

NEWSLETTER

Medichem 2006 Board Elections

In the envelope containing this Newsletter, Medichem Members will receive the ballot form for this year's Board Elections.

As announced in the last Newsletter, Board Member Peter Nmadu arrives at the end of his term of office. He has agreed to stand for re-election.

Two other candidates have also been nominated (appearance ranked in alphabetical order by last name):

ao. Prof. Godnic-Cvar (Medical University of Vienna, Austria), Dr. Peter Nmadu (NNPC Medical Center, Nigeria) and Dr. Pierre Rouzaud (France, Centre Hospitalier Purpan).

Dear Members, please show your personal interest in Medichem by casting your vote, either by fax or mail.

To be valid, the ballot form must reach the Secretary no later than September 30th, 2006. 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 in advance for your kind co-operation.

In conclusion: please vote for one of the three Board election candidates.

Doz. Dr. Robert Winker
(Vienna, Austria).



Effect of occupational safety measures on micronucleus frequency in semiconductor workers

I deeply regret that my habilitation was appointed at the same time as the ICOH-congress in Milan took place.

As such, I was unable to hold a presentation of a study, which was conducted in a German semiconductor plant.

Thus I would like to present an overview of this study in this place:

The study dealt with genotoxic effects related to chemical exposure of semiconductor workers with a follow up of **more than 12 years** (1991 – 2004).



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

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Founded 1972 in Ludwigshafen, Germany

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Briefly, we examined whether exposed semiconductor workers show an increase in genotoxic effects, as indicated by presence of micronuclei, and, if so, whether occupational safety measures protect these workers from genotoxic effects of complex mixtures of chemical waste.

We assessed genotoxic risks by detecting chromosome damage using the micronucleus test in isolated human lymphocytes. Twelve years later, after implementation of protection measures, we analyzed the micronucleus frequencies in workers of the same semiconductor plant.

A typical source of complex chemical exposure is wastes in the semiconductor industry. These wastes are potentially toxic mixtures of inorganic and organic compounds originating from the plasma etching process during semiconductor production. The process involves gases that are transformed into a highly energetic state and broken into radicals and ions using high process temperatures of 700 to 800°C and high-frequency stimulation.

These gases then react with the substrate and bring about the actual etching process. However, the radicals and ions can also recombine with each other, resulting in a high number of intermediate products.

Semiconductor industry and spontaneous abortions:

Concern that chemicals used in the semiconductor industry could cause spontaneous abortions first arose in 1982, when a cluster of spontaneous abortion was noted in the Los Paseos district (Anderson I. New Scientist. 1985).

The first study to test this possibility performed by Pastides et al. indicated a two-fold increase in the risk of spontaneous abortion among semiconductor personnel (Pastides H, et al. J Occup Med. 1988.). This finding gave rise to a series of studies on the risk of spontaneous abortion associated with exposure to wastes in the semiconductor industry. The results were conflicting, and it was unclear whether spontaneous abortions in semiconductor workers were above the reported level of 10-20 % of clinically identified pregnancies.

An approach to resolving this conflict, that we have tried, is to determine whether genetic factors such as chromosome aberrations, which can be related to spontaneous abortions, are increased in semiconductor workers.

Methods

Exposed workers and controls in a German semiconductor plant were monitored in two series: survey 1 in 1991 and survey 2 in 2004, twelve years after the implementation of occupational safety measures. The exposed group at survey 1 involved 20 employees, who

had contact with open plasma etching systems or parts of such systems during cleaning and maintenance work. The control group at survey 1 consisted of 21 unexposed operators selected randomly. Survey 2 involved 32 exposed subjects and 23 controls.

To determine whether semiconductor workers show an increase in genotoxic effects, we compared micronuclei formation in exposed workers with controls at survey 1.

At survey 2, a retrospective comparison of micronucleus formation between the two groups was carried out after the implementation of safety measures, to assess the outcome of these protective measures.

Micronucleated lymphocytes were analysed by the cytokinesis-block method according to Fenech and Morley (Fenech M, Morley AA. Mutat Res. 1985).

The following occupational safety measures were implemented during the year 1992:

1. In order to optimize work safety measures all critical work processes were analyzed.
2. Intensified educational measures for the workers were implemented.
3. Provisions for changing clothes at least once a day were created. The transfer areas were redesigned; so-called black and white wardrobes with showers and separate storage spaces for

work clothes and regular clothing were provided.

4. Mobile suction devices were installed.

5. All procedures in open reactor chambers were performed with breathing protection (full mask connected to a fresh air respirator).

6. The concentrations of potentially toxic residues were reduced by the implementation of defined cleaning cycles (N2) and whenever possible the use of cleaning plasma prior to opening of the reactors.

Results

In brief the main result was that, in survey 1, the micronucleus frequency in exposed individuals was found to be significantly elevated as compared to controls.

After implementation of protection measures a significant decrease in the micronucleus frequency of

exposed personnel was found. In addition, no significant difference in the micronucleus frequency between exposed workers and controls was observed in the second survey.

Discussion

The findings of the present study indicate that exposure of workers in the semiconductor industry to chemical waste products increases genotoxic effects. These genotoxic effects, as quantified by the micronucleus test, declined to

basal levels twelve years after implementation of defined protective measures in the workplace.

This study also points to the significance of adequate safety measures to protect against chromosomal damage in semiconductor workers.

We therefore recommend the micronucleus test for the monitoring of genotoxic effects in humans exposed to complex mixtures of chemicals.

Dr. Robert Winker
Dipl. Ing. Alexander Pilger
Prof. Hugo Rüdiger
(Vienna, Austria)

Dr. Gerhard Roos
(Regensburg, Germany)



8-Hydroxy-2'- deoxyguanosine as a marker of oxidative DNA damage related to occupational and environmental exposures

The aim of the study was to review the recent literature on 8-Hydroxy-2'-deoxyguanosine (8-OHdG) as a biomarker of oxidative stress associated with chemical exposure.

Therefore a literature survey was conducted for publications on this subject focusing on the latest publications. Pub Med was used for this literature search. The full article can be downloaded from the International Archives of Occupational and

Environmental Health under the following Internet-address:

(http://www.springerlink.com/media/9cxu7yfaqj5upjdcna9g/contributions/q/2/8/8/q288401673555202_html/fulltext.html)

Reactive oxygen species (ROS) are ubiquitous in living aerobic organisms. They result either from the cells' metabolism or from the action of exogenous physical sources (e.g., ionizing radiation, UVA) and/or chemical compounds. Oxygen free radicals can induce a variety of damage to DNA, including DNA single and double strand breaks, base modifications and abasic sites (Cadet et al. 1997; Epe 1995; Dizdaroglu 1991), and they are thought to be involved in the mechanisms of ageing and in carcinogenesis (Finkel and Holbrook 2000; Beckman and Ames 1997; Wiseman et al. 1995; Feig et al. 1994). Various agents are effective in the hydroxylation of the deoxyguanosine residue in DNA. This seems to proceed via generation of an oxygen radical, such as the hydroxyl radical (Kasai and Nishimura 1986), resulting in the formation of 8-OHdG or 2,6-diamino-4-hydroxy-5-formamidopyrimidine (Evans et al. 2004). 8-OHdG is by far the most studied oxidative DNA lesion and has gained much attention because of its mutagenic potential (Grollman and Moriya 1993).

Reliability of 8-OHdG as a biomarker of oxidative stress in humans

Despite considerable efforts to improve the analysis of 8-OHdG and to determine predictors of 8-OHdG formation, a number of questions concerning the occurrence of artifactual background and the environmental factors affecting the steady state level of 8-OHdG remain still unanswered (Collins et al. 2004). Some critical aspects related to the use of 8-OHdG in human biomonitoring studies are:

-) The measurement of 8-OHdG remains, at least partly, an analytical challenge and the results strongly depend on the method used.

-) Further investigation is needed to establish procedures that prevent artifactual oxidation of the DNA (Cadet et al. 1998).

-) There are significant inter-laboratory differences in the base levels of 8-OHdG. Projects on the quality control of 8-OHdG assays (European Standards Committee on Oxidative DNA Damage) are still far away from a consensus on the level of oxidative damage in normal cellular DNA (ESCODD 2002).

-) 8-OHdG is an unspecific marker, and a variety of confounding factors (e.g., age, gender, diet, smoking, alcohol consumption, physical activity, vitamin status) may affect the formation of 8-OHdG (Toraason et al. 1999; Chen et al. 1999; Bianchini et al. 2001). Beside this, the

presence of 8-OHdG in DNA and urine may depend on other factors, such as DNA repair capacity (Gackowski et al. 2003; Cooke et al. 2005) or inflammatory reactions (Horiike et al. 2005).

-) Effects of workplace exposures on the induction of 8-OHdG have been reported with controversial results.

-) The formation or elimination of 8-OHdG may exhibit a considerable inter and intraindividual variation (Pilger et al. 2001). Recently, levels of oxidative DNA damage ranging from 6.02 to 18.48% were detected in white blood cells from 72 healthy donors by the FPG-modified comet assay (Lee et al. 2005). In addition, a substantial interindividual variation of FPG-induced DNA strand breaks in response to treatment of these cells with sodium dichromate was found, indicating differences in the accumulation of oxidative DNA damage

-) The interpretation of urinary 8-OHdG is not unequivocal. For example, an unchanged excretion of urinary 8-OHdG at increased oxidative burden does not rule out a decreased repair capacity and an accumulation of 8-OHdG in DNA (Poulsen et al. 1998). In addition, the contribution of the nucleotide pool to the concentration of 8-OHdG in urine is not clear.

-) No significant correlation between urinary 8-OHdG and

8-OHdG in DNA could be demonstrated as yet (Foksinski et al. 2003)

Conclusion

8-OHdG is the most commonly measured marker of oxidative DNA damage. Many human biomonitoring studies have been performed in the last decade with the aim to investigate the influence of occupational and environmental exposures on the formation of 8-OHdG. However, there is still the problem with variable results and the lack of well established dose responses derived from human exposure. In addition, further work is needed to reach a consensus on the background level of 8-OHdG.

Dr. Alexander Pilger
(Vienna, Austria)



Severe Cases Of Occupational Hand Eczema May Predict Unemployment Or Days Missed From Work

Hand eczema caused by soaps and other irritants in the workplace may lead to unemployment or prolonged sick leaves from work for some individuals, according to an article in the March issue of Archives of Dermatology.

Hand eczema or dermatitis is characterized by redness and

inflammation of the hands, often due to irritants in soap, chemicals or detergents. "Occupational hand eczema (OHE) has become a disease of increasing importance during recent decades because of its serious consequences, such as frequent eruptions and risk of prolonged sick leave," background information in the article states. OHE also greatly affects quality of life (QOL). Past studies name OHE as the most frequently recognized occupational disease in Denmark and many Western countries.

Rikke Skoet Cvetkovski, M.D., Ph.D., of the University of Copenhagen, Hellerup, Denmark, and colleagues studied patients with OHE to identify predictive risk factors for the disease. Patients listed in the Danish National Board of Industrial Injuries Registry as having OHE between Oct. 1, 2001, and Nov. 10, 2002, received questionnaires regarding sick leave, loss of job, depression, health-related quality of life and their eczema's severity. A follow up questionnaire was sent one year after the first was returned. Of the 621 patients who responded to the first questionnaire, 564 (386 women and 178 men) completed the follow up.

During follow up, 25 percent of surveyed patients had persistently severe or aggravated OHE, 41 percent improved and 34 percent of patients experienced unchanged minimal or mild to moderate OHE. The groups

most affected by OHE were butchers, kitchen workers and cooks, hairdressers and patients aged 25 to 29 years. Having a severe case of OHE, being 40 years of age or older and having a low self-rated quality of life predicted unemployment and prolonged sick leave (more than five weeks in the past year). Also, patients with a lower socioeconomic status (based on education and job status) were at high risk for prolonged sick leave, a change of job and unemployment.

Predictive factors could be used by clinicians to guide treatment and to select early risk management strategies. To avoid prolonged sick leave that may lead to social and economic decline, physicians must try to identify subgroups of patients who are at greater risk of a poor outcome. The full article can be downloaded from the Archives of Dermatology:

(Arch Dermatol. 2006; 142: 305 to 311. Available pre-embargo to the media at <http://www.jamamedia.org/>)

Dr. Rikke Skoet Cvetkovski,
(Department of Dermatology, Gentofte
Hospital, University of Copenhagen)



Tuberculosis and silica exposure in South African gold miners

The aim of the study was to examine the effect of silica exposure, in the absence of silicosis, on the prevalence of pulmonary tuberculosis (PTB), which is epidemic among South African gold miners.

The article was published as an original article in Occupational and Environmental Medicine (Occup Environ Med 2006; 63: 187-192) and the full article can be downloaded from <http://oem.bmjournals.com/content/vol63/issue3/>.

Methods:

Cross-sectional study of 520 gold miners over 37 years of age. Length of service, and cumulative and average dust and quartz exposure indices were derived for each miner. Chest radiographs were read for PTB by two NIOSH "B" readers. PTB was defined as a self-reported history of PTB or PTB on chest radiograph. Logistic regression was used to adjust for age, smoking, and silicosis. PTB effects of different exposure metrics for silica, scaled on their interquartile range (IQR), were compared.

Results:

Means (ranges) were: age 46.7 (37.1–59.9) years; length of service 21.8 (6.3–34.5) years;

average intensity of respirable quartz 0.053 (0–0.095) mg/m³. PTB prevalence was 19.4% (95% CI 16.0 to 22.8) on history alone, and 35.2% (95% CI 31.1 to 39.3) on history or on chest radiograph. Length of service was poorly predictive of PTB, while all exposure indices which included dust or quartz yielded prevalence odds ratios (PORs) of approximately 1.4 (95% CI ~1.1 to 1.8) for changes of one interquartile range in exposure. Controlling for silicosis—by adjustment or restriction—did not modify these results. Drillers and winch operators had the highest PTB prevalences and the highest dust and silica exposures.

Conclusion:

Older in-service gold miners in South Africa have a high prevalence of PTB, which is significantly associated with dust and silica exposure, even in the absence of silicosis. Limitations include a survivor workforce and the use of cumulative exposures based on current exposures. Dust control is an important component in control of the PTB epidemic in South African gold mines.

Dr. J M teWaterNaude
(School of Public Health and Family Medicine,
University of Cape Town, South Africa)



Review and Meta-analysis of Risk Estimates for Prostate Cancer in Pesticide Manufacturing Workers

The aim of the study was to review cohort studies that examined the occurrence of prostate cancer in pesticide manufacturing workers in order to undertake a qualitative and quantitative evaluation of the risk as well as to assess the level of epidemiological evidence for each class of chemical compounds. The article was published as a review article in *Cancer Causes and Control* (*Cancer Causes and Control*: 2006 May;17(4):353-73) and the full article can be downloaded from <http://www.springerlink.com>.

Methods:

Following a systematic literature search, relative risk (RR) estimates for prostate cancer were extracted from 18 studies published between 1984 and 2004. All studies were summarised and evaluated for homogeneity and publication bias. As no significant heterogeneity was detected, combined RR estimators were calculated using a fixed effect model. Meta-analyses were performed both on the whole set of data and for each chemical class separately.

Results :

The meta-rate ratio estimate for all studies was 1.28 [95% confidence interval (CI) 1.05–1.58]. After stratification by specific chemical class, consistent increases in the risk of prostate cancer were found in all groups but statistical significance was found only for accidental or non-accidental exposure to phenoxy herbicides contaminated with dioxins and furans. There was no obvious indication of publication bias.

Conclusion:

The overall meta-analysis provides additional quantitative evidence consistent with prior reviews focusing on other groups exposed to pesticides (farmers, pesticide applicators). The results again point to occupational exposure to pesticides as a possible risk factor for prostate cancer but the question of causality remains unanswered.

Epidemiological evidence did not allow identifying a specific pesticide or chemical class that would be responsible for the increased risk but the strongest evidence comes from workers exposed to phenoxy herbicides possibly in relation with dioxin and/or furan contamination.

Dr. Geneviève Van Maele-Fabry
(Unité de Toxicologie Industrielle et Médecine
du travail, Ecole de Santé Publique, Université
Catholique de Louvain, Bruxelles, Belgium)



People and Events

Medichem's Chairman
Dr. Stephen Borron has been appointed Professor at the University of Texas in San Antonio.

Medichem's Secretary
Dr. Robert Winker has successfully performed his "Habilitation", which in German-speaking countries represents the prerequisite for becoming a university professor. He has been awarded the title of Univ.-Doz. Dr. Robert Winker.

Our heart-felt congratulations go to both Stephen and Robert!

Shortly after the end of ICOH's centennial congress in Milan we had to learn to our deepest regret that **Prof. Marco Maroni** had suddenly and unexpectedly died. Marco has been Board member of ICOH and a Medichem member for many years.

In the following I quote from the obituary provided by Jorma Rantanen on ICOH's website:
"Marco was a dynamic and knowledgeable scholar, scientist and educator, whose impact is seen in Italy and Europe, but extends also far beyond the national and European borders. As Director of the ICPS and a Member and Chair of the WHO Global Network of WHO Collaborating Centres in Occupational Health and the respective European Network, Marco was an untiring engine of our activities.

He was active in ICOH in various positions, including the Chair of the Scientific Committee on Pesticides and membership of the ICOH Board during the period 2003-2006 and re-elected for the tenure 2006-2009. Marco was also one of the key persons in organizing the ICOH 2006 Centennial Congress in the middle of this month.

As a person Marco was always idea-rich, optimistic and enthusiastic challenging his environments with new ways of thinking and new stimuli and initiatives always directed to the development of occupational health."

There is nothing much to add. Our thoughts are with Marco, his family and friends.

Dr. Michael Nasterlack
 Ludwigshafen (Germany)



Medichem activities

On the occasion of the ICOH – congress in Milano, Medichem organized a Mini-Symposium together with the Scientific Committee on Pesticides at the **ICOH Congress in Milan, Italy (June 11 – 16)**. According to the feedback, that I received from Medichem-colleagues the Mini-Symposium was a great success; in particular the presentations held were of good scientific quality. The following topics were treated:

-) Preparedness for chemical mass casualty incidents,

-) State of the art: Cyanide poisoning,

-) Mass psychogenic illness in the era of terrorism.



Medichem also co-sponsored an "Advanced Hazmat Life Support" (AHLS) course on June 8-9, 2006 in Rome as a "Pre-congress event" in conjunction with the Poison Center of the Catholic University of Rome..

Dr. Alessandro Barelli was organizing this pre-congress course in the Catholic University School of Medicine and Medichem sponsored part of the participation fee for participants with non-industrial background who would otherwise not be able to register. In addition to being a financial co-sponsor, Medichem provided two instructors to the courses, Dr. Jorge Morales and Stephen Borron. Medichem was able to sponsor attendance at the AHLS courses by 4 young professionals in occupational medicine from developing nations.

At the Advanced Hazmat Life Support (AHLS) course participants were trained to:

- Demonstrate rapid assessment of hazmat patients
- Recognize toxic syndromes (toxidromes)
- Demonstrate ability to medically manage hazmat patients
- Apply the poisoning treatment paradigm

- Identify and administer specific antidotes



Medichem Young Investigators Award

At the board-meeting in Monterrey in February this year, the board agreed to support a concept for a Medichem Young Investigators award. Thus, a complete "Medichem Young Investigators Award" concept was elaborated, special thanks go to Thirumalai Rajgopal as he was mainly concerned with this issue. The model should also be placed into the Medichem Handbook; The award is presented for the best contribution by a young occupational or environmental health professional (as a rule, under the age of 35 years), related to the field of occupational and environmental health in the production and use of chemicals and submitted to a selected national occupational health congress.

The Award winning contribution shall be presented with a special notation that it is made possible by Medichem, ideally preceded by a brief description of Medichem.

The national occupational health association (NOHA) will invite contributions to this competition. The NOHA congress scientific committee will select 3 abstracts meeting the above criteria, which will

be forwarded to a representative chosen by the Medichem Board. Medichem will then determine The Award winner.

The Award consists of € 500, given to the speaker to facilitate attendance and presentation at the congress. The award winner will receive a certificate and free membership in Medichem for two years. The Award winner may also use the title of "Medichem Award Winner (year ----)" in his or her curriculum vitae.



Forthcoming Events

2007, **Medichem** will organize a congress together with **Fenastac** in Monterrey, Mexico. The Fenastac-Medichem-congress will be held from the **13-15th of September 2007**. The whole 3 days will be held as a common conference and the sessions of common interest will be concentrated in the mornings; in the afternoon, parallel sessions will be held. In addition, incentives will exist for attending both Congresses, including the availability of simultaneous Spanish-English and English-Spanish translations for all presentations and a combined social programme.

FENASTAC (National Federation of Occupational Health), has become to be the most important organization of Occupational Health (OH) in Mexico. It has been recognized by Mexican public institutions

such as the Ministry of Labor, the Ministry of Health and the Mexican Institute of Social Security, as a professional organization in the OH field. Many of its members have been invited to participate in the revision and creation of Mexican laws and regulations regarding OH. FENASTAC has divided the country in nine regions and there is a Vice President for each region. The number of OH professionals included is around 3,000.

The most important scientific activities of FENASTAC are as follows: organize every year the National Congress of OH in Mexico, organize regional OH courses according to the requirements of local societies/associations, to increase OH skills, promote scientific work and publications among the members.

Dr. Jorge A. Morales
(Mexico)



Welcome to New Members

Dipl. Ing. **Alexander Pilger**,
Medical University of Vienna
(Austria),
ao. Prof. Dr. **Jasminka
Godnic-Cvar**, Medical
University of Vienna (Austria),
Dr. **Fernando Araujo
González**, Mexalit Industrial,
S.A. de C.V., (Mexico), Dr.
Rosella Marchi, (Italy),
Dr. **Alessandra Revello**
(Italy)

