



International Neurotoxicology Association

DRAFT INA Newsletter DRAFT

PRESIDENT'S MESSAGE

Helsinki, April 1, 1999

Dear Colleagues,

This is my first message to you as your new President. First, I want to express my thanks for the trust you have shown to me as reflected by the results of the ballot on the INA Executive Committee. After the election, I have been in close contact with our Past-President, Gerhard Winneke, and our Treasurer, Beverly Kulig. They both continue to work actively for INA, and have provided invaluable support and help for me when starting my term in the office. Miki Aschner and Larry Fechter, both from the US, are the new President-Elect and Secretary, and we three had our first *ad hoc* meeting during the 38th Annual Meeting of the Society of Toxicology in New Orleans in March. I will discuss some of these issues below, and they will be discussed also in the Executive Committee meeting in Leicester in July during the INA-7.

INA has existed for 12 years. During these years, it has organized a series of excellent biennial Congresses that have promoted the science of neurotoxicology, and established INA as an international organization. The Association has been informal, and has not had written rules. Now the time has come to move forward, and become more organized, without forgetting the benefits of a small and informal INA setting. In addition to preparation of a written constitution, INA will also make steps to become a member of the International Union of Toxicology (IUTOX), as was agreed in the INA Business meeting in Szeged, in Hungary, in 1997.

By increasing our international visibility we can serve our members more effectively than before. Being a part of a larger international community will provide a larger forum for our members to speak for, and promote, the science of neurotoxicology. A valuable goal in the future will be to serve our young student members. We need stable finances to make sure that INA can organize excellent Congresses also in the future. We also have to improve the stability of INA further to help raising funds from sponsors to support our Congresses, the flagship event of INA. We have increased our visibility by creating the Jacob Hooisma Lecture which honors one of the founding fathers of INA, and brings an outstanding scientist to give a special lecture in the Congress. This year, David Ray has done an excellent job by creating an exciting program for the INA-7 Congress.

We also need to develop the INA Newsletter as even

more effective means of communication. Kevin Crofton has kindly agreed to take over this important activity from Beverly Kulig, who has, in addition to being the Treasurer of INA, also served as INA Newsletter Editor. For the future, we also have to assure that interactions between the local organizers and INA Executive Committee continue to be close in creating the program of the upcoming Congresses. Various options need to be considered: can the organizers be individuals without a committed affiliation, or should a local organization, a local toxicological society, or a local or national scientific organization, also commit itself to this INA activity. A constructive solution that provides enough freedom, flexibility and security shall be sought for. The Executive Committee and the INA Business meeting should consider a possibility that the bidders of future INA Congresses shall provide a financial plan and a tentative program outline for the Congress for the evaluation and comparison of the bids.

I look forward to seeing you all in sunny Leicester enjoying the exciting scientific and enjoyable social program of the Conference.

Truly yours,
Kai Savolainen

INA-7 Update

Plans for INA-7 are well advanced. All of the 36 invited speakers are now in place, and registrations and abstracts are beginning to come in. You will find full details of the meeting on either the INA-7 web site:

<http://www.le.ac.uk/cmht/der2/>

or the INA website:

<http://home.att.net/~ina99/>

You can find registration forms and abstract instructions. If you cannot use the web site for any reason, then contact David Ray by fax (+44 116 2525 616) or mail (MRC Toxicology Unit, Lancaster Road, Leicester, LE1 9HN, U.K.).

The meeting will be held at the self-contained Oadby Campus, with bar, lecture theater, poster and exhibition areas all convenient for the accommodation. The programme has the usual poster sessions, plus a special student session, and sessions on organophosphates, PCBs, clinical toxicology, susceptible sub-populations, molecular target modeling, sensory system toxicology, and neurodegeneration. In addition there is a strong emphasis on the application of new approaches to toxicology (genetic, morphological, neurochemical, and functional), with talks given by experts in these fields. There will also be a lively debate on the usefulness of animal versus

clinical toxicology, and an even more lively football match. As usual the middle day of the meeting will be devoted to sightseeing (Warwick Castle), and there will be a full programme for accompanying persons - who will be very welcome in the heart of the UK.

Please book early as I will not sleep well until I know that the meeting is set to break even!

David Ray

Student Awards at INA-7!

Marcello Lotti and Beverly Kulig are chairing a student poster session at INA-7. A panel of 4 judges will select the three most outstanding posters and cash awards will be made to the students at the business meeting. We would like to have as many student submissions as we can. So please, give some thought and encouragement to your students to enter their work in Leicester.

For more information please contact Beverly (see last page for contact information) or Marcello (Marcello Lotti, MD, Università di Padova, Istituto di Medicina del Lavoro, Ospedale Giustiniano, Via Giustiniani 2, Padova 35128 ITALY phone: 39-4982-12548, fax:39-4982-12550, email: lottitox@ux1.unipd.it).

INA-7 Business Meeting:

The President and Executive Committee of INA extend an invitation to the business meeting of INA to be held on July 8, 1999 from 17.15-18.45 in Leicester, UK at the INA-7 Meeting. The agenda is see below. If you have topics that you would like to see added to the agenda, please forward them to Kai or to Larry.

AGENDA

1. Opening: Kai Savolainen, President of INA
2. Election of Chairman and Secretary of the meeting
3. Election of two scrutineers and two auditors
4. Acceptance of the agenda
5. President's report
 - *Introduction of new members of the Executive Committee, and Editor of the Newsletter
6. Treasurer's report
7. Secretary's report
8. INA Membership Fee
9. Proactive plans of INA (IUTOX Membership)
10. Report on preparation of INA-8 in Portugal in 2001
11. Venues of future INA Congresses (2003, 2005)
12. Farewell of to previous Members of INA Executive Committee
13. Close of Business Meeting

Future Locations for INA Meetings?

As we begin focusing energy on our presentations for INA 7 to be held in Leicester, UK and dream about INA 8 in sunny Portugal, it's also time to begin planning for INA 9 (2003) and 10 (2005). Have you considered hosting INA and sharing your homeland with your colleagues?

We intend to consider bids for hosting future INA meetings at our business meeting in Leicester. We ask that individuals or groups wishing to host the meeting develop

plans prior to the Leicester meeting and be prepared to make a 10 minute presentation (perhaps with picturesque slides?) of the proposed site. The bid to host the meeting should suggest possible scientific themes for the meeting, the initial list of organizers, and whether the meeting will be co-sponsored by a national society (e.g. a national toxicology society), university or institute. Such co-sponsorship is desirable because it improves opportunities for financial support and broader scientific input.

A bid should also provide a proposed budget that includes projected costs for room and board and meeting registration. Also, the opportunities to obtain outside support for the meeting is helpful. The objective here is to determine whether a conference site is economically feasible for the membership and the society.

So bring your slides of beautiful sunsets over the water, magnificent waterfalls, or old picturesque towns where you propose that we meet. And also develop a working plan as a touch of reality to accompany the slides. Proposed bids should be submitted to Kai Savolainen or Larry Fechter prior to the Leicester meeting. You may also contact Kai or Larry for more information on developing a bid.

INA Members Elect New Executive Committee

The results of our last election are in! The new officers are Miki Aschner, President-elect and Larry Fechter, Secretary. Kai Savolainen will take on the role of President, Beverly Kulig will continue as Treasurer, and Gerhard Winneke will serve on the Executive Committee in the role of Past President. Also, Kevin Crofton has agreed to take over the role of Newsletter Editor. He has let it be known that he welcomes all contributions! Kevin has already done a fine job establishing our web page.

Names and contact information for all members of the Executive Committee of INA are printed on the last page of this newsletter. Please contact your officers with ideas, questions, suggestions, etc. Remember the society is here to serve you. Your participation will ensure the continuing success of INA.

Membership News:

You should have already received a notice from Beverly Kulig extolling the virtues of membership in INA. Dues are only 35 dollars (US) per two years. This is a major source of funds for the society so please remember to pay your dues. If you are not currently a member please join.

In order to increase membership we are asking all members to contact colleagues and ask them to join. Send them a copy of this newsletter, an email, or give them a phone call!

Send a note to Beverly or the Editor and we will send you membership information. Membership information and applications are also available from the INA website at:

<http://home.att.net/~ina99/member1.html>

Is Your EMAIL Address Correct?

Have you received any recent email from INA? If not, perhaps your email address is missing from our database. Or, we have any old version that no longer works.

The next time you check your email please send a message to crofton.kevin@epa.gov. All you need to do put "INA and your name" in the subject line.

INA By-Laws:

The INA treasurer Beverly Kulig is currently working with lawyers to incorporate INA and formally adopt the by-laws. Hopefully, the by-laws will be available for discussion at the upcoming meeting in July.

INA WebSites:

INA now has an official website:

<http://home.att.net/~ina99/>

You can find copies of old newsletters, meeting information, membership application and more. If you have any suggestions or items you would like posted on the website just send a note to Kevin Crofton (crofton.kevin@epa.gov)

There is also a website for the INA-7 Meeting.

<http://www.le.ac.uk/cmht/der2/>

Thanks to efforts of Kevin Crofton and David Ray for making these site possible.

International Research Opportunities:

In this new section of the INA Newsletter we are attempting to disseminate information about international research opportunities. Please send the Editor information about any international research opportunities.

Fulbright Scholar Program: provides US scientists with overseas travel opportunities ranging from 2-12 months information from www.cies.org <<http://www.cies.org>>

Burroughs Wellcome Foundation Travel Awards:

provides US scientists with opportunities to visit laboratories in Europe for 1-2 months. Applications and information are available through the Society of Toxicology.

Fogarty Center of NIH: Provides research training opportunities for non-US scientists seeking to undertake training at a US laboratory. Information from www.nih.gov/fic/opportunities/index.html <<http://www.nih.gov/fic/opportunities/index.html>>

Future Meetings of Interest:

June 27-July 1, 1999: The 9th Annual Summer Neuropeptide Conference will be held at the Marriott's Casa Marino Resort in Key West, Florida, USA. For further information, please contact: Dr. Jacques Bradwejn, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, ON K1Z 7K4 Canada. Fax: (613) 722-5871.

June 30 -July 3, 1999: Neurobehavioral Teratology Society Meeting, (NBTS) Keystone, Colorado; abstract deadline was 01/25/99.

<http://nbts.bsbe.umn.edu/nbtshomf.html>

June 24-27, 1999: The eighth annual meeting of IBNS will be held in Nancy, France, June 24-27, 1999

<http://www.utsa.edu/Academics/COSAE/LifeSciences/IBNS/frindex.htm>

July 4-10, 1999: INA-7, International Neurotoxicology Association Meeting (Leicester, England)

<http://home.att.net/~ina99/>
<http://www.le.ac.uk/cmht/der2/>

August 28 - September 3, 1999: New Gordon Research Conference (GRC) entitled Neuroethology: Behavior, Evolution and Neurobiology. To be held in Oxford, UK.

<http://www.grc.uri.edu/>

August 28-September 1, 1999: The 17th International Australasian Winter Conference on Brain Research (AWCBR) to be held in Queenstown, New Zealand.

<http://psy.otago.ac.nz:800/awcbr/awcbr.html>

September 11-17, 1999: Degeneration and Regeneration in the CNS: From Biology to Diseases. FENS Summer School, 2nd Elba School on Neuroscience to be held in Elba, Italy.

<http://www.univie.ac.at/fens-schools/Links99.html#anchor670557>

October 15-19 th, 1999: Conference entitled: "Neurotoxicology, pathology and protection in Brain Disease States" to be held at Mojácar, Southern Andalusia, Spain.

<http://www.cermente.com/moj99.htm>

October 17-20, 1999: The 17th International Neurotoxicology Conference (Little Rock, AR) Children's Health and the Environment: Mechanisms and Consequences of Developmental Neurotoxicology; abstract deadline is 09/01/99. For information please contact: Prof. Joan Cranmer, Department of Pediatrics, University of Arkansas for Medical Sciences, 1120 Marshall - Rm. 304, Little Rock, Arkansas 72202 USA. Tel: 501/320-2986; Fax: 501/320-4978; cranmerjoanm@exchange.uams.edu

http://www.neurotoxicology.com/html/conference_series.html

October 23-28, 1999: Society for Neuroscience Meeting (Miami Beach, FL). Abstract deadline was 04/26/99.

<http://www.sfn.org>

December 10-17, 1999: Nervous System Reaction to Neuronal Loss and Injury, FENS Winter School. To be held in Kitzbühel, Austria.

<http://www.univie.ac.at/fens-schools/Kitzbuehel99.html>

In The News

The following is a new section of the INA Newsletter. In it we will highlight some recent news items of interest to neurotoxicologists. If you have suggestions for future items, or wish to contribute an item, please contact the Editor.

MINAMATA DISEASE IN THE AMAZON: THE TIP OF THE ICEBERG - Montreal, January 29, 1999.

The recent revelation of 3 cases of Minamata disease, identified by Japanese researchers in a village on the Tapajos River in the Brazilian Amazon, is only the tip of the iceberg concerning the situation of mercury pollution in the Amazon. Over the last ten years, an increasing number of studies have reported mercury contamination of fish in the various rivers of the Amazon region, and relatively high mercury levels in the hair of riverine populations for whom fish constitute the dietary mainstay. Up until recently, it was believed that the widespread mercury contamination came primarily from the use of this metal in gold-mining. Our research group from the University of Quebec in Montreal and the Federal Universities of Para and Rio de Janeiro have shown that the mercury released into the atmosphere from the gold-mining activities, while highly toxic for the miners and workers who burn the gold-mercury amalgam and the populations living around the gold-mining areas and the shops in the towns and cities that further burn the amalgam, remains in the local environment. Our studies and others strongly suggest that in areas remote from the gold mines, the mercury in the extensive Amazonian waterways comes from soil lixiviation of natural mercury following 'slash and burn' agricultural practices. Following deforestation, mercury leaches from the soil which contains high levels of this metal. (For a description see: Roulet et al. *Science of the Total Environment* 1998; 223:1-24).

Our international research group has likewise examined early neurological deficits in riverine populations who do not display clinical manifestations of Minamata disease. These studies reveal that motor and visual functions decrease with increasing hair mercury, at levels well below 50 ppm. (median values: 11 ppm). These findings show that even in the absence of overt disease, mercury is affecting the well-being of these populations (See: Lebel et al. *Neurotoxicology* 1996; 17:157-167; Lebel et al. *Environmental Research* 1998; 79:20-32).

The tremendous biodiversity in the fish resources is reflected in the differences in mercury levels in the abundant fish species. This in turn, is reflected in hair mercury concentration of fish-eaters. Herbivorous fish contain very little mercury and those who eat predominantly herbivorous fish have less mercury than those who eat predominantly piscivorous fish. There are seasonal variations in hair mercury levels, dependent on the bioavailability of different fish species during the rainy and the dry seasons (See: Lebel et al. *Water, Air & Soil Pollution* 1997; 97:31-44).

The Amazonian ecosystem is very complex and much

work must be done to understand what is happening and instigate mitigation measures. Researchers from Canada and Brazil, with local NGOs are currently involved in a pilot project in a small village on the Tapajos River, whose objective is to work with the community to find short, medium and long term solutions. Since fish is the major source of protein and is beneficial to their health and well-being, the short term solution seeks to inform the villagers of the mercury levels in various fish species and work with them to modify their diet in such a way as to increase the proportion of fish with low mercury levels. On the medium term, the factors that favor methylation will be determined, allowing us to identify 'hot spots' in the river. And, on a more long term basis, we have begun to work with the local farmers on reforestation projects...

There is much to be done in this area. In 1989, UNAMAZ, the Union of Amazonian Universities held a meeting on mercury, pointing out the growing dangers of mercury in the Amazonian environment. Ten years later, in January 1999, we organized a meeting in Santarem, a city at the junction of the Amazon and Tapajos Rivers to establish a collaborative network of researchers and NGOs working on the issues of mercury contamination in the Amazon. NGOs from the region and researchers from Santarem, Belem, Brasilia, Manaus, Bahia, Rio de Janeiro in Brazil and from Venezuela, Peru, Ecuador, Canada and the United States attended the meeting and set up the Forum on Mercury Contamination of the Amazonian Ecosystem on the outreach campus of the Federal University of Para in Santarem. We will soon be setting up a website. The International Development Research Center has provided funding to initiate this endeavor and we are seeking funding from other sources to pursue it.

For information, you can contact Dr. Pascale Martineu (martineu.pascale@uqam.ca), Dr. Donna Mergler (mergler.donna@uqam.ca) or Dr. Marc Lucotte (lucotte.marc_michel@uqam.ca).

NEUROTOXIC DINOFLAGELLATE

Recent research has shown that a dinoflagellate that lives in coastal waters of the Southeastern United States can excrete an extremely potent neurotoxicant. The following are descriptions of some of the research and health effects of this toxicant.

From the NC State University Pfiesteria Web Site
<http://www.pfiesteria.org/pfiesteria/pfiest.html#Toxic>

The toxic dinoflagellate, *Pfiesteria piscicida*, has been implicated as the primary causative agent of major fish kills and fish disease events (finfish and shellfish; 103 to 109 finfish) in North Carolina estuaries, coastal areas, and aquaculture operations. *Pfiesteria* and closely related toxic species ("Pfiesteria-like complex") have also been confirmed in fish kill/disease areas and aquaculture facilities outside North Carolina from the mid-Atlantic to the Gulf Coast. Fish kills caused by *P. piscicida* usually occur in the warmest part of the year, and often precede low dissolved oxygen levels in the estuaries.

Thirteen researchers who worked with dilute toxic

cultures of *Pfiesteria* sustained mild to serious adverse health impacts through water contact or by inhaling toxic aerosols from laboratory cultures. These people generally worked with the toxic cultures for 1-2 hours per day over a 5-6 week period. The effects included a suite of symptoms such as narcosis (a "drugged" effect), development of sores (in areas that had directly contacted water containing toxic cultures of *P. piscicida*, as well as on the chest and face), uniform reddening of the eyes, severe headaches, blurred vision, nausea/vomiting, sustained difficulty breathing (asthma-like effects), kidney and liver dysfunction, acute short-term memory loss, and severe cognitive impairment (= serious difficulty in being able to read, remember one's name, dial a telephone number, or do simple arithmetic beyond $1 + 2 = 3$). Most of the acute symptoms proved reversible over time, provided that the affected people were not allowed near the toxic cultures again. Some of these effects have recurred (relapsed) in people following strenuous exercise, thus far up to six years after exposure to these toxic fish-killing cultures. Moreover, subcutaneous injection of crude toxin preparations from fish-killing cultures have induced serious learning impairment and memory loss in experimental laboratory rats (work by Drs. Levin and Schmechel at Duke University, see Levin et al., *Environ Health Perspect* 105:1320-1325, 1997). The discovery, the "hard way," that *Pfiesteria* is unusual in its ability to produce toxins which can aerosolize, led to requirements by state and federal officials that all further work with toxic fish-killing cultures of this dinoflagellate be conducted in biohazard level III containment systems in a limited-access facility. These precautions must be followed for any research with live toxic cultures of *Pfiesteria*.

From INA Member Ken Hudnell

The US EPA was asked to assist the North Carolina Department of Health and Human Services in a clinical study of human health risk from exposure to *Pfiesteria piscicida*, the toxic dinoflagellate thought to be responsible for massive fish kills in estuaries. Dr. Kenneth Hudnell of NTD measured visual function in the potentially exposed estuary and unexposed offshore fishers and crabbers. Only the vision data showed

significant differences between the cohorts. Visual contrast sensitivity, an indicator of neurological function in the visual system and the ability to see visual patterns, was about 30% lower in the estuary workers. Extensive analyses indicated the many socio-demographic, life-style, medical, and occupational neurotoxicant exposure factors did not account for the group difference. Hours spent at active fish kills, however, was significantly associated with contrast sensitivity in exploratory analyses. Since none of the estuary cohort participants had contacted a fish kill for at least 3 months, and the Maryland study indicated that cognitive effects (severe learning and memory deficits) seen shortly after exposure had abated by 3 months (Grattan et al., 1998. *The Lancet*, 352:532-539), the vision data is the first indication of a persistent health effect in humans.

Dr. Hudnell is currently conducting studies with Ritchie Shoemaker, MD, who first alerted the state of Maryland to adverse health effects in people contacting fish kill areas in Chesapeake estuaries. Their initial results suggest that: 1) the vision deficit is seen in asymptomatic people who recreate on or live by Maryland estuaries where *Pfiesteria*-related fish kills have occurred, suggesting they may have a lower level of exposure than those presenting with acute effects; 2) that treatment with a polymer reverses the vision deficit and the acute effects of "Estuary Associated Syndrome", apparently by removing toxin(s) from bile during enterohepatic recirculation and; 3) the vision deficit generalizes to people who have been exposed to toxins from another dinoflagellate, ciguatera.

Evidence suggests that the incidence of human and ecological health effects from Harmful Algal Blooms (HABs e.g. neurotoxic, paralytic, and amnesic shell fish poisonings, red and brown tides, ciguatera, *Pfiesteria*, and cyanobacteria) is increasing worldwide, making this an emerging area of health and ecological research.

For *Pfiesteria* information see:

<http://www.pfiesteria.org/>

For HAB information see:

<http://www.redtide.whoi.edu/hab/>

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