



NEWSLETTER

Medichem 2007 New Board and election of chairman

With the last Newsletter you received the call for candidates for this year's Medichem Board election. Thanks to all of you who answered, and also thanks for the helpful and encouraging comments which I received.

The following Medichem members were nominated to the secretary and consented to stand as Board candidates:

Andreas Flückiger (Switzerland), Koichi Kono (Japan), Michael Nasterlack (Germany), Todor Popov (Bulgaria), Shrinivas Shanbhag (India), Thirumalaj Rajgopal (India), and Avi Wiener (Israel).

Since this year, 9 Medichem Board members arrive at the end of their terms of office there are fewer candidates as there are vacancies on the Board, and this year's Board election generally goes with a "silent vote".

According to Article 5 Sect. 4.1 the total number of the full Board is limited to a maximum of 17. The Past Chairman serving his one year on the Board after chairmanship shall not be included in this maximum number. Thus, including Stephen Borron for serving one year after the maximum of two chairmanship-periods on the board, this time the board is

limited to 18 members.

Two members were nominated for the position of Medichem-chairman: Thirumalaj Rajgopal (India) and Konrad Rydzynski (Poland).

Dear Members, please therefore vote for one of the two nominated candidates as the new chairman of Medichem. Please show your personal interest in Medichem by casting your vote, either by fax or mail. The necessary ballot form for the election is attached with this Newsletter.

To be valid, the ballot form must reach the Secretary no later than August 31st, 2007. Only Medichem members in good standing may vote.

Forms coming from anonymous voters have to be considered void. It goes without saying that the names of those voting will only be used to identify voters as members in good standing and will be known to no-one other than the Secretary. I would like to thank you for your kind cooperation.

In conclusion: please vote for one of the two chairman election candidates.

Doz. Dr. Robert Winker
(Vienna, Austria)



July 2007



MEDICHEM - Occupational and
Environmental Health in the
Production and Use of Chemicals

**Founded 1972 in Ludwigshafen,
Germany**

**Honorary President:
Prof. Dr. med. Dr. h. c.
Alfred M. Thiess**

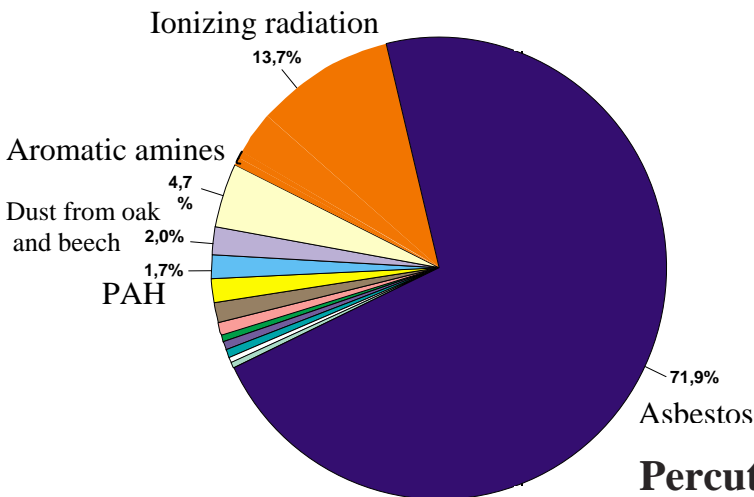
Chairman:
Dr. Stephen W. Borron
International Toxicology
Consultants, LLC
1025 Connecticut Avenue NW,
Suite 1000
Washington, DC 20036-5417 (USA)
Phone: +1-202-588-0620
Fax: +1-202-478-0444

Secretary:
Doz. Dr. Robert Winker
Medical University of Vienna
Division of Occupational Medicine/
Internal Medicine IV
Währinger Gürtel 18-20
1090 Vienna (Austria)
Tel.: (43) 664 5018662
Fax: (43) 1 408 8011

Treasurer:
Dr. Andreas Flückiger
F.Hoffmann-La Roche Ltd.
CH-4070 Basel (Switzerland)
Phone:+41-61-688 37 38
Fax: +41-61-688 16 51

Board Members:
Dr. P.J. Boogaard (Netherlands)
Prof. Dr. J. Godnic-Cvar (Austria)
Dr. E.-N. Emmanouil-Nikoloussi
(Greece)
Dr. J. Ger (Taiwan)
Prof. K. Kono (Japan)
Dr. A.B. Kotzé (South Africa)
Dr. J.A. Morales (Mexico)
Dr. M. Nasterlack (Germany)
Prof. T. Popov (Bulgaria)
Dr. T. Rajgopal (India)
Dr. F.G. Rose (U.K.)
Dr. S.O. Salomon (Argentina)
Prof. F.W. Schmahl (Germany)
Dr. L.M. Yee (USA)

Since almost 5% of all cancers in Germany from 1973-2003 were assigned to aromatic amine exposure (see figure below), aromatic amines represent a very relevant exposure in chemical industry



(data related to the figure can be ordered from the Main Association of Commercial Trade Associations in Germany or obtained under <http://www.hvbg.de/d/bia/pub/ueb/index.html>).

The incidence of bladder cancer due to occupational exposure in Germany has been increasing in the last years (Golka K, 2005). Occupational exposure to aromatic amines seems to be the main occupational source for bladder cancer in Germany.

However there are few studies to date, which focus on the examination of percutaneous uptake of aromatic amines.

A very recently in Occupational and Environmental Health published study by Korinth et

al. (Korinth et al., 2007), reported that increased use of skin barrier creams enhances the percutaneous uptake of aromatic amines in vivo.

Occup Environ Med;
64:366 -372:

Percutaneous absorption of aromatic amines in rubber industry workers: impact of impaired skin and skin barrier creams

BACKGROUND: Several aromatic amines (AA) could cause bladder cancer and are an occupational hygiene problem in the workplace. However, little is known about the percutaneous absorption of chemicals via impaired skin and about the efficacy of skin protection measures to reduce internal exposure.

AIMS: To determine the impact of skin status and of skin protection measures on the internal exposure to AA in workers manufacturing rubber products.

METHODS: 51 workers occupationally exposed to

aniline and o-toluidine were examined. The workplace conditions, risk factors for skin and the use of personal protective equipment were assessed by means of a self-administered questionnaire. The skin of hands and forearms was clinically examined. Exposure to aniline and o-toluidine was assessed by ambient air and biological monitoring (analyses of urine samples and of haemoglobin adducts).

RESULTS: Haemoglobin-AA-adduct levels in workers with erythema (73%) were significantly higher ($p < 0.04$) than in workers with healthy skin (mean values: aniline 1150.4 ng/l vs 951.7 ng/l, o-toluidine 417.9 ng/l vs 118.3 ng/l). The multiple linear regression analysis showed that wearing gloves significantly reduced the internal exposure. A frequent use of skin barrier creams leads to a higher internal exposure of AA ($p < 0.03$). However, the use of skincare creams at the workplace was associated with a reduced internal exposure ($p < 0.03$).

From these findings we assume that internal exposure of the workers resulted primarily from the percutaneous uptake.

CONCLUSIONS: The study demonstrates a significantly higher internal exposure to AA in workers with impaired skin compared with workers with healthy skin. Daily wearing of gloves efficiently reduced internal exposure. However, an increased use of skin

barrier creams enhances the percutaneous uptake of AA. Skincare creams seem to support skin regeneration and lead to reduced percutaneous uptake.

Only few publications mention that skin protection at the workplace may also have negative effects. Korinth et al. (Korinth, Geh et al. 2003) demonstrated that in an in-vitro experiment the percutaneous absorption of solvents was increased through skin treated with skin barrier creams. In addition to date, the above displayed study, reported that increased use of skin barrier creams enhances the percutaneous uptake of aromatic amines in vivo. Baur et al. (Baur, Chen et al. 1998) report that in probands with clinical symptoms of a type I allergy to latex, the application of a skin protection cream increased positive test results in terms of wearing gloves.

In fact, the agent was able to trigger a positive reaction only in gloves with a low allergen content. The authors suspect that skin protectors enhance the release of allergens, favor penetration of the skin, and may thus trigger allergic reactions.

Although the risk-benefit profile of skin protection agents from the scientific point of view is controversially discussed, the fact that preventive application of a protective agent on the skin facilitates removal of work substances such as oil and

reduces the need to cleanse the skin with abrasive and potentially irritating agents or other anhydrous cleansing agents is beyond debate (Mathias 1990).

Doz. Dr. Robert Winker
(Vienna, Austria)



Effectiveness of skin protection creams in the primary prevention of occupational dermatitis

The study aimed to investigate, whether the publicized effects of skin barrier creams can be replicated in a real occupational setting during activities that expose the skin. At this place I would like to present an abstract of our work:

In industrial countries in the western hemisphere, the annual rate of new occupational skin diseases is estimated at approximately 0.5 to 1.9 new diseases per 1000 employed persons per year. In more than 90% of cases the diseases are skin eczema; usually it is allergic and/or irritative contact eczema.

Despite intensive use of protective creams and preventive occupational skin protection as part of a three-step skin protection plan, the number of confirmed cases of suspected occupational disease has remained high in the last

few years. Occupational skin diseases have headed the list of reported occupational diseases in Austria and Germany for many years. In 2004, 26% of the reported 55869 cases of occupational disease in Germany were assigned to the occupational disease number 5101 while 22% of the 1218 reported cases of occupational disease in Austria were assigned to the occupational disease no. 19 (Main Association of Commercial Trade Associations 2006, and unpublished data of the General Accident Insurance, respectively).

Strategies to prevent occupational irritative contact eczema are based on the use of a suitable skin protection cream before work, cleaning the skin, and skin care after work.

Some preparations for the above mentioned purposes have proved their value in routine use. However, many of the advertised properties of skin barriers, agents for skin care and skin cleaning have not been adequately proven according to the strict criteria of evidence-based medicine.

Evidence of the efficacy of skin protection agents is mainly based on in vitro and in vivo laboratory investigations. The extent to which these investigation models are applicable to actual occupational exposure is to date a matter of debate.

In animal experiments, blood levels of a solvent after percutaneous absorption

through a layer of barrier cream on the skin were measured (Boman, Wahlberg et al. 1982). On guinea pigs, the benefit of skin protectors was assessed by performing the repetitive irritation test (Frosch, Schulze-Dirks et al. 1993; Frosch, Schulze-Dirks et al. 1993). In several investigations, the reduction of an experimentally produced irritation or a known type IV sensitization after previous application of a skin protector was compared in vivo with untreated controls (Grevelink, Murrell et al. 1992; Pigatto, Bigardi et al. 1992; Frosch and Kurte 1994). In the actual occupational setting, however, individuals are simultaneously exposed to a number of potential irritants or allergens and not just a single irritant or allergen. Therefore Wigger-Alberti et al. (Wigger-Alberti, Spoo et al. 2002) recommend a combination of two irritants in order to simulate actual occupational conditions during testing.

A multicenter study was performed to achieve standardized testing conditions for skin protectors. An in vivo five-day repetitive irritation test under occlusive conditions was compared with a 12-day test (Schnetz, Diepgen et al. 2000). Despite ongoing revision and improvement of test and evaluation methods (visual score, measurement of transepidermal water loss, skin color and vascularization, by the use of biophysical techniques and occasionally additional histological investigations) it is still not

clear whether and to what extent these models can be applied to occupational skin exposure. Larger controlled clinical trials (including a control group that receives no protective measures) confirming the benefit of these preparations under real workplace conditions are not yet available.

The important question raised by Wiggert-Alberti and Elsner (Wigger-Alberti and Elsner 1998) as to whether skin protection is a cause of, or effectively prevents, skin diseases cannot be answered on the basis of the scientific literature published thus far.

Therefore we decided to investigate, in a large randomized controlled trial, whether the publicized effects of skin barrier creams can be replicated in a real occupational setting during activities that expose the skin. Simultaneously we intended to determine whether the differentiation of products into those designed for skin protection and those designed for skin care are merely based on a theoretical scientific concept or whether this distinction is applicable and justifiable for practical use.

Methods

Subjects and study design

A prospective, randomized, four-tailed controlled pilot trial was performed to compare the effect of skin protection and

skin care with a control group (only cleaning).

Two typical occupational skin diseases concerned branches were chosen for consideration of subjects-enrollment: The construction and timber industry.

Occupational exposure to moisture, dirt as well as mechanical load is very high in the selected branches. A total of n=1006 workers (nB=503 from building industry and nT=503 from timber industry) were recruited to take part in the study. Each subject was randomly assigned to one of the following groups:

A: skin protection, cleaning and skin care, B: skin protection, C: skin care and D: only cleaning.

In the longitudinal run workers were seen for at least three time points (intervals of approximately 4 months in between).

The study was approved by the ethics-committee of the medical faculty of the University of Vienna.

All subjects gave written informed consent before entering the study. Procedures followed were in accordance with institutional guidelines.

Clinical investigation

At the clinical investigation a dermatologist assessed the condition of skin in a blinded manner and the individual was assigned to one of the following categories: no eczema, mild, moderate and severe eczema. In addition photographs were taken at each time point. In the event of

a diagnosed eczema or one confirmed by the patient's medical history, any eczema that needed treatment (cortisone) was treated as an exclusion criterion.

In order to assess the epidermal barrier, the subject's transepidermal water loss was measured under standardized conditions. This served as an objective physiological skin parameter to quantify damage to the epidermal barrier. The measurement was performed using the Tewameter – a device that measures the loss of moisture and allows assessment of the condition of skin and its progress over time. The examinations were always performed at the same investigation sites of the respective company. As far as possible every proband was tested under the same standardized conditions (temperature and atmospheric humidity). The room temperature was kept constant by the use of an air-conditioner. To ensure that the probands adhered to the recommendations for the individual groups over a period of one year, they were repeatedly informed and trained at every control investigation. One staff member was appointed in charge of counseling the employees individually. We retrospectively asked each proband how often he/she had actually used the products on average per week because the participants' compliance was a very important aspect of the study. In addition, at the last control investigation the

proband was asked about their subjective perception. The probands indicated, on a scale, whether the condition of their skin had remained the same, improved, improved significantly, or worsened. Potential confounders such as social status, lifestyle factors, atopic skin diathesis, leisure activities, the use of personal protective measures and contact with other work materials were registered at the time of recruitment, based on the probands' occupational-medicine history and dermatological history.

Primary and secondary outcome measures:

The primary outcome measure for assessing the effectiveness of skin protection and skin care was defined prospectively as the difference in the occurrence of eczema (mild, moderate and severe) compared with the control group. As secondary outcome measures, the change in transepidermal water loss and subjective perception were compared between the 4 groups.

Results

Concerning differences in the occurrence of eczemas, we found no difference at the third visit for the building industry and for the females working in the timber industry. When analyzing eczemas of the male timber workers, the control group had the highest percentage of eczemas (20%), followed by skin protection in combination with skin care (10%), skin protection alone

(8%), and skin care alone (4%). When evaluating the secondary outcome-measurement changes in the TEWL-scores, the biggest improvement was found for the group skin protection and skin care in combination followed by skin care alone. Females in the timber industry started with better TEWL-score than males, which may be assigned to a better overall skin care.

Discussion

The objective of this study was to determine whether skin protection and skin care in combination or applied by itself are effective in the primary prevention of occupational dermatitis in the timber and construction industry.

Taken all secondary-outcome measurements together, the main result of the present study was that it provided no clear evidence of the efficacy of skin barriers for the primary prevention of occupational dermatitis in the timber and construction industry. A uniform trend was observed for an improvement in TEWL-scores concerning skin care or skin care in combination with protection. However, this improvement in TEWL-scores was not noted for the group B, only skin protection except on a descriptive basis for women. To our knowledge this is the first large randomized, controlled trial, to assess the effect of skin protection and skin care compared to a control group under real working conditions. Taeger (Taeger, Pesch et al. 2007) recently

published preliminary results of an ongoing study with a similar design to ours. However only 90 subjects, who were exposed to cooling lubricants were enrolled so far. At the second visit there were no differences between subjects treated with skin protection or skin care concerning transepidermal water loss, skin humidity, skin pH-value, skin scaliness and skin-roughness.

In general since no large randomized trials to date exist with a similar study question we can say that there are no findings to which we can compare our results directly. However, several studies addressed the issue of skin protection in the primary prevention of occupational dermatitis in other ways. Drexler et Kütting tried to divide the clinical studies conducted thus far on the subject of skin protection into three groups (Kutting and Drexler 2003): In the first group the efficacy of skin protection agents was taken for granted; the target criteria in this group were the acceptance (Bauer, Kelterer et al. 2002) or correct application (Wigger-Alberti, Maraffio et al. 1997) of skin protectors.

The second group consisted of a few clinical studies that have proved the efficacy of skin protection agents but are not representative because of small case numbers, selection of inclusion criteria (for instance, inclusion of diseased persons: this rendered the investigation therapeutic and not preventive

in nature), the absence of an untreated control group, or a brief observation period (Berndt, Wigger-Alberti et al. 2000; McCormick, Buchman et al. 2000; Perrenoud, Gallezot et al. 2001).

The third group consists of studies that, in fact, have shown the disadvantageous effects of skin protection (Duca, Pelfini et al. 1994; Baur, Chen et al. 1998; Draelos 2000; Fowler 2000; Fowler 2001).

In conclusion, the present study showed that barrier creams have no effect on primary prevention of occupational eczema.

However, skin care after work – which results in regeneration and maintenance of the skin barrier – was shown to be effective in two selected industry-branches.

Since extrapolation of the results to other industry branches is not possible, additional large randomized trials, which include a control group without protective measures are necessary to study primary properties of skin protection.

Doz. Dr. Robert Winker
o. Prof. Hugo W. Rüdiger
Dr. Bayda Salameh
Ao. Prof. Gerhard Tappeiner
(Vienna, Austria)

o. Prof. Hans Drexler
(Erlangen, Germany)



Organic Solvent Exposure and Hearing Loss in a Cohort of Aluminum Workers

Objectives:

Organic solvent exposure has been shown to cause hearing loss in animals and humans. Less is known about the risk of hearing loss due to solvent exposures typically found in US industry. The authors performed a retrospective cohort study to examine the relationship between solvent exposure and hearing loss in U.S. aluminum industry workers.

Methods:

A cohort of 1319 workers age 35 years or less at inception was followed for a five-year period. Linkage of employment, industrial hygiene, and audiometric surveillance records allowed for estimation of noise and solvent exposures and hearing loss rates over the study period. Study subjects were classified as "solvent exposed" or not, on the basis of industrial hygiene records linked with individual job histories. High frequency hearing loss was modeled as both a continuous and dichotomous outcome.

Results:

Typical solvent exposures involved mixtures of xylene, toluene, and/or methyl ethyl

ketone (MEK). Recorded solvent exposure levels varied widely both within and between jobs. In a multivariate logistic model, risk factors for high frequency hearing loss included age (OR=1.06, $p=0.004$), hunting or shooting (OR= 1.35, $p=0.049$) noisy hobbies (OR=1.74, $p=0.01$), baseline hearing level (OR=1.04, $p<0.0001$) and solvent exposure (OR=1.87, $p=0.004$). A multivariate linear regression analysis similarly found significant associations between high frequency hearing loss and age ($p<0.0001$), hunting or shooting ($p<0.001$), noisy hobbies ($p=0.03$), solvent exposure ($p<0.001$), and baseline hearing ($p=0.03$).

Conclusion:

These results suggest that occupational exposure to organic solvent mixtures is a risk factor for high frequency hearing loss, although the data do not allow conclusions about dose-response relationships. Industries with solvent-exposed workers should include such workers in hearing conservation programs.

Dr. Peter M Rabinowitz
(Yale University School of Medicine, United States)



Forthcoming Events

The Conference **regulating chemical risks** will be held

from the 16th to 17th of August, 2007 in Stockholm, with keynote presentations as well as plenary discussions, combined with workshops.

Conference Theme

The conference addresses regulation of chemicals and particularly the risks associated with them. The growing number and global diffusion of both chemicals themselves and regulation of chemicals imply a tremendous challenge for both research and policy. In Europe the most recent development of this is the emergence of the REACH programme of the European Union. Global developments are also of considerable interest however, and regulation on the national level is still very diverse.

The multidisciplinary nature of understanding and meeting this challenge is reflected in the conference, which welcomes contributions from both natural and social science. The conference is open for both academics and practitioners, including people representing the media, industry, government and NGOs. Although the geographical focus is on the development in Europe, observations from other parts of the world that are useful for comparative analysis are greatly appreciated.

Organisers

The conference is organized by the Centre for Baltic and East European Studies (CBEEES) at Södertörn University College in collaboration with

Karolinska Institutet and the Royal Institute of Technology.

The organising committee consist of Assoc. Prof. Johan Eriksson, Assoc. Prof. Michael Gilek, Dr. Christina Rudén and Assoc. Prof. Camilla Hermansson, situated at Södertörn University College.



State-of-the-Art Conference (SOTAC) / International Commission on Occupational Health (ICOH)

General Information can be found under the following Internet-address:

<http://www.acoem.org/sotac.aspx>

The conference will be held from Friday, October 26th until Sunday October 28th 2007 in Vancouver, Canada.

The American College of Occupational and Environmental Medicine (ACOEM) is partnering with the International Commission on Occupational Health (ICOH) during SOTAC 2007 in Vancouver, BC.

This conference will offer scientific sessions on a variety of occupational health topics, postgraduate seminars, and guest activities. Pre-conference courses are on Wednesday and Thursday, October 24-25. On October 24, a one-day course entitled "Lessons from the Field: Firsthand Experience Handling Outbreaks and Emerging Infectious Diseases in Medical Centers" will be offered. Also, two-day courses

to be offered include: Basic Curriculum in Occupational Medicine, Segment 1; Medical Review Officer (MRO) I; and Musculoskeletal Exam and Treatment Techniques. In addition, the 2007 SOTAC/ICOH meeting will offer a special global perspective on health care worker health, bringing together key international experts to present emerging scientific information in these areas.

The scientific sessions will be developed jointly by the SOTAC Planning Committee of ACOEM and the ICOH Health Care Worker Health Organizing and Scientific Program Committees.

In addition to the educational sessions designed to stimulate discussion, there will be work site visits, poster sessions, networking opportunities, receptions, group meal opportunities, pre and post conference sightseeing, and business meetings.



Querétaro/Mexico congress 2007

In September, 2007 Medichem will hold its 33rd Annual Congress in Queretaro, Mexico, in conjunction with FeNaSTAC, the national federation of societies of occupational medicine in Mexico. The program, entitled "Responsible Use of Chemicals" is anticipated to be an excellent one. The congress will take place in Sept. 13th to

15th. Joint sessions will be held in the mornings, including a joint opening ceremony. In the afternoons, Medichem and Fenastac will have their own sessions.

Simultaneous translation (Spanish/English) will be provided at the joint morning sessions. At our homepage or at the Internet side

<http://www.12congresost.com/index.php?seccion=1&idioma>
= more information about the congress is available.

The congress-costs for Medichem members are USD 450.00, No Medichem Members pay USD 500.00, to attend the congress. The Hotel Costs for a single or double room are USD 86.00 (65.00 euros) + tax (15%) and services (2.5%).

In addition a second AHLS course is planned as a Pre-Congress activity. The first was sponsored in Rome in conjunction with the ICOH congress in Milan. Again Medichem will co-sponsor an Advanced Hazmat Life Support Course. Medichem will provide two instructors, Stephen Borron and Jorge Morales to teach in the 3 day course and provide scholarships to occupational health professionals.

Elia Enriquez Viveros (Mexico)



Welcome to New Members

Dr. **Denis Barnaby**, P&G
Industrial Peru SRL (Peru),

Dr. **Elizabeth Barba**, P&G
Industrial Peru SRL (Peru),

