

NEWSLETTER

Message from the Secretary

Dear Colleagues:

As we reach the end of 2009 and my first year as MEDICHEM Secretary, I find myself reflecting on the challenges and opportunities MEDICHEM faces in the coming years. As the global recession hits at all levels, we on the Board are aware that membership may decline, travel to Congresses may become more difficult, and we may lose sustaining members.

On the other hand, engaging young professionals at the local level and gaining their interest can be a wonderful opportunity for MEDICHEM to expand and energize its ranks.

In this issue, I have included an overview, Board member presentation abstracts, and weblinks to a recent MEDICHEM workshop in Thessaloniki, Greece that attracted many Greek young professionals who also presented papers. I'm pleased to say, we welcome in this issue two new young members who joined following this event.

Also in an effort to attract new young members, at the request of our new Board member, Dr. Robert Winker, the Board voted to provide a NOHA (National Occupational Health Award),

at the upcoming meeting of the Austrian Society of Occupational Medicine in 2010. The NOHA will be announced in the Austrian Journal "Österreichisches Forum Arbeitsmedizin" and the abstract will be published in an upcoming issue of the MEDICHEM Newsletter.

A description of the various MEDICHEM awards is provided on our website. The Board would like to encourage members who are active in other local Societies of Occupational Medicine to consider ways to introduce MEDICHEM to the Society and especially to young professionals. We hope to develop a short presentation in the next year that members might consider using for these local or regional meetings.

I wish you all the very best as we prepare to enter 2010.

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



New Board Member Elected

We are pleased to announce that the newest Board member, Dr. Robert Winker, has been elected for the term 2009-2012. Thanks to all who voted in this past election.

We would also like to offer our thanks to Dr. Jasminka Godnic-Cvar for her term of service.



November 2009



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. Thies

Chairman:
Dr. Thirumalai Rajgopal
Hindustan Lever Limited
Hindustan Lever House
165/166 Backbay Reclamation
Mumbai - 400 020 (India)
Tel: +91-22-2285 55 83
Fax: +91-22- 2281 91 97

Secretary:
Dr. Diane J. Mundt
ENVIRON International Corporation
28 Amity Street, Suite 2A
01002 Amherst, MA (U.S.A.)
Tel.: +1-413-256-3556
Fax: +1-413-256-3503

Treasurer:
Dr. Steffen Hitzeroth
Procter & Gamble Service GmbH
Sulzbacher Str. 40
65824 Schwalbach a. T. (Germany)
Tel: +41-61-688 37 38
Fax: +41-61-688 16 51

Board Members:
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Alfred M. Thiess Celebrates 88th Birthday

On October 3rd 2009 MEDICHEM's founder and Honorary President Prof. Alfred M. Thiess celebrated his 88th birthday.

Born in Hermannstadt, Romania he came to Germany to study medicine in Frankfurt. In 1954, he joined BASF where he was head of the Occupational Medical Department from 1963 until his retirement in 1986. During this time he was one of the major forces behind the development of occupational medicine in Germany.

He intensified the application of occupational epidemiology in an industrial setting and fostered health promotion not only in the sense of "one-time" campaigns, but with a focus on subsequent evaluation of its success. Additionally, he was a teacher at the Mannheim Medical Faculty of the University of Heidelberg, found the time to actively participate in numerous national and international expert groups and, not least of all, founded MEDICHEM in 1972.

In recognition of his achievements he received numerous awards and honours, more than I can report in this short article, and probably even more than I am aware of. But one of these, by far not the most prestigious one, but just through its title, characterizes

Fred Thiess so nicely that I want to mention it here: It is the "Service Above Self Award" issued by the Rotary Club. Why that award?

Only recently I found a notice in the *Hermannstädter Zeitung* (a German language newspaper that appears in Romania) from April 2009, where he is mentioned (for the umpteenth time) as the driving force behind the support provided through the Rotary Club Ludwigshafen for some social event. This was obviously only a little glimpse of all the activities initiated and personally led by Fred Thiess since the opening of the iron curtain, directed at helping schools, hospitals and other social institutions in this region to overcome the many shortcomings accumulated under the dictatorial regime of the past.

These activities were always more important to him than honours and recognitions directed to himself. This was the reason, for instance, why the German Society of Occupational and Environmental Medicine (DGAUM) had to wait for one more year until he was ready to accept the most prestigious award for his lifetime achievements to be issued by this society, the Franz-Kölsch award. This is because at the proposed date for this award, Fred had already scheduled a truck convoy to Siebenbürgen, Romania. Already in 2002 the city of his ancestors, Urwegen, Romania, had bestowed on him Honorary Citizenship in

recognition of his untiring and generous support over many years.

Dear Fred Thiess, your MEDICHEM friends and colleagues congratulate you on your achievements in the past and send you the very best and warmest wishes for the future. Keep your health and energy for many more years to the benefit of yourself, your dear wife Gisela, your family, and of course for the MEDICHEM community.

Dr. Michael Nasterlack,
Ludwigshafen (Germany)



MEDICHEM Workshop held in Thessaloniki, Greece

Dr. Elpida-Niki Emmanouil-Nikoloussi, MEDICHEM Board member, and her colleagues hosted a local workshop in conjunction with the mid-year meeting of the MEDICHEM Board.

The Workshop, **Risk Assessment and Human Exposure to Hazardous Materials**, was held 21-24 October 2009 at the Aristotle University of Thessaloniki, Greece.

Several Board members presented papers at the workshop, which are included in this Newsletter. In addition, I am pleased to include the presentations of two new MEDICHEM members who also offered papers at the Workshop.

The Board congratulated Dr. Nikoloussi for hosting this successful event, as well as our mid-year meeting. More information, scientific program and abstracts can be found on the Workshop website: <http://www.medicchemworkshop2009.gr/index.php>.

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



Risk Assessment and Human Exposure to Hazardous Materials

The following are presentations offered by MEDICHEM Board members and two new MEDICHEM members, at the recent Workshop in Thessaloniki, Greece.

Epigenetics: the Link between Environment and DNA Modulation

Leda Kovatsi, MD, PhD; Aristotle University of Thessaloniki, Greece

The 3×10^9 nucleotides included in the human genome, organized in 46 chromosomes, could be viewed as a “book series” in which the punctuation is still missing. It is now accepted that word spacing and punctuation is “imprinted” in the human genome by “epigenetic modification”.

This term refers to modifications of chromatin structure such as DNA

methylation and histone modification. These “epigenetic marks” alter the structure of chromatin and influence gene expression.

Methylation occurs naturally on cytosine bases at CpG sequences and is involved in controlling the correct expression of genes.

Alterations in the DNA methylation status are usually associated with chromatin structural changes, and gene silencing or activation during cell differentiation, growth, and development, as well as in cancer and other diseases.

Environmental factors including toxins, or even dietary habits, can change epigenetic patterns and thereby induce changes in gene activation and cell phenotype.

The influence of the environment, via epigenetic regulation, on the phenotype is now well documented. Studies on monozygotic (MZ) twins, which are considered to be genetically identical, have shown phenotypic discordances between them, which include the incidence and/or time of onset of various pathologies, such as schizophrenia. Recent reports have highlighted the role of epigenetic mechanisms, especially DNA methylation, in this process. It was shown that MZ twins are epigenetically impossible to differentiate at an early age, but exhibit prominent differences with respect to the distribution and overall content

of methylated cytosine at an older age. Most importantly, epigenetic differences were more prominent among twins which had lived independent lives.

In view of the above, it is now clear that DNA epigenetics constitutes the main and previously missing link among genetics, disease, genetic predisposition and the environment.

A Meta-Analysis of Formaldehyde Exposure and Risk of Leukemia and Nasopharyngeal Cancer

Diane J. Mundt, Ph.D.,
Kenneth A. Mundt, Ph.D.,
Renika R. Montgomery, MPH;
Annette Bachand, Ph.D.,
ENVIRON International Corporation, USA

We conducted meta-analyses of the epidemiological literature on formaldehyde exposure and risk of leukemia and risk of nasopharyngeal cancer.

We abstracted study results and confounder information from cohort and case-control studies, and evaluated heterogeneity and possible publication bias.

No evidence of serious heterogeneity or publication bias was seen. For leukemias, the summary RR was 1.05 (95% CI: 0.93, 1.20) for cohort studies and the summary OR was 0.99 (95% CI: 0.71, 1.37) for case-control studies. Based

on cohort and case-controls studies, no significant differences were seen by leukemia subtype, job type or region.

Summary estimates for nasopharyngeal cancers were not elevated, after excluding a single plant with an unexplained cluster of nasopharyngeal cancers (cohort RR=0.72, 95% CI: 0.40, 1.28). The summary estimate was increased for case-control studies overall, but the summary OR for smoking-adjusted studies was 1.10 (95% CI: 0.80, 1.50).

Previous meta-analyses did not explore other factors that could influence or confound results. By limiting analyses to stronger case-control and cohort study designs, considering the effects of smoking and ignoring anomalous results from a single plant, our meta-analyses provide little support for a causal relationship between formaldehyde exposure and leukemia or nasopharyngeal cancer.

Use of Biomonitoring for the Identification of Previously Unrecognized Workplace Hazards

Michael Nasterlack, MD;
BASF, Germany

Human Biomonitoring (HBM) in the strict sense is defined as the assessment of human exposure to chemicals by measuring the chemicals or their metabolites in human

specimens, most commonly in blood or urine. HBM has long been used in occupational medicine as one tool for assessing and controlling exposure to chemicals in the workplace. It supplements - not replaces! - information gathered through, e.g., ambient air monitoring.

HBM results in occupational medicine can usually be interpreted with respect to biological limit values (e.g., BEI, BAT), which have been derived based on toxicological data and set with the aim to protecting workers' health. In the absence of health-based limit values, statistically based or empirically derived reference values may be used to address the question of "normal" exposure and to identify potential exposure from unexpected sources.

Under routine conditions HBM is used to assess the effectiveness of technical measures and/or personal protective equipment to reduce chemical workplace exposures. In cases of accidental spills and contamination, HBM may provide important information on the acquired dose and associated health risk, and thus on the necessity for further diagnostic or therapeutic measures.

Finally, new and sometimes surprising insights into previously unrecognized hazards may result from the use of HBM during the assessment of unclear health conditions with questionable association to working

conditions. The latter is illustrated with case reports of intoxications with nickel-tetracarbonyl, and an unexpected exposure to ortho-toluidine.

An Overview of EU Regulation REACH

Evangelia Nena MD, PhD;
Democritus University of Thrace,
Alexandroupolis,
Greece

The new EU chemical policy REACH, concerning Registration, Evaluation, Authorisation and restriction of chemicals came into force on June 1st, 2007.

REACH is trying to create a single regulatory system for dealing with chemical substances, providing safety information to users, since the EU chemical legislation has been a patchwork of Directives and Regulations that did not produce sufficient information about the effects of chemicals on human health and the environment, in order to assess and control chemical substances effectively. REACH has placed greater responsibility on industry to manage the risk of chemicals and has put obligations concerning consumers' information about the presence of hazardous substances on subjects. It encourages also the replacement of dangerous chemicals with safer ones.

During the Registration process, each producer and importer of chemicals in

volumes > 1 tonne/ year must register with the European Chemical Agency (ECHA) and submit information on their properties, uses and safe ways of handling them. The Evaluation process enables public authorities to examine the registration dossiers and the substances at concern.

Authorisation is required for use of chemicals that cause cancer, mutations, or reproductive disorders, or that accumulate in human body or the environment. In this case authorisation is granted only to companies that can show that the risks are adequately controlled, or the social and economic benefits outweigh the risks when no alternative substances or technologies exist.

Restriction of a substance can be imposed on the manufacture, placing on the market, or use of certain substances when the risk for human health or the environment is unacceptable.

REACH has the potential to inspire new standards worldwide and not only in EU countries, aiming to provide information not only to manufactures and importers, but also, down the supply chain, to distributors and consumers. On the other hand, limitations do exist such as the wide scope, the ambiguous use of language, and the lack of consensus regarding the costs and benefits.

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Exposure to Heavy Metals due to Environmental Pollution and Pregnancy Outcomes

Elpida-Niki Emmanouil-Nikoloussi, DDS, PhD, MD, PhD ; Aristotle University of Thessaloniki, Greece

Studying the role that environmental toxicity and environmental factors play in causing birth defects is extremely challenging and current understanding is evolving.

Heavy metal toxicity, birth defects and pregnancy outcomes due to environmental exposure can include metal ion involvement in natural systems, toxic metal ions in biological systems, neurotoxic metal ions causing human diseases, metal ionic-DNA interactions influencing transcriptional regulation of oncogenes, metal ionic assembly of lattices through physiological and biomimetic substrate binding for (bio)catalytic purposes.

In all of the aforementioned cases, multidisciplinary approaches are employed to build fundamental knowledge for the subsequent pursuit of the development of technologies, enabling metal ionic detection, utilization, regulatory control of environmental pollution, birth defects and disease prognosis and potential prevention and therapies.

Heavy metal toxicity can result in damaged or reduced mental and central nervous function, lower energy levels, and damage to blood composition, lungs, kidneys, liver, and other vital organs.

There are several studies showing that preterm exposure to environmental pollutants as heavy metals can markedly increase the teratogenicity of different type of those metals. Repeated exposure as this , fact which often occurs to workers; during embryogenesis and organogenesis result in severe incidence of embryonic/foetal

death due to intrauterine exposure to heavy metals, via their open halls of work, or via the food chain with remnants of those ; exposure which in many cases is masking the teratogenic potential.

This review paper focuses to give evidence and demonstrations on preterm exposures to environmental pollutants as heavy metals , which can markedly increase the teratogenicity and also can influence the reproductive toxicity. Research studies on experimental animals and epidemiological studies on human population exposed to heavy metals during pregnancy fact which often occurs to workers are reviewed and discussed.

Principles of Health Risk Assessment in the Chemical Industry

Dr. Teodor Popov, Professor, Sofia, Bulgaria

The effectiveness of the prevention of occupational health hazards depends on the knowledge of their occurrence, distribution, mechanism of generation and consequences to health. Chemicals, which occur in high numbers (about 100,000) at the workplace, require systematic approach for risk assessment (RA).

Risk is an abstract issue, describing the probability of expected frequency of an adverse health effect, arising from exposure to a chemical. Risk is not a measure of actual health estimation of an

individual or a group. Thus, a disease or injury is not identical with risk, but they are consequences of realization of risk.

RA is a prediction about what might happen in the future to the exposed people and at which probability.

The risk assessment process includes: Risk identification (RI); risk determination or estimation (REST); risk characterization (RC) and risk evaluation (REV).

RI answers to the question "Is the chemical hazardous and if yes, what is the type of hazard".

Risk determination (Risk estimation, REST) is intended to provide quantitative data on the relationship between the exposure and the adverse health effect. Exposure assessment (EA) is inevitable for the dose-response assessment. EA is the determination or estimation of the magnitude, duration, frequency, route of exposure.

RC aims to provide a synthesis of the estimation of exposure levels and health risk. RC indicates how risk varies with exposure. RC provides the primary basis for making risk management decisions. RS is designed to support risk managers by providing scientific evidence about risk they need for decision-making.

Risk evaluation (REV) can be considered as a continuation of RC and it deals with the consequences of risk realization. REV provides

social value for an identified estimated risk. REV balances negative consequences of a risk event with social benefit of the particular activity.

Conclusions: RA is a method to prevent damage based on the prediction of what might happen in the future.

Occupational Risk Assessment and Management in the Fertilizers Industry

Dr. Avi Wiener, Mark A. Levi, Stuart Marsh.; Faculty of Civil and Environmental Medicine, Technion, Haifa.; Rambam Medical- Center, Haifa.

The constituents of phosphate based fertilizers in Israel are extracted from phosphate- rich rocks as well as from the Dead Sea. Hazardous natural and by-product contaminants may include arsenic, fluorides, selenium and radioactive isotopes.

There is a risk of exposure of workers to sulfuric acid mist as well as to anthophyllite fibers. Risk assessment based on a survey of the literature yielded various occupational toxic effects including malignancies and metabolic impairments among workers in this field.

We conducted a comprehensive hygienic and medical survey to assess the risk for specific occupational diseases among workers in the fertilizer industry in Israel. The study comprised 4559 workers,

of whom 1385 are presently active, while 3234 are former workers. All of them were hired at two separate plants and worked for at least 5 consecutive years between 1965 and 2005.

Standardized incidence rate (SIR) for all cancer disease among the active and the past workers were 0.71 (95% C.I. 0.45; 0.97) and 1.01 (95% CI 0.84; 1.00) respectively. No specific malignant disease could be attributed to any occupational exposures in these industrial plants.

At one of the plants twenty seven workers were exposed to anthophyllite fibers, and twenty five of them (86%) developed pleural plaques. One of the workers underwent a pleural adhesion procedure due to unilateral massive pleural effusion, while another worker underwent lung lobectomy due to a huge round atelectasis. No one in this group of workers developed lung asbestosis, lung cancer or malignant mesothelioma, and none of the workers at either plant was found to experience any form of acute or chronic occupational intoxication.

We therefore conclude that occupational exposure to various potentially harmful chemicals in the phosphate based fertilizers industry in Israel imposed no risk for cancerous disease to its workers.

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IARC Monograph 100: A review of human carcinogens - Part F -- Highlights

The following is taken directly from the IARC website <http://monographs.iarc.fr/ENG/Meetings/100F-introduction.pdf>.

In October 2009, 23 scientists from 6 countries met at the International Agency for Research on Cancer (IARC) to re-assess the carcinogenicity of a number of chemical compounds, complex mixtures and occupational exposures previously classified as *carcinogenic to humans* (Group 1) and to identify additional tumour sites and mechanisms of carcinogenesis. These assessments will be published as the sixth and last part of Volume 100 of the *IARC Monographs*. A few highlights are given below.

Dioxin (2,3,7,8-TCDD), which in 1997 was classified in Group 1 based on strong mechanistic evidence, now has sufficient evidence in humans. This highlights the ability of mechanistic information to provide robust evidence of carcinogenicity and suggests that preventive actions can be taken without waiting for cancers to be observed in exposed humans. The same mechanistic events involved in dioxin carcinogenesis have also been established for other dioxin-like compounds, and the Working Group extended the Group-1 classification to

2,3,4,7,8-pentachlorodibenzofuran and 3,4,5,3',4'pentachlorobiphenyl, which are indicator chemicals for a larger class of dioxin-like chlorinated dibenzofurans and dioxin-like polychlorinated biphenyls (PCBs).

Formaldehyde, which in 2004 was classified in Group 1, was confirmed as carcinogenic to humans. There is *sufficient evidence* in humans of an increased incidence of nasopharyngeal carcinomas, and the Group 1 classification is also supported by strong mechanistic evidence.

In addition, the epidemiological evidence on leukaemia has become stronger, and new mechanistic studies support a conclusion of *sufficient evidence* in humans. This highlights the value of mechanistic studies, which in only 5 years have replaced previous assertions of biological implausibility with new evidence that formaldehyde can cause blood-cell abnormalities that are characteristic of leukaemia development.

Occupational exposure as a painter causes cancers of the lung, urinary bladder and pleural mesothelioma in humans. Due to the diversity and complexity of the exposures, it is difficult to identify causal agents or a causal mechanism, although there is strong evidence that the exposures are genotoxic. The Working Group found *limited evidence* of an association

between maternal exposure to painting before and during pregnancy and an increased risk of childhood leukaemia in the offspring. These findings confirm those of a previous Working Group (2007).

Further conclusions of the IARC Working Group can be found at: <http://monographs.iarc.fr/ENG/Meetings/vol100F-evaluations.pdf> for chemicals listed in the July 2009 issue of this Newsletter.



Welcome to New Members

Dr. **Sheilah N. Bernardino**, P&G Philippines Medical Leader (Philippines)

Dr. **Leda Kovatsi**, Aristotle University of Thessaloniki (Greece)

Dr. **Evangelia Nena**, Occupational physician, Democritus University of Thrace (Greece)



Condolences

MEDICHEM extends condolences to the family of MEDICHEM member **Dr. Morris Arthur Cooke (Mac)** of Harborne Birmingham, who died on Sunday 2nd August 2009. Dr. Cooke was previously Professor of Toxicology, Occupational Physician and Dermatologist.



Upcoming Events

4th International Conference on History of Occupational and Environmental Health

The ICOH Scientific Committee on the History of Prevention of Occupational and Environmental Diseases, announces the 4th International Conference to be held in San Francisco June 19-22, 2010, jointly organized with the University of California San Francisco, UCSF.

The meeting will be held at **Holiday Inn Fisherman's Wharf**. For additional info, please email paul.blanc@ucsf.edu.

Pre-Announcement

The US National Institute of Occupational Safety and Health (NIOSH) will announce in December a call for abstracts for the upcoming **Nanomaterials and Worker Health: Occupational Health Surveillance, Exposure Registries, and Epidemiological Research** conference to be held in Keystone, Colorado 21-23 July 2010. Additional information will become more widely available in December.

2010 EPICOH-MEDICHEM Congress Occupational Health under Globalization and New Technology Taipei, Taiwan

A joint meeting of **EPICOH** and **MEDICHEM** will be held in Taipei, Taiwan **20-25 April, 2010**. Prof. Jung-Der Wang is the Chairperson for the EPICOH portion of the program, and Prof. How-Ran Guo will chair the MEDICHEM.

Broad topic areas for the Congress include: Globalization, New Technology, Methodology, Exposure Assessment, Health Outcomes, and Interventions.

Dec. 31, 2009 Abstract acceptance notification

Jan. 31, 2010 Deadline for early bird registration. Early registration for members is **400 USD** and **175 USD** for students/trainees and participants from developing countries.

For more information, visit the meeting website at: <http://www.epicohmedichem2010.tw>, or send an email to: epicohmedichem2010@gmail.com.