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14th Newsletter

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Goodbye Michael

INA was born in Italy at a NATO-ANSI course on Neurotoxicology in Belgirate in the summer of 1984. Here the tune was set for INA meetings to come in that it was held in a more or less secluded place at the border of the Lago Maggiore; that there was a nice mixture of sixty 'students' and twenty 'teachers' for ten days and that it was very fruitful from the scientific and from the social point of view. Those present certainly will remember the roof-parties. Probably at such an occasion the idea must have occurred to Michael Csicsaki to start with a "neurotoxicology Interest Group". He asked in september 1984 us for the need and the expectations of such a group. The group started in that year with 35 members. From the beginning it was decided that membership should be open to everybody working in the field of neurotoxicology. Michael sent a questionnaire to all of us and based on that he compiled four databases:

- a special interest register
- an INA collaboration request register
- an INA advice offers directory, agents, methods, problems etc.
- an INA traineeship offers directory

It must have been a lot of work to create and update these registers, but it was worthwhile. It is a unique situation that a club of 'friends in science' offers an opportunity to help each other and to ask for advice based on such registers.

In the last five year Michael was the driving force behind the Newsletter and the administration of the members. He founded INA and provided continuity for the last 5 years. We have had two excellent conferences and we are looking forward to the meeting in 1991 in Italy. It is a pity that Michael now has to decide to stop with all the paperwork.

Michael we thank you on behalf of the INA members for all the time and energy you spend on INA It is an honour that we may continue your job in preparing the Newsletter and in maintaining the different registers. We wish you good luck in your new job and happiness with your family in your new home.

Keep in touch with INA and neurotoxicology!

Jacob Hooisma, Hans Muijser, Liesbeth Hoogendijk.

**Scientific Committee: Sandra Allen (UK), Gordon Pryor (USA), Anders Iregren (Sweden), Gerhard Winneke (FRG)
Huw Jones (UK), Herbert Lowndes (USA), Luigi Manzo (Italy), Thomas Walsh (USA).
Jacob Hooisma, secretary (The Netherlands)**

SUMMARY OF THE 3RD SESSION OF THE 2ND MEETING OF THE INTERNATIONAL NEUROTOXICOLOGY ASSOCIATION, SITGES, SPMN

The third symposium was entitled "Sensory systems as targets for neurotoxic agents: the visual, auditory and mechanoreceptive systems".

The request made to the invited speakers by the organisers to provide a multidisciplinary review in consideration of their co-participant's diverse subject areas resulted in wide ranging presentations and discussions alike.

Dr Ernie Harpur provided a clear introduction to auditory neurotoxicity (ototoxicity), specifically, "Cochlear pathology and pathophysiology induced by drugs" while Dr Larry Fechter elaborated further on this theme in his lecture entitled "Impaired cochlear metabolism as a basis of cochlear dysfunction". In concert, both presentations provided insight into the basis for the prediction of ototoxic substances for different 'target' regions of the auditory system, eg. cochlea versus vestibular system and the differences in hair cell damage associated with their spatial distribution. As with the selectivity shown by neurotoxic agents for cell types or discrete areas in the PNS or CNS, ototoxins display similar biochemical specificities which are related to functional properties. The effects of ototoxins on the structural or metabolic integrity of a component-part of the auditory system may be predicted by anatomical or functional

SUMMARY OF THE 4th SESSION

The subject of the morning session of the last day of the 2nd INA meeting was "monitoring of effects of neurotoxic agents on exposed workers". The session, which was chaired by Donna Mergier and Anders Iregren, focused on measurement methods for detecting the subtle changes in neurophysiological and psychological functioning that can be caused by exposure to low levels of neurotoxic substances, and the use of human performance data in risk assessment.

In a very short introduction to the session Anders Iregren underlined the differences between the investigative approach used in clinical evaluation of diseased individuals with suspected neurotoxin-related illness, and the approach required for studying the relationship on a group level between exposure and indicators of early alterations of nervous system function. The laud approach relies on very sensitive measures, which are effective in establishing dose-response relationships and thus meaningful in group comparisons. These methods have to be highly reliable, valid, non-invasive, well standardised and easy to administer to large populations. The information provided is used for the identification of potential human neurotoxins and actions directed towards the environment, rather than for making decisions regarding individuals.

Sensory functions, neurobehavioral performance, subjective symptoms, and mood have all been demonstrated to be vulnerable to neurotoxin exposure. Donna Mergler reviewed the methods used for field assessment of sensory functions. She examined the literature on early sensory changes associated with workplace neurotoxin exposure, including chromatic discrimination, visual contrast sensitivity, vibrotactile perception thresholds, and olfaction. She stressed the need to incorporate sensory measures into current field batteries, and the growing interest in examining the relationship between sensory and neurobehavioral deficits. The varying requirements on performance tests for use in different situations were reviewed by Francesco Gamberale. His lecture also included methodological considerations regarding design in various applications within neurobehavioral toxicology, as well as short descriptions of a number of different psychometric approaches. Anders Kjellberg reviewed methodological problems in the measurements of symptoms and mood, and the relation between these subjectively reported measures and performance and psychological responses. He discussed recent theoretical and methodological developments regarding the dimensionality of mood, and presented a new two-dimensional Swedish mood adjective check list. The final invited speaker, Bernard Weiss, examined how human performance data are and could be used in risk assessment, using examples from lead and other neurotoxins. He emphasized the importance of performance loss for an exposed population by demonstrating the overall effects of lowered scores on the upper percentiles.

Twenty-seven posters were presented in the afternoon session, entitled "Neurotoxic effects on exposed workers: Industrial and clinical studies". The posters described studies of workplace exposure to carbon disulphide, lead, manganese, mercury, pesticides, polychlorinated biphenyls, styrene, trichloroethane, trichloroethylene, and solvent mixtures found in patients, printing inks, histology preparations, plastics, and others. One study examined brain tissue and cerebro-spinal fluid following fatal accidental over exposure to megluminamidotriozat, while another study presented new analytical methods for assessing metal content in scalp hair and the brain.

A wide variety of measures of neurotoxic effects were presented in these posters: symptoms and mood questionnaires, traditional paper-and pencil test batteries as well as computer-assisted performance tests, non-invasive physiological measures of blink reflex, color vision, hearing, coordination, vibration and sway, and, electrophysiological methods, including nerve conduction velocity, evoked potentials, electromyography, and heart rate.

Studies using quasi-experimental designs showed pre-post shift differences for various performance tasks among workers exposed to styrene, and workers exposed to toluene and xylene in paints. For the latter group changes were observed throughout the week. In addition, peak/post season differences were reported for workers and residents exposed to pesticides.

Longitudinal studies reported improved performance following industrial hygiene changes resulting in lowered exposure to styrene and increase nerve conduction velocity following cessation of exposure to lead.

A large number of comparative exposed/non-exposed cross-sectional studies were presented, demonstrating I) higher symptom reporting among exposed workers as compared to non-exposed workers, and among active workers as compared to retirees, and II) performance decrements on certain tests among workers exposed to low levels of manganese (simple reaction time, finger tapping, memory), solvents (psychomotor function, auditory and visual memory), and polychlorinated biphenyls (simple reaction time, memory, mental flexibility, attention).

Cross-sectional studies of workers reported hearing loss in relation to exposure to carbon disulphide and noise, and a good correlation between digit symbol performance and trimethyl lead. Color vision loss, observed among patients from an occupational health clinic was related to visual task deficits. In a study of hormonal levels prior to and following neurobehavioral testing of styrene exposed workers, pre-test levels of ACTH and beta-endorphins were lower than post-test levels, while pre-test serum prolactin levels were higher than post-test, irrespective of exposure.

A review was presented on the use of neurobehavioral research in recommending safe workplace exposures to organic solvents, which stressed the importance of human experimental studies using single solvents and combinations of solvents under both sedentary and simulated workload conditions.

Some general conclusions may be drawn from these varied investigations: I) Improved methods of measuring exposure and neurotoxic alterations indicate effects below current permissible levels. II) There is some evidence of at least partial reversibility following cessation of exposure or hygienic improvements, underlining the importance of continuing to develop sensitive measures of neurotoxic injury. III) Short-term exposure effects have shown to be useful in predicting the potential for more serious long-term effects.

It is clear that more research is required in this area to increase our understanding of the process involved in human neurotoxic injury, and to adequately identify early neurobehavioral and neurophysiological alterations, which may not be life-threatening, but which do represent diminished health and well-being for the exposed persons. Research in this area must provide a more complete picture of neural and psychological changes and address such questions as the relationship between exposure parameters (peak exposures, continuous exposures, synergism with physical activity and other workplace hazards, etc) and neurotoxic endpoints.

Donna Mergler & Anders Iregren

NEXT MEETING

In our opinion it was high time that the preparation for the meeting got started. If we were to wait until INA had been structured and an executive committee had been established, the next meeting might have to be postponed for some time. However, this gave a problem when decisions had to be made. Ideally, such decisions should be made by the INA membership, obviously that is not so easy to organize. Neither, however, should this be done by Michael and our small TNO group alone. Therefore, we asked for the time being the current scientific committee to serve as a forum for selection of a meeting place. Such a selection was necessary, since there were two very attractive offers. One invitation was from Dr. Lies Desi to come to Szeged in Hungary, the other one came from Dr. Luigi Manzo from Pavia, Italy. The result of the deliberations was that Luigi Manzo was asked to organize our next meeting in the spring of 1991. The members of the scientific committee, however, would like to recommend to the future executive committee to consider Hungary for 1993, provided the Americans still hold the same opinion they expressed so strongly in Sitges.

New Scientific Committee

It was very gratifying to learn that such a great number of INA members was prepared to serve in the new scientific committee. However, there is one drawback to such a situation. When there are so many able volunteers a choice has to be made, which is then very difficult to do. Therefore, the members of the previous scientific committee also have discussed a procedure to establish a new scientific committee and there was general agreement that about half of the members should be replaced. The previous committee had a rather well balanced representation of different disciplines, which we wanted to maintain. Consequently, the following procedure was adopted: each member indicated by whom in his discipline he or she would like to be replaced.

The outcome is that the new scientific committee will consist of the following new members and only two "old hands", presented in pairs in which they should work together:

Sandra L Allen
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Gerhard Winneke
Med. Institut f. Umwelthygiene
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Luigi Manzo (and our host)
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Thomas J. Walsh
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For the time being, I will act as secretary to this committee:

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If you have any bright new ideas or if you would like to make suggestions for the next meeting, please send them to any of the committee members who is involved in the area of research to which your suggestion is relevant. Alternatively, contact the secretary, and I will take care of it. Do not hesitate to do so, because any INA meeting should serve its membership, by addressing those issues which you as a member regard to be important.

Goodbye to old members of the Scientific Committee

As a result of the constitution of a new SC, six members of the old one will not return. These members are Stephen Bondy, Lucio Costa, Beverly Kulig, Marcello Lotti, Donna Mergler and Eduardo Rodriguez-Farre. Many of them were involved in INA from its early beginning, when there was only the idea in Belgirate to start a group of neurotoxicologists. Thanks to their enthusiasm and efforts it was possible to organize two successful meetings. Personally, I feel that without their help, it would not have been possible to organize the Lunteren meeting and I think that the Sitges' organizers share my feelings on this. Our special thanks are due to Eduardo for his contribution in the committee and for chairing the local organization that provided us with the splendid meeting in Spain.

On behalf of the INA membership, I would like to thank all these members for their invaluable assistance. As you can see from the list of candidates for the executive committee, many of them care for INA so much, that notwithstanding the large amount of time they already devoted to INA, they are willing to take care of our society also in the future.

Bylaws

We did not receive any comments on the bylaws as published in the 'NA Newsletter. Therefore, we assume that all of you find them acceptable in the present state. David Ray is now looking for legal assistance to have INA registered as a charity in the United Kingdom. Changes in the bylaws if so required by law will be published in a forthcoming newsletter. However, finalizing the registration will be the first task of the executive committee.

Elections

We had some hope that the registration of INA could have been accomplished before electing an executive committee, a somewhat more logical sequence. Since this may still take some time, we propose to go ahead, while adhering to the statutes as if registered.

Some considerations about the Executive Committee

Before embarking on an explanation of the election procedure, we would like to share with you some of our feelings about the executive committee. 'NA originated from the idea that our society should be a meeting place for experienced neurotoxicologists and novices in the field. It should help to stimulate young scientists by providing an informal meeting ground and it should stimulate cooperation between different disciplines.

Our feeling is that one should try to have this reflected in the composition of the executive committee. Of course no rules exist for guaranteeing such an outcome, however, when deciding on our personal votes we want to keep this in mind and if you agree with us you could try to do the same.

Procedure

You have received this Newsletter directly by mail and not as usual distributed to you by the local representative, because we wanted to be sure that all members were going to receive this Newsletter at about the same time. If you are a full member of 'NA, i.e. when you have fulfilled all obligations to be a full member, you will find enclosed in this letter a voting bill. You are expected to mark squares behind the names of six candidates and to return your votes to the secretary of our department miss. R. Oosterhoff, whose address is printed on the bill. In order to secure the secrecy of voting, the secretary will take care of the votes, so please, do not enclose other mail addressed to us. The counting procedure, also carried out by the secretary, will be very simple. Those six persons with the highest number of votes will be chosen to form the first executive committee. According to the bylaws, it is then up to the chosen members to divide the different offices among themselves. Your votes should be with our secretary not later than:

15th February 1990

We are happy to receive copy and/or abstracts for the next Newsletter.

Candidates

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School of Public Health
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Marcello Iotti
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Istituto di Medicina di Lavoro
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Oregon Health Sciences University
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Introduction of candidates by themselves

We have asked the candidates to introduce themselves in a few lines and to give their opinion on INA as a society, in order to help you to make your choice. Their contributions you will find on the following pages (not included in the online version).

Adress changes:

**Leif Simonsen
National Institute of Occupational Health
Lerso Parkalle 105,
DH-2100 Copenhagen 0, Denmark**

Membership cancelled by:

Prof.Dr. W. Meier-Ruge

Announcement:

We received a letter from our Swedish colleagues. It is published here. Don't hesitate to discuss with them directly or in the next edition of the INA Newsletter.

What is an international meeting in neurotoxicology?

The recent 2nd Meeting of the INA in Sitges was an excellent example of a truly international meeting, with participants from 24 countries on 4 continents, and invited speakers of seven nationalities. All of the participants that we have spoken to have expressed their great satisfaction with the meeting, and we would thus like to congratulate the organizers!

At the end of July 1989 we received the "Announcement/Call for papers" from the organizers of the so called "7th International Neurotoxicology Conference" to be held in Little Rock, Arkansas, USA, September 18-21, 1989. With the deadline for submission of abstracts for this meeting being August 1, we regret that we were practically prevented from contributing to this meeting.

Looking through the announcement for the Arkansas meeting, we observed that only one of the invited speakers was from Europe. All the other speakers are from universities in the United States, or from other organizations in this country. Since all of the sponsors and practically all of the invited speakers are american, why do our US colleagues bother calling this an "international" conference?

We would very much appreciate the opinions of the members of INA, as well as those of the organizers of the Arkansas meeting!

Francesco Gamberale

Anders Iregren

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**We wish you a merry Christmas
and a happy New Year**