

American
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Update from the Secretary-Treasurer

Martin Caravati, MD, MPH



For this month's newsletter, I refer you to some important Academy information provided to you by our new Secretary-Treasurer. Dr. Caravati has been working hard to learn the many tasks that this job requires. The Academy is fortunate to have his talents as we continue to move the organization forward.

Membership in the Academy is steadily growing with a 10% increase over this time last year. The increase is almost entirely in the category of "active" members and the total count as of March 2007 is 746 members. Jerry Leikin, as Chair of the Membership Committee, and Mike Greenberg, as President-Elect, are actively

pursuing collaborations with other toxicology societies to increase our membership.

Renewing members are the mainstay of our organization. Membership dues are the largest component of the Academy's revenue. For budget planning, journal distribution, and cash flow purposes, it is important that members renew and pay dues in a timely manner. The cost of collecting delinquent dues detracts from our ability to fund programs to the fullest extent. Thank you for paying dues on the first request. Speaking of dues, your subscription to *Clinical Toxicology* is included as a direct benefit. The cost of the journal to the Academy will increase by 30-35% this year in anticipation of an increased number of issues. The Board of Trustees will do everything to keep dues payments at their current level as a benefit to members.

The Academy is currently in a stable financial position. Membership dues, the Pre-meeting symposium, provision of CE, and the NACCT main congress provide
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AACT Partners with EAPCCT to Support Clinical Toxicology in Central Europe

Martin Caravati, MD, MPH, Secretary-Treasurer, AACT
Irma de Vries, MD, Treasurer, EAPCCT

The Academy has partnered with the European Association of Poison Centers and Clinical Toxicologists (EAPCCT) to sponsor Central European clinical toxicologists and poison center information specialists. The program includes full membership in the EAPCCT, receipt of *Clinical Toxicology*, a reduced rate registration for the annual EAPCCT Congress, and free admission to the EAPCCT pre-congress continuing education day.

Depending on the financial situation in a country, sponsorships are available for applicants from the following countries: Bosnia Herzegovina, Bulgaria, Estonia, FYROM, Hungary, Latvia, Lithuania, Romania, Russia, Serbia and Montenegro, and Ukraine. Applicants

can be working in a poison control center or clinical department and need to be under 40 years of age.

Currently, 10 sponsorships are awarded. Selection criteria for this first group were acceptance of quality abstracts for oral or poster presentations at the EAPCCT Congress. It may expand to 15 sponsorships in the future.

The Academy donates its royalty revenue from the publication of *Clinical Toxicology* and any net income from providing Continuing Education credits at the EAPCCT Congress in support of this program. The start of this program was discussed in 2006 between Nick Bateman (EAPCCT) and Mike McGuigan (AACT).

An Anticholinergic Celebration of Jamestown's 400th Anniversary

Trevonne Thompson, MD Senior Fellow: Toxikon Consortium

Timothy B. Erickson, MD, FACEP, FAACP, FACMT: University of Illinois at Chicago

Recently, in May 2007, England's Queen Elizabeth II visited the United States to celebrate the 400th Anniversary of the founding of Jamestown, Virginia, the first permanent English settlement in the New World. Every toxicologist worth their historic salt should associate Jamestown with *Datura stramonium* also known as Jamestown weed, Jimson weed, Locoweed, Angel's Trumpet, Thorn Apple, Devil's Trumpet, Mad Apple, Stink Weed, Sacred Datura, Green Dragon, and Devil's Trumpet. Jamestown weed received this name from the settlement, where British soldiers were secretly drugged with the plant while attempting to suppress Bacon's Rebellion.

In 1676, Nathaniel Bacon led the first rebellion in the American colonies. The elite farmers on the Atlantic coast, called the "tidewater gentry," owned much of the premiere farmland with a disproportionate amount of political clout, much to the objection of the majority comprised of small farmers, indentured servants and slaves. These farmers, unable to afford the best lands, were forced to the back country making them more vulnerable to attack by Native Americans. Back country farmers also had difficulty moving their goods to markets and were issued higher taxes. The governor of Virginia, Sir William Berkeley, levied an additional burdensome tax for the construction of ineffective forts to defend the colonists. Bacon drew support from the colonists and demanded a commission to raise a militia to fight the "Indians of the frontier." After returning to Jamestown, conflicts ignited between Bacon and Berkeley and their fellow supporters. The Baconites overpowered the Berkeley clan and the governor was forced to retreat. Bacon's followers ravaged the city, destroyed the symbols of the aristocratic government, and seized property. Later that year, Berkeley led a counter siege with British soldiers against Bacon, which resulted in the burning and destruction of Jamestown in September, 1676. Bacon died as a result of "flux and lice" on October 26, 1676.

According to historic accounts, the British soldiers fighting Bacon were unknowingly poisoned with the Jamestown weed and spent several days "chasing feathers, making monkey faces, generally acting like lunatics, and indeed failed at their mission."

"Some of the soldiers sent thither to quell the rebellion of Bacon (1676); and some of them ate plentifully of it, the effect of which was a very pleasant comedy, for they turned natural fools upon it for several days: one would blow up a feather in the air; another would dart straws at it with much fury; and another, stark naked, was sitting up in a corner like a monkey, grinning and making mows [grimaces] at them; a fourth would fondly kiss and paw his companions, and sneer in their faces with a countenance more antic than any in a Dutch droll.

In this frantic condition they were confined, lest they should, in their folly, destroy themselves—though it was observed that all their actions were full of innocence and good nature. Indeed, they were not very cleanly; for they would have wallowed in their own

excrements, if they had not been prevented. A thousand such simple tricks they played, and after 11 days returned themselves again, not remembering anything that had passed.'

- Robert Beverly, *The History and Present State of Virginia*, 1705

Apart from colonial Virginia, *Datura* has also been described throughout history as a poison famous for its mind-altering properties. References to the plant are made in Homer's *Odyssey*, and Shakespeare's plays: *Hamlet*, *Romeo and Juliet*, and *Anthony and Cleopatra*. In Haiti, *Datura stramonium* is referred to as "zombie cucumber." The voodoo religion uses zombie cucumber and other ingredients in an ointment to decide if a person is lying or telling the truth. If the person is telling the truth, the person survives. If a person is lying, the person dies and becomes a zombie.

In modern times, exposure may be accidental by gardeners or farmers clearing fields. The toxic effects are seen most commonly in adolescents, who intentionally misuse the weed for hallucinogenic and euphoric effects. Serious morbidity and rarely death result from the toxic anticholinergic properties. Clinically, the patient may present "blind as a bat, mad as a hatter, red as a beet, hot as hell, dry as a bone, the bowel and bladder lose their tone, and the heart runs alone." *Datura* is used as a readily available alternative to illegal drugs. Some American states do have laws regulating its use and distribution. It is typically consumed as an herbal tea, but can also be ingested or smoked. Overall, it has a low demand as a recreational drug, because it has a reputation of producing a poor and unpleasant high. If toxicity is severe, the patient may require hydration, active cooling, and administration of benzodiazepines or the antidote physostigmine.

So, with your next spot of Earl Grey tea, raise a cup and extended little finger to Jamestown and Bacon's Rebellion; add one lump of zombie cucumber, steep, and enjoy.

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In The Literature

David Juurlink MD, PhD

Prospective Study of Hydroxocobalamin for Acute Cyanide Poisoning in Smoke Inhalation. Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. *Annals of Emergency Medicine* 2007;49(6):794-801

Background

Among fire victims, smoke inhalation is responsible for a greater number of deaths than burns. Cyanide is one of the most feared products of combustion—it kills quickly, and because diagnostic testing is not generally available, its presence must be inferred from clinical information. Consequently, antidotal therapy must be given in the absence of diagnostic certainty. With the exception of sodium thiosulfate, antidotes such as amyl nitrite and sodium nitrite pose considerable risks to the patient. These include hypotension, which is often present prior to treatment, and methemoglobinemia, which further compromises oxygen delivery. Recently, hydroxocobalamin has emerged as an appealing alternative, with relative safety demonstrated in volunteers¹ and compelling evidence of efficacy in a canine model of cyanide poisoning.²

Methods

This was a prospective case series of patients aged 15 years and older who were extricated from residential fires in Paris between 1987 and 1994. All patients had clinical signs of inhalational injury (soot in the mouth, etc.) and were suspected of having cyanide exposure. Patients with extensive burns, major trauma, and those with obvious pregnancy were excluded. After examination by a physician at the scene, patients received hydroxocobalamin 5 grams intravenously over 15 to 30 minutes, in addition to supportive care. Up to two additional doses were given at the discretion of the treating physician. Other cyanide antidotes were not employed, and there was no comparison group. The investigators did not specify the primary outcome measure, but an extensive amount of clinical and laboratory data was collected on each patient.

Results

The study included 69 patients with a median age of 44 years. The majority of patients had neurologic impairment, and 39% had coma. Roughly two thirds of patients were eventually determined to have cyanide exposure (median cyanide level 52 $\mu\text{mol/L}$; interquartile range 0 to 250). The majority also had evidence of carbon monoxide exposure and underwent treatment with hyperbaric oxygen. The investigators collected only short-term outcome data, and complete follow-up information was not available for all patients.

Of the 69 patients treated with hydroxocobalamin and admitted to the critical care unit of the study hospital, 50 (72%) survived. As expected, survival varied as a function of cyanide poisoning status and history of cardiac

arrest. In fact, the majority of deaths occurred in patients who had experienced cardiac arrest at the scene, while most others died of complications related to hospitalization. Among patients later confirmed to have cyanide poisoning, survival was inversely proportional to the cyanide level.

Among patients with neurologic impairment prior to antidote administration, 71% experienced complete neurologic improvement, 9% experienced persistent neurologic sequelae, and 29% died. The time course of these improvements in relation to antidote therapy was not specified. Because a placebo group would have been unethical, and because no other antidote was used for comparison and cointerventions varied among study patients, it is not possible to precisely quantify the effect of hydroxocobalamin.

Hydroxocobalamin was generally well tolerated. Hypertension is a known effect of hydroxocobalamin,³ and many patients in this study experienced a favorable change in blood pressure following the first infusion of hydroxocobalamin. The mean increase in systolic blood pressure was 15 mm Hg (range -60 to 160). Only 3 patients developed frank hypertension, the definition of which was not provided. Other adverse effects (chromaturia, etc.) were minimal.

Implications for Practice

With an “eye of faith”, these data suggest that hydroxocobalamin may improve the neurologic and hemodynamic status of patients with combustion-related cyanide poisoning who are treated at the scene. As the authors freely admit, a prospective case series cannot prove the efficacy of hydroxocobalamin. To do so would require a comparison group and, ideally, a randomization process. However, use of the antidote was associated with clinical and biochemical improvements in some patients. In conjunction with other converging lines of evidence,^{1,3} it is reasonable to infer that at least some of these improvements might be the direct result of treatment with hydroxocobalamin.

What this study does tell us is that hydroxocobalamin is relatively safe for prehospital treatment of critically ill smoke inhalation patients with suspected cyanide poisoning, regardless of whether cyanide is actually present. In this regard, it is clearly superior to the traditional antidote kit. Safety trumps efficacy, especially when the latter is unknown, and many clinicians will likely opt to use hydroxocobalamin over methemoglobin-inducing agents when given the choice.

Some additional points are worth noting. Antidote therapy is a time-sensitive intervention, and few jurisdictions have the advanced prehospital care available in Paris. Whether or not the possible benefits of hydroxocobalamin persist after the sometimes lengthy transport to hospital is unknown, as is the drug’s place in therapy for less seriously poisoned patients. Finally, the drug is relatively expensive, it has a modest shelf life, and there is presently no reimbursement from the manufacturer for outdated supplies.⁴ A formal cost-effectiveness analysis of this antidote would be welcome.

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In Memory of Dr. Howard C. Mofenson

Tom Caraccio and the staff of the Long Island Regional Poison and Drug Information Center

Dr. Howard Mofenson, a pediatrician, and Medical Director of the Long Island Regional Poison and Drug Information Center for more than 40 years, died on April 7, 2007 from heart failure.

Dr. Mofenson was a lifelong resident of Mineola, who liked to say his medical career was forged on the battlefield in Europe. Serving as a 19 year old medic under Gen. George Patton in World War II, he lost part of his leg and had to have a plate inserted in his skull after a bomb exploded as he was crossing a bridge.

After recovering from his wounds, he attended Ursinus College in Collegetown, Pa., where he met Lois, his wife of almost 60 years. He graduated from Jefferson Medical School in Philadelphia in 1951.

He returned to his hometown to set up practice, becoming the first pediatrician in Mineola. Dr. Joseph Greensher joined him as his partner in 1962. He and Greensher, now the Medical Director at Winthrop-University Hospital in Mineola, were partners for 20 years.

Dr. Greensher said they became interested in the poison center in the early 1960's after many children had died from taking aspirin. Dr. Mofenson began to study clinical toxicology and he became the first Director of Long Island's Poison Center, currently housed at Winthrop University Hospital.

Dr. Mofenson recognized quite early on the need for developing not only the Long Island Center but also the other poison control centers in New York State. According to Dr. Lewis Goldfrank, who accompanied him to many meetings with the NY State Poison Centers at the time, "Howard always added to the group's knowledge of how our system should work and how our problems should be solved. He contributed extensively to the breadth and depth of the system that we now call the New York State Poison System. He was a leader in developing our entire effort across the country."

He was also a much beloved teacher at Stony Brook University's medical school, where he was awarded an excellence-in-teaching award five times. He inspired his first daughter Lynne to become a doctor. According to her, he made house calls long after other doctors had given up the practice. Once, when she was in graduate school studying clinical psychology, she went with him to the hospital, where he was treating a child with a brain disorder. It was at that moment that she decided to switch her career to become a pediatrician. She is currently a pediatric infectious disease physician at the National Institutes of Health in Bethesda, Md.

Dr. Mofenson clearly loved medicine and children. He often would get calls from patients that he treated many years ago as a child who would inform him of their progress on a certain condition just so he

would know. He was an amazing diagnostician who often picked up on things no one else did. This keen "detective" sense proved extremely valuable for solving many of the toxicology cases that were a mystery to physicians who confronted patients with unusual signs and symptoms.

In the Poison Center, Dr. Mofenson was known for his constant attendance to details and meticulous analysis of knowledge. The staff considered him a walking encyclopedia of medical and toxicology information. He will probably be remembered most in the field of toxicology for developing the concept of toxicological syndromes which he called "toxidromes." He diligently typed up everything he read from medical journals into protocols that would then be used on a daily basis in the center.

The staff particularly liked to hear about the latest medical news he had read and looked forward to the discussions which followed. The medical or pharmacy students rotating through the center would also relish the many lectures and lively discussions that he gave. No question was ever foolish and it never failed that these students bonded to him by the end of their rotations. Dr. Mofenson also had no qualms about letting anyone know how he felt on issues, especially physicians. If he felt a clinician was overlooking some important point in a patient's care that needed to be addressed, he would make sure that physician understood loud and clear why he should follow his advice. Under his tutelage Dr. Mofenson's standards became the Poison Center's standards. This is part of his legacy.

His concern for his staff was exemplary. Virtually every staff member has sought his advice at one time or another—whether it was medical or personal. Sure enough, he would always follow up with a "how's your mother doing," or "how did your son make out?" If one of the staff was out ill for an extended time, they would get a phone call from him to see how they were doing. Along with the staff, he cheered their happy milestones. The work place was more like an extended family. The staff is very grateful.

Over the years, Dr. Mofenson became a leading expert in poisonings, having published chapters in 41 textbooks and 216 articles on pediatrics and medical toxicology.

He and his wife, Lois, have three children, three grandchildren and one great-grandchild.

Dr. Mofenson was the staff's mentor, advisor, and friend. The Poison Center says farewell to a superb man who was loved and respected. The Center will miss him, and we will never, ever forget him.

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All AACT Elections Will Be Conducted by Electronic Ballot

E. Martin Caravati, MD, MPH, Secretary-Treasurer, AACT

Since the 2007 President-Elect election and By-laws change by electronic ballot was so successful, the Board of Trustees voted at the 2007 mid-winter meeting that all future AACT elections are to be held by electronic ballot. The electronic ballot will be accessible through any computer with Internet access via a web link. This is cost effective in terms of staff time and postage.

All future notifications of upcoming elections will be sent to members by e-mail if possible. For those who do not have e-mail access, notification of elections will be made by postal mail but you will still need to vote via the Internet.

The AACT asks that you please notify the AACT membership office of any changes to your e-mail or mailing address. If you know that you will not have e-mail access in the future, please provide a current mailing address.

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Update from the Secretary-Treasurer

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the bulk of revenue. Operational/administrative expenses (management, accounting, insurance, etc) are approximately 22-25% of revenue, with the remainder going to funding the mission and programs of the Academy. The Academy will undergo a full

financial audit this year as required by the bylaws. Budget requests to the Board of Trustees for the 2008 fiscal year should be made in writing to President Bond by September 1, 2007 for consideration at the Fall Board meeting.

Respectfully,
Martin Caravati, MD, MPH