

Newsletter: April 2011

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

Founded 1972 in Ludwigshafen, Germany

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Message from the Secretary

Dear Colleagues:

As many of us in the Northern Hemisphere move out of a long and cold winter into spring, we also are moving closer to the upcoming MEDICHEM Congress in Heidelberg, Germany. Our hosts have been working to finalize details of the meeting, links to which you will find in this issue.

Also, it is once again time to solicit requests for Nominees to the MEDICHEM Executive Board. All nominations must be submitted to the Secretary by June 15th, 2011. Nomination papers for Board members are included with this newsletter. This year, the following MEDICHEM Board members will complete their terms of office: Peter Boogaard, Stephen Borron, Adriaan Combrinck, Elpida-Niki Emmanouil-Nikoloussi, Jiin Ger, Jorge Morales Camino, Diane Mundt, Abed bin Onn and Edwin Whiteside. Board Members are elected for a term of 3 years, but may be re-elected for further terms, if they have the support of the Board and the Membership.

This year, candidates are NOT eligible from the following countries: Austria, Bulgaria, Croatia, Germany, India, Israel, and Japan.

The ballot with slate of Nominees will be sent with the next Newsletter in July 2011.

I look forward to meeting you all in June at our meeting in Heidelberg.

Dr. Diane J. Mundt
Boston, MA (USA)



MEDICHEM 2011 – See you there!

From Dr. Med. Maren Beth-Huebner, Chair of the Organizing and of the Scientific Committee of MEDICHEM 2011

The first draft of the comprehensive Scientific Program of the 39th International MEDICHEM Congress on Occupational and Environmental Health in the Production and Use of Chemicals: "Occupational Health in a Changing World" from 2 - 5 June 2011 in Heidelberg, Germany, is available. Please have a look at www.medichem2011.org or at this link:

http://www.medichem2011.org/webcom/show_article.php/c-10000059/nr-11/lkm-4784/i.html

There is still time to register before April 15th for the optional excursion to the cradle of MEDICHEM, Ludwigshafen, by invitation of the BASF SE. Also the deadline for booking the congress hotel at the special rate via our congress website is April 15. The Registration Form and further information can be found at the meeting website www.medichem2011.org. Please send completed registration forms to medichem2011@bgrci.de.

Come to Heidelberg, Germany, from 2 - 5 June 2011!

We are greatly looking forward to welcoming you in the world famous old university town, Heidelberg



MEDICHEM 2011 – Invitation to Publish Presentations

The editors of *Archives of Industrial Hygiene and Toxicology* have invited those who have had papers accepted to the MEDICHEM 2011 Congress in June to publish a full manuscript in the Journal. . We look forward to seeing your full manuscript in this publication! Please see the Editor's invitation below:

As the 39th International MEDICHEM Congress is drawing near, we invite Congress participants to submit papers related to work that will be presented at the Congress to *Archives of Industrial Hygiene and Toxicology*, a journal closely related to the field that is covered by the activities of MEDICHEM. All papers will undergo peer review and there will be a footnote referring to the MEDICHEM Congress 2011 accompanying all published papers. If ten to fifteen papers are submitted, one entire issue can be dedicated to the MEDICHEM Congress. All accepted papers will be printed free of charge and also will be permanently available online for free on the journal's web page. Details and previously published articles are also available online at the following web sites:

<http://www.versita.com/science/medicine/aiht> and <http://hrcak.srce.hr/aiht>

Archives of Industrial Hygiene and Toxicology is a peer-reviewed international biomedical journal published since 1950 by the Institute for Medical Research and Occupational Health in Zagreb, Croatia. It publishes contributions relevant to all aspects of occupational and environmental health and toxicology (scientific papers, professional papers, reviews, short communications, case reports, observations, technical papers and letters to the editor). The journal is abstracted and indexed in *Science Citation Index Expanded*, *Scopus*, *PubMed/Medline*, *Toxline* and a number of other services. In June 2011, the journal will receive its first impact factor to be published in *Thomson Reuters Journal of Citation Reports*. Its current *h-index* is 5. *Archives* is advised by an international editorial board that includes several past and present MEDICHEM Board members, former MEDICHEM president and former MEDICHEM secretary. A full list of Advisory Editorial Board members is also available on the journal website.

Nevenka Kopjar, PhD, Editor-in-Chief

Martina Piasek, M.D., Ph.D, Member of Executive Editorial Board

Archives of Industrial Hygiene and Toxicology



COGNITIVE FUNCTION IN ELDERLY MARATHON RUNNERS:

CROSS-SECTIONAL DATA FROM THE MARATHON TRIAL (APSOEM)

As the MEDICHEM Secretary is based in Boston, Massachusetts, USA, the home of the Boston Marathon, which is run every April, this article by Dr. Robert Winker, member of the Board, may be of even broader interest!

Dr. Winker writes: The study aimed to investigate whether intensive endurance exercise training is associated with better cognitive performance and increased brain-derived neurotrophic factor (BDNF) and insulin-like growth factor (IGF).

The accelerated aging progress is encountering a changing structure of labour with regard to aspects of productivity (job enlargement) and demands for qualifications (job enrichment). These changes result in dramatic consequences for the situation of the workforce, which implies a great challenge for occupational medicine. Consequently, maintaining working capacity and quality of life in an aging workforce can be considered as an important goal for occupational medicine.

Here I present an abstract of our work, which was published in the Wiener Klinische Wochenschrift (Wiener Klinische Wochenschrift (2010) 122 (23-24), pp. 704-716).

Background: Cognitive impairment of the elderly contributes to morbidity, loss of quality of life and impairment of work ability in aging western societies. Thus strategies to maintain cognitive function at an advanced age imply a great challenge to Occupational Medicine.

Aim: To study whether intensive endurance exercise training is associated with better cognitive performance and increased brain-derived neurotrophic factor (BDNF) and insulin-like growth factor (IGF).

Methods: Active elderly marathon runners or bicyclists older than 60 years were recruited and matched with an inactive control group according to age, sex, and education years. After exclusion of various diseases according to the study protocol, 56 athletes and 58 controls could be selected for follow-up studies. The influence of endurance training on cognitive function was assessed by the use of the Vienna Neuropsychological Test Battery and the CERAD test battery. Other relevant outcomes were the levels of BDNF, IGF-1, Apo e4 carrier state and self ratings.

Results: The elderly marathon group performed better only in one specific cognitive task (the Five Point Test, $p=0.04$) and almost significantly better in one additional test (the NAI Stroop Test, $p=0.08$). Neither BDNF nor IGF-1 was related to the duration of daily exercise and no differences in the basal levels of these humoral growth factors in the exercise and the control cohort were found. Interestingly, we also found significantly decreased BDNF

levels in subjects with Alzheimer’s disease in the family in spite of the maintained normal cognitive performance (p=0.01).

Conclusion: These results suggest that extensive endurance exercise training might be beneficial for maintaining cognitive function in elderly persons. Our data demonstrate that beneficial endurance training effects are not linked to the upregulation of the examined neurotrophins. Since we found reduced BDNF-levels in subjects with a positive family history of Alzheimer’s disease, we speculate that BDNF-reduction might precede cognitive impairment.

Dr. Robert Winker,
Vienna (Austria)



UN Task Force HIV/AIDS Request for Input

Dr Murray Coombs, MEDICHEM member and member of the UNAIDS Civil Society Task Force wishes to request from MEDICHEM Members thoughts on the Corporate/Business responsibility on HIV/AIDS.

Upon the request of the President of United Nations General assembly, the UNAIDS Secretariat has facilitated the convening of a Civil Society Task Force (Task Force) to advise in key decisions relating to attendance and participation of civil society organizations in the 2011 High-Level Meeting on HIV/AIDS (HLM) and the Civil Society Hearing. The Task Force will report to UN President’s Office and will provide key civil society constituencies engaged in the AIDS response with an avenue to bring forward community input into these important UN processes. Task Force representatives will be asked to work with the UN on developing key aspects of the HLM and the Civil Society Hearing. The UNAIDS Strategy is as follows:

- By uniting movements—such as joining forces with the women’s health movement to implement the UN Secretary-General’s Joint Action Plan to Improve the Health of Women and Children—we can strengthen shared political commitment and action.
- Effective partnerships remain fundamental to successful and sustainable HIV responses. Partnerships give voice to those infected and affected, act as a catalytic force for change and provide accountability for political commitments. However, the changing environment, and its demands for new and innovative ways of working, signals the need for different kinds of partnerships—those that enable nationally owned responses, foster South-South cooperation and those that move beyond the traditional HIV and health sectors to broader development areas. These partnerships

must include political alliances that link HIV movements with movements seeking justice through social change.

- Exercise selectivity in partnership building to leverage and optimize resources, assess new and existing partnerships on the basis of shared objectives and value-added, and hold partnerships to account through strengthened mutual accountability mechanisms

Dr Murray Coombs member of the UNAIDS Civil Society Task Force (Task Force) wishes to request from the MEDICHEM membership thoughts on the Corporate/Business responsibility on HIV/AIDS. Dr. Coombs can be reached at this email address (mwcoombs@dow.com) to provide your thoughts and input on the request below before the end of May 2011.

Dr. Murray Coombs
South Africa



Benzene is a well established human carcinogen. There is ample evidence for benzene-induced leukaemia, notably for the acute myeloic type. The situation is less clear for other types of leukaemia, and it remains particularly controversial for Non-Hodgkin's lymphoma (NHL), multiple myeloma (MM) and other lymphatic neoplasms. In Germany, the Scientific Advisory Board to the Ministry of Labour has concluded in 2007 that benzene can be a cause for almost all types of lymphohematopoietic malignancies including all types of leukaemia, NHL and MM, but excluding Hodgkin's disease (HD). This assessment has since been subject to some debate. New studies and findings pertaining to this topic have been published since, and more will certainly come. It is beyond the scope of an article in this Newsletter to discuss in detail the current state of science, but I'd like to point out two comparatively recent articles that may add to this discussion. Unfortunately, they also provide examples of how new contributions to this discussion may be generated in a less than scientifically optimal way.

Occupation and risk of lymphoma: a multicentre prospective cohort study (EPIC)

(Neasham D, Sifi A, Nielsen KR, et al. (2011), *Occup Environ Med*; 68:77-81)

OBJECTIVES: Evidence suggests that certain occupations and related exposures may increase the risk of malignant lymphoma. Farming, printing and paper industry, wood processing, meat handling and processing, welding, shoe and leather manufacturing and teaching profession are among the categories that have been implicated in previous studies. The relationship between occupation and malignant lymphoma has been investigated in a large European prospective study.

METHODS: We investigated occupational risks for lymphomas in the European Prospective Investigation into Cancer and Nutrition (EPIC). The mean follow-up time for 348,555 subjects was 9 years (SD: 2 years). The analysis was based on 866 and 48 newly diagnosed cases of non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL). These were identified in the EPIC subcohorts with occupational data. Data on 52 occupations were collected through standardised questionnaires. Cox proportional hazard models were used to explore the association between occupation and risk of malignant lymphoma.

RESULTS: The following occupations were positively associated with malignant NHL after adjustment for study centre, age, sex, socioeconomic status (SES), smoking and alcohol: butchers (HR=1.53, 95% CI 1.05 to 2.48, including multiple myeloma/ plasmacytoma; HR=1.30, 95% CI 1.00 to 2.66, excluding multiple myeloma/ plasmacytoma) and car repair workers (HR=1.50, 95% CI 1.01 to 2.00, including multiple myeloma/ plasmacytoma; HR=1.51, 95% CI 1.01 to 2.31, excluding multiple myeloma/ plasmacytoma). HL was associated with gasoline station occupation (HR=4.59, 95% CI 1.08 to 19.6).

CONCLUSION: The findings in this current study of a higher risk of NHL among car repair workers and butchers and a higher risk of HL among gasoline station workers suggest a possible role from occupationally related exposures, such as solvents and zoonotic viruses, as risk factors for malignant lymphoma.

In three out of 52 occupations, elevated lymphoma risks were found, with butchers and car repair workers being affected by NHL and gasoline station workers by Hodgkin's lymphoma. Unfortunately, no information is provided on the respective risk estimates for the remaining 49 professions or job titles, where I'd expect some similarly significant risk reductions in the one or the other case. The explanation offered for the findings - benzene and infectious agents - appears a little simplistic. Were there no comparable exposures among the other jobs? Are the causes for NHL and Hodgkin's lymphoma interchangeable? Why does benzene cause Hodgkin's lymphoma (and not NHL) in gasoline station workers, and why would it produce the opposite pattern in car repair workers? Could it be that pre-existing hypotheses block the authors' view on other possible explanations?

Genetic variation in metabolic genes, occupational solvent exposure, and risk of non-Hodgkin lymphoma

(Barry KH, Zhang Y, Lan Q, et al. (2011), Am J Epidemiol; 173:404-13)

Using 1996-2000 data among Connecticut women, the authors evaluated whether genetic variation in 4 metabolic genes modifies organic solvent associations with non-Hodgkin lymphoma and 5 major histologic subtypes. P (interaction) values were determined from cross-product terms between dichotomous (ever/never) solvent variables and genotypes at examined loci in unconditional logistic regression models. The false discovery rate method

was used to account for multiple comparisons. Overall associations between the chlorinated solvents dichloromethane (odds ratio (OR) = 1.69, 95% confidence interval (CI): 1.06, 2.69), carbon tetrachloride (OR = 2.33, 95% CI: 1.23, 4.40), and methyl chloride (OR = 1.44, 95% CI: 0.94, 2.20) and total non-Hodgkin lymphoma were increased among women TT for rs2070673 in the cytochrome P4502E1 gene, CYP2E1 (dichloromethane: OR = 4.42, 95% CI: 2.03, 9.62; P(interaction) < 0.01; carbon tetrachloride: OR = 5.08, 95% CI: 1.82, 14.15; P (interaction) = 0.04; and methyl chloride: OR = 2.37, 95% CI: 1.24, 4.51; P(interaction) = 0.03).

In contrast, no effects of these solvents were observed among TA/AA women. Similar patterns were observed for diffuse large B-cell lymphoma and follicular lymphoma, as well as marginal zone lymphoma for dichloromethane. The weak, nonsignificant overall association between benzene and diffuse large B-cell lymphoma (OR = 1.29, 95% CI: 0.84, 1.98) was increased among women AA for rs2234922 in the microsomal epoxide hydrolase gene, EPHX1 (OR = 1.77, 95% CI: 1.06, 2.97; P (interaction) = 0.06). In contrast, no effect was observed among AG/GG women. Additional studies with larger sample size are needed to replicate these findings.

Fascinating indeed that some out of the multiplicity of chlorinated solvents examined here, and their interactions with different genetic polymorphisms, show comparatively strong associations with the cancers of interest (although always based on very small numbers of exposed cases). On the other hand, benzene as the only substance among the tested (or reported?) ones with a high a priori suspicion, appears to be only weakly associated with only one of the possible outcomes. I am not aware that a large body of existing literature should have led anybody to expect this pattern.

As a side note it is remarkable that the authors mention in the abstract quoted here that “the false discovery rate method was used to account for multiple comparisons.” This appears to support the significance of the results further provided in the abstract. Only at the end of the results section, but not in the abstract, we find the statement that “none of the examined interactions except ... [one mentioned here] ...possessed a false discovery rate of less than 0.2”, which means “was considered robust” according to the authors’ own definition.

How should we deal with results like these? I seem to remember from the science classes I took as a pupil that some of the most convincing and brilliant experiments, which finally led to the acceptance of the wave-theory of light, had been carried out by scientists who originally wanted to disprove this hypothesis. These experiments had been devised in a way which – after the results turned out to be contrary to expectations – did not leave any other conclusion but to accept the probable truth of the concept they originally wanted to discard.

I cannot help the impression that these present articles provide some examples for the opposite approach: scientists use datasets and turn them inward out until the results appear

to be exactly in line with what was expected or even hoped to result. It strikes me that even experienced scientists of high reputation may tend to search for the confirmation of pre-existing hypotheses rather than try to devise research strategies which might prove the contrary – and thus could even more convincingly demonstrate the validity of the hypothesis thus put to the test.

I am afraid that even 50 more studies of this type will not bring us closer to knowing the truth.

Dr. Michael Nasterlack,
Ludwigshafen (Germany)



Socioeconomic factors and suicide: an analysis of 18 industrialized countries for the years 1983 through 2007

*Prevention of suicide is a major public health issue. Annually, about one million people die as a result of suicide worldwide. During the last few decades, a wide range of risk factors have been considered such as mental illness and psychiatric disorders, trauma from losses, substance abuse and genetic disposition. We tried to evaluate the association between socioeconomic factors and suicide rates and therefore analysed time series of suicide rates, gross domestic product (GDP), unemployment rates, labour force participation and divorce rates of 18 countries by the application of panel-vector error correction models. Since the results of the project have been recently accepted for publication in the **Journal of Occupational and Environmental Medicine**, we like to briefly report the results.*

Main outcome measures were the association between the socioeconomic factors and suicide rates. Decreasing economic growth and increasing divorce rates were significantly associated with increasing suicide rates in males. For females, increasing economic growth, increasing unemployment and increasing divorce rates were significantly associated with increasing suicides. Increasing female labour force participation was associated with decreasing suicides.

The strength of our study clearly lies in its econometric methodology: cross-sectional and time series information were used within one model by applying panel co-integration. The large and homogenous sample size of 18 countries and the long time period from 1983 to 2007 are further advantages.

In summary, our study provides clear evidence that socioeconomic factors are associated with suicide rates. However this relationship differs strongly by gender. As a consequence,

we recommend that suicide risk assessment should include the monitoring of socioeconomic development.

Dr. Robert Winker,
Vienna (Austria)



A New View to Occupational and Environmental Medicine

*The following was submitted by Dr. Tee Guidotti, announcing his new textbook in occupational and environmental health: **The Praeger Handbook of Occupational and Environmental Health**. Santa Barbara, Praeger ABC Clio Publishers, 2010. 1600 pp., in three volumes.*

Dr. Guidotti wrote this book over a period of ten years, working alone, as an introduction to the theory and practice of the modern field of occupational and environmental health, primarily for residents, fellows, and physicians moving into practice in mid-career. It is intended to bring within one text the foundations of the field, the core knowledge needed by new practitioners entering the field, and essential frameworks for problem solving. It takes the strong personal view that while occupational medicine is an old, established specialty, occupational and environmental medicine (OEM) is a new and emerging synthesis that has the capacity to transform and energize medical practice on the occupational side and that creates a new mission for physicians on the environmental side. The new OEM synthesis can be a model for medicine as a whole as it grapples with population health and program management, evidence-based clinical practice, complicated causation issues and prevention, the rise of health promotion, service delivery requiring integrated care models, and the breakdown in traditional medical specialization.



Notable Passing – Dr. John Lanham

The following obituary was submitted by Dr. Noel Humphry

John Lanham passed away on Jan 3, 2011 as he sat down to enjoy his morning coffee and read the newspaper. John was a long standing member and supporter of MEDICHEM including a term as the MEDICHEM Board member for the USA. John graduated from the George Washington University Medical School in 1962 and worked in family practice until 1976 when he joined The Dow Chemical Company in Midland as one of its physicians. During his time with Dow John held a number of Regional Medical Director positions

including those of California, Canada and Europe. He returned to Midland in 1988 to become the Corporate Medical Director, a position he held until his retirement in 1993.

John was a highly committed occupational health physician who played a key role in improving the health and safety of Dow employees around the world by supporting the introduction of a number of programs which continue today, such as quality health care and health promotion. He was a physician of very high integrity, work ethic and a passion for his fellow human beings. John expected and inspired similar standards from those around him. John's wisdom and common sense approach greatly assisted the Medichem Board in its deliberations and decision making.

Outside his professional life John was devoted to his family. He was an avid flea market participant buying and selling bric-a-brac and enjoying a yarn with fellow participants. The basement of his Midland home was devoted to the storage of his purchases awaiting sale at future markets. John was also noted for his sourdough pancakes made with the yeast which he was able to preserve with great care over many years and for enjoying long walks with his dog.

John is survived by his wife Mary and their children.



Welcome to New Members

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|---|-------------------------------------|
| Dr. Asgharzade Ahmadi (Iran) | Dr. Saou-Hsing Liou (Taiwan) |
| Dr. Salman Akhtur (India) | Dr. Nomonde Mabuya (South Africa) |
| Dr. Irina Filip (Romania) | Dr. Amir Radfar (Iran) |
| Dr. Andreas Heim (Switzerland) | Dr. Annette Santamaria (USA) |
| Dr. Thomas Hesterberg (USA) | Dr Alister J Scott (United Kingdom) |
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| Dr. Frans Jongeneelen (Netherlands) | Dr. Johnny Sulistio (Indonesia) |
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