M E D I C H E M

NEWSLETTER

March 2007

Medichem 2007 Board Elections – Call for Candidates

This year, the following Medichem Board members arrive at the end of their terms of office (appearance ranked in alphabetical order by last name): Stephen Borron, Andreas Flückiger, Koichi Kono, Michael Nasterlack, Todor Popov, Thirumalai Rajgopal, Sergio Salomon, Friedrich Schmahl, and Robert Winker.

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 chairmanship on the board, this time the board is limited to 18 and therefore nine seats on the Medichem Board are to be distributed.

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

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.

This year, *candidates for Board membership must not be from Austria, Greece, Mexico, Netherlands, South Africa, Taiwan, United Kingdom, United States of America*

All candidates must be Medichem Members in good standing, and also 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, Doz. Dr. Robert Winker, by mail or fax. (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, 2007.

The ballot form for the election will be sent out along with the next Newsletter in July 2007.

Doz. Dr. Robert Winker
(Vienna, Austria)

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

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

Founded 1972 in Ludwigshafen, Germany

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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)

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

Doz. Dr. Robert Winker
(Vienna, Austria)

Increased frequencies of micronuclei in lymphocytes of workers from a hot dip galvanizing plant

Introduction:

Adverse health effects by extremely low frequency electromagnetic field (ELF-EMF) are debated for more than 25 years now and are largely based on reports of increased incidences of childhood leukaemias in the vincinity of electric power lines. A pooled analysis of several independent studies came to the conclusion, that long-term exposure to power frequency electromagnetic fields above 0.4 µT is associated with a doubling of the risk of childhood leukaemia (Ahlbom A et al., 2000). Increased risk of leukaemia was also reported in workers with a presumed occupational exposure to ELF-EMF (for example Matanoski G.M. et al., 1993).

By contrast, some studies found no association between occupational exposure to ELF-EMF and leukaemia.
A meta-analysis of 38 studies assessed a small risk of leukaemia in the order of 1.2 associated with ELF-EMF exposure at work without clear dose dependency (Kheifets,L.I. et al., 1999).

The epidemiologic controversy on the possible cancerogenicity of ELF-EMF finds its counterpart in controversial genotoxicity studies. On the basis of the available data the International Agency for Research on Cancer (IARC) has recently classified ELF-EMF as possibly carcinogenic (IARC 2002). Our group has reported a dose dependent increase of DNA single and double strand breaks after ELF-EMF exposure in exposed human fibroblasts in vitro (Ivancsits et al., 2002; Ivancsits et al., 2003). This DNA fragmentation was significantly associated with an increased frequency of micronuclei and chromosome aberrations at a magnetic flux density of 1.0 mT (25).

In the present study we determined frequencies of micronuclei in lymphocytes from workers of a hot dip galvanizing plant with the aim to identify a possible genotoxic risk from exposure to 50 Hz-EMF by induction heating. A key strength of the study is that biomonitoring took place in the same workplace either in the presence of exposure to ELF-EMF from an induction heating device of a zinc furnace, and again thereafter, when for economic reasons the induction heating was replaced by gas burners. This implementation was not associated with changes in other individual production steps.

Materials and methods:

Eighteen male workers from a hot dip galvanizing plant with induction heating were included in this study. The subjects were in the age group of 29 – 60 years and their duration of work varied from 1 to 21 years at a rate of 8 h per day for 5 days a week. Three series of biomonitoring have been performed to assess a possible lowering of genotoxic effects after exchange of the heating system. The first monitoring session was performed in December 2005 when induction heating for furnacing was still in use. Shortly therafterafter it was replaced by gas heating. The second session of monitoring was done in March 2006 and the last monitoring in June 2006.

Only seven out of the 18 workers completed all three series of biomonitoring. Peripheral blood lymphocytes samples were obtained from 14 subjects in the first session, from 14 subjects in the second session and from 11 subjects in the third session for analysis of micronucei. The 7 workers involved in all three series of monitoring were their own controls. Four unexposed

subjects (age 52 – 67 years) served as control group.

Micronucleus analysis:

Micronucleated lymphocytes were analysed by cytokinesis-block method according to Fenech and Morley with some modifications. Peripheral blood lymphocytes were separated from 5ml of heparinized whole blood on Ficoll-Paque gradients, washed twice with phosphat buffered saline (pH 7.2) and resuspended in 5 ml of chromosome medium 1A (Gibco, Karlsruhe, Germany) containing phytohemagglutinine.
Lymphocytes were cultured at 37°C for 72 h. 44 h after starting the cell culture cytochalasin B (Sigma, St. Louis, USA) was added at a final concentration of 3 µg/l. After 72 h cells were washed in hypotonic saline at 37°C for eight minutes, fixed in methanol / glacial acetic acid (4 / 1), and prepared on slides. The slides were dried and stained for 15 minutes in 5 mg / l of 4',6-diamino-2-phenylindole (Serva, Heidelberg, Germany). Only binucleated cytokinesis-blocked cells were analyzed for micronuclei under a fluorescence microscope. Micronuclei were counted when they met the following criteria: (1) clearly seperated from main nuclei and located within the cytoplasm, (2) oval or round shape, (3) less than one fourth the diameter of the main nuclei, (4) same textures as main nuclei. MN were scored in a minimum of two thousand cytokinesis-blocked binucleated (BN) cells per slide and the samples were blinded to the operator.

The scoring of micronuclei was combined with fluorescence in situ hybridization technique (FISH), using a human centromere-specific DNA probe which detects the centromeric region of all human chromosomes (Qbiogene, Heidelberg, Germany). This allows to count separately micronuclei which are originated by chromosome breaks and therefore contain acentric fragments and micronuclei containing a whole chromosome because they are originated by chromosome nondisjunction The in situ hybridization procedure followed the instructions of the assay kit. Vincristine (1µg/ml) was used as a positive control for the identification of centromere positive and Bleomycin (2mg/ml) as a positive control for centromere negative micronuclei.

Determination of metals:

The concentrations of metals were measured at the second monitoring by using graphit furnace and flame atomic absorption spectrophotometry (Perkin Elmer 5100 PC, Überlingen, Germany) in order to exclude a possible genotoxic influence other than ELF-EMF. The following metals were determined: Pb in blood, Pb in urine, Cd in blood, Cd in urine, Hg in blood, Hg in urine, Mn in blood, Mn in plasma, Mn in urine, As in urine, Cu in plasma, Cu in urine, Zn in plasma, Zn in urine, Ni in blood, Cr in blood, Cr in plasma, Cr in urine. Since there was a known exposure to lead at the workplace this metal was determined also at the first monitoring.

Measurement of 50 Hz magnetic fields:

A Wandel & Goltermann EFA-3 magnetic field analyzer system (5 Hz – 30 kHz) with an external B-field probe was used to measure magnetic fields.
The measurements were based on the DIN VDE 0848-1 (27) definitions (the German official standard) and have been performed at different frontal sites of the induction heating system: left, middle and right site; distances from the furnace and height from the floor ranged from 0 – 1.3 m and 0.1 – 1.0 m, respectively. Figure 1 shows the decay of the magnetic flux density as a function of the distance from the mid-frontal site of the furnace.

For example, a flux density up to 2513 µT was measured at a distance of 0.3 m.

Statistical methods:

Statistical analysis of data was performed using Student's t-test for dependent an independent samples. Statistical significance was set at p = 0.05. Linear regression analysis was used for correlations between micronucleus frequency and internal metal exposure.

Results:

There was a startling elevation of total micronuclei in 14 workers at the fist monitoring (21.4 ± 12.2 for workers vs 4.7 ± 0.8 MN / 500 bn cells for unexposed controls) which decreased significantly 3 months after replacement of the heating device (12.3 ± 2.4) at second monitoring. This decrease of total MN could almost exclusively be attributed to a reduction of chromosome breaks because in 7 workers which have been monitored at all three instances only the centromere negative MN were reduced (first monitoring : 13.9 ± 11.8 C-MN / 500 bn cells, second monitoring : 2.0 ± 1.7, third monitoring : 1.0 ± 0.8) whereas the elevated centromere positives remained constant (first monitoring: 9.9 ± 1.4 C+MN / 500 bn cells, second monitoring: 9.4 ± 1.4, third monitoring: 9.6 ± 1.4). The centromere negatives decreased slightly further at the third monitoring after six months. Blood lead concentrations were almost equally elevated at first and second biomonitoring (247.6 ± 65.4 and 239 ± 69.5 µg / ml). Four normal controls had blood lead levels of 63.8 ± 44.9 µg / ml. The concentrations of lead in blood were significantly correlated with the concentrations of zinc in urine (r = 0.6, p = 0.04). However, with the exception of cadmium (1.98 ± 1.5 µg / ml, controls 0.19 ± 0.16 µg / ml), all other determined metals were in the normal range.

No significant correlation between micronucleus frequencies and the measured metal concentrations was observed. In addition, the level of micronuclei was not associated with duration of work (exposure years).

Discussion:

Workers regularly exposed to 50 Hz-EMF by using induction heated zinc furnaces showed high levels of total micronuclei when compared to unexposed controls with an almost equal distribution of centromere positive and centromere negative micronuclei. The centromere negatives almost normalized after replacement of induction heating by gas heating, whereas the centromere positives remained unchanged.

There had been no evidence for significant changes in other sources of workplace exposure except the exchange of the furnace heating, that might have contributed to an altered genotoxic burden. 7 out of 18 exposed workers could be monitored three times and thus served as their own controls 3 and 6 months without occupational exposure to ELF-EMF. It therefore seems justified to assume, that the initial increase of centromere negative MN is causally related to the high ELF-EMF exposure, and that the subsequent decrease of these MN levels are causally related to the discontinuation of this exposure. This striking increase of MN in blood lymphocytes is particularly interesting because in short term in vitro experiments up to 48 hours these cells did not exhibit a genotoxic effect after exposure to 2.0 mT. It can thus be speculated that lymphocytes either behave differently in vivo than in vitro, or that short term exposure does not mirror genotoxic effect of long term exposure.

The furnace workers but not the control probands exhibited also a striking elevation of centromere positive MN which persisted at almost the same level for 6 months after the induction heating had been replaced. The origin of the elevation of centromere positive MN is less clear. These MN represent centromere containing chromosomes when the chromatides have not been pulled into daughter nuclei in anaphase of the mitotic process. This epigenetic disturbance is usually caused by agents which interfere with the spindle apparatus of chromosomes (as Colchicine or Vincristine does). One may argue that the toxic influence which has caused this disturbance must still have been present in the workplace after replacement of the

furnace heating since a persistent epigenetic effect of ELF-EMF seems to be unlikely.
The elevated levels of lead and cadmium have to be considered here as an underlying cause. There is also a hypothetical possibility that a combination of ELF-EMF and metals or other toxic influences at this particular workplace may be responsible for this long-lasting cytogenetic effect in blood lymphocytes of the workers.

In this study workers showed concentrations of blood lead from 100 to 394 µg/l without significant difference before and after replacement of induction heating. Recently, Chen et al. found significantly higher frequencies of total micronuclei and DNA strand breaks in lead exposed workers (110 – 620 µg/l) than in unexposed controls (2 – 75 µg/l). This is in line with other studies.
Danadevi et al. observed a statistically significant increase in DNA fragmentation in leukocytes of 45 workers exposed to lead for 1 to 12 years when compared with 36 unexposed controls. In addition, the blood lead concentration in this study group correlated positively with DNA damage, and the years of lead exposure showed a significant effect on DNA damage. Palus et al. (30) reported 18.63 ± 5.01 micronuclei per 1000 binucleated lymphocytes in 30 lead exposed workers (282 – 655 µg/l), whereas 43 unexposed controls had 6.55 ± 3.88 micronuclei per 1000 bn cells. Using a combination of conventional scoring of micronuclei and FISH with pan-centromeric probes, the authors identified a doubling of both clastogenic and aneugenic effects in the lead exposed group. Similar effects were found in this study for workers exposed to cadmium. Vaglenov et al. showed a clear positive correlation between lead in blood and the formation of micronuclei in peripheral blood lymphocytes, indicating a direct relationship between occupational exposure to lead and genetic damage induction. Blood lead concentrations above 1.2 µM (249 µg / L) were identified to cause a significant increase in micronuclei at levels where no clinical symptoms were observed.
From these reports one could draw the conclusion that exposure to lead is a potent source for the induction of micronuclei in humans. Therefore, the fact that significantly increased levels of lead and cadmium have been found in our study group is important for the interpretation of our results. The persistently increased levels of micronuclei after induction heating cessation are likely to be caused by chronic exposure to these metals. However, we did not find a significant correlation between blood levels of these metals and the frequency of micronuclei in the group of exposed workers.
Further biomonitoring studies have to be conducted in subjects working under conditions with long term and high exposure to ELF-EMF in order to confirm the unexpected extent of the cytogenetic effects observed in this study.

A. Pilger; H. Rüdiger
(Vienna, Austria)

Short-term air particulate exposure increases heart disease risk

According to our data Short-term exposure to particulate air pollution increases the risk of acute ischemic heart disease events, especially among people with underlying coronary artery disease

Our findings may be of significant public health importance because such exposure to relatively fine particulate matter (PM) is relatively ubiquitous in urban environments, and essentially involuntary.

In a unique study, owing to its use of a large registry of well-characterized patients who underwent coronary arteriography, and who were living in an area with long-term daily monitoring of air pollution and substantial daily variability in PM concentrations, we sought to evaluate the role of short-term increases in air pollution exposures in triggering acute

ischemic heart disease events.

We analyzed ischemic events in the 12,865 patients included on the cardiac catheterization registry of the Intermountain Heart Collaborative Study who presented with one of three conditions that indicated coronary angiography. These were: acute myocardial infarction (MI), an unstable pattern of chest pain suggesting unstable angina, a stable pattern of chest pain suggesting stable angina, and stable noncoronary syndromes necessitating angiography.

The team found that a 10 µg/m3 increase in PM of aerodynamic diameter 2.5 µm or less (PM2.5) was associated with a 4.5% increased risk of an acute coronary event.

In contrast, there was a 2.6% decrease in the rate of ischemic disease with stable presentation.

Further analysis showed that increased risk of acute ischemic events was more strongly associated with PM2.5 than with PM10. The strongest associations were with concurrent-day or the mean of the concurrent- and previous-day PM exposure, indicating the importance of more recent exposure, the authors note.

In addition, stratification by event type and individual characteristics revealed that PM2.5 effects were significantly greater among individuals with at least one severely diseased coronary vessel than those with no vessel disease.

Noting that further studies are required to evaluate long-term risk, we conclude that our study provides evidence that short-term exposure to elevated concentrations of fine particulate air pollution contributes to the triggering of acute ischemic heart disease events.

Individuals with stable presentation and without seriously diseased coronary vessels are not as susceptible to risk from short-term exposure to fine particulate pollution.

The full article can be downloaded from Circulation:

(http://circ.ahajournals.org/cgi/content/full/114/23/2443)

C. Arden Pope
(Utah, USA)

Major-General Nabil L Ebeid

Older members will know Dr. Ebeid from his role on the organizmg committee of the **9th** Medichem Congress held in conjunction with the I.CO.H. meeting in 1981 at Aswan/Cairo.

They will be delighted to know that Nabil has recently received the Egyptian State Prize for Appreciation 2006. I am sure we would all wish to extend our congratulations to him on this most prestigious Award.

Nabil had not long retired, after 30 years service, from the army medical service, where he had ended as vice president of the Military Medical Academy, when I was elected chairman of Medichem in 1992. He wrote to wish me well, apologizing for his handwriting; he had had a stroke and was having to learn to write with his other hand. In reply, thanking him, I said that his writing was more legible than mine. We have corresponded ever since, and it still is, in fact nowadays more so. We have only met once, when Nabil came to London in 1994 to receive Honorary Fellowship of the Faculty of Occupational Medicine of the Royal College of Physicians. I recall that when it came to his turn to collect his scroll, thinking to save him the effort, the Dean made to walk to where Nabil was seated. No way. Nabil rose and walked with military bearing to the platform.

In retirement, Nabil has written four books, two in Arabic and two in English, about life in Ancient Egypt. He very kindly sent me a copy of bis first book, “Egyptian medicine in the days of the Pharaohs“.

lt is a splendid book, 450 pages of text, a further 50 of references and copiously illustrated. As well as being fascinating to readers in all branches of medicine, much of it would be well within the grasp of the older schoolchild. lt is published by The General Egyptian Book

Organization Press and has ISBN 977-01-6422-4.

His second book in English, co-authored with Hamdy Omar, “Life in the time of the Pharaohs“ is also copiously illustrated, and the style is simple and flowing. lt is one of the few books to focus on the Ancient Egyptians as a people rather than Egypt as a State. This anecdote may serve one other purpose, to highlight a valuable benefit of Medichem membership----the forming of lasting and rewarding friendships.

Dr. David M Williams
(United Kingdom)

Medichem activities

In January, Medichem’s Board met in Zagreb, Croatia to discuss plans for 2007 and the Medichem’s Congress in Queretaro. The meeting was arranged by Dr. Piasek and Prof. Saric and was well organized.
During the meeting, Board Members agreed to institute a new “Young professionals program”, which was prepared by Frank Rose (see attachment).
A well-attended Mini-Symposium, featuring Medichem Board members and Croatian occupational health experts, was held to share learnings with local occupational physicians.

Doz. Dr. Robert Winker
(Vienna, Austria)

Forthcoming Events

The First World Congress on **Work-Related and Environmental Allergy** held together with the 4th International Symposium on Irritant Contact Dermatitis in the summer of 2003 in Helsinki, Finland, brought together dermatologists, pulmonologists, occupational and environmental physicians from all over the world to present research and discuss issues in the field of work- and environment-related allergies. Thoughtfully designed by Prof. Lasse Kanerva from the Finnish Institute of Occupational Health and perfectly organized by his friends and coworkers, this was a meeting of science and friendship with the special Finnish touch.

The second meeting in Weimar promises to be just exciting - with an excellent panel of international keynote speakers and new data presented in free communications and poster sessions.

It is our pleasure to invite you to the 2nd World-congress of **Work-Related and Environmental Allergy** in Weimar, European City of Culture and home of poets, artists and philosophers. You will enjoy great science in a wonderful setting of hospitality. The congress will be held from 13-16th June 2007. The electronic website can be found under www.woreal.org.
Looking forward to welcoming you to Weimar 2007.

Prof. Dr. Peter Elsner,
Dr. Sibylle Schliemann
(Jena, Germany)

The **7th International Conference on Occupational Health** for Health Care Workers will be held in Vancouver, British Columbia, Canada from Friday, October 26 to Sunday, October 28, 2007 (http://www.acoem.org/icoh.aspx). The theme of the conference is “Protecting Health Care Worker Health.”

The conference is hosted by the ICOH Scientific Committee on Health Care Worker Health and the American College of Occupational and Environmental Medicine, and supported by the ICOH Scientific Committee on Occupational Health and Development, and the Occupational and Environmental Health Programme of the World Health Organization.

Other organizations supporting the conference include the Occupational Health and Safety Agency for Healthcare (OHSAH) in British Columbia, and the School of Occupational Hygiene at the University of British Columbia.

The electronic website for abstract submission is now open (http://www.acoem.org/icoh_abstracts.aspx).

Prof. Dr. Bob Orford,
(Scottsdale, USA)

"Young professionals programme"

Frank Rose prepared a draft for the "Young professionals program". At the board-meeting in Zagreb the board agreed to support this concept. The complete "MEDICHEM YOUNG PROFESSIONALS PROGRAMME" is attached to this newsletter. Applications for the scheme are to be sent to the secretary.

Doz. Dr. Robert Winker
(Vienna, Austria)

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-sponsore an Advanced Hazmat Life Support Course. Medichem will provided two instructors, Stephen Borron and Jorge Morales to teach in the 3 day course and provide scholarships to occupational health professionals.

Welcome to New Members

Dr. **Nomonde B. Mabuya,** Ntombizomonde Helath Care Solutions (South Africa),

Dr. **J.G. Bakker,** Coronel Institute Academic medical Center of Amsterdam (Holland),

Prof. **Antonio Duenas-Laita,** University of Valladolid (Spanien),

Prof. **Hiroshi Tsuji,** Department of Hygiene and Public Helath (Japan),

Dr. **Goedele Dours,** Company Glaxco SmithKline (Belgien)