

NEWSLETTER

Medichem 2002 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 Miroslav Cikrt arrives at the end of his term of office in September 2003. He informed the Board that for personal reasons he would no longer be available as candidate.

On behalf of Medichem, we would like to express our sincere thanks to Miroslav Cikrt for his engagement in the past. We all remember him organizing a wonderful congress in 2001 in Prague. We trust that he will continue to support Medichem in the future.

It is a pleasure to announce that the Secretary has received nominations for two candidates: Dr. Peter S. Nmadu (NNPC Medical Center, Nigeria), and Dr. Abed Onn (Malaysia).

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 August 31st, 2003.

Only Medichem members in good standing may vote.
Forms coming from anony-

mous 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 two Board election candidates.

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



WHO's Network of Networks

Medichem has been listed with the *WHO's Network of Networks* for dealing with chemical emergencies. There will likely be events in the future in which we may be called upon to lend assistance. As always, our participation in these issues is voluntary and determined by the individual members. The following incident, which was communicated by Dr. Babatunde Olowokure from the IPCS Chemical Alert and Response Team may serve as an example for a problem within the scope of the Network.

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July 2003



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

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WHO's network (ctd. from p. 1)

An outbreak of acute poisoning occurred after a herbal fermented wine named 'DOH' was drunk. The herbal drink was served at a birthday party. A total of nine victims drank the wine one of whom later died. Minutes after drinking the wine, victims developed dizziness, nausea, vomiting and lost consciousness. A sample of the wine was clear in color with an unpleasant smell. It dissolved a plastic cup within 20 minutes. Tests revealed no ethanol or methanol in the alleged wine. It was sent for analysis by Gas chromatography/Mass Spectrometry (GC/MS) and Gamma-Butyrolactone (GBL) and Tetrahydrofuran were identified. GBL poisoning has never previously been reported in Thailand. The alleged wine is in a green glass bottle. The label reads: 'DOH (Elephantopus scaber) herbal fermented liquor'. It was labeled as the product of Chiang Rai winery under the brand name of "La sante" which won an award for herbal drink from Thai officials in 2000. The winery says that the bottle of wine which the victims got is not similar to the real one which belongs to the winery.

This 'wine' is rumoured to have been exported to the USA, it may also be in other countries. The relevant authorities have been informed in the USA.

Dr Babatunde Olowokure
 IPCS Chemical Alert and Response Team
 WHO HQ, Geneva (Switzerland)



Exposure to vinyl chloride monomer is usually under control in developed countries, Nevertheless, because of long latency periods we still have to face the sequelae of former exposures. Some of these, like the extremely rare angiosarcoma of the liver, are generally acknowledged as an occupational disease caused by VCM. Others, like the more frequent hepatocellular carcinoma, are still a case of debate.

Meta-analysis of studies of occupational exposure to vinyl chloride in relation to cancer mortality

OBJECTIVE: A meta-analysis was made of studies addressing occupational exposure to vinyl chloride in relation to cancer mortality. **METHODS:** Two recently updated multicenter cohort studies and six smaller studies were identified. For selected neoplasms, standardized mortality ratios (SMR) and 95% confidence intervals (95% CI) were abstracted (or calculated from raw data). In cases of lack of heterogeneity (P -value $>$ or $=$ 0.01), meta-analyses were conducted using a random-effects model. **RESULTS:** With SMR values ranging from 1.63 to 57.1, all six studies for which these ratios could be obtained suggested an increased risk of liver cancer. For four of these studies, excesses persisted when known cases of angiosarcoma of the liver (ASL) were excluded. The meta-SMR for liver cancers

other than ASL (based on the 2 large cohorts) was 1.35 (95% CI 1.04-1.77). The meta-SMR for lung cancer was 0.90 (95% CI 0.77-1.00, based on 5 studies), although higher SMR values were reported in early studies. The meta-SMR for brain cancer, based on 5 studies, was 1.26 (95% CI 0.98-1.62). For soft tissue sarcomas, the meta-SMR based on 4 studies was 2.52 (95% CI 1.56-4.07). The meta-SMR for lymphatic and hematopoietic neoplasms in the 2 large studies was 0.90 (95% CI 0.75-1.01), although 3 of the smaller studies reported significant excesses. **CONCLUSIONS:** Apart from the known risk of ASL, workers exposed to vinyl chloride may experience an increased risk of hepatocellular carcinoma and soft-tissue sarcoma; however, these results may have been influenced by the underdiagnosis of true ASL. Increased mortality from lung and brain cancers and from lymphatic and hematopoietic neoplasms cannot be excluded; mortality from other neoplasms does not appear to be increased.

(P. Boffetta et al., Scand. J. Work Environ. Health. 2003; 29: 220–229).

Dr. Michael Nasterlack
 Ludwigshafen (Germany)



And here comes another contribution to this debate (see next page)

Interaction of vinyl chloride monomer exposure and hepatitis B viral infection on liver cancer

Vinyl-chloride monomer (VCM), a human carcinogen, has caused angiosarcoma of the liver. Recent studies have shown that VCM exposure is also associated with hepatocellular cancer. In Taiwanese studies, the majority of VCM-exposed workers with liver cancer had a history of hepatitis B virus (HBV) infection. To determine the role of HBV on the development of liver cancer in the VCM-exposed workers, we conducted a case-control study from a previously established polyvinyl chloride (PVC) cohort consisting of 4096 male workers from six PVC polymerization plants. A total of 18 patients with liver cancer, and 68 control subjects matched for age and specific plant of employment were selected. Detailed history of the participants that included alcohol consumption status, cigarette use, occupation, and family history of chronic liver disease were obtained using an interviewer-administered questionnaire. When the HBV surface antigen (HbsAg)-negative subjects without history of tank-cleaning were used as the reference, the HbsAg-negative subjects with history of tank-cleaning demonstrated a 4.0-fold greater risk of liver cancer (95 % CI = 0.2-69.1). The HbsAg carriers without history of tank-cleaning revealed a 25.7-fold greater risk of liver cancer

(95% CI = 2.9-229.4). Whereas the HbsAg carriers with history of tank-cleaning revealed the greatest risk (matched odds ratio (OR_m) 396.0, 95% CI = 22.6-∞) of developing liver cancer among subjects with different VCM-exposure status and HbsAg status categories. Further analysis showed the interaction term was significant ($P < .01$). Therefore, our results suggest an interaction between occupational VCM exposure and HBV infection for the development of liver cancer. (R.-H. Wong et al., J. Occup. Environ. Med. 2003; 45: 279-383)

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Increased concentrations of polychlorinated biphenyls, hexachlorobenzene, and chlordanes in mothers of men with testicular cancer

An increasing incidence of testicular cancer has been reported from several countries in the Western world during the last decades. According to current hypothesis, testicular cancer is initiated during the fetal period, and exposure to endocrine disruptors, i.e., xenoestrogens, has been of concern. In this investigation we studied the concentrations of the sum of 38 polychlorinated biphenyls (PCBs), p,p'-dichlorodiphenyl-dichloroethylene, hexachlorobenzene (HCB), and chlordanes, in 61 cases with testicular cancer and 58 age-

matched controls. Furthermore, case and control mothers were also asked to participate, and 44 case mothers and 45 control mothers agreed. They were of similar age. In cases only the concentration on lipid basis of cis-nonachlordane was significantly increased, whereas case mothers showed significantly increased concentrations of the sum of PCBs, HCB, trans- and cis-nonachlordane, and the sum of chlordanes. Among case mothers the sum of PCBs yielded an odds ratio (OR) of 3.8; 95% confidence interval (CI), 1.4-10 was calculated using the median concentration for the control mothers as cutoff value. For HCB, OR = 4.4 (95% CI, 1.7-12); for trans-nonachlordane, OR = 4.1 (95% CI, 1.5-11); for cis-nonachlordane, OR = 3.1 (95% CI, 1.2-7.8); and for sum of chlordanes, OR = 1.9 (95% CI, 0.7-5.0). No consistent different risk pattern was found for seminoma or nonseminoma testicular cancer.

(L. Hardell et al., Environ. Health Perspect. 2003; 111: 930-934).

This is indeed a new and to the best of my knowledge unique study which adds further credibility to the often cited health significance for children of endocrine disrupting chemicals. Is anybody aware of a similar study targeted at human in-utero exposures?

Dr. Michael Nasterlack
Ludwigshafen (Germany)



While we are at environmental exposures, I would like to bring the abstract of a study on dental amalgam. Although this is not exactly what we understand as "health issues related to the production and use of chemicals", it is nevertheless a contribution to the (almost) never ending debate on the safety of mercury-containing dental restorations, in which many of us may have been involved, be it as medical expert, counsellor, or maybe as father of a child with a hole in a tooth.

Mercury derived from dental amalgams and neuropsychologic function

There is widespread concern regarding the safety of silver-mercury amalgam dental restorations, yet little evidence to support their harm or safety. We examined whether mercury dental amalgams are adversely associated with cognitive functioning in a cross-sectional sample of healthy working adults. We studied 550 adults, 30-49 years of age, who were not occupationally exposed to mercury. Participants were representative of employees at a major urban medical center. Each participant underwent a neuropsychologic test battery, a structured questionnaire, a modified dental examination, and collection of blood and urine samples. Mercury exposure was assessed using a) urinary mercury concentration (UHg); b) the total number of amalgam surfaces; and c) the number of occlusal amalgam surfaces. Linear regression

analysis was used to estimate associations between each marker of mercury exposure and each neuropsychologic test, adjusting for potential confounding variables. Exposure levels were relatively low. The mean UHg was 1.7 micro g/g creatinine (range, 0.09-17.8); the mean total number of amalgam surfaces was 10.6 (range, 0-46) and the mean number of occlusal amalgam surfaces was 6.1 (range, 0-19). No measure of exposure was significantly associated with the scores on any neuropsychologic test in analyses that adjusted for the sampling design and other covariates. In a sample of healthy working adults, mercury exposure derived from dental amalgam restorations was not associated with any detectable deficits in cognitive or fine motor functioning.

(P. Factor-Litvak et al., Environ. Health Perspect. 2003; 111: 719-723).

Dr. Michael Nasterlack
Ludwigshafen (Germany)



As we are just discussing non-chemicals, here is another one which nevertheless might be an issue for many of us in our daily work.

Electromagnetic fields and breast cancer on Long Island: a case-control study

The EMF and Breast Cancer on Long Island Study (EBCLIS) was a case-control study designed to evaluate the possible association between

exposure to electromagnetic fields (EMFs) and breast cancer. Eligible women were participants in the population-based Long Island Breast Cancer Study Project, were under 75 years of age at enrollment, were residentially stable, and were identified between August 1, 1996, and June 20, 1997. Of those eligible, 576 cases and 585 controls participated in EBCLIS (87% and 83%, respectively). In-home data collection included various spot and 24-hour EMF measurements, ground-current magnetic field measurements, wire mapping of overhead power lines servicing the home, and an interview. Odds ratios and 95% confidence intervals were based on multivariate logistic regression analyses. All odds ratios were close to 1 and nonsignificant. For the highest quartile of 24-hour EMF measurements, the odds ratio was 0.97 (95% confidence interval (CI): 0.69, 1.37) in the bedroom and 1.09 (95% CI: 0.78, 1.51) in the most lived-in room. For the highest exposure category of ground-current measurements, the odds ratio was 1.13 (95% CI: 0.88, 1.44) in the bedroom and 1.08 (95% CI: 0.85, 1.38) in the most lived-in room. These and other EBCLIS results agree with other recent reports of no association between breast cancer and residential EMF exposures. (E.R. Schoenfeld et al., Am J Epidemiol. 2003; 158: 47-58).

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Power-line frequency electromagnetic fields do not induce changes in phosphorylation, localization, or expression of the 27-kilodalton heat shock protein in human keratinocytes

The linkage of the exposure to the power-line frequency (50-60 Hz) electromagnetic fields (EMF) with human cancers remains controversial after more than 10 years of study. The in vitro studies on the adverse effects of EMF on human cells have not yielded a clear conclusion. In this study, we investigated whether power-line frequency EMF could act as an environmental insult to invoke stress responses in human keratinocytes using the 27-kDa heat shock protein (HSP27) as a stress marker. After exposure to 1 gauss (100 micro T) EMF from 20 min to 24 hr, the isoform pattern of HSP27 in keratinocytes remained unchanged, suggesting that EMF did not induce the phosphorylation of this stress protein. EMF exposure also failed to induce the translocation of HSP27 from the cytoplasm to the nucleus. Moreover, EMF exposure did not increase the abundance of HSP27 in keratinocytes. In addition, we found no evidence that EMF exposure enhanced the level of the 70-kDa heat shock protein (HSP70) in breast or leukemia cells as reported previously. Therefore, in this study we did not detect any of a number of stress responses in human

keratinocytes exposed to power-line frequency EMF. (B. Shi et al., Environ. Health Perspect. 2003; 111: 281-288). *I found this study particularly interesting because it reports the absence of findings reported in previous studies. It thus demonstrates the importance of replication studies especially in these fields where a high public awareness exists and the lay media often jump on any bad news.*

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Do you feel reassured? Read the next one!

Electromagnetic fields, polychlorinated biphenyls, and prostate cancer mortality in electric utility workers

The purpose of this study was to determine whether there was an association between occupational exposure to electromagnetic fields (EMFs) or polychlorinated biphenyls (PCBs) and mortality from prostate cancer among US electric utility workers. Data on participants, who were current and former employees of five large US electric utility companies, had been collected during 1987-1994, and the mortality of the cohort was followed through 1988. This nested case-control study contained 387 cases, men whose underlying cause of death was prostate cancer, and five controls for each case. Workers categorized in the highest 10 percent of EMF

exposure were twice as likely to die from prostate cancer as those exposed to EMFs at lower levels, after adjustment for PCB exposure, race, and active work status within the past 2 years (odds ratio = 2.02, 95% confidence interval (CI): 1.34, 3.04). The odds ratio for PCB exposure and prostate cancer mortality was 1.47 (95% CI: 0.97, 2.24) after adjustment for suspected confounding factors. Exposure to high levels of both EMFs and PCBs showed no association with prostate cancer mortality. Non-White race was strongly associated with risk of prostate cancer mortality (odds ratio = 3.67, 95% CI: 2.66, 5.06). The association between EMF exposure and prostate cancer mortality warrants further investigation.

(L.E. Charles et al., Am. J. Epidemiol. 2003; 157: 683-691).

What really puzzles me with this study is the fact that electricians in the upper decile of EMF-exposure have a doubled risk of prostate cancer, and those in the upper decile of PCB-exposure have an OR of 1.4. However, the ones who were in the upper category for both exposures showed no risk increase. Who solves the puzzle?

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Maybe it's not a puzzle but merely chance. Studies on the health impact of former PCB exposure yield especially controversial results.

A mortality update of male and female capacitor workers exposed to polychlorinated biphenyls

This analysis represents a 5-year update of a mortality study of 7075 PCB exposed capacitor workers that now includes 1654 deaths and 235,984 person-years of observation with follow-up through 1998. In hourly males and females the observed number of deaths from all-cancers and all-causes were similar to the expected numbers. In salaried males all-cause and all-cancer mortality were significantly below the expected. In salaried females, all-cause mortality was significantly below the expected and all-cancer mortality was below the expected, but not significantly. The authors again failed to find any significant excess mortality in the a priori cancers of concern or in any other cancers in the total cohort or in the highly exposed portion of the cohort. These results expand on the previous observations in this cohort, and as before the data fail to demonstrate any causal association between occupational PCB exposure and excess cancer mortality or any other causes of death. (R.D. Kimbrough et al., *J. Occup. Environ. Med.* 2003; 45: 271-282).

This study is certainly worth reading, because it contains an extensive discussion of the controversial and inconsistent results of other studies in this field.

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Multiple chemical sensitivity is one of the health issues which is very clearly linked to chemicals, although apparently only in the so-called developed countries with western lifestyle (and jurisdiction?). It seems not to be an issue in the developing world, where environmental chemical exposures can sometimes be much higher than in North American or European countries. Although most MCS-affected persons suffer genuinely and should not be viewed as malingerers, the scientific evidence for the alleged causation of their ailment through chemicals is far from conclusive. Here is another study which provides a contribution to this discussion.

Anxiety sensitivity and depression in multiple chemical sensitivities and asthma

Patients with sensitivities to multiple chemicals report symptoms of cognitive dysfunction, respiratory distress, and mood disturbance. Lifetime and current psychiatric disorders, personality traits associated with symptom reporting, and tests of cognitive function were compared between 30 subjects with Multiple

Chemical Sensitivities (MCS), 19 asthmatics, and 31 healthy controls. Relative to asthmatics and controls, more MCS subjects met criteria for current depression and somatization disorder. MCS subjects and asthmatics scored significantly higher than controls on scales of chemical odor intolerance and anxiety sensitivity, both of which were significant predictors of physical symptoms. Few differences on objective neuropsychological tests were noted. However, MCS subjects with comorbid depression performed significantly worse on a verbal memory test relative to asthmatics but not to controls. Anxiety and depression are significant contributors to the physical and cognitive symptoms of MCS subjects. (E. Caccappolo-Van Vliet et al., *J Occup Environ Med.* 2002; 44: 890-901).

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Health impacts of pesticide exposure in a cohort of outdoor workers

The mortality of 1,999 outdoor staff working as part of an insecticide application program during 1935-1996 was compared with that of 1,984 outdoor workers not occupationally exposed to insecticides, and with the Australian population. Surviving subjects also completed a morbidity questionnaire. Mortality was significantly higher in both exposed and control subjects

compared with the Australian population. The major cause was mortality from smoking-related diseases. Mortality was also significantly increased in exposed subjects for a number of conditions that do not appear to be the result of smoking patterns. Compared with the general Australian population, mortality over the total study period was increased for asthma [standardized mortality ratio (SMR) = 3.45; 95% confidence interval (CI), 1.39-7.10] and for diabetes (SMR = 3.57; 95% CI, 1.16-8.32 for subjects working < 5 years). Mortality from pancreatic cancer was more frequent in subjects exposed to 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (SMR = 5.27; 95% CI, 1.09-15.40 for subjects working < 3 years). Compared with the control population, mortality from leukemia was increased in subjects working with more modern chemicals (standardized incidence ratio = 20.90; 95% CI, 1.54-284.41 for myeloid leukemia in the highest exposure group). There was also an increase in self-reported chronic illness and asthma, and lower neuropsychologic functioning scores among surviving exposed subjects when compared with controls. Diabetes was reported more commonly by subjects reporting occupational use of herbicides. These findings lend weight to other studies suggesting an association between adverse health effects and exposure to pesticides.

(J. Beard et al., Environ. Health Perspect. 2003; 111: 724-730).

Dr. Michael Nasterlack
Ludwigshafen (Germany)



Neurobehavioural effects among workers occupationally exposed to organophosphorous pesticides

The study was carried out to identify neurobehavioural deficits among workers exposed to organophosphorous (OP) pesticides in their occupation.

This study was conducted during the period when pesticides were applied to cotton crops in the fields in Menoufiya Governorate, Egypt. Fifty two occupationally exposed male workers were compared to 50 unexposed male controls who were similar in age, socioeconomic class, and years of education (> or =12 years). All participants completed a questionnaire (assessing personal, occupational, and medical histories), general and neurological clinical examination, neurobehavioural test battery (including tests for verbal abstraction, problem solving, attention, memory, and visuomotor speed), personality assessment, and serological analysis for serum acetylcholinesterase.

After correcting for confounders of age and education, the exposed participants exhibited significantly lower performance than controls on six neurobehavioural tests

(Similarities, Digit Symbol, Trailmaking part A and B, Letter Cancellation, Digit Span, and Benton Visual Retention). A longer duration of work with pesticides was associated with lower performance on most neurobehavioural tests after adjusting for multiple comparisons. Although serum acetylcholinesterase was significantly lower in the exposed than the control participants, it was not significantly correlated with either neurobehavioural performance or neurological abnormalities.

Occupational exposure to OP pesticides was associated with deficits in a wider array of neurobehavioural functions than previously reported, perhaps because of higher exposure in this population. Moderate chronic OP exposure may not only affect visuomotor speed as reported previously, but also verbal abstraction, attention, and memory.

(T.M. Farahat et al., Occup Environ Med. 2003; 60: 279-286).

Dr. Michael Nasterlack
Ludwigshafen (Germany)



People and Events

Medichem's treasurer and former secretary-treasurer **Dr. Andreas Flückiger**, Switzerland, celebrated his 50th birthday on July 20th. His untiring energy and dedicated commitment to his tedious tasks (including everything which is linked to Medichem), his great experience, as well as

his amiable personality and his ever available readiness to help and give council have long belonged to Medichem's most valuable assets. Andreas, please accept our best wishes for the next 50 or more years.

Dr. Stephen Borron, Paris (France)
Prof. Alfred Thiess
Dr. Michael Nasterlack
Ludwigshafen (Germany)

Medichem Board Member **Dr. Thirumalaj Rajgopal** has been elected President of the Indian Association of Occupational Health 2003 – 2005. The co-operation between Medichem and IAOH will be further enhanced through the XXXIII Annual Medichem Congress to be held in 2005 in Goa, India. The congress is going to be organized by Medichem's National Representative in India, **Dr. S. M. Shanbhag**.

The following message reached us from **Daniela Fano**, secretary at the *Clinica del Lavoro L. Devoto* at the Department of Occupational Health of the University of Milan:

Prof. **Antonio Grieco** died due to a sudden and unexpected illness on April 30, 2003. He was a reputed scientist and researcher and has been Director of the Department of Occupational Health of the Milan University "Clinica del Lavoro Luigi Devoto" for over 15 years. His contribution to the development of Occupational Health at national and international level and his social commitment markedly affected the evolution of OH over the past

forty years in Italy and abroad, and significantly contributed to workers' health prevention and promotion.

Medichem's Chairman Stephen Borron wrote to Daniela Fano:

I am truly sorry to hear of the passing of Professor Grieco. It was my great pleasure and honor to meet Professor Grieco for the first time at the ICOH Congress in Iguacu in February of this year. While my time to know him was brief, I was immediately impressed with his knowledge, his appreciation for the importance of the history of occupational medicine, and his kind demeanor. His enthusiasm for the work of the internationally known Lavoro Clinic, as evidenced by his distribution of a book on its history, was contagious.

I'm certain I speak for all of Medichem and the Subcommittee on Occupational Health in the Chemical Industry when I say that I am sorry for the loss of this statesman of occupational medicine and express my heartfelt condolences to his family, his colleagues, and many friends. His loss will be mourned by all who knew him.

Dr. Stephen Borron, Paris (France)



Welcome to New Members

Dr. **Michael G. Holland**, Medical Toxicologist, Hummelstown (U.S.A.),
Dr. **Gustavo Ramón Franco Serrato**, BASF Mexicana

S.A., Mexico City (Mexico),
M. Caubo, Chemelot, Arbodienst DSM, Geleen (Netherlands),
Dr. **Sergio Leichner**, Produtos Roche Quimicos e Farmaceuticos S.A., Rio de Janeiro (Brazil),
Dr. **John RB Cooper**, Unilever, London (United Kingdom)



Forthcoming Events

XXXII. Medichem 2004 - Paris

The XXXII. Medichem Congress will take place **September 1 – 3, 2004** at the Sofitel Paris Rive Gauche Hotel. The 1st announcement with call for papers will be available soon.

Please check our website at **www.medichem.org.au** for regular updates of information.

The 5th Congress of Toxicology in Developing Countries – Toxicology in New Century – Opportunity and Challenge

Guilin, China 10–13 November 2003

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