

Neurotox News

Nr 3
November
2001



**The Scientific Committee on Neurotoxicology and Psychophysiology
of the International Commission on Occupational Health**

Dear colleagues and friends,

A new issue of the NeurotoxNews is finally distributed, and important things are happening within our committee. This issue is the first one distributed according to the revised list of committee members, and several well known names are now missing from the mailing list. Partly this is due to the retirement of some members, and partly it is due to the more strict ICOH policy regarding membership.

Since retirement is actually reducing the number of committee members, we should be thinking of ways to attract the interest of young researchers in our area. Any ideas and proposals to this end are most welcome, and the membership issue will surely be discussed during our committee meeting at the 8th Symposium in Brescia in June.

The colleagues in Brescia are working hard with the preparations for the symposium, and a preliminary program should be available soon, as will the 2nd announcement. The best of luck to Roberto Lucchini and his colleagues in their efforts to organize a successful symposium!

Time flies, and although the 8th symposium is more than seven months away, planning for the 9th symposium has begun. The letter included in this issue was recently sent to several colleagues who previously have shown an interest to organize one of our symposia. Proposals are

hopefully being planned in this very moment, and when anyone of you would be interested in doing so, please don't hesitate to have a go of your own! Every serious proposal will be considered!

The first weekend in March 2002 there will be a "mid-term" meeting for the ICOH officers in Rome. The ICOH board and most scientific committee officers will convene to discuss important issue for the future of our organization. Any ideas that you as committee members would like to convey to this forum are welcome to me or Roberto Lucchini, and we'll do our best to speak for your ideas in Rome!

These lines are being written during our first massive autumn storm in Stockholm, a fact that seems quite appropriate. The storm forms a suitable background for the changes going on at the Swedish National Institute for Working Life, with a discontinuation of all research activities that need wet laboratory areas. Still, thanks to your massive support, I will be continuing with the institute, although mainly being involved in risk assessment and less in research. Toxicological research, including our exposure chamber, will be transferred to the Karolinska Institute.

Looking forward to a stimulating future with our committee,

Anders Iregren

News from the secretary

Dear Committee members of the, the preparation of the 8th International Symposium is proceeding very well and unfortunately June 2002 is approaching quickly. You can view the 2nd **announcement** with all important information on the web site www.unibs.it/medlav. A printed version of it is currently being printed and sent to about 5000 people all over the world, including yourself. Please look carefully at the address list attached to this number and let me know if your address is correct. We have had problems with some of your emails that keep coming back as unknown addresses, so please check them !

The next deadline is **December 20, 2001** for the abstract submission and for financial aid requests by students and colleagues from the developing countries. Below are the requisites for financial aid:

Developing countries

The organizers of these symposia, where appropriate, provide financial support to some participants from developing countries, and this agreement will continue for the 8th International Symposium. Since the organizing committee has limited economical resources, financial support for participation will be given according to the following requirements:

- The applicant must be working or active within the areas of occupational and/or environmental health
- The applicant must participate actively with an oral or poster presentation
- A curriculum vitae with professional experience must be enclosed with the application
- The applicant must have a certification from his/her Institute that he/she is sufficiently fluent in English and is recommended for participation

Younger applicants with a potentially lengthy future career in the environmental health area will be given priority. An equal distribution of support between men and women and geographical areas will be guaranteed. Applications should be sent to the congress secretariat, together with the abstract, no later than **December 20, 2001**

A number of mini-symposia are being organized and will soon be posted on our web page to give everybody an idea of the ongoing process.

INA is taking an active part in the organization, and a special mini-symposium will be organized on the interactions between genetic and environmental factors on behavior.

I strongly hope that all of you will take an active part in this symposium. Oral and poster presentation are welcomed and the main topics are listed below:

1. Chemically induced behavioral changes and quality of life
2. Subjective symptoms and personality
3. Sensory organs, including visual and olfactory toxicology
4. Noise induced hearing loss by chemical exposure
5. Exposure to neurotoxicants in the developing world
6. Neurobehavioral effects due to biotoxin agents (Pfiesteria-like organisms, BSE)
7. Neurobehavioral effects from manganese and MMT exposure
8. Neurobehavioral effects from inorganic and organic mercury: interactions of different forms
9. Neurobehavioral effects from organic solvents and pesticides: an update of new acquisitions
10. Exposure to heavy metals: role played in neurobehavioral toxicity
11. Connecting human neurobehavioral tests with animal models: advantages and approaches
12. Neurotoxic influence in the developing brain
13. Confronting neurotoxicology: genes, gene expression and behavior
14. Genetic susceptibility in the exposure to neurotoxicants
15. Update of new neurobehavioral testing methodologies
16. New acquisition in neuroimaging techniques
17. Neurodegenerative disorders: genetic predisposition and chemical exposure in Parkinson's Disease and Alzheimer Dementia
18. Neurobehavioral data and symptom reporting as a ground for TLV's
19. Use of risk assessment techniques for neurobehavioral data
20. Exposure assessment of neurotoxicants: environmental and biological monitoring
21. Need for meta-analysis study to improve statistical power in neuro-epidemiology
22. Multivariate analysis to evaluate confounding and modifying factors in neurotoxicity studies

ICOH policy

You may contact Saadiyah Awak, at ICOH Secretariat icohsg@singnet.com.sg for more info

BYE-LAW 3-Fees (Section 2): "In the event of non payment of fees within the first six months of the triennial period, the defaulting member shall be deemed not to be in good standing (Article 2, section 2 of the Constitution). Members not in good standing at the end of the triennial period shall cease to be members (Article 2, section 5 of the Constitution). Such members can be reinstated under the condition that they pay the fee for the whole current triennium together with any outstanding fees from the previous triennium."

Scientific work by the Committee's members

We are happy to continue this initiative to publish scientific contributions from the Committee's members, that has been favorably accepted by many of you. We continue in this issue with a very interesting article by Sin Eng Chia on possible role played by genetic polymorphism in lead neurotoxicity. Sin Eng works in the prestigious Department of Community, Occupational and Family Medicine of the National University of Singapore. He was one of the most active and restless organizers of the very successful 26th ICOH International Congress, held in Singapore in year 2000.

We would like to encourage each member to submit contributions regarding research, preventive and regulatory aspect related to the field of neuro-behavioral toxicology. One possible future direction of our bulletin could be an extension to other Scientific Committees within ICOH so this will be a good reason to keep this scientific part of the bulletin producing new contributions.

δ-AMINOLEVULINIC ACID DEHYDRATASE (ALAD) POLYMORPHISM AND SUSCEPTIBILITY OF WORKERS EXPOSED TO INORGANIC LEAD

by Sin Eng Chia

Department of Community, Occupational and Family Medicine of the National University of Singapore

Exposure to inorganic lead (hence referred to as lead) in the environmental and occupational settings continues to be serious public health problem. At high exposure levels, lead causes encephalopathy, kidney damage, anaemia and toxicity to the reproductive system. Even at lower doses, lead produces alternations in cognitive development in children. A safe level of lead exposure has not been defined, as health risks associated with lead are found at ever-lower doses.

Pinpointing the health risks associated with low-level exposures to lead will have important implications with respect to its regulation. Health-based guidelines limiting occupational and environmental exposures to lead have become more stringent over the past decade and are now thought to protect most of the population against major adverse health effects. However, genetically susceptible individuals may not be fully protected by current regulatory standards. Better understanding of genetic factors that influence susceptibility to lead-induced intoxication could have significant ramifications for public health and intervention initiatives. The major candidate genes implicated in susceptibility to lead toxicity are: delta-Amino-Levulinic Acid Dehydratase (ALAD), the Vitamin D receptor (VDR) [Schwartz, 2000] and the hemochromatosis gene (HFE) [Barton 1994].

Polymorphisms of the ALAD gene have been associated with the accumulation and distribution of lead in the blood, bone, and internal organs in human and animals. The gene that encodes ALAD exists in two polymorphic forms that may modify lead toxicokinetics and ultimately influence individual susceptibility to lead poisoning. The enzyme is encoded by a single gene located in chromosome 9q34, which has two co-dominant alleles, ALAD1 and ALAD2 (Wetmur et al., 1991). This polymorphism G177C results in a non-conservative change in amino acid residue 59 from Lys to Asn. As the ALAD2 (59Asn) protein is more negatively charged than ALAD1 (59Lys) it has a higher affinity to lead. This increased affinity to lead is associated with higher levels of total lead in blood and tissues, and of free erythrocyte protoporphyrin levels. It is therefore thought that because ALAD2 carriers/homozygotes retain lead longer, this leads to oxidative damage and structural damage. However, subsequent studies by Schwartz (2000) and others, using the chelator dimethylsuccinic acid (DMSA) show that bioavailable lead is actually lower in ALAD2 carriers compared to ALAD1 homozygotes, suggesting that the ALAD1 allele is the susceptibility allele for neurological risk. It is also not known if the ALAD genotype correlates with lead levels

and toxicity only at high levels of exposure, or whether it is also involved at normal non-occupational situations. Finally the gene-environment interaction between ALAD genotype and smoking & alcohol ingestion, both known to inhibit ALAD production and activity, has not been systematically studied.

The high risk ALAD2 allele is the less common form, occurring in 20% of the Caucasian population and more rarely in populations of African descent. Not much work has been done among the Asian population except for the Koreans and Japanese, with the ALAD2/2 homozygote frequency less than 1%, and ALAD1/2 heterozygote frequency between 4 and 15%. A recent study by Hsieh (2000) in Taiwan indicates that, the frequency of ALAD1/2 and 2/2 individuals is low (4.6%), resulting in a statistically non-significant difference in blood lead levels between ALAD genotypes.

In addition to G177C, several other polymorphisms in ALAD have been identified. These include: 2 other silent exonic polymorphisms, 12 predicted non-validated polymorphisms in the 5' untranslated region, and other putative variants in the 3' untranslated region (National Center for Bio-Informatics: dbSNP, July 2001). These polymorphisms may either a) change the primary structure of transcripts by alternate splicing, b) affect gene regulation and hence expression levels, or c) be in linkage disequilibrium with other undiscovered functional mutations. The role of these novel polymorphisms in the pathophysiology of lead toxicity has not been investigated.

In summary, evidence is mounting to suggest that ALAD plays an important role in the bioaccumulation of lead. Exactly how ALAD, and ALAD polymorphism in particular, influences the distribution of lead to other target organs and thus its toxicity is still a question open for research (Onalaja and Claudio, 2000).

To my knowledge, there is only one paper that examines ALAD polymorphism and the effects on the nervous system. Perhaps this is one area that our Scientific Committee could look into ?

References

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Kelada SN, Shelton E, Kaufmann RB, Khoury MJ. δ -Aminolevulinic Acid Dehydratase genotype and lead toxicity: A HuGE review. *Am J Epidemiol* 2001;154:1-13.

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Schwartz BS, Lee BL, Stewart W, et al. d-aminolevulinic acid dehydratase genotype modifies four hour urinary lead excretion after oral administration of dimercaptosuccinic acid. *Occup Environ Med* 1997; 54:241-6.

Wetmur JG et al. Molecular characterisation of the human δ -Aminolevulinic Acid Dehydratase (ALAD2) allele: implications for molecular screening of individuals for genetic susceptibility to lead. *Am J Hum Genetic* 1991;49:757-763.

International Meetings

Women Work & Health III International Congress

Stockholm 2002, 2-5 June

This international and interdisciplinary congress will form a meeting place for researchers and practitioners, as well as trade union, representatives for governments and the social partners and feminist activists. The meeting place is meant to stimulate open and critical discussions, to share practical experience and scholarly work on women's working and living conditions and their health.

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17th Asian conference on Occupational Health

November 1-4, 2002, Taipei, Taiwan

Major topics:

Air pollution	Health promotion
Cancer	Law & compensation
Climate change	Musculoskeletal disorders
Dermatosis	Neurologicla disorders
Epidemiology	Radiation
Ergonomics	Reproductive hazards
Stress	Exposure & Risk
Semi-conductor	assessment
Industry	Gene-environment interaction

More information is available at
www.acoh2002.org.tw

and by E-mail
acoh2002@seed.net.tw

XVIth World Congress on Safety and Health at Work

26-31 May, 2002, Vienna, Austria

Congress themes:

- A** New technologies, New Patterns of Work Organization – New Challenges for Health at Work
- B** Methods, Procedures and Instruments of Prevention
- C** Institutional and Political Aspects of Prevention
- D** Prevention in Small and Medium-Sized Enterprises
- E** Prevention in Developing Countries

More information is available at
www.safety2002.at

and by E-mail
safety2002@auva.sozvers.at

10th Intenational Congress of Toxicology 11-16 July, 2004 Tampere, Finland

I have the great pleasure to invite all scientists related to toxicology and medical services to join us at the 10th International Congress of Toxicology in Finland in 2004. About 2,000 toxicologists and scientists all over the world are expected to participate in the ICT X Congress.

Kai Savolainen
President of ICTX

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INTERNATIONAL COMMISSION ON
OCCUPATIONAL HEALTH—ICOH



COMMISSION INTERNATIONALE
DE LA SANTÉ AU TRAVAIL—CIST

SCIENTIFIC COMMITTEE ON NEUROTOXICOLOGY AND PSYCHOPHYSIOLOGY

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TO ALL COMMITTEE'S MEMBERS

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As you know, the 8th International Symposium on Neurobehavioral Methods and Effects in Occupational and Environmental Health is taking place in Brescia, Italy, in June 2002. One of the most important decisions that will be taken during the 8th symposium is the one regarding the venue of the 9th symposium. I'm writing this letter to encourage you to apply for the organization of this symposium.

On some occasion, when the location of the 9th symposium has been discussed, you have expressed an interest that you might possibly organize the symposium. This is the reason that I'm now inviting you to investigate the possibilities for you to organize in the year 2005 the 9th International Symposium on Neurobehavioral Methods and Effects in Occupational and Environmental Health.

I kindly ask you to consider your willingness and opportunities to run the 9th symposium, and in doing this, to reflect especially on the following issues:

- Your personal time and interest in this task
- Possibilities for organizational support
- Possibilities for financial support
- Possible venues and times
- Special ideas for the scientific program

In so doing, please realize that we have asked several persons for proposals. The proposals received will be evaluated with respect to the points mentioned above, and the final decision will be made by the International Organizing Committee. The members of this committee are the organizers of previous symposia. When you have questions on the organization of the symposia or on this procedure, please contact me at the address in the letter head. This is also where proposals should be sent, if possible no later than February 1st, 2002.

Best wishes from Stockholm,

Anders Iregren
Committee chairman

◆ The newsletter

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Contributions to the newsletter are most welcome, preferably as text files via E-mail, or on diskette by ordinary mail.

Preferred file format is plain text or MSWord. The newsletter layout is now produced using MSWord.

Feel free to contact me when you have any questions or suggestions related to contributions and/or the contents of this newsletter