MEDICHEM

NEWSLETTER

March 2006

Medichem 2006 Board Elections – Call for Candidates

This year, the Medichem Board member Peter Nmadu arrives at the end of his term of office. Thus, one seat on the Medichem Board is to be distributed and according to Medichem Constitution Article 5, Medichem members in good standing can nominate candidates for the Board elections 2006.

You, Medichem members in good standing, are now asked to nominate candidates for the Board, if you want to do so.

A nomination form has been sent to you along with this Newsletter.

According to Article 5 Sect. 4.1 of the Medichem Constitution, each Board member shall be from a different country. This rule does not apply for those holding the offices of Chairman, Vice Chairman, Secretary, Treasurer, and immediate Past Chairman.

*Therefore Members from **Argentina, Bulgaria, Germany, Greece, India, Japan, Mexico, Netherlands, South Africa, Taiwan, UK or USA** cannot be candidates in this year's Board election.*

All **candidates must be ICOH members in good standing**, or **at least agree to join ICOH if elected**. Furthermore, the nomination shall only be valid if it is sent in along with written acceptance of the nomination from the candidate himself or herself. Nominations must be sent to the Secretary of Medichem, Dr. Robert Winker, by mail or fax (+43-1-408 80 11; e-mail: robert.winker@meduniwien.ac.at) . They must be in possession of the secretary no later than May 31st, 2006. The ballot form for the election will be sent out along with the next Newsletter in July 2006.

ICOH Membership

The Medichem Board acts as the "Scientific Committee on Occupational Health in the Chemical Industry" of the International Commission on Occupational Health, ICOH. While all Medichem Board members therefore also have to be ICOH members in good standing, this is not mandatory for other Medichem members. The Medichem Board, however, strongly encourages every Medichem member to also join ICOH and thus participate in the fostering of scientific progress, knowledge and development of occupational health and safety in all its aspects. Find out more about ICOH and ICOH membership at www.icoh.org.sg/membership.asp

Dr. Robert Winker
(Vienna, Austria)

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

Mechanism for impact of work stress on heart proposed

Stress at work is linked to the metabolic syndrome, say UK researchers who believe that this may offer an explanation for the link between stress and heart disease. The epidemiologists based at University College London found that individuals with chronic work stress over a 14-year period were more than twice as likely to develop the metabolic syndrome compared with their less stressed colleagues.

They suggest: "Prolonged exposure to work stress may affect the autonomic nervous system and neuroendocrine activity directly, contributing to the development of the metabolic syndrome."

The findings come from 10,308 men and women in the Whitehall II study, who were aged 35-55 years and worked at one of 20 civil service departments in London.

Work stress in the group was measured using a questionnaire on four occasions between 1985 and 1999, and identified as chronic when high perceived job demands combined with low job control and low levels of support from coworkers and supervisors at three of the four assessments. This information was then compared with components of the metabolic syndrome including abdominal obesity, high blood pressure, elevated triglyceride levels, low levels of high-density lipoprotein cholesterol, and elevated fasting glucose. Tarani Chandola and fellow researchers found a dose-response relationship between exposure to work stressors in 14 years of follow-up and the risk of the metabolic syndrome, identified as the presence of three or more of its components ($p<0.05$ for men; $p<0.01$ for women).

"Men with chronic work stress (three or more exposures) were nearly twice as likely to develop the metabolic syndrome than those with no exposure to work stress," they report. "Women with chronic work stress were over five times more likely to have the metabolic syndrome, but they formed a small group (n=18)."

Both men and women from lower employment grades were more likely to have the syndrome, confirming earlier studies showing that the syndrome has a social gradient. Unhealthy behaviors such as smoking, physical inactivity, poor diet, and excess alcohol intake predicted the risk of the metabolic syndrome in men and, less consistently, in women.

Nonetheless, the researchers say: "There was little evidence that these behaviors mediated or confounded the effect of work stress on the risk of developing the syndrome." Reporting their findings in an early online edition of the British Medical Journal, they conclude: "The study provides evidence for the biological plausibility of psychosocial stress mechanisms linking stressors from everyday life with heart disease."

(Chandola T. et al., Chronic stress at work and the metabolic syndrome:
a prospective study
BMJ, Mar 2006; 332: 521 – 525)

Dr. Robert Winker
(Vienna, Austria)

Do pesticides cause childhood cancer?

Cancer in children affects 1 in 500 - 600 children until age 15. The incidence rates appear to be stable or slightly increasing for some cancer types, while mortality is decreasing. Although it is thus a rare disease, every single case causes an enormous emotional impact on the affected children and their parents likewise.

Leukemias are the group of childhood malignancies with by far the highest incidence, representing close to a third of all cases; tumors of the central nervous system and lymphomas are respectively the second and third most frequent groups.

Little is known about the causes of childhood cancer, with ionizing radiation and some therapeutic drugs being the only well established

causal factors. Suggestive evidence exists, however, for several other factors including natural causes such as infections, and man-made causes such as electromagnetic fields, traffic exhaust, and various environmental chemicals. Among the latter, "pesticides" have been specifically scrutinized.

Epidemiological studies have reported associations between childhood cancer and either parental or child exposure to pesticides.
Reviews have been published by Daniels et al. (1997) and Zahm and Ward (1998). Collectively, these studies suggest an increase in risk of brain cancer, leukemia, non-Hodgkin's lymphoma (NHL), Wilms' tumor, Ewing's sarcoma, and germ cell tumors associated with parental occupational and non-occupational exposure to pesticides. The exposures observed occurred prior to, and during pregnancy, as well as after child birth, thus, involving different potential modes of action. While Zahm and Ward conclude that "there is potential to prevent at least some childhood cancer by reducing or eliminating pesticide exposure", according to the authors of both reviews, methodological limitations common to many studies restrict conclusions regarding the role of pesticides in the etiology of childhood cancers.

A new review was undertaken in 2004 with the aim to update the current knowledge, and to discuss potential implications for further studies. To this end a literature search has been conducted to identify and evaluate new research results on this topic issued since 1998. The literature database PubMed was searched with "(pesticides OR herbicides OR fungicides OR insecticides) AND ((children or childhood) AND cancer)". This search in July 2004 yielded 217 citations, 93 of which had appeared after the comprehensive literature reviews provided by Daniels et al. and Zahm and Ward. When papers not directly aimed at the topic of interest, not representing original research or not providing sufficient information on the study populations were excluded, 14 new studies remained and another 4 were identified from additional sources, e.g., reference lists. In order to allow a rough estimate of the potential impact of the exposures studied, if sufficient information was provided population attributable risks were calculated for case-control studies.

Collectively, the studies reviewed suggest an increase in risk of different cancer types, associated with exposure to pesticides. However the evidence is conflicting with regard to cancer types as well as to causative factors across studies. Almost each positive association reported is matched by a number of studies where these associations have not been verified. This can be due to a lack of statistical power as well as to inappropriate exposure assessment in negative studies.
The major shortcomings concern exposure assessment, where, e.g., "farming" is treated equal to "exposure to pesticides", disregarding other possible exposures, e.g., to biological or infectious agents, and hitherto unidentified lifestyle factors. Also, many exposure questionnaires used in case-control studies are based on broad and sometimes implausible categories. In most studies exposures were categorized as "ever vs. never", with no regard of exposure intensity or duration.
Caution is also warranted with regard to exposure categories used in data analysis, where chemical or toxicological stringency is often not obvious. An apparent tendency to lump together unrelated items may sometimes be the result of the authors' endeavor not to overlook meaningful associations in datasets with otherwise limited statistical power. Liberal handling of these categories, however, may sometimes have just produced results of "data quenching". Equal weight could be given to the alternative interpretation where "living on a farm" or "pesticide use" are associated with the presence of a variety of biological factors, some of which are suspected causative factors for childhood cancers, like infections, and others like several mycotoxins or bioactive plant products are proven human or animal carcinogens.
Focusing on the presence of pesticides, and not asking the question why they were used,

might even mask relevant associations to other causative agents.

Notwithstanding the weaknesses and inconsistencies regarding the available evidence for an association between exposure to "pesticides" and childhood cancer, self-complacency is not an option.

There is a tendency in some studies where indoor use of pest control products appears to be more consistently associated with childhood cancers than outdoor use. Further, suggestive evidence exists of certain gene-environment interactions where some agrochemicals may increase the risk for some cancer types in susceptible individuals. Both suggestions can be followed in future studies which draw back on new methodologies, including improved biomonitoring, assessment of new biomarkers of exposure, and gene mapping techniques. However, priority setting in the allocation of limited research and intervention funds should focus on topics where the most benefit for children's health can be expected. If, despite all doubts and uncertainties, the associations reported in the studies reviewed here were true, the calculation of the attributable fractions – where feasible – of the groups of cancers examined yields between less than 1 and 15% which could be explained through pesticides.

Conclusion: Although the association between childhood cancer and various agrochemicals has been studied for many years, no firm conclusions can be drawn from the existing study reports. "Another 40 epidemiological studies similar to the majority of those conducted thus far will not provide clarity" (Olshan and Daniels 2000).

The use of biologically and chemically implausible exposure categories like "pesticides" will bias any substance-related outcome towards null and thus mask possible existing causal relations with specific agents. On the other side, if biocide or pesticide use is but a surrogate marker for a carcinogenic principle associated with the presence of "pests", it will produce spurious positive results falsely attributed to pesticides.
Investing in the acquisition and critical review of exposure information appears to be the crucial step for causal assessment in future research.

(M. Nasterlack, Int. Arch. Occup. Environ. Health 2006, DOI 10.1007/s00420-006-0086-7)

Dr. Michael Nasterlack
(Ludwigshafen, Germany)

Carbon monoxide poisoning may damage heart

Myocardial injury occurs frequently after moderate-to-severe carbon monoxide poisoning, research published in the Journal of the American Medical Association indicates.

Injury of this nature was also associated with an increased risk of death in the long term, say the researchers led by Christopher Henry (Minneapolis Heart Institute Foundation, Minnesota).

They recommend: "Patients with suspected exposure to carbon monoxide should be screened for myocardial injury, and further cardiovascular risk stratification should be considered in all patients with confirmed myocardial injury."

The study included 230 consecutive patients treated for moderate-to-severe carbon dioxide poisoning with hyperbaric oxygen treatment and admitted at a single medical center between 1994 and 2002.

In all, 37% of the group were identified with myocardial injury, defined asa cardiac troponin I level ≥0.7 ng/ml, a creatine kinase-MB ≥5.0 ng/ml or electrocardiogram changes.

Over a mean follow-up of 7.6 years, there were 54 (24%) deaths, with 12 (5%) of these taking place in hospital. Of the 85 patients with myocardial injury, 38% died during

follow-up compared with just 15% of the 145 patients without myocardial injury (odds ratio=2.1, p=0.009).

Of the patients with myocardial injury who died, 44% died of presumed cardiovascular causes.

"Although carbon monoxide poisoning is the most common cause of accidental poisoning in adults in the United States, the focus has been on acute outcome, in particular the neurological manifestations," the researchers state.

"Our data indicate these patients have poor long-term outcome, a topic that deserves further study."

Dr. Robert Winker
(Medical University of Vienna, Austria)

Obituary - in memoriam of Dr. med. Lambertus de Boer

- Former Chief Medical Advisor of Shell-International – The Hague
- Officer in the Order van Oranje-Nassau
- First Secretary of Medichem
- First Honorary Member of Medichem
- Honorary Member of ICOH

It is with very deep regret that I have to announce to all our Medichem members that our first Secretary of Medichem, Dr. med. Lambertus de Boer passed away on January 7th, 2006. I received this very sad news from his family on Thursday, January 12th. On the same day I wrote a personal letter to express my sincerest condolence and deep feelings of sympathy to his sons, daughter in law and grand children. I asked them to consider me present in spirit at his bier ”op donderdag 12 januari van 19.30 tot 20.15 uur in Uitvaartcentrum Monuta Van der Luit”, to thank Bert for all his enormous and successful engagement for Medichem.

Medichem, and especially I, owe Bert de Boer deep and lasting gratitude:

It was in Vienna, in May 1971, on the occasion of the VI World Congress on the Prevention of Occupational Accidents and Occupational Diseases, when Dr. Lambert de Boer, then Chief Medical Advisor of Shell International, The Hague, during a ball in the historical town-hall enthusiastically agreed to my suggestion to hold an international meeting for occupational health practitioners and toxicologists in Ludwigshafen.
This led to the first Medichem Conference, which was held from 27th – 29th April 1972 in Ludwigshafen and Bert de Boer documented the birth Certificate, with the words “to keep the ball rolling … and the ball started to roll around the globe”. Together with his Secretary, Mrs. van Owem, Bert served from 1972 – 1980 as Secretary of Medichem. These eight years were very hard work, and extensive are his reports of our Congresses in 1972 Ludwigshafen – 1974 Milan – 1975 Brighton – 1976 Haifa – 1977 San Franciso – 1978 Dubrovnik – 1979 Gera - and 1980 Tokyo.
Bert's words: “Medichem is really international and not just multinational” – and on August 25th, 2002 he wrote:
“I still feel sad, I cannot join any more Medichem where we worked hard, but where we also had such a pleasant time together … but happy memories never fade”.

On May 5th, 2005, he wrote “To all friends who sent me their best wishes. Sorry I could not answer your cards. Thank you again for all your good wishes and I will try to go on for a while…”.
Bert de Boer was deeply devoted to Medichem, a person much respected, dignified worldwide. Always prodigious, tireless, dynamic, with great skill, great passion, great fairness and always great warmth. This warmth earned him the support and friendship of us all, worldwide. A doctor of great loyality – of great diplomacy. Unforgettable are his “Addresses to the Ladies” on our farewell evenings, his frugality and housekeeping

qualities, which he to instill into Medichem.
Wonderful his witty "Netherlands humour".

Bert de Boer will remain a great architect within Medichem, will remain in our hearts, together with his charming wife Sophia ("Fietje") who had also passed away too early for us.
Medichem lost his first Secretary – we will never forget him.
I lost a very good faithful friend.

Thank you, dear Bert!

Prof. Alfred M. Thiess,
(Ludwigshafen, Germany)

Lead exposure levels and duration of exposure absence predict neurobehavioral performance

During the last decade many studies have addressed the issue of neurobehavioural effects due to occupational inorganic lead exposure.

Most of these studies were focused on the question of whether lead exposure has a negative impact on the cognitive functions of exposed subjects. Due to methodological challenges only a few studies deal with the question of whether such effects are reversible or whether they remain after exposure has ceased. However, this distinction between acute and chronic effects is most significant for public health. The proof of chronic effects would have much more important implications than the proof of acute effects.

In general, current scientific literature provides inadequate evidence to conclude whether or not lead induced cognitive impairments are reversible. Studies on that topic have reached conflicting conclusions regarding the association of lead exposure and cognitive deficits. Most of them are limited by a lack of cumulative exposure assessment, small sample sizes, poor follow-up rates and follow-up periods of short duration.
We therefore investigated cognitive functions in currently lead exposed and formerly exposed men. The aim of the study was to verify the hypothesis that lead induced cognitive deficits are reversible. The detailed results are published in the March Edition of the International Archives of Occupational and Environmental Health and I will therefore only give a brief summary of the current project.

We investigated 47 lead exposed subjects with a mean blood level (PbB) of 30.8 µg/100 ml and 48 formerly exposed aged-matched subjects (PbB: 5.5 µg/100 ml) with the same socio-economic background. Both groups were matched on verbal intelligence. Cognitive functions were assessed by using the Modified Wisconsin Card Sorting Test, Block Design Test, Visual Recognition Test, Simple Reaction Time, Choice Reaction and Digit Symbol Substitution. Lead exposure was assessed by using current and cumulative measures. The sample was divided according to their exposure duration versus exposure absence into four groups for subsequent ANOVA models analyses.
The exposed group was significantly poorer in the Wisconsin Card Sorting Test including the main performance category as well as in three sub-categories and the Block Design Test. No differences were found in the Visual Recognition Test, Simple Reaction Time, Choice Reaction and Digit Symbol Substitution.
Splitting the sample according to their exposure duration vs. exposure absence resulted in better cognitive performance of subjects with shorter exposure duration and longer exposure absence in the Block Design Test and the Wisconsin Test.

Discussion:
If our reversibility hypothesis is correct, currently exposed should perform worse than formerly exposed. To specify our hypothesis on reversibility an additional rank order of cognitive impairment depending on duration of exposure and absence from exposure could be proven for the Block Design Test and the Wisconsin Test. Results showed that workers with short

duration of exposure during their work combined with long absence from exposure perform best. They were followed by workers with long duration of exposure but long absence from exposure; workers with short duration of exposure and short absence from exposure followed by workers with long duration of exposure and short absence show significantly the highest cognitive reduction. This rank order stresses the importance of absence from exposure and is a further indicator for reversibility. In other words: Cognitive deficits recover with the duration of absence from exposure.

Taken together, we showed that shorter exposure duration and longer exposure absence resulted in better cognitive performance. Additionally, our present results suggest that adverse neurobehavioral effects of lead occur in currently exposed subjects but not in formerly exposed. Hence we conclude that lead induced cognitive impairment is most likely reversible.

(Winker R. et al., Int Arch Occup Environ Health. 2006 Mar;79(3):193-8)

Dr. Robert Winker
(Medical University of Vienna, Austria)

Latest UK CVD guidelines shift focus to prevention

The criteria for the prevention of heart disease and stroke in the UK should be widened in order to increase the number patients targeted for screening and preventive treatment, updated guidelines recommend.

The latest Joint British Societies guidelines are endorsed by the British Cardiac Society, the British Hypertension Society, Diabetes UK, HEART UK, the Primary Care Cardiovascular Society, and the Stroke Association, and are more strict than the previous version produced 7 years ago. For the first time, the focus has been shifted away from just coronary heart disease to cardiovascular disease as a whole. Aiming to ensure the consistent treatment of all people who already have atherosclerotic arteries, criteria for drug treatment have been reduced from a 30% or greater risk of cardiovascular disease over 10 years to a 20% or greater risk.

This means that all patients aged over 40 years will be recommended for cardio-vascular disease screening, along with younger patients who have a family history of heart disease or stroke. For the first time, all patients with diabetes will also be included.

All patients who meet the criteria will be recommended a combination of lifestyle and risk factor interventions, along with appropriate drugs to lower blood pressure and modify lipid profiles, and, in the case of patients with diabetes, reduce glycemia. Specifically, the guidelines, which are published in the journal Heart, set out new targets for lifestyle, blood pressure, lipids, and glucose for high-risk people, including a blood pressure of no greater than 130/80 mmHg, total cholesterol of less than 4 mmol/l, and a total low-density lipoprotein level of less than 2 mmol/l.

David Woods, from Imperial College London and the British Cardiac Society, who is lead author of the guidelines, said: "The promise of preventive cardiology is to reduce the risk of having a heart attack or stroke. "With professional lifestyle intervention and appropriate use of proven drug treatments, it is now possible to have a major impact on the commonest cause of death in the country. For people at high risk, this will mean less disability and a longer life."

(Heart 2005; 91 (Suppl V): v1-v52)

Dr. Robert Winker
(Medical University of Vienna, Austria)

Medichem activities

On the occasion of its Board mid-term meeting Medichem organized a Mini-Symposium for local toxicologists, public health specialists and occupational medicine doctors in Monterrey, Mexico, on February 17, 2006.

The following topics were chosen:

1) Preparedness for chemical mass casualty incidents,

2) State of the art: Cyanide poisoning,

3) Mass psychogenic illness in the era of terrorism.

Forthcoming Events

This year, Medichem will organize a Mini-Symposium together with the Scientific Committe on Pesticides at the **ICOH Congress in Milan**, Italy **(June 11 - 16).**
Unfortunately, the exact date when the Mini-Symposium will be held, is not known yet, but will be communicated via the Medichem-homepage. The topic will be "Use of Human Data in Risk Assessment".

More information is available at www.icoh2006.it/ and from the Organizing Secretariat in charge of the congress registration, which is:

Fiera Milano Congressi c/o SP.i.c., Via Costalunga, 14 25123 Brescia (BS),
E-mail:
icoh2006@fieramilanocongressi.it

Medichem is co-sponsoring an "Advanced Hazmat Life Support" (AHLS) course on June 8-9, 2006 in Rome as a "Pre-congress event".

Dr. Alessandro Barelli is organizing this pre-congress course in the Catholic University School of Medicine.
The Advanced Hazmat Life Support (AHLS) Provider program is a 16 hour, 2-day course which trains the participant 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

More information is available at http://www.ahls.org/. You may register for the course online at www.tox.it.

Welcome to New Members

Dr. **Craig Vitrano**, BASF, Los Angeles (United States),
Dr. **Pingle Shyam,** Reliance Industries LTD., Maharashtra (INDIA),
Dr. **R. Rajesh,** Reliance Industries LTD., Jaminagar (INDIA),
Dr. **Ashok Mewara,** Reliance Industries LTD., Gujarat (INDIA),
Dr. **Chaitanya Gulvady,** Reliance Industries LTD., Mumbai (INDIA)
Dr. **Raphael Ranjan,** Reliance Industries LTD., Maharashtra (INDIA),
Dr. **Henri Hendrickx,** General Electric, Bergen (NETHERLANDS)