional corps ronds. The immunofluorescence was negative. Anti-epidermal (skin) antibodieswere also negative. This striking and alarming clinical presentation after removal of patch tests had been encountered once previously in our Contact Dermatitis Investigation Unit. The possibility that the disorder was artefactual either due to an irritant introduced under the tapes or perhaps due to a contaminant within the tape adhesive was considered but no conclusion was reached In this case the clue to diagnosis became apparent at the second patch test reading when small vesicles and bullae could be seen at the edge of where the Microporeâ had been. A diagnosis of Hailey Hailey disease (HHD) trigered by the trauma caused by the adhesive tapes and their removal was made. The relatively persistent nature of his presenting problem makes Grover's disease less likely. The affected sites healed after two weeks. Allergic contact dermatitis particularly to medicaments is reported to be a frequent complication and routine patch testing has been advocated1. There has been a previous report of blistering at the site of patch testing however he was an individual already known to have HHD2. Despite having patch tested around 30 000 people in the last 22 years this complication had not been encountered until this year. We present this case whose clinical features are distinctive as we feel similar instances may have been or will be seen by colleagues. Diagnosis may be difficult if there are no blisters in association with the painful erosions.

References

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FS01.5

Establishment of safe exposure limits for the elicitation of contact allergy

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Although the primary point of intervention for the prevention of allergic contact dermatitis (ACD) should be appropriate assessment and management of potential skin sensitization hazards, there is nevertheless a place for secondary prevention in individuals who are already sensitized. Thus it is necessary to ensure a full appreciation of the variables impacting the elicitation of ACD exist. To this end, we have been engaged in a series of investigations of the elicitation of p-phenylenediamine (PPD) sensitization. In particular, we have studied the impact of duration and frequency of exposure on elicitation. Using groups of PPD sensitized volunteers, in patch tests and repeated open application tests, we have shown that exposures of only a few minutes are often without consequence in such individuals, except where the exposure is often repeated and/or the individual is highly allergic. With volunteers who were 1+ or 2+ positive to the diagnostic patch test, and where exposure to PPD was at 0.5%–1.0% in a short contact rinse-off hair colouring product, no scalp reactions were experienced. It is our view that the establishment of safe exposure limits to contact allergens should be based wherever possible on a detailed assessment of the risk to sensitized humans.

FS01.6

A 10-rear review to determine whether exposure to p-phenylenediamine during patch tests leads to sensitisation

Simon Dawe, I White, R Ryecroft, J McFadden
St Johns Institute of Dermatology, London, UK

Our review aimed to answer the question of whether exposure to PPD in the European standard series could lead to subsequent sensitisation in a significant number of patients. We aimed to achieve this by comparing the frequency of PPD sensitivity in patients who had never been patch tested compared to those who were having repeat patch testing and who therefore had been exposed to PPD in patch test conditions. From January 1990 to December 1999 14,001 patient's with suspected contact dermatitis were tested with the European standard series in St. Johns. We selected and obtained the records of all patient's during this time period who had a positive patch test to PPD free base 1% pet. Of the 14,001 patient's tested, 1035 had previously been patch tested on at least one occasion representing 7.4% of the population. This proportion varied from 5.6% in 1994 to 11.1% in 1991 but there was no obvious trend during the ten year period. The total number of PPD positive reactions (+ to +++) over the ten year period in the whole population was 449 (3.2%). The number of PPD positive reactions in the first time testers was 419 (3.2%) compared to 30 (2.9)% in the repeat testers. Our figures over a ten-year period do not show an increase in the rate of PPD sensitivity in patients who have been previously patch tested. These figures suggest that PPD 1% pet. as used in the standard series is not actively sensitising patients who are repeatedly patch tested.

FS01.7

Prevalence of contact allergy in an adult Thai population

David A Basketter[1], I Duangdeeden[2], N Gilmour[1], P Kullavanijaya[2], J McFadden[3]
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There is only very limited data on the prevalence of contact allergy, as judged by a positive diagnostic patch test, in unselected, non-clinical populations. We carried out a 48 h patch test to 7 common allergens and to the petrolatum vehicle in a total of 2545 adult volunteers in Bangkok. The patch tests were read at 48 h approximately 1 h after patch removal. Positive results were as follows Ni 27.8%, fragrance mix 2.9%, Cr 2.6%, PPD 2.3%, colophony 2.1%, MI/MCI 1.2% and formaldehyde 0.7%. No reactions were found to petrolatum. The particularly high frequency of reactions to Ni was surprising.

However, the large female bias (approximately 75:1) strongly suggested that, despite the absence of a 96 h score, that irritancy did not play a significant part in these reactions. Reaction rates to the other 6 contact allergens appeared to confirm predictions made from the extrapolation of diagnostic patch testing or from previous published studies on smaller population groups. The rates of reaction to these allergens also are likely to reflect the extent of

exposure in the Bangkok region. Nevertheless, it is interesting to note that over 2% of this adult population appear to be allergic to the cosmetic related allergens PPD and fragrance.

FS01.8

Substance-specific modulation of TNF-Alpha and IL-1Beta in human monocytes by para-Phenylenediamine and not by its autoxidation product Bandrowski's Base

Nasrin Hamidizadeh[1], S Breuer[1], HF Merk[1], B Bloemeke[2]
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Para-phenylenediamine (PPD), an arylamine dye, is a strong allergen causing allergic contact dermatitis. Cytokines such as TNF-α and IL-1beta are key mediators in the initiation of this reaction. Both cytokines are predominantly produced by stimulated monocytes and macroghages. We investigated the responses of PPD and Bandrowski's base (BB), an autoxidation product of PPD in human monocytes. We isolated monocytes from healthy volunteers and incubated them with the allergens. TNF-α and IL-1beta mRNA expression and protein levels were estimated after 45 min, 2 h, 4 h and 24 h after allergen contact. IL-1beta and TNF-alpha were measured in cell culture supernatants by ELISA (n = 7) and mRNA expression was determined by real-time RT-PCR. We found that PPD reduced TNF-α protein secretion by 20–69.9% (n = 6). Further, IL-1beta levels were decreased by 44–98%. The same tendency was found studying IL-1beta and TNF-α mRNA steady state levels (n = 3; 1 h incubation). These effects were substance-specific and not found for PPD derivatives nor for the autoxidation product BB. These findings suggest that PPD may specifically modify immune responses by directly infering with the cellular proinflammatory cytokine network.

This study was supported by the EU.

Thursday, 10 June 2004
10:30–11:55

FS02

Metal allergy I

Cataria Foti, Italy & Chee Leok Goh, Singapore

FS02.1

The role of metallurgy in allergic contact dermatitis to metals

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The critical factor in determining if an alloy may induce metal sensitisation or elicit allergic contact dermatitis is the release rate of soluble metal ions of allergenic metals at the skin surface. Metals or alloys in direct and prolonged contact with body fluids may result in electrochemical reactions (commonly called corrosion) that release metal ions. Induction or elicitation of metal allergy results if a sufficient amount of metal ions are released and absorbed through the skin where they react with the human immune system. The virtual insolubility of most metals and alloys in aqueous media (including body fluids) limits the bioavailability of metal ions. Several factors influence the rate of corrosion: metal or alloy metallurgical structure, surface films, surface finish, geometry, process history, and composition; body fluid composition, amount, pH, electrolytic properties, dissolved oxygen and other gas content; and the service environment (e.g. temperature, flow rate, etc). A review of recently published studies on metal allergy from a metallurgical perspective provides information that helps explain why certain metals and alloys cause allergic reactions and others (e.g. most stainless steels) do not. This information is useful in predicting what alloys will cause allergic reactions under varying conditions. In order to predict allergic reactions and responses to metals and alloys, metallurgical aspects of ion release should be taken into account. This presentation will increase understanding and interpretation of results of clinical or other scientific studies (e.g. studies in vitro) of reactions and responses to metals and alloys by providing a metallurgical perspective.

FS02.2

CD4+ CCR10+ effector T cells reside at former allergic contact dermatitis sites

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Local skin memory (LSM) describes the clinical phenomenon of an accelerated and increased inflammatory allergic contact dermatitis

(ACD) response upon renewed allergen exposure. This has been ascribed to the local persistence of few, but allergen-specific, T cells. Here, firstly, we characterized effector T cells, and, subsequently, studied which of these cell populations are present at former challenge sites and might contribute to LSM. Peripheral blood T cells were stimulated with nickel sulphate. Cellular phenotypes and chemokine receptor expression profiles were analysed by FACS-staining: CLA together with CD4/CD8, CD45R0/RA, CXCR3, CCR4, CCR6 and CCR10. Skin biopsies were taken at 0, 3 and 21 days after allergen application and analysed for the same markers. Upon nickel-stimulation, amount of CD4+ CLA+ CD45R0+ T cells was increased. Together with CLA, CXCR3, CCR4 and, mainly, CCR10 expression was augmented. CCR6 expression was negative on CLA+ cells. In biopsies from patch tests, cellular infiltrates were present at 3 and 21 days after allergen application. Interestingly at day 21, residing cells were localized at the perivascularity and were characterized as CD4+ CD8− CCR10+ T cells. In conclusion, nickel-activated effector T cells can be characterised as CD4+ CD8− CLA+ memory T cells. They express CXCR3, CCR4 and, in particular, CCR10. After clinical recovery from an ACD reaction, CD4+ CCR10+ memory T cells apparently reside locally. The persistence of these CCR10+ T cells, expressing the appropriate receptor of the skin specific chemokine CCL27, can explain clinically important phenomena such as LSM and flare up reactions.

FS02.3

Nickel release from white-gold jewellery

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[2]*Legor srl, Italy*

A history of reacting to jewellery contact on the skin is a common symptom of nickel allergy; wearing cheap jewellery is a common cause of nickel sensitization. We analyzed nickel release from 770 white gold jewels with different shape and karatage from the Italian market. Jewels were stored in artificial sweat for 1 week at 30 C and nickel in sweat after the release procedure was analyzed by inductively coupled plasma detection (ICP), according to the European Standard EN1811 ''Reference test method for release of nickel''. Nickel release was above 0,5 μg/cm/week in 157 jewels (20,4%), between 0,5 μg/cm/week and 0,1 μg/cm/week in 163 (21,2%) and below 0,1 μg/cm/week in 450 (58,4%). Nickel release was above 0,5 μg/cm/week in 132 out of 432 (30,6%) 14 (or lower) karat gold jewels and in 25 out of 338 (7,4%) 18 karat gold jewels suggesting an inverse relationship between nickel release and karatage. However, when comparing jewels with the same karatage, we found no clear relationship between nickel content and nickel release in the 256 items of which the exact alloy composition was known. Data seem to indicate that other factors, besides nickel content, such as ratio between nickel and other elements, presence of grain refiners and homogenization state of the alloy play a crucial role in nickel release.

FS02.4

Differential gene expression in allergen-activated peripheral blood mononuclear cells from allergic patients

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Allergic contact dermatitis is a delayed type hypersensitivity reaction mediated by allergen specific T-lymphocytes. Allergen exposure leads to the activation of specific T-lymphocytes, which subsequently start to produce and release a vast array of cytokines and chemokines. However, the list of relevant genes taking part in the elicitation phase of contact dermatitis is not complete. In this study, we evaluate the use of the high-density microarray technology, which enable us to assess the global gene expression in allergen-stimulated peripheral blood mononuclear cells (PBMC). We included 3 chromium-allergic patients and 3 non-allergic controls in the study. Cultures of PBMC were established from each participant and stimulated with 100 ug/ul CrCl3 or media alone. The cell cultures were grown for 24 hours and the gene expression was analysed using an Affymetrix GeneChip(R) Array. Of the genes that exhibited differences of expression ($p < 0.01$) in allergen-activated PBMC from patients compared to controls, 54% (159/294) displayed increased activity and 46% (136/294) displayed decreased activity. Of the 159 up-regulated genes, 41 genes had a fold change above 1.50 and 30 genes among the 136 down-regulated genes had a fold change below -1.5. A significant number of the genes that showed differential expression in the cell cultures established from the allergic patients are known

to be involved in immune responses and inflammation. The data indicates that the method of microarrays is a valuable tool for investigating the gene expression profile in our model system for allergic contact dermatitis.

FS02.5

Nickel allergy and hand eczema – a twenty-year follow-up

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Aim: To investigate the occurrence of hand eczema after 20 years in schoolgirls previously patch-tested to nickel.
Methods: In 1982–83, 960 schoolgirls, aged 8, 11 and 15 years, were investigated for the occurrence of nickel allergy (Larson-Stymne B and Widström L, Contact Dermatitis 1985:13:289–293). The girls were patch-tested and the prevalence of nickel allergy was 9%. Twenty years later, the same individuals have received a questionnaire regarding hand eczema and factors of importance for the development of hand eczema. After two reminders, the response rate was 81%.
Results: In total 17.5% of the girls reported hand eczema after the age of 15. The 1-year prevalence of hand eczema was 12.6%. Of the previously patch-tested schoolgirls who answered the questionnaire, 63 were sensitive to nickel. In this study, the prevalence of hand eczema among those 63 was 16%, compared to 17% in the non-sensitive group (NS). Excluding persons with atopic dermatitis, the prevalence of hand eczema was 12.5% in the nickel-sensitive group, and 10% among the others (NS). 32% of the persons who had had atopic dermatitis reported hand eczema after 15 years of age, compared to 10% of those with no history of atopic dermatitis ($p < 0.001$).
Conclusion: Contact allergy to nickel in early childhood (8–15 years) did not seem to increase the prevalence of hand eczema later in life. The prevalence of hand eczema was increased by a factor of three among those with a history of atopic dermatitis, which is in accordance with earlier reports.

FS02.6

Patch test reactivity to nickel sulphate and fragrance mix in unselected children

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Objectives: Study patch test reactivity to nickel sulphate and fragrance mix in a population of unselected infants with focus on reproducibility, clinical relevance, and nickel patch test concentration.
Method: The data presented is part of a clinical epidemiological study of allergic diseases in newborns followed prospectively with questionnaire, clinical examination and testing at 0, 3, 6, 12 and 18 months of age. TRUE Test patches were used with nickel sulphate in 3 concentrations: 200, 66, 22 ìg/cm^2 and fragrance mix 430 ìg/cm^2. A positive reaction suggesting sensitisation was defined as at least palpable erythema present at both the 12 and 18 months follow-up visits.
Results: A total of 543 children (268 girls, 275 boys) were patch tested at least once, 304 children were tested at both 12 and 18 months. The prevalence of a reproducible positive reaction to nickel sulphate 200 ìg/cm^2 was 8.6% (20 girls, 6 boys). A transient reactivity was observed in 111 children (53 girls, 58 boys). A clinical relevance to nickel was found in only one child. There was no association between number of patch test procedures performed and reactions to nickel sulphate. Reproducible reactivity to fragrance mix was not found.
Conclusion: A high proportion of transient patch test reactivity to nickel sulphate 200 ìg/cm^2 was found. Patch testing with nickel in concentrations used for adults cannot be recommended in infants. The interpretation of a singular positive nickel patch test in small children must be assessed with caution. Allergic reactions to fragrance mix were not found in this age group.

FS02.7

Rates of persistent itchy nodules after fourth dose of DT vaccines

Eva Netterlid[1], M Bruze[2], M Hindsén[2], M Isaksson[2], P Olin[1]
[1]Swedish Institute for Infectious Disease Control, Stockholm, Sweden
[2]Department of Occupational and Environmental Dermatology, University Hospital, Malmö, Sweden

Background: Studies in Gothenburg, Sweden, reported unexpectedly high rates, 0.35–1.66%, of late occurring itching nodules at the site of

injection of aluminium containing vaccines. Among 455 children with itching nodules after vaccination, 352 had a positive epicutaneous test to aluminium. When switching to a new booster diphtheria-tetanus vaccine in Sweden these findings warranted a comparative study of local itching nodules that had remained at least 2 months after injection, and of aluminium contact allergy.

Methods: A prospective cluster randomised study was done in 25,232 10-year-olds. Participating schools in each municipality were randomised in a 1/1 ratio to use the old diphtheria-tetanus toxoid (DT) vaccines, Duplex® or the new vaccine, diTeBooster®. Parental reports 6 months after vaccination were obtained for 22,365 (88%) pupils in 851 schools. Patch testing with aluminium chloride-hexahydrate was performed in 9 children with an itching nodule, 6 children only pruritus and 17 children without any itching nodule after the fourth dose of DT vaccine.

Results: We identified 3–6 children per 10000 with a local itching nodule persisting for at least 2 months. There were no significant differences between the vaccine groups. Contact allergy to aluminium was not detected.

Conclusion: Our findings support the use of the vaccine presently available in the Swedish vaccination program. Continued surveillance of persistent itching nodules after vaccination with different aluminium containing DT and diphtheria-tetanus-pertussis toxoid (DTP) vaccines is however warranted.

FS02.8

Patch testing with gold trichloride can give false test results

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Background: Hydrochloric acid is formed in water solutions of gold trichloride. Hydrochloric acid in contact with aluminium generates hydrogen gas which can reduce and transform trivalent gold to elemental gold.

Objective: To investigate whether patch testing with aqueous gold trichloride can cause false positive (irritant) reactions in patients without contact allergy to gold and false negative reactions in patients with gold allergy.

Methods: 13 patients with and 13 patients without positive patch test reactions to gold sodium thiosulfate were tested with gold trichloride in 2 different vehicles, water and alkaline buffer, using 2 different test techniques, the Finn Chamber technique with aluminium chambers and van der Bend technique with polypropene chambers.

Results: Irritant patch test reactions were obtained with aqueous gold trichloride tested in van der Bend chambers in 10 patients without gold allergy. In gold-allergic patients no positive test reactions were obtained from aqueous gold trichloride in Finn chambers while 2 positive test reactions were obtained from gold trichloride in alkaline buffer tested in van der Bend chambers.

Conclusion: If gold trichloride is patch tested in wrong vehicle and with wrong test technique irritant test reactions may occur which can be misinterpreted as positive allergic reactions in patients without gold allergy as well as negative reactions in patients with gold allergy.

Thursday, 10 June 2004
12:00–12:30

KL02

Keynote Lecture

Chair: Klaus E Andersen, Denmark

Contact allergy caused by air oxidation of common materials – diagnosis and prevention

Ann-Therese Karlberg
Dermatochemistry and Skin Allergy, Department of Chemistry, Göteborg University, Göteborg, Sweden

When considering the allergenic activity of a compound not only the possibility of bioactivation by skin metabolism but also air activation by autoxidation must be taken into account.

Natural compounds (terpenes) easily oxidize at air exposure. They are found in products that are common causes of allergic contact dermatitis (ACD) i.e. colophony and fragrances.

The introduction of oxygen enables the molecules to form antigens with skin proteins via a nucleophilic- electrophilic interaction or via a radical reaction. The latter mechanism seems to be important since the primary oxidation products, the hydroperoxides, are the most potent sensitizers formed. Oxidative decomposition at air exposure resulting in allergenic oxidation products is observed also for other common compounds e.g. ethoxylated fatty alcohols used as surfactants.

It is important to test the patient with the offending compounds for diagnosis of ACD. A negative diagnosis can be due to failure in testing with the correct substances. In the case of air activated compounds, testing should not be performed with the pure substances but rather with the oxidation mixture or the most sensitizing oxidation products (the hydroperoxides). We have in multicenter-studies shown that the common fragrance terpenes, limonene and linalool, are frequent sensitizers when oxidized. This is a challenge in clinical practice since such patch test materials are not easily standardized.

Compounds, easily activated at air exposure, should be prevented from oxidative decomposition by addition of antioxidants and proper handling and storage. More research is needed in this area.

Thursday, 10 June 2004
13:30–14:00

KL03

Keynote Lecture
Chair: Tove Agner, Denmark

Contact dermatitis and danger models

John P McFadden,
St John's Institute of Dermatology, St Thomas Hospital, London, UK

Conventional models of the immune response are based on distinguishing self and non-self. However, the more recently proposed 'danger' model may be an illuminating alternative for studying allergic contact dermatitis. In the presence of a 'danger' signal, which in some cases of allergic contact dermatitis could be cutaneous 'irritancy' (ie cytokine release from non-immune/keratinocyte cells in response to chemical stimulus in a non-sensitising manner), the immune system would become activated, leading first to the induction of sensitisation and then subsequently to the elicitation of a contact hypersensitivity response. In most cases both the antigenic signal and signal for keratinocyte cytokine release will come from the hapten, although for example in an occupational setting, traumiterative dermatitis would be the source of the ''danger'' signal. A further prediction of this hypothesis is that reported animal experiments demonstrating low dose tolerance with contact allergens may be explained by the loss of the 'irritant' effect at lower dilutions whilst an antigenic stimulus remains present.

Thursday, 10 June 2004
14:05–15:30

FS03

Irritant contact dermatitis
Chairs: Pieter-Jan Coenraads, The Netherlands & Donald Belsito, USA

FS03.1

The hand eczema severity index (HECSI). A study of inter- and intraobserver reliability

Elisabeth Held[1], *R Skoet*[2], *T Agner*[2], *J Duus Johansen*[1], *L Theil Skovgaard*[3]
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[2]*Department of Dermatology, Gentofte Hospital, University of Copenhagen, Gentofte, Denmark*
[3]*Department of Biostatistics, University of Copenhagen, Panum Institute, Copenhagen, Denmark*

In clinical studies on hand eczema (HE) an objective and accurate assessment of the severity of the disease is needed. The present study was undertaken in order to develop and validate a scoring system called the hand eczema severity index (HECSI) designed for clinical assessment of HE. Twelve dermatologists (observers) assessed 15 HE patients (11 women and 4 men) twice with an interval of 30 min. To minimise recall bias only the hands and wrists of the patients were visible to the observers. Agreement between the observers was determined by using the intraclass correlation coefficient (ICC). ICC for total HECSI score was 0.79 at time 1 and 0.85 at time 2 respectively. When looking at ICC for the different items in the scoring system (extent of lesions, anatomical location and intensity of clinical signs) best agreement was found for extension followed by anatomical location and least agreement was found for the scoring of clinical signs. ICC for intraobserver agreement was 0.90. A regression correlation coefficient of 0.993 was found (simple linear regression analysis of time 1 scores against time 2 scores) indicating high reproducibility. Overall good agreement existed for both inter- and intraobserver reliability although some inter- and intraobserver variation existed.

FS03.2

Visual scoring of skin irritation reactions – what are the limits?

DA Basketter, Marie Marriott, L Peters, K Cooper
Unilever Safety and Environmental Assurance Centre, Sharnbrook, UK

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 is to demonstrate the possibilities and limitations of the grading of skin irritation reactions by subjective visual assessment. In the present work, we have recorded a wide range of relatively minor skin irritation reactions using a high quality digital camera. The skin reactions recorded have then been graded by independent observers according to their appearance on a computer monitor. 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 bioengineering 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.

FS03.3

Bioimpedance revealing irritation by toothpastes in skin and mouth

Ingrid Nicander[1], *I Rantanen*[2], *E Söderling*[2], *S Ollmar*[3]
[1]*Huddinge University Hospital, Department of Dermatology, Huddinge, Sweden*
[2]*University of Turku, Institute of Dentistry, Turku, Finland*
[3]*Karolinska Institutet, Division of Medical Engineering, Huddinge, Sweden*

The aim of the study was to compare the effects of a SLS toothpaste formulation with and without betaine on skin and oral mucosa using electrical bioimpedance (IMP). Two groups, in total 47 participants, were recruited. In the skin group (27 participants) four test sites on the volar forearms were used: SLS paste, SLS + betaine paste, betaine paste, and one unoccluded control site. In the oral group (20 participants) the same toothpaste formulations were used. The test substances were applied in 12 mm Finn chambers for 24 hours at randomised test sites on the skin, and in 18 mm Finn chambers for 15 minutes on the oral mucosa. Visual examination and readings with IMP were taken before application and 24 hours after removal of the chambers for the skin, and for the oral mucosa before and 15 minutes after exposure. Information was extracted from the impedance spectra using four indices based on magnitude and phase at 2 frequencies, emphasising different aspects of the impedance properties of the tissues. The SLS-containing pastes showed for both skin and oral mucosa some positive visual grade 1 reactions. Significant changes were found for the impedance indices, and the reaction patterns of the indices differed between the skin and the oral mucosa. We conclude that very slight reactions of skin and oral mucosa are detected by IMP. Furthermore, betaine containing toothpaste does not irritate neither skin nor oral mucosa, but the effect together with SLS is insignificant.

FS03.4

Irritant dermatitis following tape stripping

Hanne Nybæk[1], *DB Knudsen*[2], *LF Nielsen*[2], *T Karlsmark*[3], *GBE Jemec*[1]
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[2]*Coloplast A/S, Humlebæk, Denmark*
[3]*Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark*

Repeated tape stripping of the skin associated with e.g. the use of stoma care products can cause irritant dermatitis. This experimental study in 12 healthy volunteers was designed to assess the effects of 3 chemically and physically different adhesives commonly used in stoma care products. Two different frequencies of stripping (daily vs twice weekly) were tested, and the various parameters of inflammation and barrier integrity were studied with established non-invasive methods (Measurement of erythema, conductance, and Trans Epidermal Water Loss (TEWL)) on day 0, 4, 6, 10, 16, 22 and 28. All adhesives caused increases in all the studied parameters during the 28 day period compared to the corresponding non-stripped values. Furthermore, daily stripping caused significantly greater inflammation and barrier disruption than stripping twice weekly. In conclusion, it was possible by measuring skin erythema, conductance and TEWL to detect different patterns of inflammatory changes and barrier disruption in areas treated with the 3 adhesives. As expected, more frequent stripping caused greater changes. These differences did however appear at different times during the study period, suggesting that the chemical and mechanical properties of the adhesives may affect the skin differently.

FS03.5

Evaluation of the irritancy potential of adapalene and tretinoin in volunteers of different ethnic origins

Chee-Leok Goh[1], A T-J Goon[1], V Sorba[2], P Soto[2], A Kaoukhov[2]
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[2]Sophia Antipolis, France

Objectives: To compare the cumulative irritancy potential of adapalene gel, 0.1% to that of tretinoin gel, 0.025% following repeated applications to the skin of human volunteers of different ethnic origins.
Methods: Single center study, randomized, investigator blind, intra-individual, comparison in healthy volunteers, 18 years of age and older. Volunteers were randomized to apply each product daily to one or the other half-face for 21 days. On the forearms products were applied under occlusive conditions for 4 days. Criteria for evaluation were signs and symptoms (erythema, desquamation, dryness, stinging/burning, pruritus) on the face and on the forearms (irritation, stinging/burning, pruritus, and biophysical measurements: colorimetry-a* and Trans-epidermal Water Loss (TEWL)). Overall safety evaluation was based on adverse events information collected throughout the study.
Results: Seventy-three (73) volunteers from 4 ethnic groups (Chinese, European, Indian and Malaysian volunteers) were randomized. On the face the between treatment differences in olerability parameters were similar in all ethnic groups, thus allowing to conclude that adapalene was significantly better tolerated than tretinoin in all ethnic groups. This also allowed us to compare overall irritation susceptibility of different ethnic groups using the sum of clinical sign scores. An overall ethnic effect could be shown ($p < 0.001$): Chinese being most susceptible (33.5), followed by Indians (26.9), Malaysians (23.6) and Europeans (14.1). Forearm evaluations showed significantly better tolerability for adapalene than for tretinoin. However in each patient TEWL measurements correlated poorly with clinical assessments. Throughout the study more treatment related adverse events occurred with tretinoin than with adapalene.
Conclusions: Adapalene gel, 0.1%showed a better cutaneous tolerability and safety profile than tretinoin gel, 0.025% for all four ethnic groups. An interethnic difference in the irritation susceptibility could be shown.

FS03.6

Efficacy of MAS063D ('Atopiclair') in irritant contact dermatitis

Hongbo Zhai, I Villarama, Z Hasan Hafeez, HI Maibach
University of California, Department of Dermatology, San Francisco, USA

Objective: To determine the efficacy of a topical, MAS063D, in managing the clinical signs and symptoms of experimentally induced irritant contact dermatitis (ICD).
Methods: Two patches of ICD were created using sodium lauryl sulfate (SLS) in 20 consenting volunteers. MAS063D was applied to one patch and a vehicle-only control to the other. Measurements were taken at baseline, 24, 48 and 72 hours as follows: blood flow volume (BFV); skin color (a*); transepidermal water loss (TEWL); patient's view of itch and visual scoring. Results: The objective measurements of BFV, a* and TEWL all showed statistically significant benefits of MAS063D over the vehicle-only control. BFV and a* were significantly better at all time points ($p = 0.046$, $p = 0.045$ respectively at 72 hours) and TEWL at 48 and 72 hours ($p = 0.02$ at 72 hours). MAS063D demonstrated benefit in the visual scoring of irritant contact dermatitis that was not statistically significant. Patient-assessed itch was low at baseline; significant improvement was neither expected nor demonstrated although a small benefit of MAS063D over vehicle was seen in the mean values.
Conclusions: BFV and a* are both good indicators of local erythema. TEWL is a good indicator of skin integrity. MAS063D therefore demonstrated statistically significant benefit over vehicle on three clinically meaningful outcomes of SLS-induced ICD, and therefore may benefit irritant contact dermatitis.

FS03.7

Tape stripping procedure: influence of anatomic site, application pressure, duration and removal

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[1]Philipp-University, Marburg, Germany
[2]University of California, San Francisco, USA
[3]TOPALIX, Topical Product Development, San Francisco, USA

Background and Objectives: Tape stripping is a common method for investigating stratum corneum (SC) physiology as well as bioavailability and bioequivalence of topical drugs. However,

little is known concerning the influence of procedures (anatomic site, pressure, pressure duration, tape removal rate) inherent in each stripping protocol.

Methods: Tape stripping was performed using tapes on the forearm, forehead and back. On the forearm different pressures (165 and 330 g cm^{-2}), durations of pressure (2s and 10s), and removal rate (slow and rapid removal) was performed. Changes in skin physiology were evaluated by measurement of transepidermal water loss (TEWL) and hydration.

Results: A significant influence of all parameters on the TEWL-increase as a function of tape strip number was observed. The fastest increase was demonstrated on the forehead, followed by the back and, lastly, the forearm. Rapid removal produced a protracted increase in comparison to the slow removal. 10s pressure induced a faster increase of TEWL than 2s pressure. Likewise, the 330 g cm^{-2} pressure induced an earlier increase than the 165 g cm^{-2}. Skin hydration was not influenced by the variables tested.

Conclusion: Tape stripping results are influenced dramatically by all investigated parameters. A standardized procedure is necessary for a comparable study design. A dynamic SC stress test to more closely investigate SC cohesion is proposed based on the present observations.

Thursday, 10 June 2004
14:05–15:30

FS04

Cosmetic dermatitis

Chairs: An Goossens, Belgium & Patricia Engasser, USA

FS04.1

Formaldehyde allergy – clinically relevant threshold reactions

Claus Zachariae[1], *B Hall*[2], *M Cottin*[2], *KE Andersen*[3], *T Menné*[1]
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[3]*Department of Dermatology, University Hospital of Odense, Odense, Denmark*

The objective of the study was to establish eliciting threshold concentrations of diazolidinyl urea (Germall II) – derived formaldehyde in formaldehyde and/or in diazolidinyl urea – sensitive patients, using a leave-on face cream formulation in a repeated open application test (ROAT) applied to different anatomical regions.

150 patients with known formaldehyde allergy were reviewed for inclusion in the study. 108 patients were contacted and in 65 patients the formaldehyde sensitisation was reconfirmed by a patch test. Four groups of 10 formaldehyde allergic subjects were exposed to 0.05%, 0.15%, 0.3% and 0.6% diazolidinyl urea, corresponding to approximately 50, 100, 200 and 400 ppm free formaldehyde, respectively.

Additional 10 individuals allergic to the formaldehyde donor – diazolidinyl urea itself – were exposed to 0.15% diazolidinylurea, corresponding to approximately 100 ppm free formaldehyde and 10 healthy non-allergic individuals were exposed to 0.6% of diazolidinylurea (approximately 400 ppm free formaldehyde).

A ROAT was performed in a scheduled sequence: upper arm, neck and face.

Contact allergy reactions were elicited in 39 out of 58 formaldehyde-sensitive and in 5 out of 7 diazolidinyl urea-sensitive individuals.

Elicitation responses were dose- and anatomical region – dependent.

No reactions were observed at the lowest dose, suggesting that an elicitation threshold was attained in the study.

FS04.2

Immunotoxic effects of arylamine dyes

Claudia Skazik[1], *L Wilbers*[1], *S Breuer*[1], *HF Merk*[1], *D Kunz*[2], *B Blömeke*[3]
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[2]*Department of Clinical Chemistry, University Hosptial RWTH Aachen, Aachen, Germany*
[3]*Department of Ecotoxicology/Toxicology, University Trier, Trier, Germany*

Allergic reactions to arylamine dyes are well-known causes for allergic contact dermatitis (ACD). These compounds are found in synthetic and natural materials, hair dyes, sun screen, photographic additives as well as temporary tattoos. Cross-reactions between different para-compounds have been frequently observed but the underlying mechanisms are not fully elucidated. We investigated the immunogenic capacities of p-phenylendiamine (PPD), Bandrowski's base (BB), 2-methyl-1,4-phenylendiammoniumsulfat (PTD), 4-aminoazobenzene (AAB), disperse orange (DO), disperse yellow (DY), 4–4-diaminophenylmethan (DDM), bismarckbrown (BBY) and 2-mercaptobenzothiazole (MBT) by measuring the proliferative responses of T-cells on polyclonal and monoclonal level

(thymidine incorporation). T cell responses were based on CD4+ and CD8+ T cells. Recently, we characterized PPD/BB T cell clones (TCC) as predominantly CD4+/CD45RO+ cells with a alpha/beta T cell receptor (Sieben et al., 2002). We isolated T cell lines (TCL, n = 16) and T cell clones (TCC, n = 20) from totally 11 PPD-allergic persons and 5 exposed persons. We established TCLs and TCCs to 4 para-amino compounds. We found some PPD and/or BB specific TCCs with no cross-reactivity to the other compounds tested. Some TCCs showed a narrow range of cross-reactions (BB, BBY, MBT), while others reacted to 6 different para-amino compounds. We observed similiar patterns of crossreaction for the TCLs. The stimulation indices (SI) varied between 2.2 and 14.0. Our preliminary results on cross-reactions between para-amino compounds support recent findings in mice (Wulferink et al., 2002) demonstrating a limited discriminatory capacity of T cells carrying an alpha/beta T cell receptor. Further studies on the mechanisms of cross-reactivities and the cytokine profiles are now under investigation. This study was supported by the Interdiciplinary Center for Clinical Research and Biomaterials (IZKF, Germany) and the Deutsche Forschungsgemeinschaft (Germany).

FS04.3

Hair dyes, prediction of sensitization potential with QSAR

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Objectives: To identify substances and tonnage data for use for hair dyes registered in Europe. To predict the sensitization potential of each substance and to rank the substances due to their sensitization potential. Further to group the substances in clusters based on their physical chemical properties with a cluster analysis.
Methods: The Inventory list of Cosmetics Ingredients (INCI), new regulation on cosmetics, tonnage data for use and Toxnet were used to identify and quantify the hair dyes. Salts were disregarded. A QSAR (Qualitative structure-activity relationship) model called TOPS-MODE, based on local lymph node assay (LLNA) data and physical chemical properties were used to predict the sensitization potential and make a cluster analysis.
Results: Out of 315 hair dye substances 229 meet the inclusion criteria. Most of the hair dye substances 75% were predicted to be strong to moderate sensitizers. Less were predicted to be weak 22% and only a small part 3% were predicted to be extremely weak or non sensitizing. The 8 most used hair dye substances were predicted to be strong to moderate sensitizers. Ppd is the most used hair dye allergy marker but some azodyes were predicted to be more potent than para-phenylenediamine (ppd).
Conclusions: Most hair dye substances are predicted to be strong to moderate sensitizers, which explain why some people gets hair dye dermatitis. A patch test series with potent, much used azodyes, might prove useful in diagnosing ppd-negative patients, with hair dye allergy. The cluster analysis grouped the substances which can be helpful choosing substances for clinical patch test.

FS04.4

Decreased MDBGN conc. in a product is counteracted by increased exposure

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Background: Some types of cosmetic products such as creams and soaps are commonly used several times a day, especially in occupational use-situations. Little is known about how the daily frequency of application of an allergen in a product influences the allergic response.
Objectives: This study investigates the allergic responses elicited in pre-sensitised individuals when exposed to a specific amount of allergen applied either in 1 application per day or distributed over 4 applications per day. As model allergen is used the cosmetic preservative methyldibromo glutaronitrile (MDBGN). Patients/Methods: 19 contact allergic individuals and 12 controls participated in a double-blind, randomized repeated open application test (ROAT) using two coded aqua/ethanol (80:20) solutions preserved with 100 ppm

and 400 ppm MDBGN, respectively. 12 cm^2 areas on the lower arms were applied 2 drops either once daily of the 400 ppm solution or 4 times a day for the 100 ppm solution.

Results: Most patients developed dermatitis following application of approximately equal amounts of MDBGN on both arms not distinguishing whether the allergen was applied as a 400 ppm solution once daily or a 100 ppm solution 4 times daily. Controls were negative.

Conclusions: Applications with 400 ppm MDBGN once daily or 100 ppm MDBGN 4 times per day had, in a ROAT study, approximately equal capabilities of provoking allergic dermatitis in agreement with well-known patch test data that dose per unit area is more important than concentration of allergen in the product. This may complicate risk assessment and regulation of cosmetic allergens. Further studies, however, are needed before more general conclusions can be made.

FS04.5

Iodopropynylbutyl carbamate (IPBC) 0.2% is suggested for patch testing of patients with eczema possibly related to preservatives

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Iodopropynylbutyl carbamate (IPBC)is a preservative that has been increasingly used for skin care products and cosmetics within the last years and the first cases of contact sensitization have meanwhile been reported. Therefore, a surveillance for IPBC contact allergy is now necessary. Our study was aimed to find out a suitable test concentration of IPBC for this purpose. The data 8106 patients tested by 23 centres of the German Contact Dermatitis Research Group (DKG) and the Information Network of Departments of Dermatology (IVDK)in the time from May 2001 to July 2003 with IPBC in concentrations of 0.1%, 0.2%, 0.3%, and 0.5% were retrospectively evaluated. Criteria considered to determine the optimal test concentration of IPBC were the reaction index, the positivity ratio, the rate of crescendo reactions, and the relation of IPBC-reactions with MOAHLFA-indices, with irritant reactions to sodium lauryl sulfate, and with positive reactions to the most common standard contact allergens and 4 other preservatives. For statistical evaluations the exact McNemar test was applied and odds ratios were calculated according to the profile likelihood method, as derived from logistic regression analyses. The rate of positive reactions to IPBC increased from 0.5% with IPBC 0.1% to 1.7% with IPBC 0.5%, but there was a problem with sensitivity or specificity with both of these 2 concentrations. Therefore, we focused on IPBC 0.2% (0.8% positive reactions) and IPBC 0.3% (1.3% positive reactions) for further detailed analyses. An evaluation of the related parameters revealed that with IPBC 0.2% as compared to IPBC 0.3% a higher percentage of crescendo reactions, a higher reaction index, a lower number of doubtful reactions, a plausible association of positive reactions with reactions to other preservatives, nd no association with a pronounced skin irritability was found. In conclusion, we recommend to start with IPBC 0.2% for patch testing of all persons with contact dermatitis that may be related to preservatives.

FS04.6

Dose/unit area and time – key factors influencing the elicitation capacity of MCI/MI

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The objective of the study was to investigate, using the Repeated Open Application Test (ROAT), two key parameters of exposure – allergen concentration (dose/unit area) and time in terms of the elicitation capacity of methylchloroisothiazolinone and methylisothiazolinone (MCI/MI) in MCI/MI-sensitised individuals and to explore the inter-relationship between these two key factors. The study was designed as a double-blind, placebo-controlled, dose-response ROAT preceded by a Diagnostic Patch Test (DPT). 79 patients with a known MCI/M allergy were contacted, 29 were diagnostically patch tested and 25 had their allergy confirmed. 25 MCI/M-allergic subjects and 10 healthy non-allergic control subjects

were challenged with 2 ppm of MCI/MI/unit area of skin for 4 weeks. After a wash out period of at least 4 weeks the subjects were challenged with 7.5 ppm of MCI/MI/unit area of skin for 4 weeks. A ROAT with 2 drops of solution twice a day was conducted on the volar aspect of the left and right forearms on a 3×3 cm area resulting in dose/unit area of MCI/MI of 0.025 mg/cm^2 and 0.095 mg/cm^2 for 2 ppm and 7,5 ppm MCI/MI respectively. The elicitation capacity of MCI/MI in MCI/MI sensitive patients is dependent on the exposure dose/unit area and time The results of this study will be a useful addition to the risk assessment information available for MCI/MI. The risk assessment for the use of MCI/MI in rinse off consumer products is unaffected by the results of this study.

FS04.7

Atypic T-cell infiltrate by isothiazolinone. Question to discuss

Ana Giménez-Arnau[1], *A Toll*[1], *F Gallardo*[1], *J Roman*[2], *RM Pujol-Vallverdú*[1]
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Methyl(chloro)isothiazolinone is an effective preservative and a major cause of cosmetic allergy in most European countries. On the face unusual clinical presentations are seborrhoeic dermatitis, lupus erythematosus, lymphocytic infiltrate, photodermatosis or atopic dermatitis. Three patients who suffered a chronic, recurrent, itchy and generalized cutaneous erytematous-desquamative and eczematous eruption with a common pathologic event, an atypical lymphoid infiltrate, whose induction by a contact allergen can be discussed are presented. The first, a 59 years old man showed a biopsy with an atypical dermal-epidermal T cell infiltrate of mycosis fungoides and monoclonal TCR-rearrangement. The second, a 74 years old man showed an atypical lymphoid infiltration with polyclonal TCR-rearrangement and a second biopsy showed an eczematous pattern. The third, a 50 year old man with pathology of plaque parapsoriasis with atypical lymphoid infiltrate. The three patients showed strong positive reaction to methyl(chloro)isothiazolinone (0.01%aq.) Trolab,,µ. Avoiding the allergen the cutaneous eruption disappeared and any recurrence has been observed yet. Pathologic criteria for mycosis fungoides remains controversial and could not be done only on the basis of cellular density or the percentage of atypical T-cells. Autoinvolutive mycosis fungoides shows the unknowledge of its pathogenesis. How some allergens could affect on the cellular life needs further studies. We highly recommend to patch test all patients with atypical cutaneous T-cell infiltrates.

FS04.8

The U.S. Cosmetic Ingredient Review: process and products

Gerald McEwen
The Cosmetic, Toiletry, and Fragrance Association, Washington DC, USA

The U.S. Cosmetic Ingredient Review (CIR) program has evaluated safety in use data on approximately 1300 ingredient since 1976. The review process, which relies on open public meetings and the active participation of the public, the U.S. Food and Drug Administration, and the cosmetics and chemical industries, has identified many cosmetic ingredients that should only be used under limited conditions. Adhearance to the limitations on use in the conclusions of the CIR reports, in the U.S., appears to have limited exposure and patient population sensitivity to some widely used cosmetic ingredients that have produced high rates of reactions in Europe. The advantages of the CIR process for the public and the medical community; the deliberations leading to the use limitations on two example ingredients, and sources for attendees to locate CIR Reports and conclusions will be presented.

Thursday, 10 June 2004 16:00–17:00

FC01

Free Communication – Occupational dermatoses I

Chairs: Rosemary Nixon, Australia & Mihály Matura, Sweden

FC01.1

Occupational contact dermatitis from methylisothiazolinone

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Background: The preservative methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) has been used extensively in various products since the 1980s. Recently, a biocide containing only MI and not MCI has been launched on the Swedish market for use in industrial settings, paints and glues. ***Objectives:*** To describe sensitization to the unchlorinated isothiazolinone 2-methyl-4-isothiazolin-3-one (MI) in 2 workers, a technician after a chemical burn and a painter, both exposed to a preservative containing MI. Methods: Patch testing

with serial dilutions of MCI/MI, MCI, MI, 2-n-octyl-4-isothiazolin-3-one (OIT) and a commercial preservative containing MI in the 2 workers.
Results: The patients reacted positively to MCI/MI and to the separate active ingredients (MCI, MI). The patch test reactivity to MI was higher than the reactivity to MCI, which is a reversed pattern to what is usually seen in patients sensitized to MCI/MI. Both patients also had positive test reactions to OIT.
Conclusion: MI may sensitize on it's own, and in patients allergic to MI, cross-reactions are also seen to MCI.

FC01.2

Contact allergy to grease-a case report

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Institute of Dermatology, Lund Unviersity Medical Faculty, Malmö, Sweden

Objectives: Contact allergy to grease is a rare cause of occupational allergic contact dermatitis and therefore this case is presented. Thin layer chromatograms were used for patch-testing and helped identify the contact sensitizer in the grease.
Methods: Patch-testing, thin layer chromatography and GC-MS. Case report: A previously healthy man working in an industry where brakes for trains were produced presented in the clinic after having developed a rash in the face, on the neck, volar aspects of the arms and dorsum of the hands. The patient's work in part consisted of putting grease on metal parts. The patient was patch-tested with our standard series, a MWF series and materials from work. He tested positively to the grease. A visit to the industry showed a much greater exposure to grease than was suspected. The investigation that followed was performed to identify the sensitizer in the grease. Thin layer chromatography was performed and the patient was tested with chromatograms.
Results: The patient had positive reactions to several allergens in the series including rubber sensitizers of the PPD type and disperse orange 3. A positive reaction was obtained to a spot on the chromatogram of the grease and investigation by GC-MS identified N-phenyl-1-naphtylamine as the sensitizer.
Conclusions: This case underlines the importance of patch testing with work materials and visiting the work environment. A rare case of contact allergy to grease was found and patch-testing with thin layer chromatograms helped identify the allergen, N-phenyl-1-naphtylamine. The identification of the allergen was made by GC-MS.

FC01.3

The Finnish Machinist Study – new results

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[3]Finnish Institute of Occupational Heath, Department of Epidemiology and Biostatistics, Helsinki, Finland

Objective: The aim of the study was to get information on the chemical exposure and the prevalence of skin and respiratory symptoms among Finnish machinists.
Methods: A cross-sectional study was carried out on a population of 961 Finnish machinists. Skin and respiratory symptoms, atopy, exposure at work, etc. were inquired by a telephone interview. Working conditions were assessed and the data were combined with the data from the interview. Technical office personnel in the same companies were used as a control group.
Results: A third of the interviewees reported prolonged rhinitis. A fifth had continuous or relapsing hand or forearm dermatitis, cough, phlegm production or eye symptoms. Wheezing, dyspnea, laryngeal symptoms, or relapsing low fever were reported by 8–2%. 5% reported having asthma. In total, 35% of the machinists considered the skin or respiratory symptoms as work-related.
Conclusion: This study shows that work-related skin and respiratory symptoms are common among machinists in Finland. Those reporting symptoms have been examined in more detail at FIOH. New results of the statistical analysis and medical investigations will be presented.

FC01.4

Occupational skin diseases in different metal-working industries

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Objectives: To analyse the yearly incidence rates and causes of occupational skin diseases (OSD) in different metal-working industries.
Methods: Between 1990 and 1999, all new cases of OSD and their causes were prospectively recorded in all metal-working enterprises of Northern Bavaria. We calculated the incidence rates according to the average employed

population. Furthermore, we analysed the different allergens, irritants and constitutional factors (e.g. atopy) in the affected metal workers.

Results: In metal workers, a total of 700 OSDs were registered which comprise 18.8% of all OSDs in our register. They were classified into metal-surface processors (260 OSDs, yearly incidence per 10,000 employees = 10.4), metal processors (129 OSDs, 5.9), locksmiths and automobile mechanics (119 OSDs, 2.5), electrical industry (69 OSDs, 1.4), machinists (47 OSDs, 11.6), mechanics (40 OSDs, 6.6), electroplaters (22 OSDs, 20.6) and solderers (14 OSDs, 13.4). The proportion between allergic (ACD) and irritant contact dermatitis (ICD) varies conspicuously. While electroplaters and solderers predominantly suffer from ACD (82% resp. 71%), in other occupational groups ICD is more common: mechanics (60%), locksmiths and automobile mechanics (59%) or metal-surface processors (53%). The type IV allergens differ widely depending on the occupational exposure. The most important allergen in solderers is colophony, in electroplaters nickel sulphate and potassium dichromate. There is a wide range of allergens in metal working fluids and it is mandatory to patch test patient's own working materials due to the fact that important allergens are not yet included in the screening series.

FC01.5

Occupationally based type IV hypersensitivity in dental professionals

Daniel Hogan[1], C Hamman[2], P Rodgers[2], C Siew[3]
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The study's objective was to determine the frequency of type IV hypersensitivity in dentists, dental hygienists, dental assistants or dental students attending annual Health Screenings at the 1997, 1998, 2000, 2002 and 2003 American Dental Association (ADA) Annual Sessions held in various major American cities. We patch tested: 1997–59 dentists and 21 non-dentists; 1998–40 and 13; 2000–21 and 7; 2002–33 and 6; 2003–25 and 4. We patch-tested participants using T.R.U.E. Test panels and/or Finn chambers containing Trolab allergens. Due to the time constraints of the ADA meeting dates, patches were placed for 48 hours and skin reactions read at 0 and/or 24 hours after patch removal. Overall, 49% of patch-testing participants tested positive to at least one allergen. The most prominent dental-related allergens were rubber compounding agents and methacrylates. Positive reactions in the former were due to thiurams (10%) and carbamates (12%). Positive reactions to acrylates were most frequent to ethylene glycol dimethacrylate. All acrylate allergies were in dentists; typically theses dentists had chronic fingertip dermatitis. Preservative allergies were also common, including thimerosal (31%) and benzoyl peroxide (11%). Glutaraldehyde and formaldehyde each produced 3.5% of positive reactions with no evidence of cross-reactivity Common allergies that may be occupationally related were nickel (20%) in tools and orthodontic appliances and fragrance mix (16%) containing eugenol and cinnamates. These results indicate that allergies other than type I hypersensitivity to NRL proteins occur in dental professionals with current or past dermatitis.

FC01.6

Hand dermatitis of hairdressers. Study of protective gloves permeation

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Contact dermatitis among hairdressers is common and is one of the most frequent occupational dematoses due to continual exposure to water, detergents, hair dyes, permanent waves and metal equipment. Use of individual protection systems – as gloves – is considered a good measure of prevention. Few data exist about the real permeation resistance (PR) of gloves, also in term of time of PR. We tested two types of djsposable latex gloves different by thickness and density of the manufacture material. We used a permeation cell composed of two separated parts: in the upper part we introduced the hair colouring formulation and in the lower one the collection medium (NaHSO3 1% in water); the two parts were separated by a portion of the glove material. A 100 microL volume of the collection medium was collected and injected onto a HPLC apparatus after 1, 2, 4 and 24 hours. A diode array detector was utilised selecting two wavelengths in the UV range (240 and 275 nm) with a linear concentration gradient up to 60% of methanol/acetonitril mixture. We can simultaneously analyse 9 oxidation dyes and the detection limits were sufficient to determine these substances at very low concentrations. We obtained respectively a breakthrough time less

than 24 hours for the lower thickness glove and of over 24 hours for the other one; the latex gloves are suitable for prevent the skin contamination during the preparation of the colourings mixture in the hairdresser activity. The obtained data show those latex gloves, of both thickness, have a very high PR. On the other hand, the use of latex gloves has been associated with the more frequent recognition of immediate-type hypersensitivity responses related to latex products. The prosecution of the study will evaluate the PR of latex-free gloves.

Thursday, 10 June 2004
16:00–17:00

FC02

Free Communication – Miscellaneous

Chairs: Kristiina Turjanmaa, Finland & Hee-Chul Eun, South Korea

FC02.1

A diene identified as a prohapten metabolised to epoxides in the skin

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[2]Medicinal Chemistry, Department of Chemistry, Göteborg University, Göteborg, Sweden
[3]National Institute for Working Life, Stockholm, Sweden

To predict the sensitising capacity of a chemical, the only existing reliable method is testing in animals and alternative methods are requested. One approach is to use databases that predict the toxicity of novel compounds by comparing the chemical structure with data stored in the database. A chemical (hapten) must contain a chemically reactive site to be able to bind to skin macromolecules and a good predictor for sensitising capacity is the electrophilic character of the molecule.

Objectives: The aim of this study was to investigate the sensitising capacity of 5-isopropenyl-2-methyl-1-methylene-2-cyclohexene, a conjugated diene with no electrophilic positions or any other structural alert for skin sensitisation.

Methods: 5-Isopropenyl-2-methyl-1-methylene-2-cyclohexene and two possible epoxide metabolites of the model compound were synthesised. Sensitisation and elicitation experiments were performed using the predictive guinea pig method FCAT. The diene system was analysed in the computer based knowledge system DEREK (Deductive Estimation of Risk from Existing Knowledge).

Results: The model diene was found to be a potent contact allergen able to sensitise the control animals after only one dermal exposure. Both epoxides gave elicitation in the animals sensitised to the diene indicating that they are formed from the diene in the skin during induction. The diene system was considered as a non-sensitiser in DEREK.

Conclusions: This study demonstrates that conjugated dienes can be metabolised to strong contact allergens in the skin and that it is important to consider possible metabolic pathways when constructing predictive databases, otherwise potent prohaptens might be considered as harmless chemicals.

FC02.2

Patch tests with gluten and gliadin in children with coeliac disease

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[2]Department of Pediatrics, Ravenna, Italy

Atopy patch tests (ATPs) are believed to be a useful diagnostic procedure for atopic dermatitis (AD), aiming at the detection of delayed reactions to aeroallergens and food allergens. Our aim was to investigate immune responses to gluten and gliadin in children affected by coeliac disease by performing APTs, and to compare these data to the ones observed in AD patients. 31 children, 15 males and 16 females (mean age $\pm$ s.d. $= 5{,}5 \pm 3{,}8$ years) affected by coeliac disease underwent APTs with gluten and gliadin. Among these, 15 children were on gluten-free diet at the moment of our examination and 3 patients were affected by AD. 83 AD children not affected by celiac disease, were used as controls. 19,4% and 12,9% of children with coeliac disease proved positive to APTs with gluten and gliadin, respectively. No difference in the frequency and intensity of APT responses were present between the patients on gluten-free diet and the children not on diet. Among AD patients 12% reacted to gluten, whereas no positive reactions to gliadin were observed. Going on these findings, the cellular-mediated reactivity to gliadin in patients with coeliac disease may show a clinical expression by positive APT reactions to gliadin. These represent a specific finding in subjects with coeliac disease when compared to AD children.

FC02.3

Thimerosal- is it really irrelevant?

Arieh Ingber, D Slodownik
Hadassah Medical Center, Hebrew University, Jerusalem, Israel

Objective: Recently, several investigators claimed that thimerosal is one of the most irrelevant allergens existing in screening for contact dermatitis.
Methods: 508 patients who were suspected to have allergic contact dermatitis were patch tested at our clinic. They completed a questionnaire including medical, demographic and occupational details. We used the standart tray of Chemotechniqe Diagnostics (MalmÖ, Sweden) and additional series which were case relevant. The relevance of the allergic reaction to thimerosal was scored from 1–6.
Results: 19 patients (3.7%) had an allergic reaction to thimerosal. Six (31.5%) had a definite relevance and eight (42.1%) had a probable relevance. Only three patients (15.8%) had an irrelevant reaction. SPIN value was 2281. We found a high proportion of mechanics (42.1%) among the patients who had positive reaction to thimerosal ($P < 0.0001$).
Conclusion: Although previous reports found thimerosal highly irrelevant, our daily experience being supported by the above data, indicates that positive reactions to thimerosal could be relevant for many patients.

FC02.4

Meteorological factors and standard series patch test reactions

Janice Hegewald[1], A Pfahlberg[1], A Schnuch[2], B Kränke[3], W Uter[1]
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[2]IVDK, University of Göttingen, Göttingen, Germany
[3]Department of Environmental Dermatology and Allergy, University of Graz, Graz, Austria

The existence of seasonal patterns to patch test reactions has been described, but with conflicting causal interpretations. The potential seasonality of patch tests may be due to irritation, changes to skin barrier or changes to immunological functions caused by meteorological fluctuations. For example, increased skin irritability due to cold winter weather and low humidity may cause an increase in irritative/doubtful and weak positive (false positive) reactions. To investigate the extent of the association between weather and patch test results, consecutive patients ($N = 73691$) patch tested with the standard series of the German Contact Dermatitis Research Group (DKG) at German or Austrian IVDK (www.ivdk.de) centres were matched with weather data collected at a nearby (30 km radius) weather station. Temperature and absolute humidity (AH) on the day of patch test application and the two preceding days were averaged to represent the environment most likely to have influenced the skin condition at the time of testing. The results of 24 standard series substances were analyzed with multivariate logistic regression. Half of the standard series substances examined, including fragrance mix, nickel sulphate, and formaldehyde, exhibited evidence of a relationship with meteorological conditions. Fragrance mix and p-Phenylene diamine exhibited the strongest evidence of an association to weather, with the odds of the reactions in all three reaction categories (ir/?, +, ++/+++) increasing during winter conditions. Due to the association between weather and patch test reactivity, the potential effect of meteorological conditions should be considered in the interpretation of patch test reactions.

FC02.5

Investigation of reactions to dental materials

David J Gawkrodger
Royal Hallamshire Hospital, Department of Dermatology, Sheffield, UK

In dentistry there are many potential allergens and irritants. Patients may have an adverse reaction in minutes, hours or days after dental procedures. Dentists use many metals e.g. mercury in amalgam restorations, which may give an oral lichenoid eruption, and gold, and platinum group metals for inlays, crowns or bridges, which may give allergic reactions. Dentists, for dentures, use acrylate resins extensively and traces of which can give rise to allergic symptoms, though most cases are not 'allergic' in origin. Dental personnel have a high frequency of occupational skin problems and may complain of hand dermatitis or itching, facial eruptions or respiratory symptoms. With regard to oral lichenoid lesions, the proportion of patients allergic to mercury on patch testing varies according to series, from 67% down to 8%. In some cases, the mechanism can be irritant as well as allergic. Gold can cause lichenoid eruption or other changes. The role of palladium is still very difficult to judge. Cheilitis is particularly difficult to investigate, as there are many causes. The aetiology is irritant in 33%, allergic contact dermatitis in 25% and atopic eczema in 20%. Benzoates, antioxidants or flavourings in foods sometimes cause lip swelling. Hand dermatitis is common in dental personnel.

Common causes are irritancy, latex contact urticaria, and allergic contact dermatitis to acrylates, Myroxolon, fragrance, thiuram and colophonium. In the investigation of reactions in dental patients many things need to be considered and often the cause is not related to the dental materials suspected.

FC02.6

Metal allergy in Singapore

Anthony Teik-Jin Goon, C-L Goh
National Skin Centre, Singapore

We will analyze incidence of allergy to nickel, cobalt, chromate and gold for 2001–3 and compare this with previous studies in the same centre (1992–92, 1986–90, 1984–85) to look for changing trends in metal allergy in Singapore. We have noted that the prevalence of nickel and chromate allergy in our centre is rising again.

Friday, 11 June 2004
08:00 – 09:05

FS05

New drugs & diagnostics

Chairs: Niels Veien, Denmark & Jean-Marie Lachapelle, Belgium

FS05.1

Treatment of hand eczema

Niels K Veien
Dermatology Clinic, Aalborg, Denmark

Hand eczema is a common skin disease that often becomes chronic, and treatment of the disease is often challenging. Skin protection is of great importance for the prevention of hand eczema and is a fundamental aspect of the treatment of hand eczema. Emollients have been shown to be successful in the primary prevention of hand eczema as well as in reducing eczema activity. Topical corticosteroids are still the mainstay of treatment, but randomised controlled trials of their efficacy are needed. A combination of tacrolimus and topical corticosteroids may reduce the risk of steroid-associated side-effects. UV-therapy and Grenz rays can also suppress hand eczema. Systemic treatment with immunosuppressants such as cyclosporine and methotrexate show promising results, and acitretin may suppress keratotic hand eczema. Treatment possibilities for hand eczema, indications and side effects will be discussed.

S05.2

Advances in emollient therapy and superficial wound treatment

Ian Steel
Croda Chemicals Europe Ltd., Research and Marketing, Goole, UK

Study objectives Two studies involving human volunteer subjects have been conducted. These studies compared the ability of several ultra-pure medical grade lanolins (Medilan^{TM} range, Croda Chemicals Europe Ltd.) and Petrolatum USP to reduce the signs and symptoms of dry, cracked hands (Study One) and to promote the healing of superficial wounds (Study Two). Methods Study One, a two-week treatment period immediately followed by a 9-day (no treatment) regression period, investigated the signs and symptoms (dryness/scaling, cracking and/or abrasions and pain/itch) of dry, cracked hands. Clinical signs and symptoms were evaluated separately and their severity scored at the time of observation. A retrospective global assessment of overall improvement from baseline was also recorded using digital 35 mm photographs. Study Two investigated the repair of de-roofed cantharidin-induced blisters. Wound sites were evaluated and ranked on a daily basis. High-resolution photographs (20x) were also taken throughout the study prior to daily treatment. Results summary In Study One, at the end of the two-week treatment period and the 9-day regression period, hands treated with ultra-pure medical grade lanolins were superior to hands treated with Petrolatum USP. In Study Two, and particularly at day 10, it was shown that wounds treated with one type of ultra high purity lanolin were unequivocally superior to those treated with Petrolatum USP. Conclusion Ultra-pure medical grade lanolins have been shown to be superior to White Petrolatum USP in their ability to reduce the signs and symptoms of dry, cracked hands and to promote the healing of superficial wounds.

FS05.3

New characterization and chemistry of Germall 115 and Germall II

Søren Vig Lehmann[1], U Hoeck[1], J Breinholdt[2], CE Olsen[3]
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[2]Drug Discovery, Novo Nordisk, Måløv, Denmark
[3]Chemistry Department, The Royal Veterinary and Agricultural University, Copenhagen, Denmark

Germall 115 and Germall II are well known cosmetic preservatives, widely used as such since

the early 1970's and 1980's, respectively. This investigation reveals that they have mistakenly been regarded as pure chemical entities with specific structures by the majority of the chemical society. In fact Germall 115 and Germall II both consist of complex mixtures of numerous and fast degradable allantoin-formaldehyde condensation products and may not even contain the conventionally assigned chemical structures of imidazolidinyl urea (Germall 115) and diazolidinyl urea (Germall II). Equilibrium between different structures may be formed in different cosmetic formulations/test materials. This may have led to the discrepancies in the literature: Are the Germalls themselves sensitizers or are the allergic reactions caused by formaldehyde release? The identification and structure assignment of (4-hydroxymethyl-2,5-dioxo-imidazolidin-4-yl)-urea (HU) will be presented, as it is the major and chemically stable degradation product of both Diazolidinyl urea and Imidazolidinyl urea. A guinea pig maximization test has been performed to determine the potential of HU to induce delayed contact hypersensibility in guinea pigs. Separate chemically stable TRUE Test patches containing the mixtures have shown clinical efficacy.

FS05.4

Contact sensitization in Italian children over a 7 year period

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Our aim was to investigate contact sensitization in children over a 7 year period and to compare these data to our previous findings. From January 1995 to December 2001, 1094 children with suspected allergic contact dermatitis were patch tested with our paediatric series of 30 substances. 404 were affected by atopic dermatitis. 570 children (52.1%), 300 girls and 270 boys, proved to be sensitized. Among them, 291 (51%) were polysensitized. Neomycin, nickel sulfate, wool alcohols, thimerosal, ammoniated mercury, and propolis gave the highest number of positive responses. No significant differences were observed in the prevalence of contact sensitization among the patients with atopic dermatitis and non atopics. However, in the latter the frequency of positive responses to nickel sulfate and Kathon CG was significantly lower than in the former. The face (25%), the hands (23%), and the flexural areas of the limbs (18%) were most frequently affected in children with positive patch tests. In this study population the frequency of sensitized children was significantly higher than the one found from 1988 to 1994, in particular for neomycin, nickel sulfate, wool alcohols, ammoniated mercury, propolis, potassium dichromate, mercaptobenzothiazole and thiuram mix. Our data demonstrate that contact sensitization is more and more frequent in children referring to our department and that the importance of some allergens, such as neomycin, wool alcohols, propolis and potassium dichromate, is increasing in the paediatric age with respect to previous results.

FS05.5

The European Standard Series in 8 European countries – first results of the ESSCA network

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Since January 2001, the European surveillance system on contact allergies (ESSCA) has developed a suitable infrastructure with the financial support of EU funding (QLK4-CT-2001–00343 and –2001–2812), and has started to collect patch test data. These comprise a standardized clinical history and patch test results with the European standard series, contributed by the 12 centres in 8 European countries listed above. So far, with the 2003 data collection not yet completed, 7636 patients' test results have been pooled and analysed; current data pertaining to 2002 and 2003 will be presented. Anamnestic data reflect partly the specialties of some centres (e.g., the % of occupational and hand dermatitis ranging

between 6 and 29% and 18 and 56%), partly different selection criteria or possibly also definitions (e.g., 7–32% with underlying atopic dermatitis, 40–69% of patients age 40+). The leading allergen was nickel sulfate (15.7%, age- and sex-standardized), with however, large inter-national variation (the lowest standardized prevalence, 9.7%, was observed in Gentofte, Denmark, where nickel regulation had long been introduced). The prevalence of contact allergy to Myroxylon Pereirae resin (7.8%) has almost reached the frequency found with the fragrance mix (8.3%). In the two centres using the True Test™, both percentages were even lower, which may be indicative of a systematic effect. Within a few years, ESSCA is expected to meet its objective of increased consumer safety by post-marketing surveillance by continuously monitoring contact allergy across Europe.

FS05.6

New standardized allergens: the experimental TRUE Test® Panel

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TRUE Test® is the only standardized patch test system for the diagnosis of allergic contact dermatitis based on 24 fully stable and reproducible formulations. New standardized patches are in process of development for TRUE Test® Panel 3. The allergens chosen are well-known sensitizers and include preservatives, steroids, metals and others. 14 new patches are included in an Experimental panel which is tested in several European clinics. 11 of the patches contain new allergens while 3 patches consist of improved TRUE Test® formulations with Neomycine sulphate, Fragrance mix and Potassium dichromate. A number of the patches from the Experimental panel will be selected for TRUE Test® Panel 3. The overall purpose with pharmaceutical development of patch test materials for TRUE Test® is to obtain a precise dose, bioavailability and stability in every single patch. The patches have to be chemically stable for at least 2 years at refrigerated temperature. The selected preservatives on the Experimental panel are Methyldibromoglutaronitrile, Germall 115, Germall II and Bronopol. All 4 patches have proven to be difficult to stabilize because of the natural reactivity of the allergenic substances. The steroids chosen are Budesonide, Tixocortol-21-pivalate and Hydrocortisone-17-butyrate. All 3 steroids are stable in TRUE Test® formulations. Other allergens on the Experimental panel are Ammoniated Mercury, Goldsodiumthiosulphate, Parthenolide and Disperse blue 106, where the latter consists of a complex mixture. Chemical stabilization of the patches as well as clinical studies will be presented.

Friday, 11 June 2004
08:00–09:05

FS06

Fragrances

Chairs: Peter Frosch, Germany & Jeanne Duus Johansen, Denmark

FS06.1

Contact allergy to oxidized fragrance terpenes.

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Terpenes are among the most widely used fragrances, found not only in fine fragrances but most often incorporated in domestic and occupational products. Terpenes oxidize easily at air-exposure. Our previous studies have proved that limonene, linalool and caryophyllene are not allergenic in themselves but easily form allergenic products due to autoxidation. The aim of this study was to study the frequency and characteristics of allergic reactions in Europe to some oxidized fragrance terpenes.

Method: Consecutive dermatitis patients in six European dermatological centers were patch tested with oxidized terpenes. Questionnaires, standard and additional fragrance patch test materials were used in the diagnosis of fragrance allergy.

Results: Oxidized limonene was tested in 2411, while oxidized linalool, linalool hydroperoxide, oxidized caryophyllene, caryophyllene oxide and oxidized myrcene in additional 1511 patients. Of the patients tested 2.6% showed positive reaction to oxidized limonene, 1.3% to oxidized linalool,

0.5% to oxidized caryophyllene and 1 patient to oxidized myrcene. 1.1% of the patients reacted to linalool hydroperoxide, while testing with caryophyllene oxide resulted in few positive Results: 60% of the patients reacting to oxidized terpenes had fragrance related contact allergy and/or positive history for fragrance related dermatitis.
Conclusion: Oxidized limonene and linalool are common allergens in dermatitis patients tested consecutively in Europe. Our results indicate that autoxidation of fragrance terpenes contributes to fragrance allergy to a great extent. This observation emphasises the need of testing with chemicals that patients actually come in contact with and not only ingredients that were originally applied in the commercial formulations.

FS06.2

Autoxidation of linalool and impact on the sensitizing capacity and allergenicity

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Linalool is one of the most frequently used fragrance chemicals in scented products and a large population is exposed to it. It is therefore important to study the allergenic properties of linalool, and the effect of autoxidation.
Objectives: To study the autoxidation of linalool and identify formed oxidation products, to investigate the impact of autoxidation on the sensitizing capacity and to study the frequency of contact allergy to oxidized linalool among consecutive dermatitis patients.
Methods: Linalool was air-exposed and the degradation followed with GC. Oxidation products were identified with GC-MS and NMR. Pure linalool, 2 different states of oxidized linalool and 3 oxidation products were tested for their sensitizing capacity in the local lymph node assay (LLNA). Consecutive dermatitis patients were patch-tested with oxidized linalool and a fraction of oxidized linalool.
Results: Linalool started to decompose immediately when air-exposed. Several oxidation products were identified among which 3 (2 hydroperoxides and an alpha, beta-unsaturated aldehyde) contain structural features that make them potential allergens. LLNA showed that the 3 oxidation products were moderate allergens, and that the sensitizing potential of linalool increased with longer air-exposure times. In the patch-test study positive reactions were observed to oxidized linalool in 1.65% of the patients.
Conclusions: The extensively used fragrance chemical linalool is not allergenic in itself. The autoxidation process that takes place at air-exposure leads to the formation of sensitizing oxidation products. The frequency of consecutive patients reacting to oxidized linalool shows that the experimental findings are clinically important.

FS06.3

Chloroatranol – clinical studies and exposure analysis

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Objectives: To investigate the elicitation potency of chloroatranol – a newly identified allergen in the natural fragrance extract: oak moss absolute. Further to compare chloroatranol and atranol and relate the findings to exposure assessed by chemical analysis.
Methods: A serial dilution patch and repeated open application test was performed in 13 chloroatranol sensitized patients and in 10 healthy controls. Further the relative potency between chloroatranol and atranol in equimolar patch test concentrations was studied and exposure assessed by chemical analysis (liquid chromatographic-tandem mass spectrometry) of perfumes on the European Market.
Results: Elicitation occurred in 92% (12/13) to the repeated open application of 5 ppm chloroatranol in ethanol within 14 days of exposure and in none of the controls ($p < 0.001$). Patch testing with eqimolar concentrations of chloroatranol and atranol indicated almost similar elicitation potency. Exposure assessment showed that chloroatranol and atranol were widespread in perfumes. Chloroatranol was found at 10 ppm and atranol 74 ppm (90% percentiles).
Conclusions: Chloroatranol and atranol are strong elicitors. The current exposure to these fragrance allergens in perfumes is likely to cause clinical symptoms in sensitised individuals.

FS06.4

Milia as sequelae to allergic contact dermatitis, a case report

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Milia are small sub epidermal keratin cysts. They may be seen following bullous diseases disrupting the dermo-epidermal junction. They may occur rarely as a complication to contact allergic reactions. An oak moss allergic patient participated in a dose response ROAT with chloratranol, shown to be a potent allergen in oak moss. The patient reacted to choratranol at patch testing down to 0.0063 ppm, and started a ROAT by application of 2 drops of a 5 ppm solution to an area of 3 × 3 centimetres on the volar aspect of one forearm. After 1 day severe oedematous dermatitis was observed and blistering was seen at day 2. The test was stopped and the patient treated with systemic prednisolone. At a 3 month control visit milia were seen at the application site on the forearm but not on the back where the patch tests were applied. The patient had no subjective symptoms and the milia were easily removed with a sterile needle. The presence of milia as sequelae seems to reflect the depth and severity of the allergic contact dermatitis developed months earlier. This observation underlines the potency of chloratranol as a very strong allergen.

FS06.5

Fragrance sensitization in geriatric nurses

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Objective: The incidence of occupational hand dermatitis in geriatric nurses (GN) is increasing. 102 GN were involved in a program of secondary individual prevention at the University of Osnabrück. Prior to participation a patch test was performed in 99 of 102 IG by the dermatologist in charge. Sensitization to the fragrance mix was noted in 16% of cases. However, not once the fragrance mix was splitted. One of the GN was presented for further work up, revealing sensitizations to cinnamic alcohol and aldehyde, hydroxycitronellal, isoeugenol, lyral as well as ylang-ylang oil.
Method: Patch tests according to the DKG guidelines were performed. To reveal the composition, fragrance oils were submitted to gas chromatography.
Results: Additional patch tests to various ylang-ylang oils employing various concentrations reveal different patch test reactions. Further work up employing gas chromatography of different ylang-ylang oils will be presented and relevance of patch test will be discussed. Hence cinnamic alcohol is frequently employed by the perfume and cosmetic industry, further patch tests of cinnamic alcohol in petrolatum at various concentrations as well as given cinnamic-alcohol-containing-products are performed. Relevance of patch test results will be presented and discussed with respect to the current discussion of labelling skin sensitizers.
Conclusion: At present the fragrance mix is not commonly splitted. Dermatologist in practice test the fragrance mix. When patch testing naturally occurring fragrance oils, origins and extracts thereof must be considered, because they may contain different allergens relevant for sensitization.

FS06.6

Mucosal symptoms elicited by fragrances; a population-based study

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Objectives: To investigate symptoms from the eyes and airways, elicited by perfume and fragrance products and associations between such symptoms and skin prick test reactivity, metacholine bronchial hyperreactivity (BHR), contact allergy, and eczema in a population based sample.
Methods: A questionnaire on mucosal symptoms elicited by fragrance products was mailed to 1189 persons who had participated in a Danish population-based study of allergic diseases in 1997/98. The study included measurement of BHR, skin prick testing, patch testing and history of hand eczema.
Results: The response rate to the questionnaire was 80%. Symptoms from the eyes or airways elicited by fragrance products were reported by 42%. There were no significant associations between these symptoms and skin prick test reactivity. Positive and independent statistical significant associations were found between BHR, perfume contact allergy and hand eczema, and symptoms from the eyes and airways elicited by

fragrance products, also when adjusting for nickel contact allergy, age, gender psychological vulnerability, educational level and social class.
Conclusions: Individuals with BHR, hand eczema and/or perfume contact allergy, as opposed to those without, are more frequently and more severely bothered from the eyes or airways after volatile exposure to fragrance products. The lack of association with skin prick test reactivity indicates that IgE mediated allergic mechanisms do not play a major role in the development of these symptoms. Having hand eczema has the greatest impact on reporting mucosal symptoms elicited by fragrance products.

FS06.7

The new fragrance mix II – test results of a multicentre European Study

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A new fragrance mix (FM II) with 6 frequently used chemicals was evaluated in consecutive patients patch tested in 6 dermatological centres in Europe. 28% FM II contained 5% Lyral, 1% citral, 5% farnesol, 5% coumarin, 1% citronellol and 10% alpha-hexyl cinnamic aldehyde (AHCA); in 14% FM II the single constituents' concentrations was lowered to 50% and in 2.8% FM II to 10%. Each patient was classified regarding a history of adverse reactions to fragrances: certain, probable, questionable and none. The frequency of positive reactions to the currently used 8% fragrance mix (FM I) and the new mix in 1703 patients was as follows: FM I, 6.6%; 2.8% FM II, 1.3%; 14% FM II, 2.9%; 28% FM II, 4.1%. The number of doubtful/irritant reactions was 7.2% for FM I and ranged from 1.8% to 10.6% for FM II.

8.7% of tested patients had a certain fragrance history. Of these 25.2% were positive to FM I, reactivity to FM II was dose-dependent and ranged from 8.1% to 17.6% in this subgroup. Comparing 2 groups of history – certain and none – values for sensitivity (sens) and specificity (spec) were calculated. Sens: FM I, 27.2%; 2.8% FM II, 8.7%; 14% FM II, 15.9%; 28% FM II, 21.5%. Spec: FM I, 96.3%; 2.8% FM II, 99.5%; 14% FM II, 98.7%; 28% FM II, 97.9%. 31/70 (44.3%) patients positive to 28% FM II were negative to FM I. In the group of patients with a certain history a total of 6 patients was found reacting only to FM II. Simultaneous break-down testing with the single constituents produced positive reactions in 54.3% for 28% FM II and 48% for 14% FM II. Lyral was the dominating single constituent with positive reactions (37.1% for 28% FM II, 36% for 14% FM II), followed by citral, farnesol, citronellol, AHCA and coumarin. Chemical analysis for the 6 constituents of FM II was performed on 25 products used by 12 patients being patch test positive to FM II. Lyral was detected in 76% of these products, citral in 16% and AHCA in 8%. In conclusion, the new FM II detects additional patients with contact allergy to fragrances missed by the currently used FM I. The medium concentration, 14% FM II, is probably the most useful one for diagnostic screening.

Friday, 11 June 2004
09:10–10:15

FS07

Legislation & prevention

Chairs: Carola Lidén, Sweden & Ian White, UK

FS07.1

A survey of occupational hand eczema in Denmark

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Background: The need for prevention to reduce the number of occupational hand eczema is high. Occupational hand eczema is the most frequently recognised work-related disease in Denmark. Previous findings have shown that almost half of all cases develop a chronic condition with persistent

dermatitis, and the annual cost to society is immense.

Aims: The aim of this study was to survey the trends and development of occupational hand eczema in Denmark and thereby help to ensure future successful prevention of chronic disabling occupational hand eczema.

Methods: 758 patients with recognised occupational hand eczema were included prospectively in the period October 2001- November 2002. Data on diagnoses, disease duration, severity, absence from work and occupation was obtained from The Danish National Board of Industrial Injuries and an additional questionnaire was administered by mail.

Results: 621 patients answered the questionnaire (response rate 82%). Irritant contact dermatitis was the most frequent diagnosis and the female/male ratio was 2:1. High prevalence was found in particularly wet occupations. 19 per cent had sick leave more than 5 weeks per year and the mean disease duration was 4.8 years (median 2.1 years). 68.2% had chronic changes.

Conclusion: The results showed a marked gender difference in the pattern of diagnosis and occupation. The impact of occupational hand eczema is still high with prolonged absence from work and a high percentage of chronic disease. The results of the study give important suggestions for future preventive strategies for health authorities.

FS07.2

Occupational contact dermatitis and workers' compensation

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Statistics for occupational contact dermatitis (OCD) in Australia are gathered from workers' compensation (WC) data and research has indicated that occurrence is underestimated by as much as 400%. This study investigated reasons which might influence decisions whether to claim WC or not. A questionnaire was posted to 168 individuals diagnosed with significantly work related OCD at a specialised occupational dermatology clinic, therefore fulfilling valid claim criteria under the WC scheme operating in the state of Victoria. 70 completed responses were analysed. Ages ranged from 18–65 and only 40% had claimed workers' compensation, with those under 45 y less likely to claim. Females were significantly ($P < 0.05$) less likely to claim, as were respondents who had dermatitis present for less than 6 months. At the time of diagnosis, 37% of respondents were health care workers, 10% hairdressers, 7% food handlers, and 29% worked in hospitals, 24% manufacturing, 10% hairdressing salons, and 7% each vehicle maintenance, food service and trades. 31% no longer worked for the same employer, however 90% of respondents were still employed. Those who did not claim WC lost less time from work than those who claimed, but more non-claimants still had skin problems quite often or constantly than did claimants. 28.6% of non-claimants had all or some of their medical and/or lost time costs paid by their employer, and only 18% of claimants had all of their costs paid by their employer or WC insurer. Although the sample size was small, interesting data was also obtained from the qualitative responses.

FS07.3

Skin sensitisation thresholds: a legislative perspective

David Basketter
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Current EU legislation for skin sensitisers is a simple device, which crudely distinguishes between chemicals which possess significant sensitising potential and those which do not. Where a chemical is clearly positive in predictive tests or by human experience, it is classified and labelled R43: May cause sensitisation by skin contact. Use of such a chemical at 1% in products would require appropriate labelling. Additional labelling requirements in relation to elicitation also exist, or are planned, which variously impact cosmetics, detergents and a wide range of other consumer products. Improvements to this basic system are presently under consideration and largely are focused on a consideration of options to categorise sensitising chemicals according to their potency. Central to this activity has been the demonstration of the utility of the local lymph node assay (LLNA) as a predictor of the human potency of skin sensitisers. Arising from this, both industry (ECETOC) and regulatory bodies in the EU have taken proactive steps to initiate improvement in the existing legislation. However, at a wider regulatory level, the debate currently centres on whether formal validation processes are required to progress potency categorisation at the OECD level, and if so how many categories and with what threshold levels. Political niceties here represent a barrier to progressing improvements in human health protection.

FS07.4

Co-operation between dermatologist and occupational health physician

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[3]Governmental Organisation for Facilitating Medical Care of Employees, The Hague, The Netherlands

The Dutch government has recently taken initiatives to improve the protection of labourers against diseases which are related to their work, and most especially, to reduce the rapidly increasing number of patients who have to definitely stop working and who, eventually, end up being dependent on social welfare. Firstly, a number of new laws have been adopted which define the responsibilities of both the employers and the employees. Secondly the cooperation is stimulated between the Dermatologist and the Occupational Health Physician of the patient. The latter is (according to law) employed by the employer of the patient and regularly visits the place of work. We now had the opportunity to treat and study both the social, medical and occupational aspects of a patient's case simultaneously.

We decided to eliminate the existing hesitation of consulting or referring, as well as the barriers created by matters of procedure, bureaucracy and waiting lists. In our paper we discuss the above-mentioned laws and regulations, and the way in which cooperation takes place between the doctors. We will present figures showing the effects of this approach on sickleave.

FS07.5

Sensitive skin: What is it? What strategies meet its challenge?

Patricia Engasser
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Sensitive skin is a neolgism used by consumers for a self-perceived intolerance to environmental factors including skin care products and cosmetics. Consumer complaints focused industry on this concept and dermatology has gradually recognized it also. Identified associations range from endogenous skin disorders to irritant (including sensory) and allergic reactions. Impaired barrier function has been implicated in some instances. The consumer with sensitive skin frequently experiences adverse reactions to cosmetics, but what information is available to help them choose products they can tolerate? To answer this question, a survey is being conducted among cosmetic manufacturers inquiring if they market products for consumers with sensitive skin. They are asked what steps they take in the design of these products to insure tolerance, and what testing is done on these products that may be unique. Does the post-marketing data show these products fulfilled their goal and these cosmetics are well tolerated by this group? The manufacturers are surveyed as to what precautions they regard as important for 'sensitive skin' individuals in choosing and using cosmetics. The results of the survey are incorporated into patient recommendations.

FS07.6

Efficacy of UVB radiation versus skin protection in the prevention of hand dermatitis in baker apprentices

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In-vitro and in-vivo data suggest the efficacy of various skin protection measures in the prevention of hand dermatitis (HD). The aims and objectives of this intervention study was to quantify the efficacy of skin protection (SP) measures and UVB hardening in the prevention of HD. SP measures were compared against UVB hardening in a controlled clinical trial of 94 apprentices. The apprentices were assigned to the intervention arms class-wise. Baker apprentices involved in a previous follow-up study served as an additional historic control group representing no intervention. The apprentices were interviewed and examined in a standardised way at the beginning of the vocational training and at four follow-ups. Transepidermal water loss (TEWL) was measured at the back of the hands. Point prevalence of HD in the groups after 6 months was highest in the controls (C) (29.1%) followed by the UVB-group (19.4%) and the SP group (13.3%). UVB hardening and SP measures were associated with a reduction in HD prevalence by 9.7% (95%CI −8.5 to 28.1) and 15.8% (95%CI −2.4 to 33.9), respectively. Unadjusted logistic regression analysis showed atopy (OR = 4.74, 95%CI 1.12–20.11, $p = 0.035$) and skin care (OR 0.39, 95%CI 0.16–0.86, $p = 0.023$) to be independent risk factors. Application of SP measures reduced the OR for HD 0.8 (95%CI 0.17–3.70) and 0.33 (95%CI 0.09–1.23) fold compared to the UVB and C group, respectively. The trends in the clinical results

were confirmed by statistically significant differences in TEWL values. Apprentices in the SP group consistently had a lower prevalence of HD compared to the apprentices in the UVB and C group. These trends were reinforced by statistically significant differences in TEWL levels. A multicentre trial is recommended to confirm the efficacy of SP measures in a larger randomised study.

Friday, 11 June 2004
09:10–10:15

FS08

Quality of life and compliance

Chairs: Thomas L Diepgen, Germany & Berndt Stenberg, Sweden

FS08.1

What kind of knowledge generates patients' actions? – an empirical study in relation to allergic contact dermatitis

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During the last two decades the incidence of contact allergy to preservatives in consumer products has increased. It is of crucial importance for the prognosis that sensitised patients avoid contact with the allergens, and they are informed how to take precautions, e.g. by reading the descriptions of contents on consumer products. Discrepancy between 'doctors orders' and patients' actions is often taken as an expressions of patients' lack of knowledge. However, sociologically inspired studies show that differences in social experiences and in social life circumstances non-consciously lead to socially different ways of coping with illness. This study investigates in a sociological perspective, how people handle contact allergy in everyday life and the social genesis of their actions. Interviews were carried out with 8 women selected according to medical and sociological criteria. The study indicates that patients with contact allergy comply with 'doctors orders' in different ways depending on patients' resources, possibilities and social class. The study also indicates, that information given by health staff to a considerable extent is directed to patients from the higher social classes, who possess the ability to read the linguistic difficult names of the preservatives and to a lesser extend to patients from lower social classes, who do not possess this ability.

FS08.2

Gender, race, age & occupation effect quality of life (QoL) in ACD

Donald Belsito, D Kadyk, S Hall
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Objectives: This study was conducted to investigate the relationship between QoL scores for patients with ACD and confounders, such as gender, race, age, and occupation.
Methods: A total of 428 subjects with ACD were, at varying times after diagnosis, mailed a QoL questionnaire modified from Skindex-16 to include an additional 5 items pertaining to occupational impact. The QoL scores were analyzed by gender, race, age, and occupation to ascertain factors that impact QoL in subjects with ACD.
Results: Three of the four confounders examined have a significant connection with QoL in patients with ACD. Non-Caucasians had significantly worse QoL scores than Caucasians within the functioning scale, and had more emotional distress secondary to their disease. There were no statistically significant gender-related differences in QoL scores, although females felt a higher degree of embarrassment and depression. Age significantly impacted items within the functioning and occupational scales, with subjects nearing retirement age and older reporting better QoL. In contrast, younger subjects, especially those in the 5th decade, were more likely to have difficulty pursuing daily activities, have more fear that they might need to leave their jobs, and have more concern for their financial futures. Office workers, students, and homemakers were primarily diagnosed with non-occupational ACD, while more industrial, health care and other wet workers suffered from occupationally related ACD. In the analyses of QoL by occupation, industrial workers reported significantly more impaired QoL than subjects in other professions.

FS08.3

Health-related quality of life and hand eczema

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Aims: The aims were to study health-related quality of life (HRQL) in patients with hand eczema,

and to compare two different instruments for assessment of HRQL.
Methods: 100 consecutive hand eczema patients (51 females and 49 males) at an occupational dermatology clinic completed the generic questionnaire Short Form-36 (SF-36), and the dermatology specific Dermatology Life Quality Index (DLQI). To compare the instruments factor analysis, with a polychoric correlation matrix as input, was performed, thus taking the ordinal aspect of the data into account.
Results: HRQL was affected by hand eczema, measured with both SF-36 and DLQI. The mean (SD) sum scores of DLQI was 7.4 (5.8), no difference between genders. However, the SF-36 showed more impaired HRQL for females than for males in the mental health dimension. There was a high correlation between the instruments for physical health, but lower for mental health.
Conclusions: Hand eczema has an impact on HRQL, and both SF-36 and DLQI are suitable instruments. Our conclusion from the factor analysis is that the SF-36 measures mental health better than the DLQI. The choice of instrument to be used in a specific study depends on the purpose of the study. A generic instrument has the advantage of making comparisons with other diseases possible. The SF-36 also appears suitable for use in hand eczema studies where gender differences in HRQL are of interest.

FS08.4

Prognosis of hand eczema – a 15-year follow-up

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Aims: To study long-term prognosis of hand eczema and to identify factors of importance for the prognosis.
Methods: A cohort of 1238 individuals with verified hand eczema diagnosis was established by a population-based prevalence study in Gothenburg, Sweden, in 1982–83. In 1998 a questionnaire was mailed to all individuals with available addresses ($n = 1115$). The response ratio was 78% (868/1115).
Results: 66% reported periods of hand eczema since 1983, and 44% during the past year. 12% stated continuous symptoms. No significant difference was found between the sexes. 74% of those who reported symptoms after 1983 considered that their hand eczema had improved. Significant differences in the persistence of hand eczema were related to the age at onset of hand eczema, skin atopy, and the extension of eczema at examination. Contact allergy related significantly to occurrence of hand eczema during the year before follow-up. 32% had visited a doctor, 7% reported sick leave periods, 2% sick pension and 3% change of occupation due to hand eczema.
Conclusions: In this population-based study, a majority of individuals with hand eczema reported periods of eczema during a 15-year follow-up, implying that hand eczema is a longstanding disease. Young age at onset, history of childhood eczema and extension of the hand eczema were prognostic factors. Hand eczema did entail consequences like change of occupation, sick leave or pension in more than 10% during a 15-year period.

FS08.5

Does childhood atopic dermatitis influence the future working life?

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[4]*National Institute for Working Life, Stockholm, Sweden*

Aim: To investigate the risk of adult hand eczema and possible influence on later working life in persons with childhood atopic dermatitis.
Method: After reviewing medical records from the school healthcare in Stockholm regarding individuals born 1960–69, 600 individuals where signs of atopic dermatitis were noted ("cases") and 600 matched controls without eczema or allergic disease ("controls") were identified. 405 cases and 378 controls answered a questionnaire regarding past and present skin disease, choice of job, exposure at work and possible change of job due to eczema.
Results: Hand eczema was more than 3 times more common among cases, 42%, compared to controls, 13% ($p < 0.001$). Hand eczema during the past 12 months was reported by 24% of the cases and 9% of the controls ($p < 0.001$). The proportion of individuals working in jobs with high-risk for hand eczema was equal between the groups, as well as exposure to water, detergents, chemicals and hand washing. Among the cases 9% reported change of job due to eczema compared to 2% of controls

($p < 0.001$) and sick leave 10% compared to 2% ($p < 0.001$).

Conclusions: Childhood atopic dermatitis is a risk factor for hand eczema. As the proportion of individuals in jobs with high-risk for hand eczema and the exposure was the same in cases and controls measures preventive measures are important to reduce consequences like sick leave and change of job.

FS08.6

Persistent post-occupational dermatitis: a case series

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Objectives: Persistent post-occupational dermatitis (PPOD) was mentioned by Wall and Gebauer in 1991 to describe ongoing skin disease precipitated by occupational contact dermatitis (OCD). There has been little formal recognition or clarification of this condition.

Methods: Approximately 1600 records from our Occupational Dermatology Clinic were searched to identify likely cases. PPOD was difficult to diagnose as relatively few patients had been reviewed after initial assessment.

Results: A number of patients with reasonably clear histories of persistent occupational contact dermatitis were identified, which followed either irritant or allergic occupational contact dermatitis. These included a 57 yr old male who worked with photographic chemicals, a 51 yr old female food handler and a 25 yr old female food handler who were all diagnosed with irritant contact dermatitis and yet experienced persistent dermatitis even after avoiding the irritants that were associated with causing their dermatitis. A 51 yr old process worker allergic to acrylates, a 28 yr old laboratory worker allergic to rubber accelerators and coconut diethanolamide in her hand wash and a 48 yr old epoxy applicator allergic to epoxy resins experienced recurrent dermatitis for years after avoiding their causative allergens, although with gradual decrease in the frequency of outbreaks of dermatitis. Unfortunately, many patients experienced difficulties with workers' compensation because the persistence of their dermatitis was thought by some medical examiners negate its work-relatedness.

Conclusion: There needs to be greater recognition and understanding of PPOD. We are planning to follow-up patients from our clinic to better study and define this condition.

Friday, 11 June 2004 10:45–11:15

KL04

Keynote Lecture

Chair: Thomas L Diepgen, Germany

Dose response aspects of contact allergy

Jeanne Duus Johansen
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It has been shown by series of experiments that the induction of contact allergy depends on the concentration of allergen per unit skin rather than the total dose delivered. This means that a high concentration of allergen delivered to a small area of the skin comprise a higher risk of induction than if the same total amount is applied to a larger skin area. Attempts have been made to exploit this knowledge in risk assessment models for induction of contact allergy. The concentration (dose per unit skin) applied at induction also determines the sensitivity of the individual at elicitation. It also seems that smaller concentrations of allergen are required to sensitise individuals with pre-existing contact allergy than those without. Once a person is sensitised to a substance, the sensitivity of the individual in combination with the level of exposure to the allergen, determines whether clinical symptoms will occur. These dose-response relationships can be studied in sensitised individuals by re-application of a serial dilution of the relevant allergen either under patch test conditions or by repeated open applications. Thresholds for no-response or minimum effect levels may be determined for different allergens and used systematically for preventive purposes. Practical examples of such successful prevention exist regarding nickel and chromium allergy, providing both primary and secondary preventive effects. Further understanding of the dose- response relationships is important in diagnosing contact allergy and advising the patient relevantly.

Friday, 11 June 2004 11:20–12:45

FS09

Medicament allergy/drug eruptions

Chairs: Derk P Bruynzeel, The Netherlands & Åke Svensson, Sweden

FS09.1

Diacetylmorphine (heroin) allergy

Aliet J Hogen Esch[1,2], S van der Heide[2], W van den Brink[3], DP Bruynzeel[4], PJ Coenraads[2]
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[3]Central Committee on the Treatment of Heroin Addicts, Utrecht, The Netherlands
[4]Free University Medical Center, Amsterdam, The Netherlands

Since heroin is delivered to a selected group of drug addicts under supervision of nurses in the Netherlands, we reported about several nurses who presented with work-related eczema and positive patch tests to heroin. To investigate the prevalence of heroin contact allergy among all workers in this heroin delivery project, a study was started using questionnaires. Altogether 31 nurses reported work-related complaints out of 100 who returned questionnaires. Besides reports of eczema, mainly of eyelids (probably airborne) and hands, there were mucosal and respiratory complaints. Patch tests were performed in 25 nurses with complaints; in 9 of them a heroin contact allergy could be confirmed. In 6 out of these 9 nurses this was combined with mucosal or respiratory complaints. There were also 6 nurses with mucosal or respiratory complaints without a contact allergy. Contact dermatitis from opioids, such as morphine and codeine, has been documented among opioid industry workers, nurses, doctors, pharmacists, and in patients. In conclusion heroin appears to be a potent contact allergen, causing contact dermatitis. Mucosal and respiratory complaints however, cannot be explained by this contact allergy; they might be caused by a type-1-allergy to heroin, or by a direct histamine liberating effect. Opioids are known histamine liberators causing urticaria, rhinitis and anaphylactoid reactions; therefore intracutaneous tests with heroin are unreliable. In an ongoing research project it will be attempted to detect specific IgE to heroin in the 12 workers with mucosal or respiratory complaints; within the next few months results will be available.

FS09.2

Contact allergy to a commercial alcohol prep swab

James S Taylor, E Erkek, Y-H Leow, D Jacobsen
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Allergic contact dermatitis to prepackaged disposable alcohol prep swabs is infrequently reported. A 60-year-old woman developed repeated episodes of dermatitis at sites of injections and venipunctures. History and patch testing revealed contact allergy to Kendall Webcol alchol prep swabs. There were negative patch test results to isopropyl alcohol (IPA), but positive reactions to the Webcol swab, to the inner surface of the packaging foil, to two other brands of alcohol swabs, and to bacitracin. UV absorbance profile analysis revealed the presence of UV absorbing materials at peaks of 221 and 280 nm within commercial IPA samples, including one from Kendall, which were absent from reagent grade IPA. Reports of similar cases identified IPA, propylene oxide, or both as the allergens; when swab ingredients were negative, compound allergy was proposed. A recent report from Korea identified dodecyldiaminoethylglycine and IPA as the allergens in the commercial disinfectant swab. Although the exact allergen is undetermined in our case, it may represent a chemical compound or contaminant that is used or acquired during the manufacturing of the swabs or foils.

FS09.3

Can Flutivate® cream be safely used in formaldehyde-allergic patients?

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[2]National Skin Centre, Singapore

Objectives: To study the healing time of an experimental eczema treated with Flutivate® cream, a potent corticosteroid containing a formaldehyde releasing preservative, in patients allergic to formaldehyde and controls not allergic to formaldehyde.
Methods: 24 individuals allergic to nickel, 7 of whom were also allergic to formaldehyde, had a nickel-allergic contact dermatitis experimentally induced on both upper arms. The dermatitis was treated twice daily for a maximum of 3 weeks or until healing with either Flutivate® cream or Betnovate® cream, a corticosteroid with the same potency but containing another preservative, which was tolerated by all 24 study persons. The study was double-blind and randomized.
Results: In 12/17 controls (71%) the nickel-allergic contact dermatitis healed completely when treated with Flutivate® cream compared to 2/7 formaldehyde-allergic patients (29%) ($p < 0.05$).
Conclusion: Flutivate® cream should not be used by individuals allergic to formaldehyde.

FS09.4

Methyldibromo glutaronitrile in leave-on products

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The rapidly increasing frequency of contact allergy to methyldibromo glutaronitrile (MDBGN) is of concern. This study investigates the allergic response elicited in pre-sensitised individuals from exposure to a leave-on product preserved with 50 or 100 ppm MDBGN.

Material and methods: Eighteen volunteers with contact allergy to MDBGN and 10 healthy controls were exposed to repeated open allication tests (ROAT) with two moisturisers with a high and a low lipid content, respectively, both containing MDBGN in a concentration of 50 ppm. The ROATs were performed on the left and the right side of the neck for 14 days, or until a positive reaction was seen. If a positive reaction did not develop within the first 14 days the application with analogous moisturisers containing 100 ppm MDBGN continued for further 14 days.

Results: Eleven (61.1%) developed dermatitis on the test area, and 10 (55.5%) developed a positive reaction to 50 ppm moisturiser. Reactions to the low- moisturiser were the most frequent. the controls all had negative ROATs.

Conclusion: A concentration of 50 ppm MDBGN in a leave-on product was found to elicit an allergic reaction in more than half of sensitised individuals when applied on the neck.

FS09.5

Patch testing with allopurinol and oxypurinol in drug eruptions

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Background: Drug eruptions as maculopapular rash, hypersensitivity syndrome, Stevens-Johnson syndrome or toxic epidermal necrolysis occur in about 2% of patients taking allopurinol. The allopurinol oxidation product – oxypurinol – seems to be responsible for these hypersensitivity reactions. Opposing what occurs during the study of drug eruptions induced by other drugs as carbamazepine or amoxiciline, patch testing with allopurinol is usually negative.

Objective: To evaluate skin reactivity to allopurinol and oxypurinol by patch testing in patients with a previous history of drug eruption related with allopurinol.

Methods: 10 patients (6 females and 4 males) with drug eruptions induced by allopurinol with a high imputability index (6 hypersensitivity syndromes, 2 Stevens-Johnson syndromes, 1 erythroderma and 1 toxic epidermal necrolysis) were patch tested with allopurinol in vaseline (10 and 20%) and with oxypurinol in vaseline (10 and 20%), acetone (10 and 20%) and alcohol (10 and 20%).

Results: Patch tests with allopurinol and oxypurinol were invariably negative after 48 and 96 hours in all patients tested.

Conclusion: Patch testing with oxypurinol as well as with allopurinol is usually negative and therefore is not helpful in the confirmation of these hypersensitivity reactions to allopurinol.

FS09.6

Capsaicin contact dermatitis

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Capsicum peppers are widespread both in and out the kitchen. ''Human hand'' is a contact dermatitis resulting from the direct handling of peppers. Capsaicin also is found in topical agents for treatment of postherpetic neuralgia, diabetic neuropathy and arthritis. The oleoresin of capsicum is considered a powerfull irritant capable to induce irritant contact dermatitis and non-immunological contact urticaria. A 81 year-old man with a severe itchy macular and papular rash induced by Capsidol® initially located over the shoulder and sudden spread over the thorax is presented. A dense dermal mononuclear cell infiltrate and spongiosis suggested the diagnosis of contact dermatitis. Negative open tests and a positive patch test reaction (++ 96 hours) using the trade cream Capsidol® (capsaicin 5%) led us to contact with the Pharmaceutical Company Viñas. They provided us the components of the cream: capsaicin, isopropyl myristate, estearic acid (DERVACID 3148), propylene glycol, glycerin monomyristate (ESTOL3650GMM), AMPHISOL K, Cetyl alcohol (NACOL 16–85), benzyl alcohol, diazolidinyl urea (GERMALL II), p-hydroxybenzoate–methylsodium (NIPAGIN M sódic), p-hydroxybenzoate propyl (NIPASOL M). Capsaicin in benzyl alcohol at 0,075% was open tested with negative results. Only

patch test with capsaicin was positive (++) at 48/96 hours and the excipient components at the appropiate concentrations were all negative. Patch test biopsy showed an eczematous pattern. Twenty controls showed negative results. This case is probably an allergic reaction but shows how still remains difficult to distinguish among allergic and irritative cutaneous reactions.

FS09.7

Standardisation of the "strip" patch test: a multicentre study

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Objectives: The strip patch test (SPT), proposed by Spier and Sixt (Hautarzt 1955;6:152–9), is a modification of the patch test (PT). This technique is used to enhance penetration through the stratum corneum for poorly penetrating substances such as medicaments. So far, a standardised procedure is lacking. This multicentre study aims at standardising the SPT procedure.
Methods: A total of 83 healthy volunteers participated. In each subject, we determined the number of strips (A) until the surface became glistening and then calculated the median number of strips in the sample ($\bar{A} = 26$). We ascertained the median number of strips in the sample ($\bar{a} = 11$) that was necessary to achieve a first statistically significant and medically relevant increase of the TEWL revealing a critical stratum corneum strip depth. For the finally calculated number of strips for each subject ($a/A = (\bar{a}/\bar{A}) \Leftrightarrow a = A \times (\bar{a}/\bar{A})$), the actual increase in test sensitivity was substantiated employing SLS 0.125% aqueous.
Standardisation results: Perform stripping at one upper part of the back until the surface becomes glistening: gently press a 25 mm diameter adhesive tape downward vertically for about 2 seconds and then remove it in one quick movement at the angle in direction of adherence; continue stripping with a new tape cut on exactly the same skin area. Multiply number of strips by the correction factor ($cf = \bar{a}/\bar{A} = 11/26 = 0.4$). Perform calculated number of strips likewise on the contralateral site and then apply there the test preparation for 24 hours.
Conclusions: If clinically an allergic contact dermatitis is expected but PT is negative, the SPT might reveal the potential allergen.

FS09.8

Drug-induced Baboon syndrome: SDRIFE at strife with systemic contact dermatitis?

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The term baboon syndrome was introduced 20 years ago. It was proposed for a particular eruption mimicking the red gluteal area of the baboon after systemic exposure either to the contact allergens nickel and mercury or to oral ampicillin. Previously this phenomen was e.g. termed flexural exanthema to mercury. Since then similar incidences have been reported after systemic exposure to betalactam antibiotics and other drugs, sometimes under different terms. Clinically sharp demarcation of a V-shaped erythema is present in inguinal/genital and gluteal/perianal areas. Additionally papules, vesicles and hemorrhagic lesion may be found. In most patients presence of exanthema in other anatomical flexural regions (axilla, elbow, knee, ventral neck) has been identified. However, involvement of the plantar/palmar regions, face and mucosal sites has not been documented. Typically blood tests are normal and systemic symptoms are absent. Histological results vary but a predominance of superficial perivascular infiltrate with mononuclear cells has been reported. Occasional positive patch tests or stimulation of lymphocytes in the LTT may be suggestive for a type IV allergic reaction. Since the drug-related baboon syndrome shows clinically and histologically different findings to systemic contact dermatitis and acute generalized exanthematous pustulosis (AGEP), it should be seen as a separate entity. The mainstay for the diagnosis of systemic contact dermatitis requires contact sensitization and elicitation by a contact allergen. In contrast in the

baboon syndrome and AGEP history for sensitization is often negative, although sometimes positive patch and LTT results can be found. AGEP, on the other hand, requires a distinct score including systemic signs and leucocytosis. In all three symptoms typically occur within 1 to 2 days. The term baboon syndrome does not reflect the whole range of symptoms and signs. And, although it is easily remembered, the comparison to an animal may be insulting. Therefore, we suggest that drug-induced baboon syndrome should be separated from the contact allergen-induced form, and should be recognized as a separate entity within the spectrum of drug eruptions. For this reason we propose the acronym SDRIFE (symmetrical drug related intertriginous flexural exanthema). This refers to the distinctive clinical pattern of this drug eruption without implicating any pathomechanism, which has not been clearly elucidated. The following criteria are proposed: 1) Exposure to a systemically administered drug, 2) Sharply demarcated erythema of the gluteal/perianal area and/or V-shaped erythema of the inguinal/perigenital area, 3) Involvement of at least one other intertriginous/flexural fold, 4) Bilaterally or symmetrically affected areas, and 5) Absence of systemic symptoms and signs.

Friday, 11 June 2004
11:20–12:45

FS10

Occcupational dermatoses

Chairs: Agustin Alomar, Spain & Marléne Isaksson, Sweden

FS10.1

Current spectrum of contact allergens in metalworking fluids

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The current spectrum of contact allergens in metalworking fluids (MWF) is illustrated based on (I) recent patch test data from the Information Network of Departments of Dermatology (IVDK) concerning metalworkers tested in 2002/2003 due to suspected MWF dermatitis, (II) a study on occupational contact allergies performed in the IVDK 1999–2001 (FaSt study), (III) a patch test study in five centres of the German Contact Dermatitis Research Group (DKG) with components of MWF not routinely tested, and (IV) information from the interdisciplinary task force on allergy diagnostics in the metal branch. Potential allergens are found in various MWF components, mainly in emulsifiers, rust preventing agents, preservatives, and anti-wear-additives. Various special additives also may contain potential allergens. Currently, the most important MWF allergens are: – oxidation products from resin acids, e.g. abietic acid, in distilled tall oil, a frequently used base material of MWF. Contact allergy to these is detected by patch testing with colophony. – monoethanolamine, diglycolamine – used as rust preventing agents and emulsifiers. – formaldehyde and various formaldehyde releasers, mainly oxazolidine derivatives – used as biocides. Other biocides, e.g. Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI), Benzisothiazolinone (BIT) or Iodopropynyl butylcarbamate (IPBC) are also used in MWF and should hence be tested routinely. While odour masks for MWF are available, little is known about the extent of their usage. However, this allergen source should be considered in cases of fragrance allergy. Cobalt apparently is a relevant MWF allergen only in carbid metal processing.

FS10.2

Occupational contact dermatitis in health care workers

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Objectives: 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.

Aim of our study was to analyse the reports of OSD in Health care workers (HCW) in the register of OSDs of 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 5285 cases of OSD were assessed prospectively and registered from

1990–1999. Data of total employment were provided by the German Federal Employment office. ***Results:*** A total of 3097 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 accounted for 7.3 per 10,000 workers. In 1990 the incidences in this occupational group accounted for 11.4%, in 1999 for 5.0% per 10,000 workers with highest incidences in younger age groups. In the evaluated health care workers from the register of OSD in Northern Bavaria 54% (n = 260) had irritant and 51% (n = 244) had allergic contact dermatitis including 19% (n = 89) who suffered from both. Of the 482 HCW 13% had occupational relevant Type IV allergy to glutaraldehyde, 12% to thiurams, 6% to nickel (II) sulfate, 4% to formaldehyde or fragances, respectively, 2% to thimerosal, potassium (II) chloride, chloromethyl-isothiazolone and p-phenylendiamine (free base) each.
Conclusions: HCW belong to the occupational groups at exceedingly high risk for OSD. Higher frequencies of OSD occur in younger age groups. Irritant and allergic contact dermatitis are equally common causes of OSD in HCW. Sensitization to certain allergens (e.g. glutaraldehyde, thiurams and latex) are most often of occupational relevance, whereas others although frequently found (e.g. sensitization to nickel-II-sulfate, cobalt-II-chloride, fragance-mix) rarely are of occupational relevance.

FS10.3

Occupational allergic contact dermatitis from drugs in pharmaceutical workers

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Occupationally-induced reactions to medicaments occur in two exposed groups. The group that we discuss consists of employees of pharmaceutical and chemical companies involved in the production of drugs. We describe some patients who developed allergic contact dermatitis to specific drugs. Two of them we related to occupational exposure to simvastatin and other to n-acetyl-cysteina. Also one to diphendiprone. The diagnosis of airborne contact dermatitis was confirmed by patch test in all cases. We will do a review in this aspect on occupational contact dermatitis to foccus attention on the increasing importance of this aspect in pharmaceutical workers.

FS10.4

Colophony allergy as a cause of occupational dermatitis

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Objective and methods: To evaluate the importance of occupational colophony exposure among occupational dermatitis patients we analyzed data of occupational dermatitis caused by colophony on the basis of the Finnish Register of Occupational Diseases (FROD) and among the colophony allergic patients studied in the Finnish Institute of Occupational Health (FIOH)in 1993–2002. Finnish physicians are obligated to report cases of occupational diseases to the FROD. Insurance companies remit patients to FIOH, mainly recommended by company doctors or dermatologists.
Results: Altogether 128 cases (68 females and 60 males) of occupational dermatitis caused by colophony were reported to the FROD since 1993 to 2002 accounting for 3.4% of all occupational allergic contact dermatitis cases and another 67 had it as a second diagnosis. Mean age of the patients was 42 years, being lowest among engineering workers (34 years) Among colophony allergic patients studied in FIOH 46/89 had an occupational dermatitis caused by colophony; 14 of them as a second diagnosis. Engineering, metal working, wood working, agricultural or medical work were most common occupations. Among colophony allergic patients without an occupational dermatitis (22) or an occupational dermatitis caused by other causes (21)working with food materials and agricultural work were most common. Principal causative agents of occupational allergic contact dermatitis from colophony were cutting fluids, soldering fluxes, tall soft soap, adhesives and varnishes. Variable individual sources were occasionally detected. Mean exposure time was 12 years.
Conclusion: Occupational dermatitis caused by colophony is difficult to diagnose, since non-occupational colophony exposure is common.

FS10.5

Occupational allergic contact dermatitis from isothiazolines

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VUMC University Medical Centre, Amsterdam, The Netherlands

Several employees of a construction adhesives-producing plant developed skin problems. Within

few weeks, 4 out of 12 workers got itchy eczematous lesions at the face, lower arms and hands. All of them reported on a work-relationship with recoveries during holidays and sick-leaves. This prompted the responsible occupational physician to contact our occupational dermatological clinic for further examination. First, we got an overview of the chemicals and pathways used for the production of the highly specialized plastic products. After working place examination, extended medical histories of the employees were taken. All affected workers were patch tested with the European Standard series, epoxy resins, preservatives and own working materials. After an occlusion time of 48 hours, skin tests were read at day 2 and 4 according to the ICDRG guidelines. Examination of the plant revealed that all affected workers were employed at the blending unit where, in particular dusty, ingredients were mixed. Few months prior to the development of skin problems, 2-n-octyl-4-isothiazolin-3-one (OIT) preservative had been introduced in the production pathway in partial exchange for chloro/methylisothiazolin-3-one (CIT/MIT). Personal protection measures were rarely provided.

All 4 tested workers were found patch test positive to CIT/MIT, 3/3 positive to OIT and 1/3 positive to 1,2-benzisothiazoloin-3-one (BIT) and methyldibromoglutaronitril. Industrial usage of preservatives can result in frequent sensitisation of exposed employees. Adequate protection and prevention advices are required. This study highlights the need for extended (occupational) medical histories and working place examination to identify individual risk factors and to trace potential hazards at the working place.

FS10.6

10 years experience with the Allergen Bank

Klaus Ejner Andersen
Department of Dermatology, Odense University Hospital, Odense, Denmark

The Allergen Bank supplies dermatologists on request with special contact allergens for aimed patch testing of suspected contact dermatitis patients. Easy access to patch test materials beyond the standard patch test series makes it possible for the dermatologists to make an early diagnosis of special cases of allergic contact dermatitis. The Allergen Bank was established in 1992, and the concept described in Acta Derm Venereol 1996; 76: 136–140. The Allergen Bank service is financed through an annual subscription fee, and about 60 Danish dermatologists are currently subscribers.The use of the service has increased steadily over the years. In average, the dermatologists order 6–7 allergens for each patient. The dermatologists use pattern of the bank service varies considerably, probably reflecting what they have available in their clinic of extra allergens beyond the standard series, as well as their patient selection and interest in contact dermatitis. Based on the test results reported back from the dermatologists to the Allergen Bank a total of 197 positive reactions from 107 different contact allergens were found in 2002. This is a yield of approximately 7% positive patch tests related to the number of allergens ordered. The pro's and con's of the Allergen Bank function will be reviewed.

FS10.7

A surveillance network for occupational contact dermatitis utilizing general practitioners

Rosemary Nixon[1], T Keegel[1,2], A Noonan[1], H Saunders[1], K Frowen[1]
[1]Occupational Dermatology Research and education Centre, Skin and Cancer Foundation, Melbourne, Victoria, Australia
[2]Department of Public Health, University of Melbourne, Melbourne, Victoria, Australia

Objectives: The Surveillance by General Practitioners of Occupational Contact Dermatitis Project (Spot) has been designed to provide disease estimates for occupational contact dermatitis within a defined geographic area in Melbourne, Australia.
Method: Spot collected reports of occupational contact dermatitis from four separate sources: general practitioners, dermatologists, a Dermatology Outpatient clinic, and an Occupational Dermatology Clinic. Case definition was stratified into two levels, suspected and confirmed. All cases of suspected occupational contact dermatitis reported to Spot were assessed and required to undergo diagnostic confirmation, including appropriate patch testing by an occupational dermatologist. The rates generated by Spot were compared to the rates generated by Victorian workers' compensation data (Victorian Work Cover Authority) for "Contact dermatitis and other and unspecified dermatitis."
Results: To date, a total of 125 suspected cases have been reported to Spot. 56 cases of occupational contact dermatitis have been confirmed with an incidence rate of 12.5 per 100,000 full-time workers and a prevalence rate of 28 per 100,000. This can be compared to the rate from Victorian WorkCover Authority of 4 per 100,000

(with information not available for incidence or prevalence).
Conclusions: Although limited by resources, clinician and worker participation rates, Spot provides a better estimate for occupational contact dermatitis in an Australian urban setting than that currently available through workers' compensation statistics. The information generated by Spot will provide an important contribution towards the characterisation of occupational contact dermatitis in Australia.

FS10.8

Prevention of occupational contact dermatitis

Thomas L Diepgen
University of Heidelberg, Department of Clinical Social Medicine, Heidelberg, Germany

Occupational contact dermatitis (OCD) take the first rank of all occupational diseases in many countries. The incidence rate is believed to be around 0.5 to 1.9 cases per 1000 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. Occupational Contact Dermatitis (OCD) has become an issue of increasing importance world-wide, 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 occupational contact dermatitis in Europe, demonstrates possibilities of prevention based on recently conducted epidemiological studies, and ends by highlighting important future health service and population research issues. The following questions will be discussed:

- How common are OCD in different industries and what is the extent of underestimation
- What kind of regulations are needed to prevent OCD
- How to deal with high risk individuals (atopics)

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

Friday, 11 June 2004
13:45–14:15

KL05

Keynote Lecture

Chair: Halvor Möller, Sweden

The value of skin testing in the study of drug eruptions

Margarida Gonçalo,
Portugal

Abstract not available at the time of printing.

Friday, 11 June 2004
14:20–15:30

FS11
Plant dermatitis

Chairs: Evy Paulsen, Denmark & Christopher Lovell, UK

FS11.1

Primula obconica – a falling allergen

Maureen Connolly[1], J Mc Cune[2], E Dauncey[2], C Lovell[1]
Bristol Royal Infirmary, Bristol, UK Centre for Economic Botany, Royal Botanic Gardens, Kew, UK

Objective: We believe the incidence of primula contact allergic dermatitis has fallen since the introduction of primin-free primula onto the European market and thus our study aims were twofold. Firstly to see if the incidence of primula contact allergic dermatitis was truly on the decline and secondly to confirm the presence and document retailers' knowledge and awareness of primin-free primula in the UK.
Methods: A questionnaire was sent to 22 contact dermatitis departments throughout the UK and Ireland looking at the number of primin positive patch tests in the years 1995/96, 1998, 2000 and 2002 compared with the total number of patch tests. 10 seed suppliers and 12 plant retailers were asked to complete a telephone survey.
Results: We showed a significant fall in the yearly incidence of contact allergy to primin from 0.785% in 1995/96 to 0.457% in 2002. This downward trend was statistically significant ($p = 0.001$). The telephone survey showed 90% of seed suppliers were aware that the older varieties of P. obconica could cause an allergic reaction whereas only 60% of them were aware that new primin-free varieties were now being bred. 50% of suppliers were in fact selling these primin-free varieties with 60% of them stocking a primin-free variety exclusively. 90% of retailers were not currently selling any variety of P. obconica.

Conclusion: Our study shows that the incidence of primula contact dermatitis is falling. The overall trend is moving towards primin-free varieties provided they continue to be horticulturally viable long term.

FS11.2

Contact allergy to herbal teas from Asteraceae plants

Kerstin Mårtensson[1], M Hindsén[1], B Gruvberger[1], H Möller[1], Å Svensson[2], M Bruze[1]
[1]Department of Occupational and Environmental Dermatology, Malmö University Hospital, Malmö, Sweden
[2]Department of Dermatology, Malmö University Hospital, Malmö, Sweden

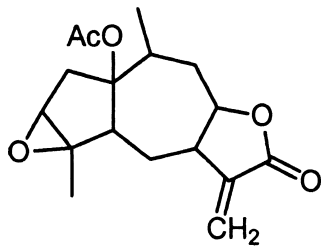
Objective: A possible contact allergy to herbal teas, in particular those derived from the Asteraceae plant family, was investigated in patients allergic to sesquiterpene lactones (SL).
Method: Twenty patients with a contact allergy to SL were recalled and patch-tested with aqueous, ethanol and acetone extracts of 8 different herbal teas based on Asteraceae plants as well as with parthenolide and other SL.
Results: In 18/20 patients with SL allergy there were positive test reactions to the Asteraceae teas, mainly to those based on German chamomile, dandelion and milfoil. Among the SL, parthenolide was the most frequent co-reactor.
Conclusion: Most patients with a contact allergy to SL are allergic to commercial teas derived from the Asteraceae plant family as well.

FS11.3

Contact allergy to the sesquiterpene lactone calocephalin

Monica Hindsén[1], LP Christensen[2], E Paulsen[3]
[1]Department of Occupational and Environmental Dermatology, Malmö University
[2]Hospital, Malmö, Sweden
[3]Department of Food Science, Danish Institute of Agricultural Sciences, Research Centre Aarslev, Aarslev, Denmark
[4]Department of Dermatology, Odense University Hospital, Odense, Denmark

Background: A 63-year old female gardener developed eczema on her hands, arms and face. She suspected cushion bush, Calocephalus brownii F. Muell., a plant introduced in Sweden by her. This plant belongs to the Asteraceae family.
Methods: Patch testing with our standard series, plant series and acetone extract of cushion bush. The predominating sesquiterpene lactone (SL) calocephalin identified in the plant extract was patch tested in the patient and 20 controls. Calocephalin was isolated from the plant extract of cushion bush by column chromatography and preparative high-performance liquid chromatography (HPLC) and identified by mass spectrometry and nuclear magnetic resonance (NMR) spectroscopy.
Results: The patient was negative to the standard series but positive to parthenolide and to the cushion bush extract. Likewise, positive reactions to cushion bush extracts were seen in SL-mix positive but not in negative patients. Parthenolide was not present in the plant extract as shown by gas chromatography-mass spectrometry (GC-MS) analysis, while the guaianolide calocephalin was identified as the major SL. The patient tested positively to calocephalin while the controls tested negatively.
Conclusion: The plant cushion bush can cause occupational allergic contact dermatitis and the major contact sensitizer in the plant is the SL calocephalin.



Calocephalin

FS11.4

Garlic-fingered chefs – a study of contact dermatitis to garlic in curry chefs

Viginia Hubbard, P Goldsmith
Barts and The Royal London NHS Trust, Department of Dermatology, London, UK

Allergic contact dermatitis to garlic is described in caterers and can be an important occupational hazard.

Our department serves an area with a large Bengali population. We noted a relatively high number of curry chefs and housewives have hand dermatitis. We wanted to see whether garlic was an important sensitiser in this group.

We use diallyl disulphide to test for garlic sensitisation. We reviewed the notes of all patients who had been patch tested to this over a 12 month period. We recruited further curry chefs by visiting local restaurants. We also asked local GPs to refer suitable patients for patch testing.

We identified 26 patients who were patch tested to diallyl disulphide. Of this group, 13 were curry chefs and 11 housewives. 4 patients were found to have an allergic reaction to diallyl disulphide – all were chefs. All had presented with dermatitis of the non-dominant hand. 1 was atopic.

Advice was given on avoidance of contact with garlic and onion (a cross-reactant). Unfortunately this proved difficult in practice. 1 patient required acitretin with a good result. 1 patient responded well to hand PUVA.

Previous studies have shown a high incidence of occupational garlic dermatitis but some of these have tested with garlic plant or extract which can be a powerful irritant and produce misleading Results: Diallyl disulphide, allylpropyl disulphide and allicin have been identified as the allergens in garlic. Diallyl disulphide is considered the main allergen. This study shows the importance of testing for garlic allergy in caterers.

FS11.5

Toxicodendron dermatitis in the United Kingdom

Stephen Walker[1] *J Williams*[1], *J Lear*[1,2], *M Beck*[1]
[1]*Contact Dermatitis Investigation Unit, Manchester, UK*
[2]*Department of Dermatology, Manchester Royal Infirmary, Manchester, UK*

We describe two cases of Toxicodendron dermatitis, one acquired in the United States but presenting in the United Kingdom, the other a recurrent dermatitis following importation to the UK. Poison ivy, poison oak and poison sumac are native to North America and belong to the genus Toxicodendron. This group of plants is of interest to the dermatologist because they contain a mixture of potent sensitisers which cause a severe allergic contact dermatitis. The dermatitis can present to the dermatologist in Europe after an individual has been in contact with the plant whilst visiting an endemic area. The plants have the potential to grow in the UK and it is therefore possible for an individual to be sensitised and subsequently to develop the rash without leaving the UK. A 35-year-old American man who lived in the UK visited his family in Marietta, Georgia USA. Shortly before his return to the UK he cut some plants back in his mother's garden. Two days following his arrival back in the UK he developed a widespread pruritic and painful vesicobullous eruption. He required admission for intensive potent topical corticosteroid therapy and the eruption settled over the next two weeks. The plant he had been pruning was subsequently identified as poison sumac (Toxicodendron vernix). A 54-year-old woman living in Wales was referred to the Contact Dermatitis Investigation Unit because during the summer months for the previous four years she had experienced an intermittent, intensely pruritic, vesicular and in parts linear eruption affecting her face, arms and legs. This responded slowly to potent topical corticosteroids. She is a keen gardener and suspected that it was related to a plant in her garden. She was patch tested to our Standard Series, Plant Series and all the plants in her garden. She showed ++ allergic reactions to sodium metabisulphite, propolis and a strong vesicular reaction to the leaf of one of the plants from her garden Inspection of the plant revealed that it had three leaflets per stem. She had taken a cutting whilst visiting friends in Pennsylvania in 1996 and on returning to the UK had planted it in her garden. It grew but had never flowered or produced seeds. Once the cause of her dermatitis had been confirmed our patient took the necessary protective measures and removed the plant including its roots from her garden. She has not experienced any further problems with her skin. She contacted her friends in the USA who knew precisely where she had picked the plant. A further specimen was taken to the local Conservation Office where it was confirmed to be poisonivy. Poison ivy and poison sumac belong to the genus Toxicodendron which is native to North America and Mexico. They cause an allergic contact dermatitis when there is exposure to a bruised portion of the plant. This leads to the oleoresin, urushiol coming into contact with the skin. 25–60% of North Americans are reported be allergic to poison ivy and its relatives. The importation of plants into the UK is restricted by law. It is clear that this plant grew in its new habitat but did not extend beyond the confines of the garden. With frequent and more extensive air travel it seems reasonable to speculate that similar occurrences have taken place and that plants not endemic to Europe should be considered in those with suspected plant dermatitis.

FS11.6

Contact dermatitis to Iris in a florist

Yves Dejobert[1], *L Arzur*[2], *A S Thellart*[2], *P Martin*[1], *M Torck*[3], *P Frimat*[2], *F Piette*[1], *P Thomas*[1]
[1]*Service de Dermatologie CHRU, Lille, France*
[2]*Institut de Médecine du Travail CHRU, Lille, France*
[3]*Pharmacie Centrale CHRU, Lille, France*

Objective: To detect a possible allergen in a florist with occupational dermatitis. Patient and methods: a 27-year-old atopic female working in a

greenhouse since 10 years presented with a 3 months history of severe eczema involving hands, face, eyelids and neck requiring a stop of the work. Tests were performed with European standard series (Trolab®), additional series, plant series, (Chemotechnique Diagnostics®) and flowers. Readings were performed at D2 and D3 according ICDRG criteria. Results: positive patch tests were parabens +/+ nickel sulphate ++/++ cobalt chloride −/++ palladium chloride ++/++ thiomersal ++/++, Iris petal ++/+. Then various colours of Iris were tested and pale blue, yellow and white petals were positive ++/++ but purple blue petal was negative. The proximal yellow part of purple blue petal and orange part of yellow petal were also positive ++/++. The leaf and pistil of Iris were negative. One control with a white Iris petal was negative. Then the patient presented flare up of her dermatitis in the presence of Iris, at home, without handling them, that could make suspect an airborne contact dermatitis. Even after examination by a botanist, the precise identificaton of these Iris was not possible. Positive patch tests to unspecified Iris (petal and leaf) have already been reported in a florist who was allergic to safflower (Van der Willigen A.H. and al, Contact Dermatitis, 1987, 17,184). Conclusion: this case could evoke the responsibility of anthocyans, which play a role in the colours, but essential oils or other components are also possible responsibles.

Friday, 11 June 2004
14:20–15:30

FS12

Plastics and rubber

Chairs: Kristiina Alanko, Finland & James S Taylor, USA

FS12.1

Allergic contact dermatitis from plastic gloves

Kristiina Aalto-Korte[1], K Alanko[1], ML Henriks-Eckerman[2], T Estlander[1], R Jolanki[1]
[1]Finnish Institute of Occupational Health, Helsinki, Finland
[2]Turku Regional Institute of Occupational Health, Turku, Finland

Plastic gloves are made of polymers including polyvinylchloride, polyvinylalcohol, polyethylene and polyvinylacetate. Additives such as plasticizers, stabilizers, UV light absorbers, fungicides, bactericides, flame retardants and colourants are added to the polymer, and these are potential allergens. Contact allergy to plastic gloves is rare. The allergen responsible for the sensitization usually remains unknown. An organic pigment, Irgalite Orange F2G, and bisphenol A have both caused contact allergy from household-type PVC gloves. 1 patient with allergic contact dermatitis from his PVC gloves reacted also to tricresyl phosphate and triphenyl phosphate, chemicals known to be used as plasticizers in PVC. A plasticizer, di(2-ethylhexyl) phthalate (DOP), caused 1 case of contact urticaria from the vinyl chloride slip guard of cotton gloves. 1 patient with contact urticaria from his polyethylene gloves reacted to 3 antioxidants, octadecanoic acid methyl ester and di-tertiary butyl phenol of the gloves on scratch testing. We report 3 additional cases of allergic contact dermatitis from PVC gloves due to bisphenol A. 2 of the patients reacted also to para-tertiary butyl catechol, a polymerization inhibitor in PVC. In chemical analysis, the connection between sensitization to para-tertiary butyl catechol and the use of vinyl gloves could not be proven. We analysed 16 brands of disposable PVC gloves for medical use, covering at least 80% of the Finnish market. We found a very small amount of bisphenol A in 1 brand, and no para-tertiary butyl catechol in any of the gloves. However, bisphenol A should be remembered as a possible allergen in PVC gloves.

FS12.2

Occupational allergic contact dermatitis from UV-cured adhesive

Stefano Francalanci[1], S Giorgini[1], M Gola[1], S Sestini[2], S Moretti[3]
[1]Unit of Allergological Dermatology, Florence, Italy
[2]I Dermatological Clinic, Florence, Italy
[3]II Dermatological Clinic, Florence, Italy

A 35-year-old woman presented with a 8-month history of scaling, hyperkeratotic and fissured lesions of the fingertips of the first three fingers of both the hands. She referred the healing of the dermatitis during the summer holidays. She was employed in a small firm where she was used to glue together silver components with glass ones of decorative pieces. For this aim, she applied a glue (Loxeal UV 30–20) cured by exposition to UV light coming from a proper lamp. The material safety data sheet (MSDS) indicated that the glue contained hydroxyethyl methacrylate (HEMA) and hydroxypropyl methacrylate (HPMA). Patch tests performed with the standard SIDAPA

series gave negative results; patch tests carried out with an additional one (acrylic adhesive series) showed positive reactions towards glue components (HEMA,HPMA) and towards other acrylates (possible cross-reacting). An inspection performed in the work-place showed that the patient was in contact with the glue not only when she applied it on the components, but particularly when she handled the bottle cap (splashed with the glue) in its opening and closing. After the changing of her occupation, the patient has not presented relapse of the dermatitis. The UV-cured acrylic resins are known for some time to be a frequent cause of occupational allergic contact dermatitis in dentists and in printing industry. The case reported shows a different exposition source towards these resins, i.e. from UV-cured acrylate adhesive employed for sticking metal pieces with glass ones.

FS12.3

Occupational contact dermatitis to phenol formaldehyde resins

Michael H Beck
Contact Dermatitis Investigation Unit, University Department of Dermatology, Dermatology Centre, Hope Hospital, Manchester, UK

Phenol formaldehyde resins were the first synthetic plastics to be used commercially, being patented as Bakelite in 1907.There are two main types of phenol formaldehyde resin [PFR], resols [phenol reacted with excess formaldehyde in alkaline conditions] and novolacs [formaldehyde reacting with excess phenol in acid conditions]. Novolac resins may require cross-linking agents to cure them but resol can be hardened by heat alone. Usually sensitisation occurs when the resins are handled in partially condensed form. Modifications and additives to these resin systems increase the range of potential allergens. PFRs have electrical resistance and binding properties resulting in their widespread use in electrical appliances, glues, laminated floorboards, plywood, fibreglass including insulation, brake linings, clutch facings, grinding wheels, foundry sand moulds, abrasive cloths and papers, plastic moulds, telephones and steering wheels.
Study aim: To analyse retrospectively the causes, occupations and investigations of patients demonstrated to have dermatitis from occupational contact with PFRs.
Summary of Results: 27 dermatitis cases were identified (4 irritant and 23 allergic). The commonest causes were from contact with PFR used in fibreglass materials, in binders e.g. brakes, foundry sand, and from adhesives.
Conclusions: Patients should be investigated for contact allergy by patch testing them with their own resins. PFR-2 identified by M. Bruze was the best commercially available allergen to screen for contact allergy. Concomitant allergy to formaldehyde and PTBP formaldehyde resin is rare. The possibility of allergy to reactive diluents should be considered in those exposed to epoxy novolac systems.

FS12.4

An analytical method for p-tert-butylphenol-formaldehyde resin

Erik Zimerson
Department of Occupational and Environmental Dermatology, University Hospital, Malmö, Sweden

p-tert-Butylphenol-formaldehyde resin (PTBP-F-R) is frequently reported to give positive patch test reactions with uncertain clinical relevance. A possible explanation is deficient knowledge of the sources of exposure. An analytical method for PTBP-F-R could be used to investigate products in the patient's environment. Most individual PTBP-F-R substance constitute less than 1% w/w of the resin contributing to analytical difficulties.
Objective: To develop an analytical method for PTBP-F-R and to use it to investigate some patients' products.
Methods: 10 identified PTBP-F-R substances in silylated form were used as reference substances in gas chromatography-mass spectrometry (GC-MS) analysis.
Results: The recording of ion chromatograms for the 3 largest mass peaks in the MS for each reference substance was used to avoid interference of disturbing substances. Demonstration of a PTBP-F-R substance was defined as the simultaneous detection the 3 defined mass peaks at the expected retention time and with the same relative intensities as found with the corresponding reference substance. A minimum criterion for the demonstration of PTBP-F-R was the demonstration of 3 PTBP-F-R substances. PRBP-F-R was demonstrated in watchstraps, shoes, glues and ECG-electrodes. p-tert-Butylcatechol, a PTBP-F-R substance but also an antioxidant, was demonstrated in: an ECG-electrode, watchstraps, a prosthesis, a protective mask, a glue, an oil for bikes and in a nail polish.
Conclusion: An analytical method for PTBP-F-R was developed, which when applied to products could show the presence of PTBP-F-R substances and PTBP-F-R in products and indicate contact of clinical relevance.

FS12.5

Chemical analysis of MDI in petrolatum patch test preparations

Malin Frick[1], E Zimerson[1], D Karlsson[2], Å Marand[2], G Skarping[2], M Isaksson[1], M Bruze[1]
[1]Department of Occupational & Environmental Dermatology, Malmö University Hospital, Malmö, Sweden
[2]Work Environment Chemistry, Stockholm University, Hässleholm, Sweden

Objectives: Diphenylmethane-4,4'-diisocyanate (MDI) is a very common isocyanate which is used in the plastics industry in its' polymeric form in the production of polyurethane products such as rigid and flexible foams, elastomers (rubbers) and coatings. Previous reports on MDI-related contact allergy have shown a pattern where patients seem to react to their own MDI-based work material but not to the commercial patch test preparations of MDI. Therefore, we performed chemical analysis of 14 commercial patch test preparations of MDI.
Materials and Methods: MDI preparations from 8 European and 4 American dermatology departments as well as preparations obtained from 2 major European suppliers of patch test allergens were analyzed with respect to MDI content using liquid chromatography mass spectrometry (LC-MS).
Results: None of the preparations obtained from dermatology departments contained more than 12% of the concentration stated on the label. In most cases the MDI content was only a few percentages or less of the concentration stated. In only 1 commercial preparation the MDI content came close to the declared concentration.
Conclusion: 7 of the 14 preparations were analyzed before the expiry date. Yet, only 1 of them contained a concentration that came close to that stated on the label. Thus, using these preparations patients will be tested with a much lower concentration than intended leading to a high risk of false-negative reactions and thereby underdiagnosis of allergic contact dermatitis from MDI.

FS12.6

Sensitizing capacity and cross-reactivity of phenyl glycidyl ether

Ann Pontén, E Zimerson, M Bruze
Department of Occupational and Environmental Dermatology, University Hospital, Malmö, Sweden

Phenyl glycidyl ether (PGE) is an aromatic reactive diluent used in epoxy resin systems. The sensitizing capacity of PGE, as well as the cross-reactivity between PGE and the most important contact allergens in epoxy resins based on bisphenol A and bisphenol F, i.e. diglycidyl ether of bisphenol A (DGEBA) and the 3 isomers of diglycidyl ether of bisphenol F (p,p′-DGEBF, o,p′-DGEBF, and o,o′-DGEBF), were investigated in a guinea pig maximization test (GPMT). Statistical significance was calculated with one-sided Fisher's exact test. PGE was found to be a strong sensitizer (24/24 sensitized animals, $p < 0.001$). Induction with DGEBA resulted in a statistically significant number of animals reacting to PGE ($p = 0.006$), but when induced with PGE, the animals did not react significantly to DGEBA. When induced with PGE, significant numbers of animals reacted to p,p′-DGEBF (13/24 animals, $p = 0.0011$) and o,p′-DGEBF (11/24 animals, $p = 0.004$). Induction with p,p′-DGEBF and o,p′-DGEBF resulted in a high number of reacting animals when tested with PGE (23/24 animals, $p < 0.001$ for both isomers). No statistically significant cross-reactivity between PGE and o,o′-DGEBF was found.
Conclusion: According to our results in the GPMT, sensitization to DGEBA, which is the main constituent in the most common epoxy resin, may result in contact allergy to PGE, whereas sensitization to PGE seldom causes contact allergy to DGEBA. Sensitization to PGE may cause contact allergy to epoxy resins based on bisphenol F.

Friday, 11 June 2004
16:00–17:00

FC03

Free Communication – Occupational dermatoses II

Chairs: Arieh Ingber, Israel & Elisabeth Held, Denmark

FC03.1

Experience from joint occupational health/ dermatology clinics

Yat Wing Wong, S Powell
Churchill Hospital, Department of Dermatology, Oxford, UK

Background: A monthly consultant led occupational health/dermatology clinic was started in 1999 providing rapid access to staff with suspected occupational skin disease including natural rubber latex (NRL) allergy and teaching for the occupational health staff.

Objectives: To evaluate the characteristics and outcome of staff attending this clinic and to assess patient satisfaction.
Methods: A retrospective case note survey was performed from staff attending the clinic from 1999 to 2002. A questionnaire was sent to them >3 months following consultation.
Results: A total of 116 patients were identified (12 male, 104 female), and 85 (73%) were nurses. 77 (66%) patients were referred with hand eczema (HE). Of the 45 patients referred with adverse reactions or exacerbation of hand dermatitis following the use of latex gloves, only 4 had positive prick tests and were considered to have NRL allergy. Patients with significant HE or occupational exacerbation of HE were referred for patch testing (n = 36). Of the remainder, most could be discharged after a single visit. 49/95 (52%) questionnaires were returned, 34/45 (76%) patients found the consultation useful. As a separate study, the data recorded within the patch test clinic looking at health care workers (HCW) referred both from this clinic and from other sources was analysed. This showed relevant positive patch tests in 16/49 (33%) patients. In 55/99 (56%), an occupational cause was likely.
Conclusion: Occupational skin disease in HCW is common, attendance at the clinic was beneficial and a single visit was sufficient in most cases.

FC03.2

Cumulative incidence of self reported skin disease in hydrotherapists working in swimming pools

Aneta Lazarov[1], *K Navo*[2], *A Pardo*[2], *P Froom*
[1]*Contact Dermatitis Clinic, Meir Hospital, Kfar Saba, Sackler Faculty of Medicine, Tel Aviv, Israel*
[2]*National Institute of Occupational and Environmental Health, Israel*

Objective: To assess the cumulative incidence and characteristics of self reported skin disease in hydrotherapists.
Methods: Hydrotherapists, who had completed a hydrotherapy training course answered a questionnaire in reference to newly appeared skin disease. Data were analyzed statistically.
Results: 190 subjects presently working as hydrotherapists were studied. Of them 75.8% were female and 24.2% were male. 80% of the hydrotherapists worked up to 10 000 cumulative hours defined by the formula: working hours per weeks × number of weeks per year × years of work in the pool. 85 of the subjects (45%) reported on the development of skin disease for the first time after starting work at the swimming pool. 21 (11.8%) had a preexisting skin disease. The most frequent symptoms included pruritus, burning, stinging, erythematous patches and xerotic skin on the extremities, trunk and folds. A statistically significant relationship between the cumulative working time and the incidence of dermatological pathology compatible with contact dermatitis was found.
Conclusions: The incidence of self reported skin diseases, developing for the first time or due to exacerbation of preexisting dermatological conditions, in hydrotherapists working in swimming pools is high. Statistically significant relationship between the cumulative hours of immersion in the pool and the incidence of the dermatological pathology was observed suggesting a dose response relationship between exposure and effect.

FC03.3

Identification of subjects with atopic dermatitis in questionnaire studies

Karen Frydendall Jepsen, M-A Flyvholm, K Mygind
National Institute of Occupational Health, Copenhagen, Denmark

The performances of three different questions from The Nordic Occupational Skin Questionnaire (NOSQ-2002) were compared with respect to their ability to identify subjects with atopic dermatitis. NOSQ-2002 was used in an intervention study on the prevention of work related skin diseases among gut cleaners. The questions were: ''Have you ever had an itchy rash that has been coming and going for at least 6 months, and at sometime has affected skin creases?'' (A1), ''Have you ever had eczema on the fronts of the elbow or behind the knees?'' (S5a), and ''Have you ever had ''childhood'' eczema?'' (S5b). Question A1 is the single UK-working party question on atopic dermatitis; questions S5a & S5b are national atopic dermatitis questions previously used in different Nordic studies. A total of 255 of 622 (41%) gut cleaners answered ''yes'' to question A1. Questions S5a and S5b gave rise to 14% and 5% positive answers, respectively. The high frequency of positive answers to question A1 could be due to the occupational exposure of gut cleaners. Their working environment is wet and often involves both forearms and hands, hence often leading to eczema of elbow creases. In conclusion, compared to other Danish studies

the UK question seems to lead to over-reporting. Question S5a seems to give a reliable frequency of atopic dermatitis in adult populations at risk for work-related skin diseases.

FC03.4

Eczema, skin symptoms and risk factors among hospital employees

Bodil Bach[1], M-A Flyvholm[2], E Villadsen[2]
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Hospital employees and especially nurses have a high frequency of work-related skin diseases. The purpose of the present study was to collect baseline data in order to plan an intervention project with focus on skin problems among different hospital job groups reporting high frequencies of work related skin problems or eczema. Self-administered questionnaires based on a standardized questionnaire for work-related skin diseases and exposure (NOSQ-2002) were used. A total of about 1.900 employees from all job groups at the hospital where invited to participate. Due to anonymous distribution of the questionnaires it was not possible to administer reminders. The overall response rate was 65%. Among the 1.246 respondents the frequency of self-reported eczema within the last year varied between different departments from 7% to 44%. Assessed by job group the eczema frequency varied from 8% to 31%, with the highest frequency found among nurses and assistant nurses.

FC03.5

Characteristics of wet work in nurses

Frank Jungbauer, F Steenstra, PJ Coenraads
Academic Hospital Groningen, Department of Dermatology, Groningen, The Netherlands

Background/objectives: The health care sector is known for its high prevalence of hand dermatitis, mainly because of the high exposure to wet work in nursing activities. Wet work can be activities with wet skin and activities with glove use (skin occlusion). A prevention program to reduce wet work exposure should be based on knowledge about activities that are components of wet work. We observed the frequency and duration of skin exposures to irritants with nursing activities.
Method: Duration and frequency wet work activities were assessed in parts of the health care sector: 53 randomly chosen nurses were observed during their morning shift. Hand skin exposure to water, soap/detergents and occlusion by using gloves were recorded during 112 different 8-hour morning shifts.
Results: In nursing wet work activities make up 9% (dialysis ward), 16% (regular ward) and 24% (I.C.-unit) of the duration of one shift. On a regular ward duration of wet work is mainly divided into 34% patient washing, 31% glove use and 26% hand washing. These main wet work activities have a short exposure cycle of 1.4–3.6 minutes. Hand washing, excluding the use of hand alcohol, and patient washing (without gloves) form both one third of the frequency of wet work activities.
Conclusions: Wet work activities take up a substantial portion of nursing activities and are characterised by frequent short-term exposures. Effective prevention programs on reducing the risk of hand dermatitis in nursing should primarily focus on the high frequencies of hand washing and patient washing. Using gloves in the procedure of patient washing will reduce the frequency of exposure to water and soap with 24%, at the expense of increasing exposure to occlusion by these gloves.

FC03.6

Exposure of the hands to wet work in nurses

Frank Jungbauer, G Lensen, PJ Coenraads
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Background/objectives: Prevention of hand dermatitis among nurses can be achieved by reduction of wet work exposure. Kwodledge about the amout of wet work in nursing is import implementing hand dermatitis prevention plans. Wet work exposure in nursing can be assessed by questionnaire or observation.
Method: Duration and frequency of wet work activities were assessed by a questionnaire in a population of 1471 nurses.In addition a randomly chosen sample of 53 nurses from this population was observed on duration and frequency of wet work during 112 different morning shifts.
Results: questionnaire: wet work between 26 minutes (at a dialysis ward) and 100 minutes (in nursing homes). For frequency a range between 12 and 21 episodes of wet hands during morning shifts was reported. In nursing homes and regular wards gloves were reported to be used less than once during a shift.
Observation: A duration of wet work of 10 minutes (dialysis ward), 28 minutes (regular ward) and 19 minutes (I.C.-unit) and 45 minutes in a nursing home. Frequency: between 19 and 43 episodes of wet hands during morning shifts.

Conclusions: A questionnaire does not accurately assess the quantity of wet activities; it overestimates the duration of wet work and underestimates the frequency of wet work. On regular wards the exposure to irritants is mainly associated with the frequency of wet hands instead of the duration of wet hands. On specialised care units skin exposure is mainly a matter of occlusion by gloves.

Friday, 11 June 2004
16:00–17:00

FC04

Free Communication – Cosmetic & irritant dermatitis

Chairs: Walter Larsen, USA & Genovaite Lapinskaite, Lithuania

FC04.1

Some new and unexpected allergens in cosmetics

An Goossens
Katolieke Universiteit Leuven, Dermatology (Contact Allergy Unit), Leuven, Belgium

Labels on cosmetics with statements such as 'recommended by dermatologists', 'allergy-tested', 'hypo-allergenic', and more recently 'for use on intolerant' or for 'sensitive skin' have become very popular. Indeed, many ingredients are used precisely because of their low irritancy potential. However, this does not preclude the occurrence of contact allergic reactions from such cosmetic products. During the last few months several of these substances have been identified as allergens. Examples are: – Alkylglucosides, e.g. coco-, decyl-, and laurylglucosides, which are condensation products of the corresponding fatty alcohols with glucose, are widely used as emulsifiers in skin-care products, mild surfactants and cleansing agents, as well as in fragrance products, hair dyes, sunscreens and tanning products. – Ethylhexylglycerin (syn.: octoxyglycerin) is used as a skin conditioning agent (and for miscellaneous purposes). – Methoxy PEG-17 and PEG-22/dodecyl glycol copolymers, which are alkoxylated alcohols and synthetic polymers, are used as emulsion stabilizers and suspending and viscosity-increasing agents, and also as skin-conditioning agents. – Butylene glycol and pentylene glycol are aliphatic alcohols with applications similar to those of propylene glycol, which is considered to be more irritant and allergenic. These agents are widely used in a wide variety of cosmetic products because of their solvent, humectant and antibacterial effects. Butylene glycol is also usd as a fragrance ingredient and as a skin conditioner.

FC04.2

Sensitization to propolis in 1255 children undergoing patch testing

Francesca Giusti, R Miglietta, S Seidenari
University of Modena and Reggio Emilia, Modena, Italy

Propolis is an ancient remedy well known for its beneficial properties. The aim of our study was to estimate the frequency of sensitization to propolis in our pediatric patch test population. 1255 children, 583 boys and 672 girls, aged from 7 months to 12 years, were patch tested for suspected allergic contact dermatitis with our pediatric series of 30 allergens including propolis. Out of these, 37% were affected by atopic dermatitis. Among the 1255 children tested, 113 (9%), 60 boys and 53 girls reacted to propolis. In subjects reacting to propolis the dermatitis involved the face in 4% of cases, the trunk in 3%, the hands in 2,2%, and the flexural skin folds of the limbs in 1,7%. The wider and wider use of propolis in "natural products" and biocosmetics, even in the pediatric age, could explain the high frequency of positive patch test responses to propolis we observed.

FC04.3

Allergy to phthalic anhydride/trimellitic anhydride/glycols copolymer in nail varnishes

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[2]Hôpital Pasteur, Paris, France
[3]Hôpital du Bocage, Dijon, France

Introduction: Nail varnishes are well-known sensitizers, and the most frequent allergen is nowadays tosylamide/formaldehyde resin (TFR). We present 3 cases of allergic contact dermatitis (ACD) due an unusual ingredient.
Case reports: The 1st patient presented with atopic dermatitis that progressively worsened, involving face and neck for several months. The 2nd patient had history of occupational allergy to glutaraldehyde, and presented with head and neck dermatitis. The 3rd patient had severe onycholysis and dermatitis of perionychium, face, neck and décolleté. European standard series was negative in all patients, as was TFR, (meth-) acrylates and cosmetic series when tested. Patch tests with patient's own varnish(es) were ++, and breakdown identified phthalic anhydride/trimellitic anhydride/glycols copolymer (PTG) as the allergen (tested 1 to 5% pet.).
Discussion: PTG results of condensation of phthalic anhydride, trimellitic anhydride, ethylene glycol, and neopentyl glycol monomers. It belongs to the copolymer class, and is used in

confection of nail polish and enamels, like TFR or phthalic anhydride/glycerine/glycidyl decanoate copolymer. Our patients had long lasting dermatitis, common in ACD to nail varnishes. Sensitivity was proved by patch testing with patient's own cosmetics. Allergic contact dermatitis to PTG seems to be rare, but has to be considered particularly in patients with negative standard patch tests. An alternative is the use of tosylamide/formaldehyde-based nail polish.

FC04.4

Impact of exposure duration on the induction of contact allergy

David A Basketter[1], N Gilmour[1], D Tonucci[2],
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[2]HillTop Research, Cincinnati, Ohio, USA

It has been demonstrated for a wide range of contact allergens that the degree to which sensitisation is induced is highly dependent on the dose per unit area of material applied to the skin. For a given skin area, the concentration of the contact allergen applied may be conveniently expressed as a percentage. However, although a number of other variables affecting induction have been examined, little attention has been paid to the impact of the duration of skin contact. For example, in the human repeated insult patch test the 9 inductions exposures may be applied for either 24h or for a combination of 48h and 72h, the latter ensuring continuous exposure during the 3 week induction period.

Under these latter conditions, it is known that the contact allergen p-phenylenediamine (PPD) sensitises quite efficiently; historical data with 1% PPD in petrolatum resulted in a sensitisation rate of 47/88 (54%). Applying the same dose per unit area, we examined the impact of reducing the exposure time to 9×5 minutes spaced over the same 3 week period. Under these conditions, PPD sensitised only 2/102 (2%) of subjects. The data suggest that one route to the limitation of the extent of contact allergy would be to limit the duration of skin exposure.

FC04.5

Influence of ambient meteorological conditions (temperature and absolute humidity) on a routine NaOH-irritation test in occupational dermatology

Swen Malte John[1], Hans-Joachim Schwanitz[1], Wolfgang Uter[2]
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[2]Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen/Nuernberg, Erlangen, Germany

Dry air and cold weather have been shown to influence skin irritability. We have recently proposed a routine irritant patch test to assess skin irritability in a standardised fashion in occupational dermatology. The effects of local meteorological parameters on this test were studied.

In 556 consecutive persons (276 female [median age: 36], 280 male [median age: 42]) with former occupational skin disease, who were seen for medico-legal evaluation from Feb. 2000 to Aug. 2003, a swift modified alkaline resistance test (SMART) was conducted simultaneously in the volar forearm and the dorsum of the hand. The test comprises a 0.5 M NaOH-challenge for 2×10 minutes with intermediate TEWL-measurements and a clinical assessment with an NaCl 0.9% control site. TEWL was measured according to current guidelines. The outcome of each patient was related to standardised data on the local temperature [T] and absolute humidity [aH] on the day of examination, obtained by the German Meteorological Service.

There was no relevant correlation between '*basal* TEWL' or 'TEWL *after* NaOH' and 'aH' or 'T', respectively. There was no association between meteorological conditions and demographic characteristics potentially relevant for susceptibility to irritants and, hence, no indication of confounding. In a logistic regression model increasing 'aH' (OR 0.91, 95% CI: 0.87–0.96 per 1 mg/l humidity) and 'T' (OR 0.94, 95% CI: 0.81–0.97 per °C) were associated with a decreasing likelihood of a clinically positive reaction to irritation.

Although there are only slight seasonal effects detectable, they should be taken into consideration when interpreting the test.

FC04.6

Characterisation of dendritic cell responses to ascaridol, an autoxidation product of tea tree oil

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[2]Department of Pharmacy, University Bonn, Bonn, Germany

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[4]*Department of Ecotoxicology/Toxicology, University Trier, Trier, Germany*

A large number of monoterpenes and their degradation products are likely skin sensitizing agents (Hausen et al., 1999). Terpenes are very common e.g., as constituents of cosmetics, food and other daily used products.

We investigated responses to the endoperoxide 1,4-epidioxy-2-p-menthen (ascaridol), an autoxidation product of tea tree oil, using monocyte derived dendritic cells (MDDC). Therefore, we isolated peripheral blood mononuclear cells (PBMC) from 9 healthy donors by the standard Ficoll-Paque gradient centrifugation.

Monocytes were isolated by adherence and incubated in media (RPMI 1640) containing GM-CSF (800 units/ml), IL-4 (1000 units/ml) and 10% autologous serum. The immature MDDC (day 6) were characterized by flow cytometry (CD1a+, CD14 −, CD40, CD45, CD80, CD83, CD86, HLA-DR and CCR-7) and incubated with various concentrations of ascaridol (1–70 μg/ml). After one hour incubation time LPS was added (1 μg/ml) for 23 h. Cell culture supernatants were collected after 24 h for cytokine analysis.

IL-12p40, IL-12p70 and prostaglandin E2 were measured by ELISA, TNF-alpha and IL-2 were measured by flow cytometry (FACS). Methods of the quantification of steady state mRNA levels were established for IL-12 and CCR7 (real-time RT-PCR). Ascaridol enhanced significantly IL-12p70 production (120% up to 396%) by MDDC as well as mRNA levels for IL-12 and CCR7. Moreover, we detected a distinct increase of TNF-alpha (110% up to 146%) secretion, IL-2 (135%) and PGE2 (102% up to 155%).

Totally, these results suggest that ascaridol may be a potent modulator of maturation and antigen presenting function of dendritic cells, and we performing further experiments to verify this hypothesis.

This study was supported by the Deutsche Forschungsgemeinschaft.

Saturday, 12 June 2004
08:45–09:15

KL06

Keynote Lecture
Chair: David A Basketter, UK

Gene expression profiling in allergic contact dermatitis

Ian Kimber[1], RJ Dearman[1], CA Ryan[2], GF Gerberick[2]
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[2]*Procter&Gamble Company, Miami Valley Laboratories, Cincinnati, OH, USA*

The successful acquisition of skin sensitisation requires orchestrated cellular and molecular interactions that collectively result in the induction of a cutaneous immune response of the required quality and vigour. Pivotal roles are played by epidermal Langerhans cells (LC), and by the mature immunostimulatory dendritic cells (DC) into which they mature. LC serve as sentinels of the adaptive immune system with responsibility for surveying changes in the local microenvironment and for processing antigen (and chemical allergens) encountered at skin surfaces. Following such encounters LC are mobilised and stimulated to migrate, via afferent lymphatics, to regional lymph nodes. While in transit they lose the properties of antigen processing cells and acquire instead the characteristics of mature DC that are able to interact effectively with, and present antigen to, T lymphocytes. To gain a greater understanding of the molecular events that induce and regulate cutaneous immune responses to chemical allergens, we have used microarray transcript profiling and related experimental approaches to characterise changes in gene expression and protein production associated with the development of skin sensitisation. Our attention has focused particularly on changes in the expression of mRNA and protein resulting from the interaction of chemical allergens with DC, and associated with the presentation of antigen to T lymphocytes.

Saturday, 12 June 2004
10:20–11:35

FS13

Intervention and prevention
Chairs: Tove Agner, Denmark & Manigé Fartasch, Germany

FS13.1

How to change habits at wet work – an implementation research study

Karen Mygind, V Borg, K Frydendall Jepsen, M-A Flyvholm

National Institute of Occupational Health, Copenhagen, Denmark

Skin problems are often regarded as part of the job in wet occupations. Bad habits as not using protective gloves and moisturizers are often justified by the workers and ignored by the management. To change habits at the shop floor, involvement of the whole organisation is necessary. The objective of an intervention in 6 gut-cleaning departments was to implement good habits by establishing a safety management system to manage skin risk. Local teams with representatives from all levels of the organisation were trained to run the process. Each team included 2–5 gut-cleaners, who should embody good habits and supervise their colleagues. Implementation research studies evaluate the understanding and acceptance of the intervention at the workplace and the association of the implementation and the reduction of work related diseases. Data are collected from questionnaires, interviews, written documents, etc. The change after one year in the frequency of eczema on hands and forearms within the past 3 months, varied in the 6 departments from a minor increase to a 2/3 reduction. 3 months after the start of the intervention the gut-cleaners in the team were asked to grade their expectations for success on a scale from 1 to 10; 10 being the optimum. The average grade varied from 4,8 to 10, indicating very different local expectations to the colleagues' acquisition of new habits. Further data and analysis will show if there is a covariance between the local changes in eczema frequency and the degree of implementation.

FS13.2

Intervention on work-related skin problems among gut cleaners

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Work-related skin problems are frequent in the food processing industry. A randomised intervention study with a one-year follow up was carried out among gut cleaners in order to prevent work-related skin problems due to wet work. The effects of the intervention were primarily measured by telephone interviews using questionnaires based on a standardized questionnaire for work-related skin diseases and exposure (NOSQ-2002).* The intervention activities included an evidence-based prevention program and an evidence-based method for implementation. Six of the 18 participating departments were randomly assigned to the intervention group and the remaining 12 departments to the comparison group. A total of 644 employees responded in the baseline interview and 622 in the follow-up interview carried out a year later. The participation rates were 87,5% and 71,6% respectively. Among the 495 participants answering in both interviews the frequency of eczema on hands or forearms within the past 3 months was reduced significantly by more than 25% in the intervention departments. A minor increase was observed in the comparison departments. This study has shown that even in jobs without the possibility to reduce high exposure to wet work work-related skin problems can be reduced by proper preventive measures.

*) Susitaival P, Flyvholm M-Å, Meding B, Kanerva L, Lindberg M, Svensson Å, Ólafsson JH. Contact Dermatitis 2003;49:70–76.

FS13.3

Development of risk reduction strategies for preventing dermatitis

Terry Brown[1], L Rushton[1], W Williams[2], J English[2]
[1]MRC Institute for Environment and Health, Leicester, UK
[2]University of Nottingham Hospital, Centre of Evidence-Based Dermatology, Nottingham, UK

Introduction: A recent survey of the UK printing industry found a prevalence of 11% of occupational contact dermatitis (OCD), much higher than previously identified.
Objective: This pilot study aimed to evaluate risk reduction strategies derived from recommendations of a literature review of preventive intervention studies and a series of focus groups of printers and observations of printers undertaking their normal duties.
Methods: Four interventions were evaluated: (1) Provision of gloves of the correct size/type, plus use of an after-work skin cream; (2) Provision of information; (3) Provision of skin checks; (4) Development of best practice skin care policy. Each intervention was evaluated in two companies over a three-month period, at the end of which printers and managers were interviewed as to the effectiveness and acceptability of each intervention.
Results: Although this pilot study was short, all interventions were acceptable to some extent. The prevalence of frank dermatitis fell over the study period, particularly in intervention (3). Intervention (1) achieved an improvement of awareness in both

management and workforce and an increase in the use of both gloves and cream. Intervention (2) highlighted problems of dissemination and the need for relevant information in an appropriate format. However. no single intervention was completely effective.
Conclusions: This qualitative research approach forms an essential first stage to improving understanding of ways in which OCD may be reduced among workers in the printing industry, and points towards the need for further testing of preventive strategies in larger-scale intervention trials, in printing and other industries.

FS13.4

Prevention of occupational hand eczema by skin-care management – results of an intervention study

Thomas L Diepgen
University of Heidelberg, Department of Clinical Social Medicine, Heidelberg, Germany

Objectives: In the prevention of occupational contact dermatitis the usage of personal skin protection measures have a high priority, however there is a lack of intervention field studies to demonstrate its efficacy. Therefore we conducted a field study in a plant of the metal-working industry and investigated the efficacy of an established skin protection programme.
Methods: First, a professional dermatological appraisal of the current status and a skin-protection analysis were carried out for 180 company employees, and a dermatological evaluation of each workplace from the aspect of prevention was conducted. Using the information obtained a skin protection programme for the whole company was devised and subsequently set up. The follow-up examination was performed eight months later.
Results: At the beginning of the study 26% of the employees were found to have skin problems related to the work they were doing. In 50% of the cases skin protection was never or only rarely used, with the right kind of skin protection almost never being applied. There was no skin protection programme in place meeting today's professional dermatological requirements, or at the most there were just the first signs of one. After the programme had been set up and suitable instruction and information given there was a follow-up observation period of eight months, during which several professional dermatological examinations of the employees were carried out and further instruction (individual prevention) was given. In the final examination only 8.7% of the employees were found to have work related skin problems.
Conclusions: We could demonstrated that the occurrence of occupationally-related hand eczema can be significantly reduced by setting up and providing instruction in a skin protection concept matched to the hazards the skin is exposed to at work. Additionally, valuable knowledge and experience were gained on implementing industrial skin protection programmes and performing intervention studies.

FS13.5

Occupational contact dermatitis: printer worker's viewpoints

Terry Brown[1], L Rushton[1], H Williams[2], J English[2]
[1]*MRC Institute for Environment and Health, Leicester, UK*
[2]*University of Nottingham Hospital, Centre of Evidence-Based Dermatology, Nottingham, UK*

Introduction: Occupational contact dermatitis (OCD) is very common in the printing industry due to contact with chemicals, paper, and wet work. It can be avoided by adequate protective measures, but the effectiveness of intervention depends heavily on the employer's and employee's awareness of this health risk.
Objectives: The study aimed to collect information on the knowledge, attitudes and beliefs of print workers about the risk of OCD and methods of prevention.
Methods: A series of focus groups were held with print workers, health and safety officers and managers to discuss their awareness of dermal risk factors, risk behaviour at work, attitudes to health and safety and options on possible preventive measures. A number of companies were also visited to observe, overtly and covertly, the normal work practices.
Results: OCD was not perceived to be either a major problem or a health and safety priority. There was general agreement about the processes and work practices that could cause skin problems. However, work practices varied considerably and did not always reflect this awareness. There was general concern about the type and availability of personal protective equipment, especially gloves and after-work skin cream. The provision of an occupational health service was generally felt to be inadequate, and no company had a policy in place that specifically addressed skin care.
Conclusions: These findings highlight the urgency to intensify health and safety education on skin

care within the printing industry. Recommendations were developed for the evaluation of a series of risk reduction strategies.

FS13.6

Risk management for workplace dermal exposure – a practical approach

Christopher Leonard Packham
EnviroDerm Services, Evesham, UK

Contact dermatitis remains one of the most common forms of occupational ill health in most industrial countries. Eliminating or minimising contact can significantly reduce the incidence and prevalence of occupational contact dermatitis. However, this is often believed by managers to be associated with either expensive measures, such as constly changes in the process or in the need for expensive new equipment, or with the provision of personal protective equipment such as gloves. Frequently, however, an analysis of the actual source of exposure can lead to a simple change that can have a significant effect in elimninating or controlling exposure. In many cases not only has this led to the elimnination of the skin problems, but also to a reduction in operating costs and/or an improvement in productivity. A structured approach to the elimination or adequate control of exposure will be explained and its benefits illustrated by a number of case studies where simple intervention methods have achieved the desired results.

FS13.7

CXCL8: a potential novel marker in predicting contact sensitisers

Susan Gibbs[1], MJ Toebak[1], PR Pohlmann[1], BME Blomberg[2], RJ Scheper[2], T Rustemeyer[1], DP Bruynzeel[1]
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[2]*Department of Pathology, VU University Medical Centre, Amsterdam, The Netherlands*

Cultured monocyte-derived dendritic cells (moDC) have been shown to provide a promising alternative for identifying potential sensitisers in vitro. Allergen induced moDC maturation results in elevated expression of the cell surface markers CD83 and CD86. Unfortunately, this increase in CD83 and CD86 expression is not sensitive enough to identify moderate and weak contact sensitisers. In this study, we investigated whether chemokine production by moDC is increased upon maturation and, ultimately, whether chemokine production can be used as a sensitive method to discriminate allergens from irritants.

Methods: MoDC were exposed for 48 hours to allergens (NiSO4, CoCl2, PdCl2, CuSO4, CrCl3, K2Cr2O7, PPDA and DNCB) and irritants (SDS, DMSO, BCl2 and propan-1-ol). CD83 and CD86 expression was analysed by flow cytometric determination and chemokine production (CXCL8, CCL5, CCL17 and CCL20) was determined by ELISA.

Results: Exposure to strong allergens caused upregulation of CD83 and CD86 expression whereas exposure to irritants did not. Remarkably, increased CXCL8 production by moDC was detected after allergen exposure whereas a decrease in CXCL8 production was observed after irritant exposure. CCL20 production was induced only by NiSO4. CCL5 and CCL17 production was increased upon exposure to both allergens and irritants.

Conclusion: CXCL8 production by moDC can be used to distinguish allergens from irritants. This chemokine is a potentially novel marker for determining the sensitising capacity of a chemical in vitro. Furthermore, our results suggest an important role for CXCL8 in the sensitization phase of ACD.

Saturday, 12 June 2004
10:20–11:35

FS14

Photo dermatitis/Metal allergy II

Chairs: Torkil Fischer, Sweden & Christophe J Le Coz, France

FS14.1

Safety of various fragrances: allergy and phototoxicity, joint study in Korea

Hee-Chul Eun[1], S An[2], H Lee[2], A Lee[1], CH Lee[1], D-W Kim[1], K-C Moon[1], Y-H Won[1], Y-S Ro[1], J-H Hahm[1], K-J Kim[1]
[1]*Korean Society for Contact Dermatitis and Skin Allergy, Seoul, South Korea*
[2]*Amore Pacific Corporation R&D Center, Youngin, South Korea*

The purpose of this study is to know the prevalence of allergic patch test responses in patients with suspected fragrance allergy in Korea and to know the photoxic potentials of limited fragrance substances. Nine dermatology departments of university hospitals and one research institute of cosmetic company were participated in this study for the past 1 year.

To inquire the specific fragrance allergens in Korea, eighteen fragrance ingredients were added to Korean standard series and fragrance series (Chemotechnique Diagnosis, Sweden). Among 422 patients, 83% were women and the most common topographic site was face. Except the fragrance mix and Balsam of Peru, Cinnamic alcohol and Sandalwood oil showed high frequency of positive responses. Among the added specific fragrance ingredients, 3-methyl-5-(2,2,3-trimethyl-3-cyclopenen-1-yl) pent-4-en-2-ol, alpha-isomethyl-ionone(methyl ionone gamma), Lyral showed high positive responses. With eighteen added specific fragrance substances, we have also performed two in vitro phototoxicity tests, 3T3 NRU phototoxicity test and photohemolysis test. 3T3 NRU phototoxicity test is a screening method for DNA or cellular damage and Photohemolysis test is a useful screening method for phototoxic chemicals that cause oxygen-dependent membrane damage. Only Lyral showed phototoxicity in photohemolysis test and no other fragrance ubstances showed phototoxicity in 3T3 NRU phtototoxicity test. We think our data are useful to know the current status of the frequent fragrance allergens in our society and the possible phototoxic potency of limited fragrance substances.

FS14.2

Photoallergic contact dermatitis from ketoprofen in Southern Sweden

Monica Hindsén, Zimerson E, Bruze M
Department of Occupational and Environmental Dermatology, Malmö University Hospital, Malmö, Sweden

Objective: In Sweden ketoprofen has been available for topical applications since 1995. Photoallergic contact dermatitis from ketoprofen has been reported since 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 structurally similar.
Methods: Photopatch testing and patch testing with 2 standard series, the ketoprofen-containing gels and their ingredients, fenofibrate and benzophenones.
Results: During the last year 35 patients have been photopatch tested with ketoprofen with very strong photopatch test reactions. 26 patients also had positive reactions to fentichlor.
27 of the ketoprofen – photoallergic patients had also been photopatch tested with fenofibrate, 17 had positive reactions. 21 had positive reactions to balsam of Peru and 13 to fragrance mix.
Conclusion: Ketoprofen is a strong photosensitizer.

FS14.3

Interleukins in patch-test blisters for the detection of contact allergy

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Objective: To investigate whether interleukins in blisters formed at patch-test sites can be used as markers of the grade of contact allergy.
Methods: Recently patch-tested volunteers with and without allergy to nickel sulfate were retested with 5 nickel sulfate patch tests and 5 control tests. 48 hours later, the test were removed and the perfusion of the test sites was assessed with a laser Doppler perfusion imaging (LDPI) technique. Then, suction blisters were made at the test sites. Blister fluids were collected separately from the allergen test sites and the control-test sites.
Results: The patch-test results prior to the study and in current study, and the results with the LDPI helped to distinguish between subjects with and without allergy to nickel sulfate. The concentration of one of the interleukins was high in the blister fluid from the nickel-test sites in all of the allergic subjects while the concentration was not detectable or low in fluid from the control sites and in fluid both from the nickel and the control sites in subjects without nickel allergy.
Conclusion: Immunological factors in fluid from blisters at patch-test sites may be important for the detection of contact allergy.
Acknowledgement: Icelandic Research Council.

FS14.4

Gold trichloride as a marker of contact allergy to gold.

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Objective: To study the usefulness of a trivalent gold salt, gold trichloride (GTC), as a marker for contact allergy to gold. Method: Patients patch test positive or negative to gold sodium thiosulfate (GSTS), 13 subjects of each, were patch-tested with dilution series of GTC and equimolar concentrations of GSTS; each series started at 0.03 mM and contained 5 steps. In order to avoid false positive and false negative test reactions the salts were dissolved in an alkaline buffer and placed on van der Bend® polypropene chambers. The tests were applied for 48 h; reading was blinded and performed on D3 and D7.
Results: Allergic reactions were observed in 9/13 gold-allergic patients with GSTS and in 2/13 with GTC. The sum of positive reactions was 18 with GSTS and 5 with GTC. Primary toxic reactions: 0 with GSTS and 2 with GTC among the gold-allergic patients; and 2 with GSTS and 1 with GTC among the controls.
Conclusion: GTC can elicit positive patch test reactions in patients with gold allergy but to a lesser degree than GSTS. GTC cannot be recommended for patch testing.

FS14.5

No suppression of nickel patch reactions by local betamethasone

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Background: Topical corticosteroids are usually banned on test areas prior to patch testing. The previous literature on the effect of topical corticosteroids is conflicting.
Methods: Patients allergic to nickel sulphate were patch tested on 4 sites with nickel on Day 0. Intracutaneous betamethasone was injected to test sites on Day −1, Day 0 and Day 1. NaCl injection on Day −1 was control. The patch test reactions were evaluated clinically and with laser doppler.
Observations: There were no differences in patch test reaction intensities on sites treated with intracutaneous betamethasone as compared to control.
Conclusions: A single local dose of potent corticosteroid does not suppress allergic patch reactions to nickel. The current practice of avoiding topical corticosteroid use prior to patch testing should be re-evaluated.

FS14.6

Oral lichenoid reactions and amalgams: no topographical relationship

Paolo Pigatto[1], E Passoni[1], R Crippa[2], C Tanzi[1], R Zerboni[1], L Brambilla[1], G Guzzi[3], S Muratori[1]
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[3]*AIRMEB-Italian Associaton for Metal and Biocompatibility Research, Milan, Italy*

Background: Several lines of evidence indicate a potential association between oral lichen-reactions and the presence of dental amalgam fillings.
Aim: We examined the relation between oral lichen reaction cases and the site of amalgam fillings in the oral cavity.
Methods: We conducted an observational study in 5 consecutive patients who had OLR and underwent to dental amalgam replacement. The number of total amalgam surfaces and OLR sites were charted. Saliva samples were taken and levels of total mercury were measured by CV-AAS method. Also we did patch-testing with dental series in all patients. Results: Our observational study revealed that oral lichen reactions may not have an association with the physical proximity the mercury tooth fillings. Unexpectedly, we noted a complete remission in patients with OLR (n = 5). The patients with OLR presented allergies to mercury (n = 4) or gold (n = 1). All patients were negative for HCV/HBV and they had not been taking any drug-induced lichenoid mucositis.
Findings: In this case report series no topographical association was found between OLR and the dental amalgam fillings. All OLR cases were in full recovery after total amalgam removal within three months. Saliva mercury concentrations were significantly elevated in all subjects. After amalgam removal the mercury levels were undetectable. We suggest that dental amalgam removal is important therapeutic option in OLR cases even if the lichenoid lesions are not adjacent to dental amalgam restorations.

FS14.7

BMS associated with allergy to metals

Paolo Pigatto[1], *E Passoni*[1], *R Crippa*[2], *C Tanzi*[1], *R Zerboni*[1], *L Brambilla*[1], *G Guzzi(3)*, *S Muratori*[1]
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Background: Burning mouth syndrome (BMS) is a burning and painful sensation of the mouth and perioral tissues. Despite several research its causes remain unknown. The treatment of BMS continues to be a challenge. This study investigated the relation between allergy to metals and long-term outcomes in 5 patients with BMS.
Methods: We studied 12 consecutive patients who had received a diagnosis of the BMS (ranging in age from 35 to 71). Mean duration of BMS symptoms was 10 months. We did patch-testing in all patients with dental series. We measured the saliva metal concentrations in each subjects. Of the 12 patients studied, 5 had symptoms which appeared to be related to type 3 BMS. Thus, they were assigned to total metals alloy removal procedures because allergic to at least one metal and had high levels of metals in saliva. No subjects had been receiving drug therapy. The primary outcome was the relief of BMS symptoms. Patients were followed for an average of 1.6 years.
Findings: Of the 5 patients who underwent to total metal alloy removal, 4 had a complete remission and one had showed notable improvement of his symptoms. Three patients were allergic to mercury. Two patients showed an allergy to gold. The saliva mercury and gold levels were significantly over the threshold limit. We also noted in three patients a full recovery of systemic dermatologic manifestations associated with BMS.
Conclusions: We believe that our exploratory investigation adds evidence that allergy to dental metals are involved in BMS.

Saturday, 12 June 2004
11:40–12:10

KL07

Jadassohn Lecture

Chair: Magnus Bruze, Sweden

Fragrance allergy: a chemical perspective for dermatologists

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Sensitivity to fragrance ingredients is acknowledged as a common and clinically important problem in Europe.

Aims of the project: The "fragrance chemical allergy" project (QLK4-CT-1999-01558) funded by the European Commission under the Quality of Life programme was to increase the safety standard of fragrance compounds and provide more transparency in the data available, and to develop prevention of fragrance chemical allergy in non sensitised (primary prevention) and in already sensitised (secondary prevention) individuals.

Primary prevention: A strategy for the rapid identification of sensitizers in complex mixture has been developed and 2 major sensitizers of oak moss, namely atranol and chloroatranol have been identified. Oxidation products, formed during storage and handling of common terpenes, have been shown to be involved in the sensitizing potential of fragrances. Quantitative Structure-Activity Relationships have been developed for 2 classes of aldehydes often present as perfume ingredients. Major fragrance allergens relevant to hand eczema have been identified.

Secondary prevention: A new fragrance mix "FMII" has been developed as a diagnostic tool for patients allergic to fragrances. An elicitation thresholds methodology has been established and validated with some important new sensitizers. The substitution strategy of sensitizing fragrance chemicals by analogues has been studied in the case of isoeugenol and demonstrated to be non relevant to consumer safety.

Expected applications of results: Data generated by this project will be used as basis for decisions to improve consumer safety such as product labelling of the most frequent sensitizing materials, making guidelines for the evaluation of safe concentration limits, making rules of handling and best-before-date and banning of the most sensitizing compounds in consumer products.

Participants: University Strasbourg (F), NIWL Stockholm (S), Unilever SEAC (UK), University Copenhagen (DK), University Witten/Herdecke (D), King's College London (UK), NERI Roskilde (DK), University Odense (DK), University Malmö (S), University Leuven (B).

Poster Abstracts

Chairs: Iris Ale, Uruguay, Klaus E Andersen, Denmark, David A Basketter, UK and Paivikki Susitaival, Finland

P01

Contact dermatitis from textile colours in three Spanish towns

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[3]University Hospital V. Arrixaca, Murcia, Spain

Objective: Prevalence of textile dye contact dermatitis (TD-CD) are lacking in many countries. Our aim is to know the frequency of TD-CD in three different areas of Spain.
Methods: 100 patients were tested with Spanish standard series and the five most frequent TD in each city. D. Orange 1, D. Orange 3, D. Blue 35, D. Blue 106, D. Blue 124 were included in Murcia and Seville, and the three last and D. Red 1, D. Red 17 in Santiago.
Results: 23/300 (15 women and 8 men) were positives to one or more TD. D. Blue 124 was the most frequent allergen (18/300), followed by D. Blue 106 (17/300). D. Red 1, D. Red 17 and D. Orange 1 were positives in 2/200. D. Orange 3 and D. Blue 35 were positives in 1/200. Eczema was located on hands in 13 cases. Clinical picture was variable. Origin of sensitization was clothing and occupational. Relevance was obtained in 20/23 cases.
Conclusions: The study confirm an high frequency of disperse dye allergy in Spain with a very different prevalence in the three areas: Seville 14%, Murcia 5% and Santiago 4%, that are probably due to social and cultural factors. We recommend the inclusion of D. Blue 106, D. Blue 124, D. Blue 35, D. Red 1, D. Red 17, D. Orange 1 and D. Orange 3 in standard series in order to detect sensitivity to textile colours that is most frequent than previously suspected.

P02

Analysis of coupled patch test reactions to nickel, cobalt and chromate

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Concomitant sensitizations to Nickel, Cobalt and Chromate are often observed among patch test patients. However, the reasons for being sensitized to two or more of these substances are not completely understood. Examination of IVDK (www.ivdk.org) patch test results with multivariate procedures has been conducted to further elucidate the mechanisms involved with these sensitizations and potential exposure factors that may have led to the concomitant sensitizations. Gender, age, occupational dermatitis, and construction work were considered and examined with multivariate logistic regression models with the dependent response variable being concurrent reactions to a metal pair versus no reactions. In addition to the aforementioned anamnestic data, examination of a poly-sensitizations variable (reactions to 1, 2, or 3 standard series allergens other than Nickel, Cobalt or Chromate) provided information regarding general susceptibility to positive patch test reactions. Combined reactions to Cobalt and Chromate were strongly linked to construction work (OR = 11.23 (7.46, 16.90)) and occupational dermatitis. Female patch test patients had a higher odds of a positive patch test reaction to both Nickel and Cobalt (OR = 4.73 (3.81, 5.87)). Sensitization to other, unrelated standard series substances was associated with concurrent reactions to all of the metal pairs. The association between construction work and Cobalt-Chromate reactions corresponds with the hypothesis that cement exposures lead to cobalt-chromate sensitizations. Individual susceptibility to delayed-type sensitizations, as represented by the poly-sensitization variable, also appears to be associated with coupled sensitizations to metals and warrants further examination.

P03

Type-I and -IV hypersensitivity to platinum salts

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VUMC University Hospital, Amsterdam, The Netherlands

A 28-year-old female analytical chemist visited our patch test clinic with initially complaints of severe hand dermatitis. Later on she developed rhinitis, bronchial asthma and tightness of the chest. The complaints seemed work related: her condition improved during holidays and on sick leaves. She worked in a laboratory with several platinum salts and used different kinds of gloves (latex, nitril, etc.).
Methods: Patch tests were performed with the European Standard series and prick tests with common inhalant allergens. Patch-, prick- and open patch tests were carried out with various aqueous dilutions of platinum chloride (PtCl2).
Results: Patch tests with 0.01–2% PtCl2 were positive on day 2, 3 and 6, and at 0.001% a follicular reaction was found. The prick-test was already positive at the lowest concentration tested (0.001%). The open patch test, carried out retro-auricular, showed a positive reaction at 1 and 2% PtCl2 after 20 min. Controls in healthy volunteers (n = 5) were all negative.

Discussion: It is well known that platinum salts can cause type-I hypersensitivity reactions like allergic rhinitis, conjunctivitis, bronchial asthma and urticaria, also referred to as platinosis. Contact dermatitis to platinum salts, however, is very rare. In our patch test clinic, 78 patients were tested between 1987 and 2001 with PtCl2 2%. Only 2 women showed a positive patch test for PtCl2. The patient presented here, stopped working with platinum salts and recovered from all complaints. We interpret our case as occupational type-I and type-IV hypersensitivity to platinum salts with mucosal and dermal manifestations.

P04

Cashiers's disease due to euro coins – a case report

Michael Häberle
Private Office, Künzelsau, Germany

A 37-year-old female cashier working in a drugstore developed a dyshidrotic hand eczema in summer 2001. Positive patch test results were obtained against nickel and cobalt. When the new euro coins were introduced in January 2002, the skin symptoms disappeared. Five months later the work-related hand eczema flared up with massive aggravation. Money-triggered hand eczema has occasionally been reported. Its low incidence is probably due to the absence of wet or irritant work. Coins are not mentioned in the EU nickel directive as "products intended to come into direct and prolonged contact with the skin". Nestle et al. (Nature, Vol 419, p 132, 2002) found that 1- and 2- euro coins released more nickel than pure nickel itself in vitro. A factor contributing to this high release of nickel is corrosion due to the bimetallic structure of these coins, which generates a galvanic potential of 30–40 mV in human sweat. A current can enhance galvanic corrosion and thereby cause more nickel release. In a thin irregular electrolyte layer such as a sweat deposit, galvanic corrosion occur primarily near the bimetallic junction owing to the high resistance to lateral current flow in the thin layer.

P05

Quantification of erythema using digital camera image analysis

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In general, Irritant skin reactions are graded by using visual scoring method for the degree of erythema, edema and scaling. The main disadvantage of this method lacks objectivity and parametric properties. The purpose of this study is to develop a quantitative evaluation method by using computerized color image analysis of skin erythema. We have described the objective measurement of the irritant skin responses by using skin surface color determination and compared it with the measurement by using traditional visual scoring method. Using R (Red), G (Green), B (Blue) value and CIE color parameters (L*a*b*) of digital camera image by using the software program, two kind of erythema index (ΔRG, Δab) and change in total color (ΔE*ab) were calculated. ΔRG value and Δab in digital camera image were highly correlated with the degree of erythema than chromameter measurements. And Δab (difference in color redness (a*) and yellow hue (b*)) with the exception of luminance (L* value) in CIE was well correlated than change in total color (ΔE*ab). Our data showed that erythema indices (ΔRG, Δab) were good parameters for evaluation of skin erythema produced by irritant reaction.

P06

Axillary irritation: methods of assessment

L Peters, Marie Marriott, DA Basketter
Unilever, Safety and Environmental Assurance Centre, Sharnbrook, UK

Axillary dermatitis can be associated with the use of underarm products. However the unique physiology of this region makes assessment of irritation problematic. Furthermore, given the type of products used in the underarm, the friction and occlusive nature of the site, it is necessary not only to concentrate on the area of application ie the area of hair growth, but also to examine the periphery. There is evidence that products tend to move to this area during the day possibly as a consequence of axillary physiology and mechanical effects. Consequent upon these various factors, predicting axillary irritation from acute patch tests on back or arm skin is problematic. In a recent comparison, we found that where approximately 10% of panellists reacted to a formulation by patch test, 50% developed axillary reactions during a 21 day use test. In addition, not all those who reacted in the patch test reacted in the axilla. Predicting axillary

effects from repeated open tests seems better but still has challenges; currently we are assessing alternative strategies to permit rapid identification of potential issues without recourse to extended in use tests.

P07

The poverty-one of the reasons for chronic toxic contact dermatitis

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The aim of the work is to present the incidence and the main reasons for this illness at women who live in very bad and poor conditions, in town and in village.

Material and methods: 137 women were included, who were inspected during the time period of 8 months in 2003. A proper therapy was introduced-per os and in loco, and all of them were controled for 14 days.

Results: All together, 137 women were inspected and they were classified by their age, place of leaving and nationality. The detail anamnesis showed that 80% are housewifes who live in poverty and who are in contact with detergents everyday, becouse they do the dish-washing and the laundry with hands, without any machines. The following therapies were applicated: corticosteroid and antihystaminic therapy per os and corticosteroid therapy in loco. After 14 days, a control look over was made, and they were given the preparation with vitamin A and lanolinum, for 14 days more. All of them were adviced to use protection gloves when they are in contact with detergents, especially for the laundry.

Conclusion: One of the reasons for the appearance of chronic toxic contact dermatitis is the low standard of living when, becouse of the poverty, people can't use machines and still in the 21th Century they wash the clothes and dishes with hands. The only help at this category of people is to give them advices for using protection gloves.

P08

Changes in Nitric oxide synthase expression in acute irritant contact dermatitis: a possible predictive tool

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There is a need for a diversity of approaches to predictive irritancy testing. In this study we examined the potential for changes in the expression of the nitric oxide generating enzyme, nitric oxide synthase, to act as a marker of skin irritation. Human volunteers were patch tested with sodium lauryl sulphate and dithranol so as to induce acute irritant contact dermatitis. Test and control biopsies were removed at various time points and skin sections immunocytochemically labelled with a range of polyclonal and monoclonal antibodies against the three nitric oxide synthase isoforms, NOS1, NOS2 and NOS3. Quantitative image analysis of keratinocytes and endothelial cells revealed major inconsistencies in the labelling of both normal and inflamed skin between antibodies, including those purported to recognise the same epitope. Of the ten antibodies tested, two, AHP303 and N2643, gave statistically significant changes in NOS2 and NOS3 expression, respectively, in well-established 48 h and 96 h reactions. Importantly, the changes were consistent for both irritants, despite their differing mechanisms of action. Further investigations are needed to assess their suitability as markers of irritation in animal and in-vivo models.

P09

Comparison between mild irritant response in haired and hairless guinea pigs

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The hairless guinea pig offers the possibility of performing irritant studies without the use of depilatory agents or clipping. Studies have shown a response to allergens and simple irritants comparable to that of the haired guinea pig. Histoanatomical studies have demonstrated differences in cutaneous structure in the two strains, differences that might influence the response to mild irritants such as topical drug vehicles. The purpose of this study was to compare the usability of hairless (HLGP) and shaved haired guinea pigs (SGP) in tolerability studies of complex topical formulations. The tolerability of 6 selected skin care formulations (SCF), known to cause a differentiated irritative response in HLGP, was studied in 15 male SGP and 15 male HLGP. All animals were treated on a 5×5 cm area on each flank twice daily for 4 consecutive days with SCF.

The irritant effects of the SCF were quantified clinically and by measurement of transepidermal water loss (TEWL) and colorimetry (a*-parameter). Both species were able to differentiate between SCF in relation to skin tolerance and although the response pattern was somewhat different in the two species the ranking of the SCF was essentially the same using TEWL and clinical scoring. However, colorimetry was found to be unsuited for the evaluation of cutaneous irritation in the SGP over a period of days as regrowth of fur obfuscated the underlying erythema. In conclusion the HLGP appears to be a more suitable model for tolerability testing of composite formulations.

P10

Comparison between mild irritant response in hairless guinea pigs and human volunteers

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Small rodent laboratory animals lack the complex cutaneous structure and function of human skin resulting in ''all or none''-responses to mild irritants so that the animals may show a less discriminative reaction pattern compared to human volunteers when studying the tolerability of topical drug formulations. This study compared the tolerance pattern of a 6 composite formulations (SCF A-F) in human volunteers and in hairless guinea pigs (HLGP). The formulations were 2 basic creams (A and B) and 4 composite creams containing either isopropyl palmitate (C), glycerin (D), canola oil (E) or (-)-alfa-bisabolol (F). The tolerability of 6 selected skin care formulations (SCF A-F), known to cause a differentiated irritative response in HLGP, was studied in 15 male SGP and 20 human volunteers. The HLGP were treated twice a day on a 5×5 cm area on each flank with a SCF for 4 consecutive days. The irritant effects of the SCF were quantified by clinical assessment, measurement of trans epidermal waterloss (TEWL) and colorimetry (a*-parameter). In humans the tolerability was evaluated clinically using the chamber scarification test. In HLGP SCF A and C were strong irritants followed closely by E, the remaining formulations were indistinguishable. In human volunteers all formulations were tolerated equally and well with the clinical score rising slightly on the first day and remaining stable thereafter. In conclusion, the HLGP appeared to be too sensitive, as formulations showing irritation in HLGP were well tolerated in a human.

P11

The complex problem of sensitive skin

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There exists within the population subsets of individuals who display heightened skin reactivity to materials the majority find tolerable. In a series of investigations, we have examined interrelationships between many of the endpoints associated with the term 'sensitive skin'. In the most recent work, 58 volunteers were treated with 10% lactic acid, 50% ethanol, 0.5% menthol and 0.1% capsaicin on the nasolabial fold, unoccluded, for 8 minutes. Sensory reactions were recorded at 2.5, 5 and 8 minutes. Urticant susceptibility was evaluated with 1 M benzoic acid and 125 mM transcinnamic acid applied to the volar forearm for 20 minutes. Visual assessments were taken at intervals for up to 4 hours after treatment. A 2×23 hour patch test was also conducted using 0.1% and 0.3% sodium dodecyl sulphate, 0.3% and 0.6% Tegobetain F50 and 0.1% and 0.2% benzalkonium chloride to determine irritant susceptibility. As found in previous studies, increased susceptibility to one endpoint was not predictive of sensitivity to another. In our hands, nasolabial stinging is a poor predictor of sensory as well general skin sensitivity. However, it may be possible to identify in the normal population individuals who are more generally sensitive to a range of non-immunologic adverse skin reactions. Whether such individuals are those who experience problems with skin care products is open to question.

P12

Measurement of skin edema by a dielectric technique (MoistureMeter-D)

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Easily applicable, cheap, noninvasive and quantitative techniques to measure edema in skin and subcutaneous tissues have not been available. Recently, a new device MoistureMeter-D based on the local measurement of the dielectric properties of the biological tissues was validated in the quantitation of systemic edema in humans. In the

present study the MoistureMeter-D was applied to quantitate local skin edema related to skin irritation. The irritation was induced in the volar forearms of 12 healthy volunteers with the topical application of 1% sodium lauryl sulfate (SLS) for 6 hours. After induction the volunteers were divided into two groups: the irritation site of group I (six volunteers) had no treatment for the irritation site while for group II (six volunteers) the corticosteroid cream was topically administered on the irritation site. A good correlation was measured between the temporal changes of edema during the three days' follow-up by the ultrasound-measured skin thickness and the edema-specific MoistureMeter-D in group I ($p < 0.001$). The reduction of edema in group II by the corticosteroid treatment was consistently measured by both instruments. The coefficient of variation for a single measurement varied between 2 and 3%. The results demonstrate that the MoistuMeter-D is an accurate instrument for the quick quantitative evaluation of local oedema and fluid retention in irritated skin.

P13

Results of patch testing with patients' own cosmetics and toiletries

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Patch testing with materials brought in by the patient is useful to identify the cause(s) of current allergic contact dermatitis (ACD). However, little is known (i) on the contribution of such tests to diagnostic success and (ii) on the spectrum of contact allergens associated with ACD to certain product categories. Between 1998 and 2002, 5911 out of 48381 patients patch tested in the centres of the IVDK (www.ivdk.org) have been tested with own cosmetics and toiletries in addition to commercial allergens. These were manually assigned to 26 categories, based on a EU classification (annex I to 76/768/EEC), which was further refined. As illustrative example, data on ''Bath and shower preparations'' are presented: out of 1333 patients tested with a total of 2336 single patches (1102 with 1%, 391 with 10% and 280 with 0.1% in water, remainder with other preparations, depending on the actual kind of product), 71 had positive reactions at the D3 reading. Only in 46 of these, reactions to potential cosmetic ingredients, tested as commercially available allergens, were observed. Among these, fragrance mix (30.0% vs. 12.9% in those not reacting positively to this product category), Myroxylon Pereirae resin (18.6% vs. 8.4%) and some biocides like MCI/MI (11.4% vs. 1.8%) and methyldibromo glutaronitrile + phenoxyethanol (12.1% vs. 5.3%) were the most common allergens. In conclusion, patch testing own products – although not without pitfalls – may (i) help to correctly diagnose ACD and (ii) give important hints on the occurrence of allergens in a particular type of (cosmetic) product.

P14

Hydrolysed wheat protein: a new allergen in cosmetics and food

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For the pas few years, mainly because of mad cow disease, hydrolysed wheat proteins (HWP) have been used in cosmetics and food as emulsifiers and stabilizers in replacement of bovine collagen. We report here contact urticaria to cosmetics induced by these HWP in 7 patients of which 6 had food allergy to modified gluten and the results of their immunological testing. These cases were regrouped through the french network REVIDAL-GERDA.

All 7 women developped contact urticaria immediatly after applying cosmetics (mainly facial cream), from different brands, containing HWP. Six of them had also anaphylactic reactions or urticaria after eating preserved foods or delicatessen which contained modified gluten. Neither had allergic reaction after eating broad or bread.

Skin tests were positive with the cosmetics, HWP contained in them and, in case of food allergy, modified gluten. They were negative with natural wheat flour. Despite that, specific IgE to wheat flour were positive in 2 cases. Specific IgE to gluten were positive in 3 patients.

Sera were also investigated for their specificity toward wheat proteins and various preparations of gluten. Individual variations of specificity were observed. All sera contained IgE reacting with both hydrolysed peptides and some native flour proteins.

It appears that, from the medical history, allergy to cosmetics preceeded food allergy. In view of these elements, may be the use of HWP in cosmetics should be questionned.

P15

A randomized double-blind controlled trial comparing extra-virgin coconut oil with mineral oil as a moisturizer for mild to moderate xerosis

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Coconut oil, a traditional moisturizer used for centuries by people in the tropics, does not have any clinical studies documenting its effectivity and safety. This study aims to determine effectivity and safety of coconut oil compared to mineral oil as moisturizer for mild to moderate xerosis. A review board-approved randomized double-blind controlled trial was conducted in 34 patients after negative patch-testing. Patients applied either coconut or mineral oil twice a day for two weeks. Quantitative outcomes for effectivity, measured at baseline and each weekly visit, were skin hydration (Corneometer CM825®) and skin lipids (Sebumeter SM810®); for safety, transepidermal water loss [TEWL] (Tewameter TM210®) and skin surface pH (Skin pH meter PH900®). Patients and investigator evaluated symptoms of dryness, scaling, roughness, and pruritus using visual analogue scales (VAS) and grading of xerosis. Both groups showed significant improvement in skin hydration and increased skin surface lipid levels. TEWL and Skin pH were not affected. Objective instrumental determinations showed no significant difference between both groups. Patient and investigator subjective grading of xerosis and VAS showed general trend toward better, though not statistically evident, with coconut over mineral oil. Coconut oil is as effective and safe as mineral oil as a moisturizer.

P16

Eyelid dermatitis with positive patch test to coconut diethanolamide

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Objective: The aim was to detect a possible allergen in a patient with eyelid dermatitis. Patient and methods: a non atopic 27-year-old female presented with eyelid dermatitis since 3 months. This dermatitis persisted despite the fact she had stopped the use of make up; she had acrylic artificial nails since 2 months and sometimes used hair dyes;patch tests were performed with Finn Chamber® tests with readings at D2 and D3, according ICDRG criteria, with European standard series, additional series (including toluenesulfonamide formaldehyde resin), cosmetic, acrylates, hairdressing series, in 3 patch test sessions, using Chemotechnique Diagnostics® allergens.
Results: The only positive patch test was coconut diethanolamide (0.5% pet.)++ at D2 and D3. After removal of the shampoo containing this allergen, the dermatitis cleared. Coconut diethanolamide (cocamide DEA), tensioactive synthesized with coconut oil is widely used in shampoos, soaps, shower gels, barrier creams, washing up liquids, metalworking fluids, hydraulic oils. Involvement of eyelids is not frequently described in the literature with this allergen.
Conclusion: Coconut diethanolamide should be added in cosmetic series, and it should be useful to test this allergen in patients with eyelid dermatitis.

P17

Allergic contact dermatitis from hydrolyzed wheat protein

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Allergic Contact Dermatitis (ACD) from hydrolysed wheat protein (HWP) is rarely reported in the literature. We describe 2 cases of ACD to this new allergen. Case1- A 39-year-old non atopic woman presented with a dermatitis of the face, mainly eyelids and neck. She had been using a new cosmetic cream for 2 months. The lesions subsided with topical corticosteroids. Patch tests with the standard, cosmetic, fragrance series and with her own products gave positive reactions only to the new cosmetic cream. We also tested all the components of this cream and only HWP gave a doubtful reaction with occlusive tests and positive reaction with ROAT. Case 2 – A 48-year-old atopic woman presented with a dermatitis of the face and hands for 1 month. She had been using a new cosmetic cream for 11 months and kept using the product without any suspicion. The dermatitis subsided with cetirizine and topical corticosteroids. Patch tests with the standard, cosmetic, fragrance series and her own products revealed positive reactions to the cosmetic cream. Again, testing all the components of the cream, only HWP gave doubtful reactions with occlusive tests and positive reactions with ROAT.
Discussion: In recent years, a number of protein hydrolysates have been introduced into cosmetic

manufacture. HWP is being used in cosmetic creams for its moisturizing properties. As far as we know, there is only one previously reported case of ACD induced by this allergen. More cases may be expected.

P18

Allergic contact dermatitis to cosmetics: a retrospective six year review

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A retrospective study was done of allergic contact dermatits to cosmetics, seen at the department of dermatology of Curry Cabral Hospital, over a six year period (1998 to 2003). Of 2848 patients patch tested during this period, 314 had cosmetic contact allergy and represented about 15.7% of all patients with at least one positive patch test. The patients aged between 13 and 82 years old, and were mostly female (78%). Skin reactions occurred most often on the face, followed by hands, neck and the eyelids. All the patients were tested with the standard series, with supplementary series when appropriate, and whenever possible, with the personal cosmetic products. 92% had positive reactions to standard series allergens; 226 patiens to allergens of the standard series, which may be used in cosmetics. The majority of reactions were due to fragrance mix, followed by balsam of Peru, p-phenylenediamine, kathon CG and colophony. Fragrance series was tested in 118 patients, with the following most frequent positive reactions: oak moss absolute, isoeugenol, hydroxycitronellal. Cosmetic series was tested in 147 patients with the following most frequent positive reactions: toluenesulphonamide-formaldehyde resin and propolis. 30 patients tested with photoallergen series, 4 reacted to oxybenzone. Skin care products and fragrances were the most commonly involved product categories. Twelve patients reacted only with their own products. The fragrances were the most frequent ingredient recorded as the cause of cosmetic contact allergy. Our standard series detected 70% of cases of allergic contact dermatitis to cosmetics.

P19

Allergic contact dermatitis to p-phenylenediamine from a temporary tattoo in a 8-year-old boy

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A 8 year old boy was seen in our department with a allergic contact dermatits to a temporary tattoo done at his arm 1 week before. It was the third temporary tattoo (called 'henna' tattoo) done over a 3 month period of school holidays. He was treated with topical corticosteroid and reobserved with an residual hypopigmentation. He was patch tested with our standard series with positive reaction to p-phenylenediamine; later test with 'henna' powder was negative. Temporary 'henna' tattoos are very popular, specially during holidays. Several cases are reported in the literature of sensitization to p-phenylenediamine, contained in the henna tincture, but few of these are pediatric cases. It is important to discouraged the use of these tattoos, due to the consequences that a sensitization to p-phenylenediamine could have in their future.

P20

Red tattoo reactions

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Tattoos are becoming increasingly popular, although reactions to tattoos remain relatively uncommon. We describe 4 patients with a variety of red tattoo reactions, one responding well to intralesional steroid therapy.

Case 1: A 50-year-old man presented with a florid, inflammatory reaction confined to the red area of his forearm tattoo. Biopsy showed a dense lymphocytic and focal macrophage response to tattoo pigment. Mass spectrometry of biopsy tissue revealed high concentrations of titanium and iron. Patch testing was negative. Intralesional steroid injection has produced a marked improvement.

Case 2: A 42-year-old man presented with an inflammatory reaction affecting the red area of his leg tattoo. Biopsy revealed a florid lymphoid reaction.

Case 3: A 30-year-old man presented with an eczematous reaction within the red/brown pigmented areas of his tattoos, which was exacerbated by sun exposure. Patch testing showed a (+) positive reaction to cadmium after 96 hours. Photo patch testing was negative. The reaction settled spontaneously within 12 months.

Case 4: A 37-year-old woman presented with a florid, indurated inflammatory reaction involving the red area of a shoulder tattoo. Patch testing revealed a (++) and (+) positive reaction to nickel

and cobalt respectively with a doubtful (? +) reaction to mercury 0.5% in petrolatum after 96 hours. Tattoo reactions, especially red tattoo reactions can present with a spectrum of histological changes, including lichenoid, granulomatous, hypersensitivity, nodular, pseudolymphomatous or sarcoidal reactions. One of our cases responded well to intralesional steroid injection and one case resolved spontaneously.

P21

Is medical motivation a good motor to collect side effects of cosmetics? Results of REVIDAL GERDA from the 1st January of 2000 to the 31st December of 2002

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Background: Why are there few declarations of side effects to public vigilance? Are there really few cases? Is there a lack of motivation?
Motivation of revidal gerda is a medical motivation. Acceleration of knowledge by each about side effects. Amelioration of the tracking of side effects. Amelioration of management of patients
Aim: to answer the question: is the medical motivation a good motor to collect the side effects of cosmetics?
Patients and methods:
REVIDAL GERDA
1/collects the declaration od S.E. of cosmetics which are sent by dermato-allergologists who are astonished by these S.E
2/shows reception for each declaration
3/wake up the vigilance of all in the event of concordant declarations
3/inform each one of all the declarations 2 times per annum
The majority of the declared S.E. is allergic
1/evocative clinical history
2/and positive reaction with a mufactured product
3/or positive reaction with an allergen of the allergotheque and presence of this allergen in the list ''ingredients'' of manufactured product (s)
here is the analysis of declarations which was made from the 1st january of 2000 to the 31th december of 2002
Results:
42 dermato-allergologists had declared 304 declarations for 398 products; 188 used for the face 58 used for the body, 38 used for hair, 31 used for legs, 30 parfums, 15 sunscreens, etc.

The declared pathology was: 12 immediate type, 281 delayed type, 10 other

For 6 products, the name alone did not make it possible to identify its use. 2 collective publications were made (many declarations about a new problem)
Conclusion: There were many declarations. The number of product is much larger than what was published before:

The under declaration is certain to the public vigilance

The medical motivation is a good motor to obtain declarations

These declarations can be useful to help patients, to publish new problems and to program prospective studies

P22

Patch testing with p-toluene diamine (PTD) preparations of different ages

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Background: PTD, a component of oxidative hair dyes, is a frequent sensitizer in hairdressers. Investigations on the stability of the patch test preparation PTD 1% pet. revealed a decline of the PTD concentration to 0.1% within 6 months, possibly due to a reaction of PTD molecules to dye complexes. This raises the question if the long-term diagnostic quality of the PTD preparation is hampered by chemical changes.
Objective: To systematically compare intra-individually patch test results obtained with three PTD patch test preparations of different age, tested synchronously in a multicenter study of the German Contact Dermatitis Research Group (DKG).
Methods: 3 PTD preparations, produced in January 2002 (batch A), August 2001 (batch B), and April 2001 (batch C), were patch tested in 177 patients from March to December 2002. Patch testing was performed blinded, with respect to the production date.
Results: There were 150 concordant reactions to batch A, B, and C, i.e. 133 negative, 1 doubtful (?), 11 weak positive (+), 3 strong positive (++ and +++), and 2 irritant reactions. In 27 patients, discordant reactions to batch A, B, and C had been observed. Altogether, 22 positive reactions were noted to batch A, and 19 to

batch B and C, respectively (difference not significant). There was no clear cut time trend concerning the occurrence of positive or discordant reactions.
Conclusions: Reproducibility of patch test reactions was within a normal range. The chemical changes mentioned above apparently do not affect the diagnostic quality of the PTD patch test preparation.

P23

Allergic contact sensitization in Spanish patch-tested patients in 2001

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GEIDC Members, Spain (2003)

Objective: The first Spanish patch-test study of patients with contact dermatitis was performed in 1977. We aimed to determine the prevalence of hypersensitivity for Spanish standard allergens in patients suspected of contact dermatitis in 2001.
Methods: A total of 3832 patients of 13 dermatological centers were patch-tested with Spanish standard series. Age, gender, occupation, dermatitis site and type, and positive patch test were tabulated.
Results: 2300 female and 1532 male patients, aged 0 to 70 years were observed with contact dermatitis. Origin of eczema was occupational in 16.66% of patients. Eczema was located on hands in 54.34% of cases. Allergic contact dermatitis in 31.02% and irritative contact dermatitis in 15.88% were the most frequent diagnosis. Positive patch tests was observed in 55.11% of patients. Prevalence of positives reaction was obtained with nickel (26.64%), cobalt (9.89%), chrome (8.66%), PPDA (5.27%), thimerosal (5.21%), fragance mix (5.03%), Kathon CG (4.04%) and thiuram mix (2.87%).
Conclusions: The results emphasize that nickel, cobalt, chrome are by far the most common allergens. A increase in the frequency of allergic patch test reactions to nickel has been noted (18,78 in 1977; 26,64 in 2001). However the contact sensitivity to cobalt, chrome and thiuram mix has decreased. Currently, allergy to cosmetics constitutes a significant portion of the cases of contact dermatitis.

P24

Increasing prevalence of sensitization to preservatives in children

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The aim of this study was to evaluate the frequency of contact sensitization to preservatives in a pediatric population and to compare the data to our previous findings referring to the period 1988–1994. From January 1995 to December 2002, 1255 patients aged 7 months-12 years, 583 boys and 672 girls, with suspected allergic contact dermatitis underwent patch testing with our pediatric series of 30 allergens including 5 different preservatives: methyldibromoglutaronitrile, methyl(chloro)isothiazolinone, imidazolidinyl urea, paraben mix, and formaldehyde. Of the 1255 children tested, 108 (8.6%), 52 boys and 56 girls, showed positive reactions to 1 or more of the preservatives listed above. In particular, 55 subjects reacted to methyl(chloro)isothiazolinone, 22 to methyldibromoglutaronitrile, 20 to paraben mix, 17 to formaldehyde, and 13 to imidazolidinyl urea. Among our preservative-positive children, 77% of patients reacted to other haptens of the series, and 44% were affected by atopic dermatitis. In comparison with our previous data referring to the period 1988–1994, a significant increase has been observed in the frequency of positive reactions to methyldibromoglutaronitrile, paraben mix, and formaldehyde. Our findings confirm the importance of patch testing children with preservatives since the wider and wider use of cosmetics in the pediatric age.

P25

Accuracy of serial dilution concentrations for intradermal skin testing: a neglectable problem?

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Skin tests are important diagnostic tools. To establish reactivity, a single allergen test concentration is considered to be sufficient. To diagnose sensitivity serial dilution or endpoint titration is recommended. Skin testing in drug allergy is complex, since pathogenetic mechanisms are diverse, and for many drugs cut-off skin test concentrations have not been established. Therefore, after a negative prick/puncture test with the stock solu-

tion, intradermal tests with serial (ten-fold) dilutions are recommended. Surprisingly in most publications dealing with serial skin test dilution, the technique is not described in detail.

Aim: Comparison of the variability of test substance concentrations produced with two serial dilution techniques conducted by experienced allergy nurses.

Methods: Two allergy nurses produced dilution series. Isosulfane blue was chosen as test substance, since it enabled easy and sensitive detection. Dilution series of isosulfan blue (aqueous solution of 10 mg/ml) from 1:10 to 1:10'000 were produced under sterile conditions by two dilution techniques: 1) Dilution in vials: 0.5 ml isosulfane blue solution was serially transferred with 1 ml tuberculine syringes to vials containing exactly 4.5 ml NaCl 0.9% 2) Dilution in syringes: 0.1 ml isosulfane blue solution with the higher concentration was aspirated into 1 ml tuberculine syringes followed by 0.9 ml NaCl 0.9%. These procedures were compared with a controlled experiment carried out using piston-stroke pipettes. The concentrations of isosulfan blue in all dilutions were determined by UV/VIS-spectroscopy and external standard calibration.

Results: In almost all samples the concentrations were higher than expected. In vials the concentrations varied from 83 to 360%, in syringes from 83 to 711% of the expected values. The dilution in vials gave consistently better results than dilution in syringes. A considerable interindividual variability was observed between the conducting nurses, however variability over time was smaller.

Conclusions: In routinely performed serial dilutions of allergen test preparation considerable deviations from the expected allergen test concentration have been observed. This might be of minor importance for an individual patient, however, in establishing e.g. cut-off concentrations for non-irritant drug concentrations or in multicenter studies such variations may result in major errors. Quality management of skin testing should not only include the recording, injection technique and test reactivity evaluation, but also the exact description of the preparation of test dilutions. In clinical routine dilution techniques should be applied, which give more accurate results.

P26

An epidemiological study of the relevance of the allergens of the standard series of the Spanish Group for the study of contact dermatitis (Grupo Español para la Investigación de la Dermatitis de Contacto, GEIDC) (2001)

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An epidemiological study is made to evaluate the present or past relevance of positivity to the allergens pertaining to the GEIDC standard series. A retrospective study was made of patients evaluated with patch tests corresponding to the GEIDC standard series by 14 GEIDC dermatologists in the course of 2001. The following parameters were evaluated: age, sex, positive allergens, and present, past and total relevance. A total of 3343 patients were studied, of which 1892 had at least one positive test (56.59%). The most relevant allergens were mercaptobenzothiazole (93,93%), thiuram mix (93%) and nickel sulfate (92.33%). In women, paraphenylenediamine was moreover also very relevant, while in males epoxy resin, butylphenol formaldehyde resin and colophony were particularly relevant. Among the less relevant allergens in both sexes, we found the following in relation to the total: quinolein (44.44%), lactones (45.45%) and caine mix (48.07%). In 1783 patients with at least one positive test, an evaluation was made of whether allergen relevance was past or present. In 60.78% of the positive tests present relevance was established. The allergens of greatest present relevance were ethylenediamine (100%), budesonide (100%), euxyl K 400 (96.96%), epoxy resin (93.33%), and Quaternium 15 (92.85%). The allergens of least present relevance were nickel sulfate (36.38%), caine mix (40%), and neomycin (41.37%).

Determination of the relevance of positive patch test is fundamental in all cases. In our study nickel and rubbers were the most relevant allergens, though nickel was essentially of past relevance. Few studies have addressed the present or past relevance of the standard allergen series.

P27

"Two feet-one hand syndrome" masquerading as occupational hand eczema

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Background: Occupational hand eczema is mainly characterised by bilateral manifestation whereas one-sided hand involvement is unusual.

Subject: We report on a 38-year old dental technician who presented with interdigital skin alterations of the left hand resistant to previous eczematous treatment. Main professional task was the production and processing of plaster or plastic dental models. While handling with dental models like smoothing by the left hand, usually this one was splashed with plaster. On clinical examination the patient showed additionally scaly lesions on the soles.
Results: No sensitisation could be ascertained performing patch and prick tests. By normal IgE-level, no specific antibodies against aeroallergens or occupational allergens such as isocyanates, formaldehyde or latex could be found. Mycological cultures of scaly lesions of the left hand and soles revealed an infection with Trichophyton rubrum. In accordance with the subjective perception, the starch-iodine test showed the left hand more sweating. We diagnosed a "two feet-one hand syndrome" and achieved healing after local antimycotical treatment.
Conclusions: In case of one-sided, suspicious work-related skin alterations of the hands, a "two feet-one hand syndrome" (i.e. bilateral plantar tinea in coexistence with a unilateral tinea manuum) should be considered as differential diagnosis. A common explanation for the fungal infection of one hand is the scratching of the already infected soles. However, within occupational fields little is published about the "two feet-one hand syndrome." An asymmetric increased palmar sweating and a one-sided chronic professional burden of the hands are discussed as predisposing factors for the unilateral fungal infection.

P28

Interleukin-8 from keratinocytes can be used to test for contact allergy

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Objective: To investigate whether secretion of interleukin-8 (IL-8) proteins by keratinocytes following in vitro exposure to a contact allergen can be used to detect contact allergy.
Methods: Suction blisters were made on skin of allergic and anergic subjects to urushiol, the contact allergen of poison ivy. Keratinocyte cultures were prepared and exposed to the allergen in vitro. Controls were the allergen solvent. Variable allergen concentrations, allergen exposure times and cell culture times were used. At the end of each culture time, IL-8 RNA and protein of the culture supernatants were analyzed by PCR and ELISA.
Results: The concentration of IL-8 in the supernatants proved to be a successful way to distinguish between subjects who patch tested positive with a non-toxic concentration of urushiol and subjects who tested negative. In the allergic subjects, a correlation was established between the dose of the allergen and the IL-8 protein concentration in the supernatants.
Conclusions: In vitro testing of contact allergies in patients makes possible an objective assessment of their allergic status without causing a booster effect or risking active sensitizations. The results indicate that the method may be used as an alternative method to animal models for testing consumer products before their marketing, thus avoiding ethical problems and problems related to interpretation of tests because of biological differences between animals and humans.

P29

Interleukin-8 in patch-test blisters is chemotactic and detects allergy

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Objective: To investigate interleukin-8 (IL-8) as a chemokine for T-lymphocytes and as a marker of magnitude of contact allergy.
Subjects, Materials and Methods: Urushiol, the contact allergen of poison ivy, was applied to allergic and anergic volunteers. Suction blisters of urushiol exposed and non-exposed skin were produced 48 h later and the fluids were analyzed for chemotactic activity for T-lymphocytes using modified Boyden chambers. Anti-IL-8-antibodies were added to the fluids to investigate their effect on the chemotactic activity. IL-8 protein concentration of the fluids was determined by ELISA and its correlation with visible test responses was investigated.
Results: Significant chemotactic activity for T-lymphocytes was only present in blister fluid from urushiol exposed skin and only from the allergic subjects. The chemotactic activity could be neutralized with the anti-IL-8 antibodies. There was an excellent correlation between the IL-8 protein concentration in blister fluids and

the clinical appearance of the inflammatory reactions at the skin test sites.
Conclusions: The results support the hypothesis that IL-8 in blister fluid is both chemotactic for T-lymphocytes and is a sensitive marker of an inflammatory response. Determination of the concentration of IL-8 proteins in blister fluid of patch tests may be of future use for objective assessment of clinically important contact allergies.

P30

Transparent plastic foils allow a short patch-test application time

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Objective: To investigate whether application of allergic patch tests with transparent semi-occlusive adhesive plastic foils yields higher test sensitivity than when tapes are used. To study whether such foils compared to tapes allow a shorter application time of tests.
Methods: We applied different doses of budesonide printed on polyester squares and vehicle control squares to budesonide allergic subjects for 4 days. Each subject was tested with a set of tests both with a tape and a foil. We assessed all tests when they had been detached and additionally those applied with foils at earlier time points. All assessments were performed both visually and with a laser Doppler perfusion imaging technique.
Results: Test sensitivity is higher with foil applications than when tapes are used and the perfusion is higher with the foils in many cases. The foils allow detachment of visually positive tests before 48 hours in some subjects, regardless of dose.
Conclusions: Test applications with transparent semi-occlusive adhesive plastic foils is sensitive and should be considered for application of patch tests when a short application time is important as when tests are carried out with occupationally hazardous allergens or when test substances containing allergens are expected to be irritating.

P31

Patch test reactions in the elderly

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The incidence of patch test reactivity depends on prior exposure, with few studies evaluating elderly
Subjects: The aim of our study was to address this issue. We reviewed results of elderly patients, (defined ¡Ý 65 years) who attended for patch testing over a five-year period from January 1999 to December 2003. Patients were patch tested to an extended European standard series and additional series depending on clinical presentation. Results showed 322 (16.4%) of 1968 patients patch tested were elderly, 196 women (60%) and 126 men (40%). Balsam of Peru (Myroxylon pereirae) was the commonest sensitizer among men 21/126 (16.7%), followed by fragrance mix in 10 subjects (7.9%) neomycin in 7 (5.6%) and carba mix in 7 (5.6%). Nickel was the most frequently occurring contact allergen in women, 32/126 (16.3%), followed by fragrance mix in 19 (9.7%), thiuram mix in 19 (9.7%), carba mix in 15 (7.7%) and Balsam of Peru in 14 (7.1%). Investigation of ACD in a multicentre study of all age groups in the UK reported nickel as the commonest allergen at 18.6%, followed by fragrance mix (10.7%) and Balsam of Peru (6.7%). Our study shows nickel and fragrance mix reactions to be lower in this elderly population at 11.5% and 9% respectively, Balsam of Peru positivity being higher at 10.9%. This study suggests that patch testing in elderly patients remains a worthwhile investigation yielding significant positive results.

P32

Dexamethasone inhibits dendritic cell activation by skin sensitizers

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Objective: Evaluate activity of a corticosteroid on dendritic cell (DC) activation induced by skin sensitizers.
Methods: Using a fetal mouse skin derived dendritic cell line (FSDC) stimulated by Nickel sulphate (50–100 ìg/ml) and DNFB (1–2.5 ìg/ml), we studied the effect of dexamethasone (DEX)

(0.01–1 ìM) on nitric oxide (NO) production (by the Griess reaction), on nitric oxide synthase type II expression (iNOS) (by immunocytochemistry and western blot) and on the activation of the nuclear factor-kappaB pathway (NF-êB) (by electrophoretic mobility shift assay – EMSA), pathways that we have previously shown to be activated by these sensitizers.

Results: NO production induced by Ni was significantly inhibited by DEX in a dose dependent way. Future studies using 0.5 ìM of DEX, showed a significant reduction of iNOS expression at 24 h induced by both sensitizers. This effect occurred in parallel with the inhibition of NF-êB activation, which was most evident at 45 min.

Conclusions: These results suggest that dexamethasone inhibits intracellular events that are relevant for DC activation induced by skin sensitizers during antigen presentation. Therefore, besides the anti-inflammatory activity of DEX usually used for the treatment of ACD, this drug can also interfere with the initial steps of skin sensitization. This work was supported by FCT (Portugal).

P33

Patch testing an extended standard series

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Objective: To examine the usefulness of the standard allergen series as a sole tool in the diagnosis of allergic contact dermatitis and consider the diagnostic benefits yielded by the routine use of an extended standard series in general dermatology practice.

Methods: From January 1, 2003, to December 31, 2003, one hundred patients attended in a general dermatology unit were recruited for patch testing. Every patient underwent testing with the standard tray recommended by the Spanish Contact Dermatitis Research Group, and simultaneously, with a supplementary series of 35 allergens. Other specific series were performed in some cases, but their results have been omitted in this study. Patients with positive allergic reactions were divided into two groups based on the clinical relevance of their reactions. These groups were subsequently stratified in four subgroups: (1) reactions only to allergens in the standard series; (2) reactions only to additional allergens; (3) reactions to both standard and additional allergens; and (4) reactions to own substances or allergens in other series.

Results: Of patients tested, 62 had at least 1 positive allergic reaction, and among these, 44 had reactions deemed clinically relevant. Of all the patients with relevant positive tests, 70.5% (31/44) reacted only to allergens in the standard tray; 11.4% (5/44) reacted to supplementary allergens exclusively; 4.5% (2/44) reacted to both standard and supplementary allergens. Finally, 6 more patients (13.6%) reacted to other sensitizers.

Conclusion: In our study, 15.9% relevant allergies would have been missed by the standard series alone. Patch testing an extended standard series increased our diagnostic capability, and might be a useful screening tool in those dermatology offices where other series are lacking.

P34

Reproducibility of the positive patch test reactions with the TRUE Test

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The patch test results of patients tested at least twice at our clinic during a period of 11 years were analyzed with regard to reproducibility of the positive patch test reactions found in the first patch testing session.

A retrospective analysis of 257 patients who have been tested with the TRUE Test at least twice between 1991 and 2002 and had a minimum of one positive reaction in the first testing session was done. Test reactions were read routinely after 3 and 5–7 days.

In the first testing session a total of 299 positive reactions were found. Of these allergens, 151 (51%) stayed positive in the second test, 31 (10%) produced a doubtful reaction, 67 (22%) a negative response, and 50 (17%) were not retested because of strong positive reactions in the first test. Of the individual allergens, positive reactions from thiuram-mix, kathon CG and colophony were the most reproducible.

If it is assumed that allergens which were not retested because of strong positive reactions would have shown positive reactions in a retest, a total of 68% of positive reactions were reproduced. A multitude of factors, such as: avoidance of relevant allergens between tests, diminished sensitivity, retesting within a period of more or less active dermatitis, different observers, methodological error, and prior false-positive responses,

influence the reproducibility of patch tests. The results will be put in perspective.

P35

Photo-, phyto- and frostbite- provoked cases of contact dermatitis cured with o3

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Objectives: To show cases of contact dermatitis (CD) provoked by different factors and possibility of their treatment with ozone application.
Methods: Description of clinical cases:

Patient S., female, 17 years old, came to dermatologist with complaints on erythema and vesicles, sense of burning on the face during two weeks. The patient works on the market, exposures by sun. As a result of a talk with the patient, new perfume as a possible reason of photoallergic reaction was suspected. The patient was successfully treated by use of ozone therapy: 6 autochemotherapy minor (AHTmin) treatments were applied. By the end of the course crusts and hyperpigmentation only were observed.

Patient T., male, 36 years old, suffered from erythema and vesicles, itching and sense of burning on both hands and arms for 3 days. During weekend he had contact with cow-parsnip plant. The patient got 5 AHT minor treatments: clinical recovery was registered.

Patient S., 36 years old, frosted his hands two weeks ago. When he came to dermatologist, erythema, vesicles, erosions and crusts on the backs of the hands were observed. Ozone therapy (AHTmin – 5 treatments plus ozonized water externally) was successfully applied: full recovery was registered.
Summary of results: Different cases of CD were successfully treated by ozone therapy use.
Conclusions: CD provoked by different factors can be cured with ozone.

P36

Risk factors of fragrance allergy revisited

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Prompted by a recent publication on contact allergy to the fragrance mix (FM) declining with age, patch test data of the IVDK (1992–2002, www.ivdk.org, n = 90824 patients) were subjected to a multifactorial logistic regression analysis, employing a finer age categorization than previously used (Uter W et al., Occup. Environ. Med. 2001; 58: 392–8), additionally adjusting for "polysensitization", operationalized as the number of additional positive patch test reactions to other standard series allergens. The aim was to disentangle a possible association between age and contact sensitization in general, and age and FM contact allergy in particular. The strongest of all associations observed was to the number of additional positive patch test reactions ("polysensitization"; OR for 1 vs. 0 additional reactions: 2.7 [95% CI: 2.6–2.9] steadily increasing to OR for 4+ vs. 0 additional reactions: 12.8 [11.7–13.9]). Independently from this, the well-known increase of FM contact allergy with age (OR 1.9 beyond age 60) and higher prevalence in female patch test patients, but only up to age 60, was confirmed, however, no decline beyond age 80 was observed. Moreover, it was found that not health care workers in general, but masseurs/physiotherapists, and, to a lesser extent, geriatric nurses have a high risk of FM contact allergy. In conclusion, our results confirm the profound impact of age, and partially of sex, on FM contact allergy, which makes stratification, standardization or adjustment a prerequisite for meaningful comparative analyses. The phenomenon of "polysensitization" deserves further attention.

P37

Autoxidation of the fragrance caryophyllene forms contact allergens

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This is part of an ongoing effort to investigate how autoxidation affects the sensitzing potential of terpene-based fragrances. We have previously shown that terpenes such as abeitic acid (diterpene), limonene and linalool (monoterpenes) form stable hydroperoxides when oxidized. These hydroperoxides have proved to be strong allergens. Its therefore of special interest to study the connection between formation of hydroperoxides caused by autoxidation of fragrance chemicals during handling and storage and an increased allergenic effect.
Objective: To investigate the autoxidation of caryophyllene (sesquiterpene) and study its effect on the sensitizing capacity.
Methods: Caryophyllene was exposed to air and the autoxidation was monitored by GC and HPLC. The major oxidation products were isolated and their structure determined. The allergenic activity of pure caryophyllene and its oxidation products was investigated in animal assays and clinical testing.

Result: Only 10% of the staring material remained after 20 weeks of air exposure. The major oxidation product was caryophyllene oxide. Substantial amounts of formaldehyde were found in the oxidation mixture. Little or no hydroperoxides were detected in the total oxidation mixture. Caryophyllene oxide and oxidized caryophyllene showed a low sensitizing capacity in animals and very few positive reactions at patch testing.
Conclusion: Caryophyllene is easily oxidized at air exposure. A low allergenic effect is observed in both sensitization studies and clinical testing. This is consistent with our earlier findings that the amount of hydroperoxides is important for the allergenic activity of autoxidized terpenes.

P38

Quantitative structure activity relationships for fragrance aldehydes

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Fragrance substances represent a diverse group of chemicals, some being associated with the ability to cause allergic skin reactions. In recent work, we evaluated two groups of fragrance chemicals, saturated aldehydes (aryl substituted and aliphatic aldehydes) and ?,?-unsaturated aldehydes. QSAR models relating the LLNA EC3 values to a measure of the lipophilicity of a chemical (log P) and s* (a measure of reactivity) were developed for both sets of aldehydes. The outcome was consistent with ?,?-unsaturated aldehydes reacting via Michael addition, whilst saturated aldehydes formed Schiff bases with proteins. In the present study we evaluated further aldehydes to test the robustness and extend the scope of the QSARs. The QSAR models were used to predict EC3 values for 4 new Michael addition aldehydes and 6 new Schiff base formers. LLNA data generated for these compounds demonstrated the original QSARs were fairly accurate but still required improvement. Development of the QSAR models has provided us with a better understanding of the potential mechanisms of action for aldehydes and hence how to avoid or limit allergy. Knowledge generated from this project is being incorporated into new/improved rules for sensitisation in the expert toxicity prediction system Deductive Estimation of Risk from Existing Knowledge (DEREK).

P39

The accuracy of material safety data sheets: reporting of skin irritants and skin sensitisers

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Objectives: In Australia the National Occupational Health and Safety Commission (NOHSC) requires that manufacturers provide Material Safety Data Sheets (MSDS) for all hazardous materials. However the accuracy of MSDS has not previously been assessed, utilizing the specified NOHSC criteria for hazardous substances.
Methods: 100 consecutive product MSDS were collected from workers with potential work-related cutaneous exposure, attending an occupational dermatology clinic. Manufacturers were contacted to verify the ingredients of each product. MSDS were evaluated using for skin irritants and skin sensitisers, and for compliance with the NOHSC criteria for hazardous substances (sensitisers present at a concentration $>=1\%$, irritants present at a concentration $>=20\%$). All sensitisers were checked for clinical significance (relevant positive patch test result) to the worker's dermatitis.
Results: On manufacturer follow-up, 58% of the MSDS satisfied the NOHSC criteria. However, 3 products omitted sensitisers, present at $<1\%$. Importantly, one sensitiser was clinically significant. 19% failed to meet the NOHSC criteria. 17 MSDS omitted sensitisers at $>=1\%$, two omitted irritants at $>=1\%$. Irritants were specified correctly in 19/22 cases, whereas sensitisers were specified correctly in only 30/71 cases ($p = 0.0003$). Non-compliant MSDS may have been as high as 42%, as insufficient information to enable assessment was provided on manufacturer follow-up regarding the percentage concentration of 1 unlisted irritant and 22 unlisted sensitisers.
Conclusion: MSDS are significantly inaccurate with respect to skin sensitisers. Sensitisers and percentage concentration are frequently omitted from MSDS, thereby providing inadequate information for the prevention of skin sensitisation for workers.

P40

A case of contact dermatitis to polyethylene glycol

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A 58-year-old female presented with a rash around an ulcer of livedo vasculitis. She had applied ActosinTM ointment (Bucaladesine Sodium) on the ulcer 1 month before. A patch test with ActocinTM ointment (as is) resulted in a ?+ reaction on D2 and + on D3. Polyethyleneglycol (10%pet.) gave a + reaction on D2 and + on D3. A skin biopsy of the positive reaction showed contact dermatitis. Patch tests to Bucaladesine Sodium and other components of ActosinTM ointment were negative. The eruption disappeared after 2 weeks of treatment with a topical corticosteroid.

P41

Contact allergy to clindamycin

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A 42-year–old non-atopic lady was treated with twice daily 2% clindamycin vaginal cream (Dalacin®) and ster-zac (bath antiseptic) for hidradenitis of the groins. She also had mild facial acne.

She developed genital pruritus and erythema which quickly became generalised which she related to the use of ster-zac. However, when she applied clindamycin to her face a few weeks later, she developed a severe reaction which became generalised.

The patient was patch tested with an extended European series, the clindamycin cream, ster-zac 1:100 and E45 which had also been used. Initially she developed an angry back picture which was difficult to assess but the standard testing was negative.

Repeat patch testing to the constituents of the topical preparations used produced a reaction to clindamycin 1%, 5% and to dalacin cream 'as is'.
Discussion: Coskey1 first described contact allergy to clindamycin in 1978. Since then there have been 6 further case reports. Mild local adverse reactions to topical clindamycin preparations such as burning, excessive dryness, itching and erythema are not uncommon, but more serious adverse events should prompt exclusion of a contact allergic component. Despite topical clindamycin being used for more than 25 years, sensitisation appears uncommon.

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P42

Cutaneous reactions from non-steroidal anti-inflammatory drugs: follow-up of 4 years

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Introduction: Cutaneous reactions due to use of non-steroidal anti-inflammatory drugs (NSAID) are frequently described. In the Contact Unit from the Department of Dermatology of Juan Canalejo Hospital, we compiled all cases studied during 4 years (from 2000 to 2003) to analyze the incidence, frequency and type of reactions derived from NSAIDs use.
Material and methods: We used a NAIDs battery (Aristegui lab.Ò) on 55 patients with clinical suspicion of adverse reaction from NSAIDs. We performed epicutaneous study on 17 and additional photoallergic study, after UVA irradiation (from 5 to 7,5 J/cm^2), on 38 cases. In some cases we patched the drug used by patient as is and/or the active substance provided by the laboratory if it was not included on NSAIDs battery. Readings were done following ICDRG criteria at 48 and 96 hours on patch tests and 24 and 72 hours on photopatch tests. Healthy controls were patched.
Results: 22 patients showed positive test: 15 cases were diagnosed as photoallergic dermatitis (etofenamate 5; dexketoprofen 4; ketoprofen 3; piroxicam 2; diclophenac 2 and aceclophenac 1). Five cases were explained as allergic contact dermatitis (etofenamate 2; fepradinol 2 and phenylbutazone 1) and two cases of fixed drug eruption from piroxicam were found.
Conclusion: In this study we observed that cutaneous reactions due to ketoprofen and piroxicam are still high. It is important to note the high incidence of allergic and photoallergic reactions from dexketoprofen, a recently introduced NSAID, reporting always a cross reaction between ketoprofen and dexketoprofen.

P43

Acute urticaria to infliximab

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Infliximab is a chimeric antitumor necrosis factor-alpha monoclonal antibody used to treat Crohn's disease and rheumatoid arthritis. Acute infusion reactions, headache, fever, chills, urticaria and chest pain were seen in 17% of patients with infliximab compared with 7% of those receiving placebo. Other adverse cutaneous reactions are fungal dermatitis, eczema, seborrhoea, hordeolum, bullous eruption, furunculosis, periorbital oedema, hyperkeratosis, rosacea, verruca, skin pigmentation, alopecia, leukocytoclastic vasculitis, lichenoid drug eruption, erythema multiforme, perniosis-like eruption, granuloma annulare and acute folliculitis. Any pathogenic mechanism has been suggested. Patch test with infliximab can induce flare-up of lesions, nausea and malaise and suggest a percutaneous absortion. A sixty years-old man with atopy background and rheumatoid arthritis treated with Remicare®, infliximab who developed a severe acute urticaria with angioedema is presented. The lesions appearance after previous endovenous administrations and the worsening spreading wheals days after the injection clinically suggested an hypersensitivity mechanism. The protocolized study drug hypersensitivity performed showed only the Prick Test positivity with infliximab at 30/60 minutes. Patch test with infliximab was negative and any adverse event was reported. Actually the patient is treated with etanercept and this drug is well tolerated. This result suggested a type I hypersensitivity mediated reaction. Urticaria could be induced as immunologic reaction of the host against the murine part of infliximab, just as it hapens with other antichimeric antibodies.

P44

A case of contact dermatitis caused by a NSAID's soluble agent

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A fifty five year-old man had experienced itching sensation when he applied analgesic plasters for his lumbago. He tried to use several kinds of analgesic plasters, however he felt itching sensation whenever he used them. He applied a plaster containing ferbinac for his left elbow joint's pain on April 2003. On the next day, an itching erythema developed on the area where the plaster was applied. He was treated with a difluprednate ointment, and his dermatitis gradually improved. He visited our clinic for precise medical examination for finding out the causative agent of his dermatitis on May 13, 2003. We conducted 48 hours closed patch testing with the plaster he used and it's ingredients. He reacted positively to the plaster containing ferbinac and crotamiton 5%p that was used for dissolute the active drug. He also reacted positively to a cream containing ketoprofen, however he reacted negatively to ketoprofen 1%p. Crotamoton was also used in the ketoprofen cream.

P45

Neomycine sulfate patch tests

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Objective: The purpose of this study is to investigate if patients with neomycin sulfate allergy may develop test responses that are unclassifiable by commonly used assessment scales but which should be considered positive.
Materials: 16 patients who tested positive to neomycin sulfate patch tests are retested with different dose levels and application times. Test areas are assessed visually up to 11 days.
Results: Three types of reactions were observed. The first type was characterized by erythema and diffuse infiltrate. Some of these had in addition either discrete papules or both papules and vesicles on their surface. The second type of reaction initially developed large perifollicular papules which later developed into coalescent erythema and diffuse infiltrate. The third type of reaction exhibited perifollicular papules only which declined over time. This type was unclassifiable by commonly used assessment scales. All types of reactions were of clinical significance.
Conclusion: The results support that universal assessment scales for patch-test responses due to

different test agents may be inappropriate for assessment of neomycin sulfate patch tests. The clinician should only consider assessment scales as an aid in the assessment of test responses and be aware that morphology of test responses may differ between test agents and test techniques.

P46

Allergic contact dermatitis to a retarding cream in a condom

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We describe a case of a 42-year-old non atopic man with a history of ano-perianal eczema in consequence of the use of anti-haemorroidal ointments and allergic contact dermatitis to Myroxylon pereirae, benzocaine, paraben mix and paraphenylenediamine. He was referred to our Unit for a strong eczematous reaction in the genital area with a marked oedema of the balanoprepuzial region that had appeared some hours after the use of a condom (Settebello-Hatù® Durex) made of natural latex and containing a retarding cream composed with benzocaine 5%, polyethylene glycol plus glycerin 94,7% and paraben 0,3% as preservative. The suspension of the use of the condom and treatment with a corticosteroid cream healed the eruption in few days. Patch testing with the SIDAPA (Società Italiana di Dermatologia Allergologica, Professionale e Ambientale) standard series, an additional rubber series, a piece of the rubber's condom washed clean of cream and the condom's cream gave positive reactions to Myroxylon pereirae, benzocaine, paraben mix, paraphenylenediamine and condom's cream. Further patch test with the other ingredients of condom's cream was negative as well as latex prick test. We discuss about the ethiologic agents and the most useful diagnostic test in allergic contact dermatitis condom-related and the preventive measures that should be adopted.

P47

Contact dermatitis to peppermint and menthol in a transdermal therapeutic system

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A 60-year-old non atopic was referred to our Unit due to the onset of severe eczematous contact dermatitis on the lumbar region, following repeated applications of a transdermal therapeutic system (TTS) with flurbiprofen for lumbar pain. Patch testing with the SIDAPA (Italian Society of Allergological, Occupational and Environmental Dermatology) standard series, the TTS as is and the constituents of TTS, including flurbiprofen 2% pet., isopropyl myristate 5% pet., polysorbate 80 5% pet., sorbitan sesquioleate 20% pet., peppermint oil 2% pet. and menthol 1% pet. gave a strong positive reaction to TTS, peppermint oil and menthol and a weak reaction to fragrance mix. Allergic contact dermatitis to peppermint oil and its principal constituent (menthol) is rare. Isolated cases of patients with oral symptoms after the use of mentholated cigarettes, toothpaste flavours and fragrances have been reported. Peppermint oil and menthol are used in TTS with anti-inflammatory activity for their anesthetic properties and their vasodilatation effects that aid topical drug penetration. Reapplication of the device to the same site, the irritant action of the vehicle or adhesive, the length of occlusion, associated with warm and humid climates, may promote sensitization to menthol otherwise rarely a cause of contact dermatitis, when used in products designed for a brief contact with the oral mucosa. In contact allergies induced by TTS-treatment patch tests are needed to make a precise identification of the causative agent.

P48

Actual risk of contact dermatitis in hairdressers

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In order to know the actual risk of contact dermatitis in hairdressers, we studied, from 1994 to 2003, 300 hairdressers of a total of 7510 patients seen in our Department of occupational skin diseases. Most of them were women (93%) with a mean age of 23.7 years. A positive patch test response to one or more of the allergens tested was presented by 215 patients (71.7%). Occupational allergic contact dermatitis was diagnosed in 174 cases (58%). The most frequent sensitizations showed by positive patch test response were to: PPD (54.3%), 4-aminobenzene (40.7%), nickel (36.7%), disperse orange (17%), p-toluene-diamine (15.3%), ammonium persulfate (14.3%), aminophenoles (14.0%), acid thioglycolic (12.7%) and kathon (10.3%). Irritant contact dermatitis (20%), no occupational allergic contact dermatitis (5.3%), atopic dermatitis (6.7%) were some of the other diagnoses

between the hairdressers. We compare these results with those of a previous study of 379 hairdressers who attended our department from 1980 to 1993, in order to evaluate the effects of the changes in the substances and techniques used in hairdressing and the occupational education in the risk of sensitization in this trade.

P49

Occupational dermatoses of machinists – Finnish statistics

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Objective: In this study the statistical data on occupational dermatoses of Finnish machinists in 1992–2001 were analysed.
Methods: The data were collected from the Finnish Register of Occupational Diseases (FROD) to which physicians are obligated to report all cases of occupational disease. Each case record consists of information on the patient and the employer, date and diagnosis, causative agents, etc.
Results: During the 10-year period, a total of 281 occupational dermatoses of machinists were diagnosed. Dermatoses consisted mostly of irritant contact dermatitis (N = 144), allergic contact dermatitis (N = 108) and unspecified contact dermatitis (N = 21). Only few cases of protein contact dermatitis and contact urticaria as well as occupational acne were reported. The main causes of irritant contact dermatitis were cutting oils and fluids, oils and lubricants, and organic solvents; the commonest inducers of allergic contact dermatitis were formaldehyde, cutting oils and fluids, metals (nickel, chromium and cobalt) and various antimicrobial agents.
Conclusion: Dermatoses were the second commonest occupational diseases of machinists, after hearing loss, and they accounted for 27% of all occupational diseases within the profession. Machinists are a large occupational group (about 19 000 employees; 0.8% of the work force) in Finland, and their dermatoses formed a noteworthy proportion (about 2.6%) of the occupational skin diseases reported during the study period.

P50

Occupational dermal exposure to permanent hair dyes in hairdressers

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Objective: To assess occupational dermal exposure to permanent hair dyes in hairdressers.
Methods: Dermal exposure was assessed in 31 hairdressers using a previously evaluated method, hand wash sampling with bag rinsing. The measurements were performed in hairdressing saloons during working hours. Hand wash samples were collected from each hand before start of the hair dyeing process, after application of the hair dye and after cutting the newly dyed hair. 13 of the hairdressers did not use gloves during application of the hair dye, and during cutting of the dyed hair no one used gloves. The samples were analysed for aromatic amines and resorcinol using an HPLC-method.
Results: After application of the hair dye PPD (p-phenylenediamine) was found in samples from 1 hairdressers (148–185 nmol/hand), TDA (toluenediamine) in samples from 12 hairdressers (range 10–735 nmol/hand) and resorcinol in 22 individuals (range 19–769 nmol/hand). In the samples taken after cutting the dyed hair PPD was found in 2 hairdressers (range 36–358 nmol/hand), TDA in 14 (range 8–361 nmol/hand) and resorcinol in 20 (range 10–725 nmol/hand.
Conclusion: Skin exposure to aromatic amines and resorcinol was detected in more than half of the hairdressers after application of hair dye and also after cutting newly dyed hair. To reduce exposure improved skin protection is important.

P51

Occupational contact dermatitis among operating room nurses

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Background: Occupation related dermatitis is a common problem in health care workers, especially in nurses, who are exposed to a wide variety of allergenic and irritant substances. The aim of this study was to assess the prevalence rate of skin symptoms among personnel handling chemical disinfectants and to examine which allergens were important.
Methods: We investigated 460 randomly selected health care workers (HCW), who had constant contact with chemical disinfectants during their work. The study was performed by means of a questionnaire, a medical exam-

ination, skin patch test using Finn chambers and glutaraldehyde, benzalkonium chloride, hydrogen peroxide and chlorine compounds at 0,1, 0,5 and 1,0% wat.

Results: 241 HCW (52,5%) described various skin symptoms they attributed to disinfectant exposure. Generally, these symptoms were mild and ranged from pruritis to hand eczema. Of these 66 (14,4%) tested were skin patch test positive. Of the 460 HCW tested, 37 (8%) had positive patch test reactions to benzalkonium chloride, 22 (4,8%) to chlorine compounds, 18 (4%) to glutaraldehyde, 6 (1,2%) to hydrogen peroxide. 5 HCW (7,6%) testing positive to disinfectants gave no history of reactivity to them. History of atopic dermatitis was found in 50 (10,9%) and it was associated with diagnosis of allergic contact dermatitis and positive patch test reactions to benzalkonium chloride. Also positive patch tests reactions were associated with frequent use of latex gloves in contrast to those, which used latex gloves while working constantly or didn't use them at all.

Conclusions: 1. Skin symptoms related to work with chemical disinfectants are common, but mostly mild. 2. Benzalkonium chloride is one of the strongest sensitizing disinfectants used in health care professions, especially for atopic persons who do not take measures of protection during exposure to it.

P52

Contact dermatitis due to computer's mouse

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Background: Introduction of informatics has facilitated the apparition of lesions affecting the hand responsible of mouse movement. Different cases of contact dermatitis related to the use of personal computers have been published in the last years and two new morphologic patterns within cutaneous pathology affecting hands have been described in direct relationship with professional occupation, named generally "computer fingers" and "computer palms".

Case report: We present a 7-patient series presenting lesions suggesting contact dermatitis after continued use (min 8 hours/day) of personal computer from a total of 700 patients revised. Patch tests including standard series of the GEIDC, series for plastics and glues and others related to specific details of each patient were performed in all cases. Six of our patients presented lesions in the 2, 3 and 4 fingers of the right hand while the other one was affected in the right hand palm. In our patients, all the epicutaneous tests were negative or without relevance, suggesting a mechanical cause to the occupational dermatitis presented.

Comments: Products used in the fabrication of ABS plastics, employed to make personal computers mouse, such as ftalates, cobalt salts and resorcinol monobenzoate have been described as possible allergens. However, concentration of these allergens is too small to ensure a causal relationship. Pressure or an excessive sweating could facilitate these reactions. Wide use of informatics nowadays obliges us to consider those factors in patients presenting chronic dermatoses in their hands. Furthermore, better ergonomics in work places could prevent this kind of occupational dermatitis.

P53

Hand contact dermatitis in jewellwery 2 cases

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The production of jewellery is currently mostly industrial and the jewellers perform only one or two stages in the manufacturing process. The jewellers make jewellery by hand in small workshops and are more polyvalent: they shape the metal with pliers or hand tools or cast it in moulds, assemble the individual parts with glues, carve metal, diamonds and other stones, clean metals with soaps and ultrasonic baths. The occupational dermatitis is of irritant nature (acid and alkalis in metal cleaners, soaps, detergents, metal dust, abrasions from polishing wheels and emery paper, heat, adhesives, etc) and allergic nature (potassium dichromate, 2-mercaptobenzothiazole, ammoniated mercury, carba mix, epoxy resin, mercapto mix, formaldehyde, nickel, colophony). We report the cases of two jewellers working in workshops.

A 47 year old atopic woman already known for a sensitivity to metals (nickel, potassium dichromate and cobalt) developed recurrent vesiculopustular erythematous lesions of both palms with occasional infections treated with systemic antibiotics and topical steroids. Patch tests were performed for the European standard series, woods, and personal series. There were positive + reactions at 96 h to colophony, palladium, and personal waxes. Information obtained through the manufacturer revealed colophony in the waxes frequently used by jewellers to fix the precious stones to woods and metal allowing the stones to be carved. A 47 years old atopic man working as a jeweller for 32 years developed recurrent eczematous lesions of the fingers of the

right hand. Patch tests were performed for the European standard series, preservatives, plastics, acrylates and personals series and were positive ++ at 96 h for urea formaldehyde, diethylenetriamine, araldite hardener and the soap used to clean the jewels. Uncommonly this contact allergy is not due to the epoxy resins themselves but to the hardener. The urea formaldehyde and the diethylenetriamine are in fact used as epoxy resins hardeners. There were no reactions to the araldite resin but there was one to its hardener.

In conclusion we report two unusual cases of hand contact dermatitis in jewellers. Because jewellers are exposed to a variety of substances, to detect the allergens the inquiry must be accurate and extensive patch testing may be required. Common allergens are compounds of uncommon substances and tools and uncommon allergens are compounds of well-known sensitizers.

P54

Prevalence of skin changes in the cleaning industry

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Background: In the cleaning industry, the hands are exposed to water and irritants, resulting in dry skin and hand eczema. The prevalence and severity of skin changes is unknown.
Objectives: To quantify the prevalence and the severity of skin changes of the hands. To compare questionnaire-based self-reported signs of hand eczema (both current and at any occasion during the last 12 months), with skin changes revealed by clinical examination.
Methods: A random sample of 231 employees in the cleaning industry participated in the study. Most of them were immigrants. They had to answer a (translated) questionnaire about signs of hand eczema. Then all of them were examined and the severity of hand eczema was graded by a scoring system1. In the comparison only objective subvariables (desquamation, erythema, fissures, infiltration, vesicles) were used.
Results: Clinical examination of the hands detected desquamation in 38%; erythema in 29%; fissures in 24%; infiltration in 12%; vesicles in 4%.

Severity scoring of hand eczema: one point in 21%; two points in 18%; three points in 9%; four points in 4%.

Signs of hand eczema reported in the questionnaire based on the current situation: desquamation in 17%; erythema in 20%; fissures in 20%; infiltration in 10%; vesicles in 12%.

Signs of hand eczema reported in the questionnaire based on any occasion during the last 12 months: desquamation in 18%; erythema in 17%; fissures in 22%; infiltration in 11%; vesicles in 15%.

False negative self-reporting by the questionnaire: desquamation in 26%; erythema in 18%; fissures in 14%; infiltration in 11%; vesicles in 3%.

False positive self-reporting by the questionnaire: desquamation in 5%; erythema in 10%; fissures in 10%; infiltration in 8%; vesicles in 11%.
Conclusions: Desquamation and erythema were the most common signs both in clinical examination and in questionnaire. The self-reported prevalence (both current and over the last 12 months) of erythema and desquamation is an underestimation of the true prevalence. Scoring hand eczema revealed that most of the employees scored one or two points; indicating that most of the clinical signs of hand eczema are minor. False negative self-reporting by questionnaire was high; indicating that these minor symptoms of hand eczema were probably not recognized by the employees. False positive self-reporting was also high; probably because they misunderstood the questions. This study illustrates the need for a consensus about the distinction between ''minor skin damage'' and ''true eczema''.

Reference

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P55

Nordic Occupational Skin Questionnaire (NOSQ-2002)

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Questionnaire-tools for surveying occupational skin diseases and exposure are needed for com-

parable epidemiological research, workplace assessments, and evaluation of workplace interventions. 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 exposures to environmental factors.

Nordic Occupational Skin Questionnaire (NOSQ-2002) includes two questionnaires designed for separate purposes. NOSQ-2002/short is a 4-page questionnaire for screening skin problems at workplaces. NOSQ-2002/long is an in-depth survey tool for research purposes. The questionnaire covers occupational history, atopic symptoms, self-reported hand or forearm eczema, exacerbating factors, consequences and life impact of dermatoses, self-reported contact urticaria on hands or forearms, skin symptoms, skin tests, exposures, and protective glove use. For the time being, NOSQ-2002 is available in English, Danish, Swedish, Finnish and Icelandic. Further translations are welcomed.

The NOSQ-2002 report includes a review of pertinent literature on questionnaire methods for skin disease studies. Questions on work and exposure can be tailored to specific populations or occupational groups, according to the instructions and recommendations given in NOSQ-2002/INFO version of the questionnaire.

The NOSQ-2002 questionnaire files can be downloaded from www.ami.dk/NOSQ. The Nordic Council of Ministers has the copyright to the NOSQ-2002 questionnaires. Use of the questionnaires is free of charge. The NOSQ-2002 questionnaires and their present and possible future translations cannot be used commercially.

P56

Occupational protein contact dermatitis from shiitake mushrooms

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Case report: A 54-year-old woman, with no family or personal history of atopy, developed skin symptoms and cough after she had been cultivating shiitake mushrooms for 12 months. The patient reported dermatitis on the backs of her hands, fingers and on her wrists, after 1 or 2 days of being in contact with shiitake mushrooms. The skin lesions and cough disappeared entirely during the holidays. Result: Prick tests to common inhalant allergens, molds and flours were negative, with the exception of D. farinae (3 mm). The prick-to-prick test was positive for shiitake gill (3 mm), shiitake stalk (3 mm) and dry shiitake (8 mm ps). The histamine wheal was 5–7 mm. Control prick tests with shiitake on 5 non-exposed subjects were negative. An open test was performed with shiitake on the flexor side of the upper arm. Within 20 minutes a positive reaction appeared comprising two wheals and flare reactions. Patch test with shiitake gave a strong toxic reaction in 2 days, which continued to diminish on days 3 and 4. Conclusion: Contact urticaria is the clinical skin symptom of immediate allergy, but repeated exposure may lead to protein contact dermatitis. However, our patient has not had urticaria symptoms from shiitake, although the prick-to-prick and open tests were positive. To our knowledge, this is the first report of protein contact dermatitis from shiitake in a patient with a positive immediate skin reaction and negative patch test result.

P57

Allergic contact dermatitis to compositae mix in children

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Background and aim: Recent studies have demonstrated that contact sensitization to Compositae is not uncommon in adults. However, to our knowledge, no data are available in children. Our purpose was to investigate the prevalence of contact sensitization to Compositae in a pediatric population.

Methods: 434 consecutive pediatric patients (205 M; 229 F; mean age 6,7,,b3,4 years) with suspected allergic contact dermatitis were patch tested with 30 haptens comprising Composite mix 5% (Tenacetum volgare, Arnica montana, Partenolide, Chamomilla recutitia, Achillea millefolium) at the Dermatology Unit of the Department of Pediatrics in Padua.

Results: 11 patients (7 M; 4 F; mean age 5,6,,b2,8 years) had a positive patch test reaction to Compositae mix. In all these patients dermatitis was localized on the face and/or on the hands. Most of them had more than one positive reaction. 6 were affected by atopic dermatitis, 2 had a personal history of mucosal atopy and one had both. In 8 patients (5 with atopic dermatitis, 2 with mucosal

atopy) the reaction was considered clinically relevant.
Conclusion: It might be useful to add Compositae mix to the pediatric screening series, when investigating dermatitis of air-exposed areas in children with atopic diseases.

P58

Multisensitization to plants: clinical case

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We observed a 65 years old male patient with pruritus, scaling erythema and liquenification areas on the face, neck, forearms and hands. For six years he had a story of episodic crisis of exsudative erythema associated with farm work. The skin biopsy showed irregular acantosis with slight hyperkeratosis and a mild multifocal lymphohistiocytic infiltrate, with many eosinophils. The patch tests with the Contact Dermatitis Portuguese Group of Study standard tray were positive for colophony, perfume mix and lactone mix. The patch tests with plant series were positive to atranorin, usnic acid, alantolactone, Parthenolide, lichen mix, Frulania dilatata, Achillea millefolium and Tanacetum extracts. Treatment was started with oral prednisone and hydroxyzine plus topical hydrocortisone and emollient cream with great improvement. The patient was advised about the avoidance of possible allergens sources. This kind of multisensitization to plants is an uncommon finding and poses diagnostic and therapeutic problems. This patient had a sustained recovery by avoiding farm work and by removal of in house plants.

P59

Patch test results to plant extracts and chemicals

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Objective and methods: We review patch test results from two special patch test series for plant allergens, 'plant extracts' and 'allergenic plant chemicals', provided by Prof. Hausen (Germany) and tested in 1992–2003. The standard series contained Sesquiterpene-lactone mix (SL mix) since 1993 (3/1998–10/1999 excluded) and Compositae mix since 3/1998. We present the cases where either SL mix or Compositae mix gave an allergic reaction and where, in addition, the series of plant extracts was tested.
Results: SL mix and Compositae mix were tested to 900 patients. Among them, plant extracts were tested in 122 and plant chemicals in 104 cases. 30 patients had an allergic reaction to Compositae mix and 17 to SL mix as well. In the plant extract series, there were more than 5 allergic reactions to feverfew(21), true chamomile(21), arnica(18), chrysanthemum(18), laurel bay leaf(13), tansy(12), gaillardia(9), yarrow(8) and pot marigold(7). In the plant chemical series, there were 9 allergic reactions to parthenolide and single reactions to primin, chlorophorin and Mansonone A.
Conclusions: Compositae mix gave a positive test reaction always together with SL mix, which gave a positive reaction in only part of these cases. The concentration of Compositae mix was lowered from 6% to 3% in 1/1999 because of cases of active sensitisation. The lower concentration seems to be reliable for detecting allergy, although it still causes active sensitisation.

P60

Permeability of gloves to plant allergens

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Objective: Study permeability of gloves to plant allergens, therefore evaluating glove efficacy for hand protection.
Material and methods: We studied 20 female patients (aged 21–71; mean 45,1 years) with ACD from plants, 10 allergic to diallyl disulfide (DAD) from Allium sativa, 8 allergic to alpha-methylene-gama-butyrolactone (AMGBL) from Alstroemeria ligtu and 2 allergic to primin from Primula obconica. Patch testing was performed applying the allergens, for 24 or 48 h, directly on the skin and over fragments of different gloves: domestic rubber gloves (RG), nitrile latex gloves (NG), vinyl gloves (VG), surgical latex gloves (LG) and polyethylene gloves (PG).
Results: VG, PG or LG gloves offered no protection for these 3 allergens. With RG and NG gloves, DAD reactivity was abolished or significantly reduced, respectively, in 5 and 7 cases. Reactivity to AMGBL wasn't abolished by any

glove material. NG abolished skin reactivity to primin; RG was efficacious only in 1 patient.
Conclusions: Advising gloves in patients with ACD from plants is difficult, as allergen permeability through gloves associated with occlusion may intensify the dermatitis, as occurred during skin testing. Nitrile latex gloves may protect from primin and garlic dermatitis, whereas they are not helpful for manipulating Alstroemeria. Although exposure time in this study is higher than in real life, results show interesting data on glove permeability to these plant allergens and support our patients' complaints that gloves didn't protect them.

P61

EPOX 2002: concomitant sensitizations to epoxy resin components

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Objective: The study EPOX 2002 is performed to detect the most frequent allergens in epoxy resin systems (ES) currently in use. In particular, concomitant test reactions are analysed to identify possible 'indicator' allergens for a future ES test series.
Methods: Multicenter study within the German Contact Dermatitis Research Group (DKG) and the Information Network of Departments of Dermatology (IVDK) with 27 ES components.
Results: From Oct. 2002 to Nov. 2003, 120 patients have been tested with the preliminary ES series. Of the 49 patients reacting to epoxy resin based on diglycidylether of bisphenol F (DGEBF), 44 also reacted to the standard epoxy resin based on diglycidylether of bisphenol A (DGEBA), i.e., 90% (95%-CI [confidence interval]: 78%-97%).

Out of 21 patients positive to 1,4-butanediol diglycidylether (BDDGE), 18 also reacted to 1,6-hexanediol diglycidylether (HDDGE) (86%; 95%-CI: 64%-97%). All 8 patients with allergic reaction to cresyl glycidylether (CGE) also reacted to phenyl glycidylether (PGE). Concomitant reactions to PGE and p-tert butylphenyl glycidylether (PTBPGE) occured in 9 patients, while 5 patients reacted to PGE without reaction to PTBPGE and 6 patients vice versa.
Conclusions: Immunological cross sensitization as well as frequent concomitant exposure to DGEBA and DGEBF epoxy resins is well known. Our data support testing a DGEBA resin as an indicator. HDDGE might serve as an indicator allergen for BDDGE; however, the sample size is too small yet to make a final decision. PGE obviously is a valuable tool to detect sensitization to CGE, but not to PTBPGE.

P62

Methacrylates in dental restorative materials

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Commercial dental restorative materials were analysed in order to get information about the occurrence and amounts of sensitizing acrylates and methacrylates. The analytical results were compared to information given in the safety data sheets.

Acetone soluble methacrylates of seven bonding materials, eight composite resins and two glass ionomers were identified by gas chromatography with mass selective detection and quantified by liquid chromatography with UV detection.

The most frequently occurring methacrylates in the bonding materials were 2-hydroxyethylmetharylate (2-HEMA) in the concentration range 0.3–28% and 2,2-bis(4-(2-hydroxy-3-methacryloxypropoxy)phenyl)-propane (bisGMA) in the concentration range 21–40%. BisGMA and triethyleneglycol dimethacrylate (TEGDMA) were the most frequently occurring methacrylates in composite resins. Their concentration ranges were 5.8–21% and 3.2–6.7% respectively. The main methacrylate of the two glass ionomers was 2-HEMA (23%) or trimethylolpropane trimethacrylate (TMPTMA, 9%).

Information about methacrylates was given in the safety data sheets for about half of the products that according to the analysis results contained methacrylates. Safety data sheets need to be improved so that the health risks for dental personnel can be reliably asessed and controlled.

P63

Prevention of occupational dermatitis in the digital age: www.2hands.ch

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In 1998 we began to develop multi-lingual educational material for apprentice schools. This material was highly graphical, consisting of overheads with explanatory notes. The kit also included clinical slides, an introductory videotape, and handcream samples. By early 2000, 300 kits had been distributed to teachers of apprentices all over Switzerland. Teachers rapidly embraced the kit thanks to its simplicity and ease of use. Feedback was also gratifyingly high among those outside teachers per se: health professionals, safety engineers and others involved in prevention, even outside Switzerland.

By 2004, however, we had made a total paradigm shift: kits were out, the Internet was in. The advantages were obvious, both in quantity and in quality. We could reach more people and we could reach them better. When we made 300 kits our budget reached its limit, but with the virtually free Internet, using only one highly developed digital course, we can now reach a potentially limitless audience. Moreover, we can refine, update and amend our material continuously.

Our main course includes defining and preventing contact dermatitis, defining the special requirements of such varied users as hairdressers, bricklayers and machinists. It also shows how to avoid misuse of protective gloves. The course still involves an intense use of graphics, but they were redrawn from scratch for the Internet to maximize simplicity, immediacy and elegance.

Conclusions: The risk of hand eczema is more than doubled in dental technicians. The work involves frequent and unprotected exposure to acrylates and wet work. Education regarding skin protection is important.

P64

Shoe contact dermatitis

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Because of its numerous etiologies, foot dermatitis can be difficult to diagnose despite of thorough history and physical examination. The differential diagnoses are challenging and include allergic contact dermatitis, dyshidrosis, juvenile plantar dermatosis, atopic dermatitis, lichen planus.

Methods: In the Cutaneous Allergology Unit of the Department of Dermatovenereology of Pedro Hispano Hospital, between 1999 and 2003, 804 patients were observed with suspicion of contact dermatitis. In 9,3% there was a history of recurrent foot dermatitis. All these patients were patch tested with GPEDC standard and shoe series and shoe fragments.

Results: Twenty-five patients revealed shoe contact dermatitis with positive reactions to the series tested, with an average age of 40 years. The dermatitis involved the dorsal aspect of the foot in 20 patients and the volar aspect in 8, the lateral aspects in 4, typically sparing the instep and flexural creases of the toes. The most common allergen were para-tertiary-butylphenol formaldehyde resin – PTBFR (12 patients-48%), mercapto mix (7 patients-28%), potassium dichromate (24%), mercaptobenzothiazole (24%).

Conclusions: The most common causes of shoe contact dermatitis were glues, followed by rubber components and chromated leather. As in other studies the most common allergen in shoe dermatitis in Portugal is PTBFR in neoprene adhesives. Rubber components (accelerators) were the second more frequent allergen in this study, probably a direct result of improved fixation of chrome and a change in footwear style and chrome sensitivity explains leather allergy. Other causes of foot contact dermatitis are iatrogenic complication, clothing (socks), cosmetics, adhesive tape and professional etiology.

P65

Patch testing to plastics in Sheffield

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We reviewed our experience patch testing to plastics at the Royal Hallamshire Hospital in Sheffield, England. The department's electronic database was searched from June 2002 to December 2003. In total 434 patients where patch tested to the British Standard Series. All positive reactions to epoxy resin and p-tert-Butylphenol-Formaldehyde resin (PTBF)where recorded. 28 of the patients tested to the Standard Series where also tested to an extended Plastics Series and again positive reactions where recorded. Type-4 mediated hypersensitivity reactions where seen in, 3 men secondary to epoxy resin, 2 men secondary to PTBF and in 1 women secondary to triethylene glycol acrylate. No irritant reactions where recorded. Epoxy resin was thought to be the cause of an occupational allergic hand dermatitis in 2 of the men. The positive reactions in the other patients where felt not to be of current

relevance to their dermatitis. Allergic contact dermatitis to plastic appears to be rare in patients attending for patch testing in Sheffield. In particular the frequency of reactions to epoxy resin, a potent sensitizer, is less than 1%. This is perhaps surprising as Sheffield is a large industrial city where exposure to epoxy resins is likely to be common. Hopefully this reflects safe workin practices in Sheffield.

P66

Occupational contact dermatitis from glues

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Objective: Exposure to adhesives and glues is common in occupation. We here analyse the data of patients with suspected contact dermatitis (CD) from glues recorded within the Information Network of Departments of Dermatology (IVDK).
Methods: Data recorded between 1996 and 2001 within the IVDK were searched for patients who underwent patch testing because of suspected contact dermatitis from glues.
Results: Overall data of 829 patients were found, among them 336 with occupational skin disease. Allergic CD was diagnosed in 171/336 patients (50.9%), irritant CD in 24.7%. CD was mostly localized on the hands (72.6%), followed by the face (13.4%) and arms (3.9%). By far the most common cause of an allergic patch-test reaction was epoxy resin (EP): 18.2% (age- and sex-standardized proportion of sensitization) reacted to the standard EP based on diglycidylether of bisphenol A. reactive diluents and hardeners which elicited a positive patch-test reaction in $>5\%$ of the patients were phenyl glycidylether and 4,4′diamino diphenylmethane respectively. Cresyl glycidylether was positive in 4.9%. (Meth-)acrylates which showed an allergic patch-test reaction in >= 5% of the patients were 2-hydroxypropyl methacrylate, hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, ethyleneglycol dimethacrylate, BIS GMA and triethyleneglycol dimethacrylate. Colophony was positive in 8.3% and p-tert-butylphenol formaldehyde resin in 4.1% of the patients respectively.
Conclusion: In our collective allergic CD was nearly 2-fold more frequent than irritant CD in patients with occupational CD from glues, epoxy resin components being the most important allergens.

P67

Hand eczema, skin exposure and glove use in dental technicians

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Aims: To estimate the incidence of hand eczema in dental technicians and to elucidate occupational risk factors.
Methods: This was a retrospective cohort study among former dental technician students (n = 2139). Controls comprised population controls (n = 2288) with similar distribution of age and sex as the dental technicians. A mail questionnaire asked for occurrence of hand eczema including age of onset, occupational exposure and use of protective gloves. The response rate was 58% (1210 dental technicians and 1316 controls answered the questionnaire).
Results: In dental technicians the incidence of hand eczema was 7.1 cases/1000 person years in males and 10.8 in females during acrylate-exposed time. In controls the incidence of hand eczema was 3.1 in males and 3.7 in females. The relative risk (RR) for males was 2.3 (95% CI 1.6–3.4) and for females 2.9 (95% CI 2.1–4.0). 48% of the dental technicians and 30% of the controls reported more than 10 hand-washings/day ($p < 0.001$). 80% of the dental technicians reported skin exposure to uncured acrylates, 14% daily. 87% had skin contact with grinding dust from acrylates, 42% daily. 38% used protective gloves when handling uncured acrylates, males 29%, females 48% ($p < 0.001$). 58% did not know for how long the normally used gloves protected the skin against uncured acrylates.
Conclusions: The risk of hand eczema is more than doubled in dental technicians. The work involves frequent and unprotected exposure to acrylates and wet work. Education regarding skin protection is important.

P68

Atopy and contact sensitisation: relationship reassessed

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Background: Throughout medical literature, there are conflicting data on the relationship between atopy and contact sensitisation. Some authors believe that atopy is a protective factor against contact allergy, whereas others say it is a risk factor. Facing this contradiction, this study was undertaken to reassess the possible relationship.
Study design: In 5 vocational schools, 1 randomly selected class in each was invited to participate. Altogether 135 students were tested, 73 females and 62 males aged 18–19 years. As markers of atopy, positive skin prick tests, Phadiatop and elevated total IgE (>120 kU/l) were selected. Patch tests were used for the detection of contact sensitivity. Skin tests included 10 contact allergens and 16 aeroallergens relevant for this population. The tests were carried out and scored according to the ICDRG and EAACI guidelines. Statistical analysis of the relationships included Fisher's chi-square test and odds ratios.
Results: Positive patch tests (at least 1+ reaction) were found in 28.1% of the study subjects, positive prick test (wheal diameter at least 3 mm) in 23.7%, positive Phadiatop in 20.0%, and elevated total IgE in 23.7%. No statistically significant relationship between atopy markers and patch test results could be found. For each analysed feature, odds ratios remained close to the value of 1. As a "positive control" for the study design, the known relationship between female gender and positive patch test could be reconfirmed (for nickel: $p = 0.003$, OR = 12.0, 95%CI: 2.7–54.1).
Conclusion: In general population, there is no (or little) correlation between atopy and contact sensitisation.

P69

A practical approach to the selection and use of gloves for workplace protection against chemical hazards

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Millions of chemical protective gloves are used every day in Europe. Unfortunately, many are not achieving the level of performance needed to protect the health of the worker, although neither employer nor user are aware of this. The way in which such gloves perform is complex and affected by a whole range of factors. A method of integrating these into a simple method for selection and use has proved to be extremely difficult. This presentation will review the many factors that affect glove performance under actual working conditions and show how a system for the selection and use of gloves for chemical protection might be developed. A novel method for testing gloves under actual working conditions so as to correctly identify performance will be proposed.

P70

Photoallergical contact dermatitis from diclophenac: cross reaction to aceclophenac

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Introduction: Cutaneous adverse reactions from topical or systemic administration of non-steroidal anti-inflammatory drugs (NSAID) are frequently described. New cases of adverse reactions from NSAIDs are reported, but the most frequently involved are drugs as ketoprofen or piroxicam. We report a case of photoallergical contact dermatitis from diclophenac with possible cross reaction to aceclophenac.
Material and methods: A 63-year-old-man, allergic to penicillin, developed eczematous lesions on hands and face, after applying a medicament containing diclophenac. Patch test and photopatch test ($5\,J/cm^2$) were performed with a photoallergen battery (Chemotechnique diagnosticsÒ), a NSAIDs battery (Aristegui lab.Ò) and aceclophenac 1%, 5% and 10% in pet. Readings were done at 48 and 96 hours in epicutaneous test and at 24 and 72 hours in photoallergic study, following the ICDRG criteria.
Results: The results of photoallergic study were as follows: diclophenac 1%, 5% and 10% in pet. and aceclophenac 10% in pet. positive at 24 and 72 hours. The remaining compounds of the NSAIDs battery were negative.
Conclusions: Diclophenac is a NAIDs derived from aryl alcanoic acid group used both topically and systemically in Spain. Some adverse reactions have been reported as exanthema, urticaria, eczema or Steven-Johnson's syndrome. We have found only two cases reported as photosensitization from diclophenac. In one of them, the clinical lesion was described as a granuloma annular-like and photoallergic study was negative. We report a photocontact dermatitis from diclophenac with positive

photopatch test. Photopatch test positive to aceclophenac may be explained as a cross reaction among group.

P71

Metabolism of delta-3-Carene by human cytochrom 450 enzymes

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Occupational exposure to monoterpenes occurs in saw mills, particle-board plants, carpentry shops and other types of wood-treating industries. The bicyclic monoterpene delta-3-Carene, one of the components of turpentine, may irritate the skin and muceous membranes and prolonged exposure may result in allergic contact dermatitis or chronic lung function impairment. The effects of low concentrations of delta-3-Carene on alveolar macrophages in vitro were examined and a dose-dependent relationship between the cell viability and the delta-3-Carene concentration was found. Little is known about the metabolism of delta-3-Carene in mammalians. In order to determine the toxic potential of this monoterpene we studied the human metabolism of delta-3-Carene in vitro. Therefore we used pooled human liver S9 and human liver microsomal cytochrome P450 enzymes. By using GC-MS analysis we found one main metabolite produced at high rates. The structure was identified by its mass spectra. The mass fragmentation indicated hydroxylation in allyl position. After synthesis of the assumed product in a four step reaction, it was characterized as delta-3-Carene-10-ol. There was a clear correlation between the concentration of the metabolite production, incubation time and enzyme concentration, respectively. Kinetic analysis showed that Km and Vmax values for the oxidation of delta-3-Carene by human liver microsomes were 0.39 μM and 0.2 nmol/min/nmol P450. It is the first time that delta-3-Carene-10-ol is described as human metabolite of delta-3-Carene.

P72

Pigmented patch-test substance and laser Doppler perfusion imaging

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Objective: To investigate if pigment of a dark patch-test substance may affect assessment of perfusion with the laser Doppler imaging technique.
Materials: 13 subjects who previously patch-tested positive with 25% balsam of Peru in petrolatum were re-tested with the same test substance and petrolatum controls applied directly by transparent foils and with much weaker and less pigmented serial doses tested with polyester squares. Readings of perfusion were performed through the test substances and the transparent foils at time intervals up to 4 days while tests were applied and for 5 days following detachment of tests. The instrument set-up of the LDPI was the same as we have suggested for non-pigmented patch-test substances tested on white skin.
Results: Results show that pigment remnants following detachment of the dark pigmented and pasty test substance containing the petrolatum vehicle were prone to affect perfusion assessments by masking detection of perfusion of parts of test sites. A real masking effect is supported by a similar effect with readings of the same tests while they were applied and by no such observable effect with the petrolatum controls or the non-pasty and much less pigmented squares.
Conclusion: The results show that pigment of patch-test substances may affect perfusion assessments with the instrument set-up suggested for non-pigmented substances.

P73

The magnitude of contact allergy responses can be quantified with imaged perfusion

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Objective: The objective of this study was to determine whether the magnitude of the perfusion

of the contact hypersensitivity response as measured by the laser Doppler perfusion imaging (LDPI) technique was associated with immunological parameters implicated in the pathogenesis of the disease.
Methods: Urushiol was applied on one of the forearms of volunteers for 48 hours while the other forearm served as a control. Twenty-four hours later, measurements of perfusion of the patch test sites were performed with the LDPI technique. To determine whether there was a correlation with immunological parameters associated with human contact hypersensitivity, suction blisters were produced at the test sites. Blister fluid was removed and examined for the cytokine interleukin-8 (IL-8).
Results: There was an extremely close correlation between the magnitude of the contact hypersensitivity response as measured by the imaged perfusion and the level of IL-8 in the blister fluid ($r = 1.00$). Compared to subjects with visually positive urushiol reactions, patients who failed to develop urushiol contact hypersensitivity despite repeated exposures to that substance had both greatly diminished perfusion and blister fluid IL-8 levels.
Conclusion: The results indicate that LDPI is a sensitive method of quantifying contact hypersensitivity reactions in humans and that the magnitude of the measurements with this technique correlates extremely well with cutaneous cytokine levels that have been implicated in the immunopathogenesis of contact hypersensitivity.

P74

Categorisation of human sensitisation potency using local lymph node assay EC3 values

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Effective evaluation of skin sensitisation demands that potential contact allergens are identified and the risk of sensitisation amongst exposed populations assessed. Sensitisation hazard is not an all or nothing phenomenon; dose response relationships can be discerned and thresholds identified for induction and elicitation of contact allergy. These parameters, under the heading of potency, are vital for the risk assessment process. The murine local lymph node assay (LLNA) is an accepted method for the identification of sensitisation hazards (a sensitiser is a chemical that induces a stimulation index 3 or more times that of the concurrent vehicle control). The LLNA has also been used to determine the potency of sensitisers, by derivation of an EC3 value, the estimated concentration of chemical required to induce a stimulation index of 3. At present, various agencies, including in EU and OECD, together with industry bodies, are considering whether and how to adapt these data into regulations which would place sensitisers into one of several potency categories. It is our view, based on an evaluation of over 300 chemicals, that five categories: extreme, strong, moderate, weak and negative represent the optimal approach and is consistent with what is understood regarding the potency of these skin sensitisers in humans. To illustrate this approach, an example dataset of 100 selected organic chemicals is shown, where the accuracy of prediction of human potency is in the region of 90%. This categorisation has utility as a simple guide for risk management strategies as well as representing an important first step in risk assessment.

P75

Molecular screening for skin sensitisation hazard in vitro using proteomics techniques

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Covalent binding of hapten to skin protein is required for sensitisation. It has long been postulated that only sensitising chemicals will modify skin protein(s), whereas non-sensitisers and irritants do not. To pinpoint the amino acid residues involved in such modifications, we employed mass spectrometry (MS) based proteomics techniques. Known sensitisers, non-sensitisers and irritants were incubated with human serum albumin (HSA). Modified HSA samples were digested by trypsin and matrix assisted laser desorption/ionisation (MALDI-MS) analyses were conducted on the digests. Nano-electrospray tandem mass spectrometry (ES-MS/MS) analyses were conducted on modified peptides purified by high performance liquid chromatography (HPLC). The HSA sequence was mapped and modified peptides identified. In HSA samples incubated with non-sensitisers and irritants there was no change compared to HSA incubated without chemical. Modified peptides were purified by HPLC and sequenced using

ES-MS/MS. Lysine, histidine and cysteine were found to be involved in covalent modifications by the sensitising chemicals used. A double adduct of one sensitiser (MCI) on His 338 of HSA molecule was also identified. More sensitisers need to be investigated to establish similarities between covalent protein modifications of chemically related compounds. The aim is to develop an assay for protein binding ability of chemicals which could form part of a battery of tests needed to replace animal testing for sensitisation potential.

P76

Allergic contact dermatitis vs. psoriasis

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Background: Psoriasis prevalence in the Spanish population is around 1.4% (2000). The last epidemiological enquire of the GEIDC (2001) showed that 55.11% of the patients revised in specialized units presented Allergic Contact Dermatitis (ACD). Concomitance of both processes has been widely studied being the opinions of the different authors controversial. Palmoplantar psoriasis seems to be the most frequent type in patients presenting delayed hypersensitivity.
Aim and methods: A retrospective study (2002–2003) of the incidence of ACD in patients previously diagnosed of psoriasis was performed in the allergy unit of our hospital. The aim of our study was to investigate the delayed hypersensitivity among psoriatic patients as well as its clinical relevance in our influence area. 604 consecutive patients were studied. Standard batteries of the GEIDC as well as complementary series (True-Test and Chemotecnique) were performed. Allergen application and posterior evaluation were done according to the ICDRG rules.
Results: We studied 26 patients affected of Psoriasis, (4,3% of total). In contrast to the general population, 9 were female (mean age 49 years) and 17 male (mean age 48,4 years). ACD suggestive lesions were located in the hands of 15 patients, feet in three of them and in 4 patients both. Patch test was negative in 8 cases. The most detected allergens were Nickel and Fragrance-mix. Occupational origin was discussed in 6 cases. Sensitivity to formaldehyde resins was demonstrated in several patients. Medicamentous origin due to ethylendiamine and Peru Balsam was also demonstrated.
Comments: Several revisions about the relationship of ACD and psoriasis have been published in the last years and most of the authors think that there are no differences between healthy, psoriatic and atopic subjects. These studies have focused on adverse drug reactions or standard series of allergens, taking not in consideration an occupational origin. We suggest epicutaneous tests as a reliable method to diagnose ACD in psoriatic patients with chronic and/or refractory lesions in hands.

P77

Incidence of psoriasis in Norway

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Investigations in several western countries, especially european, have shown an increase in the frequency of psoriasis. To investigate these trends in Norway, the following procedure was followed.

Using four standardized interview-reports the development and the frequency of atopic dermatitis was determined.

The questionnaires were conducted in the years 1968, 1975, 1985 and 1995. The results were registred electronically, and made available on the Statistical Package for the Social Sciences (SPSS) in Windows version.

In 1968 420 out of 11101 persons suffered from a skin disease, in 1975 the number had increased to 690 out of 11014 persons. These numbers still increased; in 1985 1136 out of 10576 and in 1995 1026 out of 10248 said to suffer from a skin disease.

The diagnosis psoriasis was reported by 34 persons in 1968 (8% of all skin disease), increased to 97 in 1975 (14.1%), to 149 in 1985 (13.1%), and finally to 284 in 1995 (26.7%).

In all, the infectious skin diseases decreased in number, whereas inflammatory skin diseases, such as psoriasis but also atopic dermatitis increased.

Connections to air pollution, indoor environment, especially smoking are at present under investigation.

These results indicate that psoriasis is among the most frequent skin diseases in Norway, comparable to other western industrialized countries.

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Frequency and development of atopic dermatitis in Norway

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Investigations in several western countries, especially european, have shown an increase in the frequency of atopic disease. To investigate these trends in Norway, the following procedure was followed.

Using four standardized interview-reports the development and the frequency of atopic dermatitis was determined.

The questionnaires were conducted in the years 1968, 1975, 1985 and 1995. The results were registred electronically, and made available on the Statistical Package for the Social Sciences (SPSS) in Windows version.

In 1968 420 out of 11101 persons suffered from a skin disease.

The diagnosis atopic dermatitis was not recorded in 1968, in 1975 0.7% of all skin disease considered atopic dermatitis, in 1985 1.3% and in 1995 10.1%.

The results show an increased incidence of atopic dermatitis in Norway, comparable to other western countries.

Connections to air pollution, indoor environment, especially smoking are at present under investigation.

P79

A chemical dataset for evaluation of alternative approaches to skin sensitization testing

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In recent years, the local lymph node assay (LLNA) has emerged as a practical option for assessing the skin sensitization potential of chemicals. In addition to accurate identification of skin sensitizers, the LLNA can also provide a reliable measure of relative sensitization potency; information that is pivotal in successful management of human health risks. However, even with the significant animal welfare benefits provided by the LLNA, there is interest still in the development of non-animal test methods for skin sensitization. Here, we have collected a large dataset of chemicals that have been tested in the LLNA, and the activity of which correspond with what is known of their potential to cause skin sensitization in humans. It is anticipated that this will be of value to other investigators in the evaluation and calibration of novel approaches to skin sensitization testing, in particular for the development of *in silico* methods. Prerequisite for the development of *in silico* models is always the availability of a large high quality data set, suitable for modeling. This dataset encompasses both the chemical and biological diversity of known chemical allergens, and provides also examples of negative controls. The data are a collection of published and non-proprietary industry data. All materials were tested in standard vehicules following the standard LLNA protocol. It is hoped that this dataset will accelerate the development, evaluation and eventual validation of new approaches to skin sensitization testing.

P80

Preliminary findings on the histopathology of chronic hand dermatitis

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Chronic hand dermatitis is a common and distressing condition with a complex, multifactorial aetiology. In order to better understand its pathophysiology and hopefully improve diagnosis, we have begun a systematic histopathological study of various forms of hand dermatitis, with a particular emphasis on those in which exposure to irritants and allergens is strongly implicated. Suitable patients were recruited from amongst those presenting at the contact dermatitis clinic. Detailed past and present medical and personal histories, clinical examination, patch testing and prick testing were conducted in order to classify the eczema into one of several broad entities e.g. chronic irritant contact dermatitis (CICD), with or without atopy. After performing a range of bio-engineering measurements on a pre-selected affected area of the hand, biopsies were removed and processed for high resolution light microscopy and immunocytochemistry. Age/sex matched, healthy, non-atopic individuals provided control skin from similar sites of the hand. Using a range of antibodies and quantification techniques, we examined the status and expression of certain immune-associated cells and receptor/adhesion molecules. Of note amongst these, were the differences in epidermal CD1a+ cell density between groups. Non-atopics with CICD, for example, had significantly fewer CD1a+ cells than both

atopics with CICD and those with normal skin. CD54 (ICAM-1) and several cytokine/chemokine receptors were more widely and strongly expressed by keratinocytes in those with an atopic diathesis. Although preliminary in nature at this stage, our results suggest that different forms of hand dermatitis display characteristic immunopathological features which may possibly be of diagnostic value.

P81

Occupational hypersensitivity to platinum group elements

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Objective: the increasing industrial use of platinum–group elements (PGEs), namely Ir, Pd, Pt and Rh and related hypersensitivity such as respiratory symptoms, urticaria and contact dermatitis, have led to a growing need to monitor selected populations of exposed workers. Our aim is to determine the prevalence and the clinical characteristics of hypersensitivity to the platinum-group elements; the levels of PGE measured in indoor airborne particulate matter and in biological samples (serum, urine and hair) taken from of employees in a platinum refining and catalyst manufacture; to correlate environmental exposure role and platinum salts concentrations in biological samples in the onset of allergy.

Material and methods: 132 subjects variable exposed 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 platinum salts and to other common allergens and patch test to platinum salts. Airborne PGEs was collected by personal and area samples. Biological samples (serum, urine and hair) were collected. Analitical procedure based on sector field inductively coupled plasma mass spectometry (SP-ICP-MS) for the analysis of airborne filter, serum, urine and hair was used. Results: positive prick test to platinum salts were found in 18 workers, 4 out 14 gave simultaneous positive reactions to Pt, Rh and Ir. 2 out 14 gave a positive reaction to Pt and Pd. Positive patch test reactions to Pt were found in 2 subjects, 1 out 2 gave positive reaction also to Pd.

Conclusion: the preliminary results of the investigation indicate that Pt-salts are important allergens in catalyst industry and that the clinical manifestation involves both the respiratory system and the skin.

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