

**American
Academy
of Clinical
Toxicology,
Inc.**



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AACTion

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President's Corner



Endangered Species

Michael I. Greenberg,
MD, MPH, FAACT

As we move into the year 2010 (by the way...Happy/Healthy/Prosperous new Year wishes to you all!!!) I am struck by just how vigorous and alive the disciplines that make up clinical toxicology seem.....for now. But I'm here to tell you it's not going to last and its actually looking pretty shaky; if you ask me. While trends in the past have basically allowed almost anyone to enter the world of clinical toxicology, "hang out a shingle" and call themselves a specialist in clinical toxicology, today's paradigm for clinical work requires a combination of formal training and formal certification by a publically recognized certifying body. And.....as many of us are painfully aware, the public policy paradigm has now embraced a system of continuous and continuing RE-certification of competence. If we take a hard look at some of the subsets of clinical toxicology it looks like we may be falling behind the curve in some important ways.

A quick visit to the Accreditation Counsel for Graduate Medical Education (ACGME) website (www.acgme.org) one can see that there are only about 22 accredited training programs in the specialty of Medical Toxicology in the US. These programs are allocated a total of 85 "approved [trainee]

positions" and currently there are only 48 Medical Toxicology "residents on duty" i.e. in training. A look at the web page from the American Board of Clinical Pharmacology (www.abcp.net) lists only about 17 training programs nationwide in clinical pharmacology and subsets of clinical pharmacology. These programs tend to have very few trainees although the precise numbers are not listed (or at least I could not find them). And, indeed, not all clinical pharmacology trainees enter a clinical toxicology career. There are certainly many more training programs for pharmacists but, again, it is clear that the vast majority of pharmacy trainees do not go into (or even consider) clinical toxicology as a career choice.

The above calculus is admittedly flawed and constrained by a lack of data. However, I think we are all reminded (me: when I look in the mirror....you....you have your own demons I'm sure) that our ranks are aging. My further unscientific calculations tell me that within the next ten years there will be a substantial (I dare say catastrophic) thinning of the ranks due to attrition (those who migrate back to other areas of endeavor), retirements (and worse). It does seem to me that we are headed for a situation where we will lose many more clinical toxicologists each year compared with the numbers we gain. A sad situation but I think it's the truth.

The real question is what to do about the above scenario. Unfortunately this is where I must leave you, my friends, to your own devices. If we all believe the status quo is

AACTion Wants Your News

We want to hear from you regarding promotions, lectures, publications, moves, new positions, etc. Have you (or another member you know of) been in the news interviewed by the press? We want to hear from you. News can be emailed to: rdonovan@clintonx.org

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ok for now then clinical toxicology will, like the polar bear, head down the path of extinction. Turning it around may not be doable; it may be too late and there may be a lack of will; I don't know. But, then again, it might still be salvageable. The only hope, from where I sit, is that each of us on an individual basis must seek out, recruit, encourage, and mentor at least one young person into the discipline of clinical toxicology every

year. The universe of candidates is enormous (students in medicine, pharmacy, nursing, pharmacology, etc) and it seems it's up to us as individuals to reach out to these folks. The formal organizational structure (AACT, EAPCCT, AAPCC, ACMT, etc) can only do so much. In order to succeed at preventing our own extinction my recommendation is that we need to act as individuals....only thing is, we need to do it now.

Prevention and Treatment of Amatoxin Induced Hepatic Failure With Intravenous Silibinin (Legalon® SIL): An Open Multicenter Clinical Trial

Madaus Inc, a division of Madaus GmbH (Cologne, Germany), is sponsoring an open-label clinical trial evaluating the safety and efficacy of intravenous silibinin, Legalon® SIL, to treat patients with suspected amatoxin poisoning due to the ingestion of *Amanita phalloides* or other amatoxin containing mushrooms.

Legalon® SIL will be administered to patients with amatoxin poisoning diagnosed by history, gastrointestinal symptoms, elevated liver enzymes, and/or diagnostic assay (should one become available). Patients may or may not also demonstrate abnormalities in bilirubin and/or creatinine. Treatment consists of a 5 mg/kg loading dose followed by 20 mg/kg/day via continuous infusion. The treating physician is expected to administer supportive therapy of his/her choosing but consistent with best practices. Legalon® SIL will be stopped when coagulopathy is no longer present, and when liver function tests have returned significantly towards the normal range. Patients will be followed 7-14 days after the end of Legalon® SIL therapy with follow up lab studies.

Any physician with a case of suspected amatoxin mushroom poisoning may have Legalon® SIL overnighted after calling a 24 hour hotline. When a physician calls the hotline they will be put in touch with the Principal Investigator (PI). Once the PI determines that the situation qualifies for the Legalon® SIL study, a supply of the antidote will be shipped overnight to the hospital pharmacy. Upon the completion of treatment the attending physician will submit all relevant data to the PI for follow up.

Physicians can obtain the medication by contacting a 24 hour hotline: 866-520-4412.

For additional information see:
<http://clinicaltrials.gov/ct2/show/NCT00915681>





AACT Members Participate In 'National Conversation'

Alan Woolf, MD, MPH, FAACT

The National Center for Environmental Health (NCEH) within the Centers for Disease Control & Prevention (CDC) continues to make progress with the organization and roll-out of its new initiative: '*National Conversation on Public Health and Chemical Exposures*'. This new effort was introduced to AACT members in the July, 2009 AACTion Newsletter. Now I want to update you briefly on its progress.

The NCEH is conducting this activity in partnership with EPA, ATSDR, and other state, tribal, and federal governmental agencies and environmental advocacy-related community groups, professional associations, nonprofits and members of the public. The AACT is proud to be included within these professional collaborators. The *Vision* is that chemicals can be used and managed in ways that are safe and healthy for all people. The *Goal* is to develop an action agenda for strengthening the nation's approach to protecting the public from harmful toxic exposures. The agenda will outline how best the United States can change its current functioning to meet these public health goals and achieve the **National Conversation's** vision. Areas of inquiry include:

- o Collect information about chemical use, who is exposed, and the level at which people are exposed;
- o Gain more knowledge of how chemicals affect people's health
- o Use policies and practices that tell us about risks, reduce harmful exposures, and create and use safe chemicals
- o Increase efforts to prevent, prepare, and respond to chemical emergencies
- o Protect all communities from chemical exposure
- o Create a well-informed public and healthcare provider network so people understand chemical exposure risks
- o Involve the public in government decision-making
- o Encourage teamwork among partner groups and agencies.

A Leadership Council will create a final working document with recommendations for an action plan by 2011. Work groups comprised of 20-25 nationally recognized representatives with the requisite expertise have been organized and assigned specific tasks so as to contribute ideas and data to the final plan. The 6 formal work groups are: Monitoring, Scientific Understanding, Policies & Practices, Chemical Emergencies, Serving Communities, and Education & Communication. The AACT is well-represented on two of these groups. Dan Goldstein (Monitoring), Alan Woolf (Monitoring), Mark Kirk (Chemical Emergencies), James Madsen (Chemical Emergencies), Anthony Tomassoni (Chemical Emergencies), and Michael Greenberg (Chemical Emergencies) are active participants in this dialogue.

It is anticipated that toolkits, web-based discussion strings, and other activities of the *National Conversation* will soon be posted at their website:

<http://www.atsdr.cdc.gov/nationalconversation/index.html>

AACT members are invited to visit this website periodically to keep abreast of these exciting developments with regard to the use of chemicals in the United States. Comments are being taken by the leadership of the National Conversation at the following Internet address: nationalconversation@cdc.gov

AACT members may wish to add their own thoughts and perspectives as a valuable contribution to shaping the government's environmental protection policies and practices in the future.

Archives of the Drug Information Service at Upstate Poison Center SUNY Upstate Medical University; Syracuse, NY

Jamie Nelsen, Pharm.D. DABAT

Illustrative Case: A 30 YOF was administered promethazine prior to a procedure to manage anticipated nausea. Approximately one hour later she was transferred to the ED due to a presumed adverse drug reaction. The patient is restless, nervous, rocking back and forth. She is described as AAO x 3, but "not quite right". The patient has been given diphenhydramine 25 mg IV x 1 and lorazepam 2 mg x 2 without observed response. The patients vital signs include: BP 189/98 mmHg; HR 117 bpm; RR 22 bpm; afebrile.

By the end of this review the reader should be able to:

- 1) Identify various types of dyskinesias based on presenting symptoms
- 2) Provide optimal management strategies based on clinical symptoms
- 3) Provide education regarding the etiology and care of patients with drug induced movement disorders (DIMDs)

Defining Dyskinesias: Dyskinesias broadly refer to abnormalities in motor tone and difficulty or distortion in performing voluntary movements. There are several types of movement disorders, but this review will focus primarily on the acute DIMDs.

- a) **Dystonia:** A sustained, involuntary muscle contraction or spasms resulting in abnormal postures or twisting repetitive movements. Affected body parts typically include: jaw, back, neck, eyes. Depending on the affected muscle group, difficulty with walking, breathing, speech, and swallowing may occur.
- b) **Choreoathetoid:** Abnormal, irregular involuntary movements often described as writhing or twisting. Symptoms are not painful but may result in embarrassment in social settings. The orofacial region, tongue, upper and lower extremities are often involved. Lip smacking, chewing movements, and tongue protrusion are common. (*A chronic disorder tardive dyskinesia can also result in some of these findings, although it is unlikely to present in the ED and is therefore not discussed.*)
- c) **Akathisia:** A subjective feeling of restlessness and need to move. It is clinically described as difficulty sitting still, repetitive leg movements, restlessness, and a subjective feeling of inner agitation.

Pharmacology and Management: It is important to be able to recognize and identify a particular subset of movement disorder. In doing so, you will have greater insight into the pharmacology of such DIMDs and therefore

be better able to select the most appropriate management. Please note lists of associated drugs are NOT complete.

- a) **Dystonia:** Dopamine withdrawal or antagonism (**not enough dopamine**) causes a release of acetylcholine (Ach) in the basal ganglia, resulting in increased motor tone. The optimal treatment therefore aims to block Ach binding using an anticholinergic drug, such as diphenhydramine (25-50 mg IV).
- Associated drugs include: antipsychotics, antiemetics,
- b) **Choreoathetoid:** Drugs that **increase dopamine** in the basal ganglia ultimately results in decreased inhibitory tone (GABA) which manifests as choreoathetoid movements. Notably, this etiology is the opposite of the cause of dystonia. Consequently optimal management is obtained via removal of the offending agent and a benzodiazepine (preferably diazepam for rapid onset) as clinically indicated.
- Associated drugs include: stimulants, carbidopa/levodopa
- c) **Akathisia:** Is thought to be the result of **acute dopamine antagonism** and resultant increased norepinephrine in the basal ganglia. Treatment, therefore would consist of reducing the dose (or removing) the offending agent, and using a lipophilic beta-antagonist (such as propranolol) to reduce the central hyperactivity. Management may also be augmented by a benzodiazepine.
- Associated drugs include: antipsychotics, antiemetics, lithium, SSRIs

Considerations: Based on the noted pharmacology and management strategies discussed above, it would be wise to remember a few caveats:

1. Remember to consider the half-life of the inciting drug. It is often longer than the half-life of the treating agent (diphenhydramine, propranolol) and repeat doses may be needed. The clinician should be made aware of the need for continued therapy and the patient counseled appropriately. Ultimately duration of therapy will be determined based on reappearance of symptoms once therapy is stopped.
- Ex: risperidone ($t/2 \sim 24h$) induced dystonia would warrant 48-72 h of diphenhydramine q 6-8 hours.
- Ex: fluphenazine ($t/2 12-20 h$) induced akathesia would warrant 24-72 h of propranolol q 6 hours.
2. Although patients with akathisia may have accompanying anxiety, these patients should not receive dopamine antagonists such as haloperidol or atypical antipsychotics, as this may contribute to their etiology.

It is important to distinguish choreoathetoid movements from dystonias in order to avoid inadvertently making the patient anticholinergic with a therapy (such as benadryl) that is not expected to work considering the etiology (too much dopamine).

Case Continuation:

This patient has clinical manifestations of toxicity most closely associated with akathesia. The MD has already given 10 mg ativan without response. The following was advised: 1) propranolol 60 mg oral, or can try 1 mg IV if can't take oral, 2) switch to diazepam for quicker onset, 3) avoid haldol. The MD called approximately an hour later to say that the patient had an excellent response to propranolol and

diazepam. Follow up the following day revealed that the patient was AAO x 3 and did not need additional therapy.

References

1. Lindenmayer JP. The Pathophysiology of Agitation. *J Clin Psychiatry* 2000;61(S14):5-10.
2. Richelson E. Receptor Pharmacology of Neuroleptics: Relation to Clinical Effects. *J Clin Psychiatry* 1999;60 (suppl 10): 5-14.
3. Chen JJ, Swope DM. Movement Disorders. In: Drug-Induced Diseases: Prevention, Detection, and Management. Eds: Tisdale JE, Miller DA. 2005. ASHP, Bethesda, MD.

Clinical Toxinology Short Course: March, 2010 Women's & Children's Hospital, Adelaide, Australia

Who is this course designed for?

Primarily for doctors requiring detailed and practical information on snakebite, spiderbite, scorpion stings, marine envenoming, poisonous plants & mushrooms and related topics with a global and Australian perspective. It is particularly relevant for those working in emergency medicine, toxicology, intensive care, or in rural practice. Throughout there will be an emphasis on practical clinical issues and development of clinically relevant skills. It will also be of interest to poisons information pharmacists and graduate nurses in emergency medicine. You should be fluent in English, as no language translation will be available.

When and where are the courses held?

The course runs over 6 days; Tuesday March 2nd to Sunday March 7th, 2010. The venue is the Women's and Children's Hospital, North Adelaide, SA, Australia

What does the course cover?

Course content is available on the web at:
<http://www.toxinology.com>

Is the course accredited in any way?

The course is a University of Adelaide postgraduate training course. We are seeking formal accreditation of

continuing education points with relevant colleges and possible incorporation within some college specialist training schemes.

What sort of practical clinical sessions are included?

The programme includes a number of interactive sessions discussing "clinical evolving problems" (CEPs) to develop registrant's understanding of clinical skills in toxinology and test those skills in a group setting. These are all based on real patients contributed by faculty members, drawn from their own clinical experience.

Is there any formal evaluation of my performance on the course?

Yes! Faculty will be evaluating all registrants on their interactions, especially during the clinical evolving problem sessions. On the Saturday there will be a written examination.

How To Enrol:

Please contact the Course Coordinator, Assoc. Prof. Julian White (fax ++618-8161 8024; email: julian.white@adelaide.edu.au; internet www.toxinology.com) for course details and enrolment forms.



AACT Online Membership Renewal: 2010

As we continue to find new ways to grow our services, we also are always looking to grow the clinical toxicology community of AACT.

This year we are pleased to announce the launch of online membership renewals at www.clintox.org. As a member, you can now login to your online account, and automatically be taken to the page that allows you to renew your subscription. Additionally, members can specify what SIGs they are currently part of, or would like to become a part of. Updating this information ensures that you are receiving the most up-to-date and pertinent information for your needs. If you still need a username and password to the new site, click "Need a Password" in the upper right corner. Follow the instructions and you will get online "Member Only" access immediately.

If you need any assistance logging in, please don't hesitate to call or email rdonovan@clintox.org.

And, to help make that commitment even easier, we are offering two great incentives for you to take advantage of:

- **10% Savings**: Receive 10% savings off your membership dues when you pay for two years of dues at once.
- **Even More Savings**: Receive 10% refund on your paid dues for every new full member you refer, up to 10 members, for a possibility of a complete refund!
 - Referral discounts will apply for referrals of new members that are applying for FULL membership, and using your name as the referral source on the application.

Call for Nominations: AACT President Elect

Michael I. Greenberg, MD, MPH, FAACT

An election will be held this Spring to choose a new President-Elect for AACT. This individual will take office as President-Elect following the NACCT meeting in Denver this Fall (2010) and will take office as AACT President following the NACCT meeting in 2012.

The process for developing a slate of candidates to run for any AACT office involves deliberations by the AACT Nominating Committee, the body that actually chooses the individuals to run for a given office within AACT. I would like to issue this solicitation to the general membership to put forth the names of individuals to be considered by the Nominating Committee to run for the office of

President-Elect. After personally discussing if it would be appropriate to put forth a given name with that individual, please forward that person's name and curriculum vitae to my attention at mgreenberg199@gmail.com. Self nominations for consideration by the Nominating Committee are permissible.

This solicitation will remain open until midnight on February 1, 2010, and the candidate slate will be chosen by the Nominating Committee at the Winter Board of Trustees meeting in late February.

Thank you for your continued support for the American Academy of Clinical Toxicology.

International Congress of Toxicology IUTOX Trainee Awards

Christy Ours, IUTOX

Along with the Junior and Senior Travel Fellowships to attend ICT XII in Barcelona, Spain, IUTOX has two additional opportunities for young scientists to attend this meeting!

International Congress of Toxicology IUTOX Trainee Awards

IUTOX Trainee Awards: Graduate students and post-doctoral fellows are invited to submit their International Congress of Toxicology (ICT) poster abstracts for consideration in the IUTOX Trainee Award poster competition.

Submissions will consist of: (1) The poster abstract, as it will be presented at the ICT Meeting, in electronic form (Microsoft Word or Adobe Acrobat pdf) in a 8.5" by 11" page format with a 12 or 14 font size (2) a two-page letter from the faculty advisor that indicates the significance and potential impact of the work, also in electronic form. Submissions must be received by the IUTOX Secretary General no later than January 31 of the year in which the International Congress of Toxicology is to be held. The review of nominations is the responsibility of the IUTOX Education Commission.

Winners will receive a plaque and a monetary award. **Graduate Students:** Plaques for 1st through 3rd place as well as monetary award (1st Place \$500, 2nd Place \$300, Third Place \$100). **Post-Doctoral Fellowship Award:** Only one will be awarded and it will include a plaque and \$500. Awards will be announced at the ICT meeting.

International Congress of Toxicology IUTOX Early Toxicologist Award: The purpose of the IUTOX Early Toxicologist Award is to recognize and stimulate outstanding research in toxicology by newly established investigators. The Award consists of a plaque and reimbursement of the travel expenses incurred to attend the International Congress of Toxicology (ICT); the Award will be presented once every three years, at the ICT meeting.

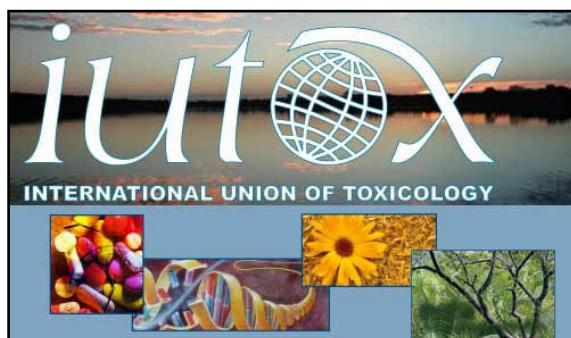
In the year of the ICT meeting, a candidate must have less than 10 years experience since obtaining his/her highest earned degree. Originality of the research, the significance of the contribution and its impact in the field of Toxicology, in addition to the clarity and excellence of data presentation, are important criteria. Candidates will not be judged in comparison with the work of more mature and experienced investigators.

Nominations should be made by the home Society, or, if the applicant does not have a national toxicology society, by his/her department.

Nominations shall be accompanied by: 1) Two letters of recommendation from senior colleagues describing the importance of the candidate's work and information on how the sponsor believes the candidate's career will advance the field of Toxicology. 2) Up to three published articles, or manuscripts accepted for publication, that are representative of the candidate's work. The contribution of the candidate to any jointly authored reprints and manuscripts should be made clear. 3) The candidate's curriculum vitae, of no more than two pages.

Nominations for this Award must be submitted to the IUTOX Secretary-General *no later than January 31, 2010*. Send applications to: IUTOX Headquarters, 1821 Michael Faraday Dr., Suite 300, Reston, VA 20190, or by e-mail. The Award recipient will be notified by March 1 of the year of the ICT meeting. Formal presentation of the Award will be made at the ICT meeting, at which the Award recipient will be invited to give a 15 minute presentation.

For additional information please contact: Christy Ours, iutoxhq@iutox.org



NAACT 2010: Get Ready!

Time to think of NACCT, 2010 in Denver! A formal "call for abstracts" will be distributed soon. All abstract submission and meeting information will be posted at www.clintox.org. Electronic submission of all abstracts will be available starting

January 18th, 2010. Deadline for submissions this year will be April 7th, 2010, at 11:59 pm, EDT. All abstract presenters, for both poster and platform sessions, must register for the NACCT.

Upcoming Meetings

NACCT 2010 October 2010

Denver, CO

www.clintox.org

American College of Medical Toxicology
8th Annual Spring Conference
March 12-14, 2010
Scottsdale, AZ
<http://www.acmt.net>

Midwest Association for Toxicology and Therapeutic Drug Monitoring (MATT)
April 29-30th, 2010
Milwaukee, Wisconsin
<http://www.midwesttox.org/annualMeeting.html>

Southwestern Association of Toxicologists
Spring 2009 SAT Meeting
April 30 - May 2, 2009
San Antonio, TX
<http://www.sat-tox.org/index.php>

American Occupational Health Conference
ACOEM Annual Scientific Meeting
May 2 - 5, 2010
Orlando, FL
<http://www.acoem.org/aohc2010.aspx>

California Association of Toxicologists

Spring Meeting
May 2010
Sacramento, CA
<http://www.cal-tox.org/>

XXX International Congress of the European Association of Poisons Centres and Clinical Toxicologists
May 11-14, 2010
Bordeaux, France
<http://www.eapcct.org/show.php?page=congress>

The Society of Toxicologic Pathology (STP)
2010 Annual Meeting
June 19-24, 2010
Chicago, Illinois
<http://www.toxpath.org/>

IUTOX 2010 Congress (XII International Congress of Toxicology)
July 11-15, 2010
Barcelona, Spain
<http://www.icoah2009.co.za/cgi-bin/giga.cgi?c=1600>

The International Association of Forensic Toxicologists (TIAFT)
Joint Meeting with the Society of Toxicological and Forensic Chemistry (GTFCh)
Bonn, Germany
August 29-September 2, 2010
<http://tiaft2010.gtfch.org/>

Society of Forensic Toxicologists (SOFT)