

STC NEWS/NOUVELLES

VOLUME XXIV, No 2, November 2005

BULLETIN OFFICIEL DE LA SOCIÉTÉ DE TOXICOLOGIE DU CANADA
OFFICIAL NEWSLETTER OF THE SOCIETY OF TOXICOLOGY OF CANADA

C.P./P.O. Box 517, Beaconsfield, Quebec, Canada H9W 5V1 <http://www.stcweb.ca>

TABLE OF CONTENTS

FAMOUS POISONS (Bill Racz).....	2
THE PERSPECTIVE OF THE PRESIDENT (Barbara Hales).....	4
ICTXI PLANNING UPDATE (Malle Jurima-Romet, Dave Josephy and Doug Arnold).	5
TRIVIA CORNER (Bill Racz).....	6
THE VIEW FROM MY CANOE (Don Ecobichon).....	6
BOOK REVIEW (Don Ecobichon).....	8
NEWS ITEMS (Bill Racz).....	9
EDUCATION CORNER (Bill Racz).....	10
CONFERENCES, MEETINGS AND WORKSHOPS.....	11

VOLUME XXIV, NUMBER 2
NOVEMBER 2005
2004-2005

President..... Dr. Barbara Hales
Past President..... Dr. Sheldon Roth
Vice-President..... Dr. Michel Charbonneau
Secretary..... Dr. Jeff Kawamoto
Treasurer..... Dr. Daniel Cyr
Executive Director..... Dr. Gordon Krip
Councillors..... Dr. Timothy J. Shrader
..... Dr. Lena King
..... Dr. Daniel Sitar

Editor: Dr. William J. Racz,
e-mail: raczw@post.queensu.ca
Tel: (613) 533-6113

FAMOUS POISONS

Bill Racz

The title of the lead article in a magazine was “12 Toxic Tales”. This peaked my interest and I immediately scanned the article; to my horror, I did not find acetaminophen on the list, but being open minded I read on, disgruntled, but I read on. Before you read further take pen in hand and list the poisons that have historical or are of public interest. Let us see if you agree with the list presented by the article.



The article examines the concept of when is a xenobiotic a poison and when is it a drug and uses arsenic and botox as examples. The article gives the famous quote by Paracelsus “All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy.”

Arsenic: Arsenic is probably the most famous and notorious poison of all time. The poison of kings and the king of poisons. It was reported that Hippocrates used arsenic to treat ulcers and later arsenic became a component in Fowler’s Solution, an agent used to treat a number of disorders. The father of chemotherapy, Paul Erlich, designed organic arsenicals as treatment for syphilis. William Osler, stated that arsenic was the best treatment for leukemia; it is still used for this purpose today.

Arsenic is odorless, tasteless and usually colorless and as it acts in an insidious manner when given in small doses over a long period of time. It was an ideal poison for those wishing to dispense with an adversary before the era of forensic medicine.

Arsenic could also be given as a larger single dose with more immediate results. This was the manner in which the compound was used by the Borgias. Alexander VI and his son Cesare, used wine laced with arsenic to dispatch their victims. Apparently they prepared wines containing arsenic with the care used to develop a great vintage. It is reported that they appointed Cardinals and Bishops and allowed them to accumulate wealth, by whatever means, and then invited them to dinner and offered the laced wine. As directed by church law the estate of the bishops and cardinals would revert to the Borgias. Many Romans stated “I am dining with the Borgias tonight” but very few stated, “I dined with the Borgias last night.”

Was Napoleon Bonaparte poisoned with arsenic or did he die of natural causes? I shall not attempt to answer this question as many historical whodunits have failed and undoubtedly I would fail as well, but I will give a few clues. It is important to consider that Napoleon had enemies, British and French Royalists who wanted him out of the way for good. Arsenic was found in samples of Napoleon’s hair. Is the source of arsenic a case of poisoning or misadventure? Arsenic was found in the wallpaper (Scheele’s green or copper arsenite) of his room and arsenic was commonly used in personal products of the day. Did his physicians over treat him with arsenic for the ulcer that was found on autopsy? Autopsy also revealed a malignancy but this was probably not sufficiently advanced to be the cause of death.

I personally prefer the story that Napoleon was poisoned by the Count of Montholon, with whose wife he allegedly had an affair. A case of revenge? I love intrigue.

In short there are as many stories about Napoleon's death as there are people who study his life, and there is no agreement about the cause of his death, among the so called experts. Agatha Christie where are you when I need you?

Snake venom. There are at least 400 species of poisonous snakes in the world, some more deadly than others. Most members of society have an aversion for snakes, including me. We have used snakes to instill fear in movie patrons, and plays. The most famous being Shakespeare's use of the asp; Cleopatra committed suicide as she held the poisonous asp to her breast. Hannibal devised a strategy where he tossed containers of poisonous snakes on the decks of the opposing fleet, thus using the serpents as a weapon of war. Snake venom is used as a research tool and to develop anti-venom.



Botulinumtoxin: The third best known poison to society is botulinum toxin. In 1971 a man in New York died of botulinum poisoning after eating tainted vichyssoise that was under processed. The threat of botulinum poisoning resulted in the addition of nitrites to prepared foods even though there were very few cases of botulinum poisoning in North America. In the last decade and half, Botox, as it is now called, has been used to control muscle spasticity in multiple sclerosis and cerebral palsy and other conditions. I understand that it is also useful for softening wrinkles. The toxin has had a remarkable journey as it moved from poison to drug.

Ricin: No list of popular poisons would be complete if it did not include ricin. Georgi Markov was assassinated in London in 1978 when he was jabbed with an umbrella that was altered to fire a small pellet of ricin.

Subsequent to this incident, ricin has been studied by toxicologists.

Tetrodotoxin: What of tetrodotoxin? Should you be offered a meal of fugu, or puffer fish, I suggest you politely decline. It might be a good time to become a Vegan. Certain species of the fugu produce tetrodotoxin which blocks sodium channels and nerve conduction; the only problem is that most experts have difficulty in distinguishing the various fugu. The toxin is produced in poison glands under the skin and stored in the liver, ovaries, gonads, intestine and skin. The impact of overindulging in fugu is exemplified by the famous Kabuki actor, Mitsugoro Bando, who feasted on fugu liver and liked the tingling sensation it created on his lips and tongue. Unfortunately for Bando, the toxin distributed to other organs and he died of respiratory arrest some eight hours later. Today fugu chefs must pass a rigorous exam and be able to dissect a fugu into edible and non-edible parts in a few minutes and produce a plate of thinly sliced fish, selling for \$500.00 a plate. Apparently "one man's poisson is another man's poison".

Cynide: Cyanide is surely the most notorious of all poisons. Zyklon b, a crystallized form of hydrogen cyanide was used by the Nazis at Auschwitz. The horror created by this agent was and is still unimaginable. It was also the agent used in the gas chambers to execute condemned prisoners.

Venoms: Poisons have long been used as instruments of war and chemical/biological warfare is not a 20th century phenomenon. The first biological weapon is attributed to Hercules who slew Hydra, the many headed serpent of mythology and then dipped his arrows into the poison to enhance their effectiveness. Indeed the word toxic

originates from the Greek word “Toxikon” or poison arrow. The citizens of Hatra repelled the Roman invaders by hurling clay pots containing poisonous scorpions. James Bond survived a potential attack by a black widow spider in one of his better movies. Thus poison carried by spiders and scorpions must be considered among the top ten poisons. Did not tarantula and scorpion venom help elucidate the structure of the potassium channel and lead to a Nobel Prize?



Modern warfare (terrorism) includes anthrax laced letters in the US and sarin released into a Tokyo subway. Last year dioxin was administered to Ukrainian President Yushchenko in an attempt to prevent him from winning the presidency. Any of these three could be on a list of modern toxins and toxicants.

The last agent that I will include on the list is mercury and derivatives. These compounds are environmental contaminants

and are found in our food source. But that is not why I would include the organo-mercurials, it is because I think they have been given a bad rap. Karen Westerhan died 5 months after spilling a “tiny drop” of dimethylmercury on her gloved hand. The mercurial allegedly penetrated the glove and being lipid soluble was absorbed through the skin. This single exposure is claimed to be responsible for her death. I do not buy the explanation! Paracelsus must be spinning in his grave. To accept this single exposure as the cause of death requires a complete disregard of our knowledge of the dose response relationships and toxicokinetics of dimethylmercury. I do not doubt that Dr. Westerhan died of mercury poisoning but the exposure was most likely long term and via inhalation.

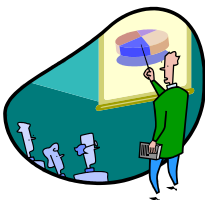
One final note, poisons have been used since before the birth of Christ to dispense of ones political foes. To prevent being killed by poisoned food most members of the nobility employed food tasters. It was a lucrative and often a short career.

THE PERSPECTIVE of THE PRESIDENT

Barbara Hales

Dear Society of Toxicology of Canada members

It is time to make your travel plans and register to attend STC’s 2005 Annual Symposium (December 5 and 6, 2005). Special thanks to the Program Committee, and especially Louise Winn, for putting together an outstanding slate of speakers focused on exposures and child health. Better yet, submit an abstract before the November 8 deadline! New this year, several of those who submit abstracts will be invited to give platform presentations.



This is a special time for STC and for all Toxicology researchers in Canada as July 2007, and with it the International Congress of Toxicology (ICTXI) in Montréal, approaches. This is also a special event for us because it will be the 30th anniversary of ICT1 which was held in Toronto in 1977. We have set as our goal to host the best ICT meeting possible, showcasing Toxicology in Canada to the world. The first announcements (please visit the website at www.ict2007.org) are out and the game is afoot. I should like to encourage all of our members to get involved! Encourage your

students and postdoctoral fellows to join STC and participate in our activities, too. Because of our focus on the international meeting in 2007, for this one year only, we will forego our annual symposium. Our December 2007 annual general meeting will be held in July during the ICT congress. Support STC and get involved in planning

ICTXI in Montreal. Let us know how you would like to help.

See you in Montréal in December!

Barbara Hales
President

ICTXI PLANNING UPDATE

Malle Jurima-Romet
Dave Josephy and Doug Arnold

Planning for the 11th International Congress of Toxicology (ICTXI), which will be held in Montreal, July 15-19, 2007, is continuing, and the pace is picking up. The most recent meeting of the Organizing Committee was held at the Palais des Congrès on September 26th. The official ICT XI website (www.ict2007.org) is a well-organized, attractive, and up-to-date information package for the Congress. (Parts of the web site are bilingual.) Among other items, the web site includes an "Expression of Interest" reply form, a Sponsorship Opportunities Prospectus, traveler and accommodation information, etc. Registration information will be posted soon.

Banquet, and Closing Ceremonies, and Accompanying Persons Program. A special tribute will be held to commemorate the first ICT meeting (Toronto 1977). (If you are aware of any memorabilia or photographs pertinent to ICTI 1977, please let us know!).

Michel Charbonneau has agreed to Chair the Financial Contributions Committee and is charged with raising a quarter of a million bucks. If you happen to have a quarter of a million bucks, please give him a call. If you happen to know someone who has a quarter of a million bucks, please give him a call. Especially, if you can assist Michel by providing contact information for potential sponsors, please contact him at:

michel.charbonneau@iaf.inrs.ca.

The Scientific Program Committee received more than 150 proposals for symposia. These were reviewed and ranked by the International Scientific Program Committee (ISPC). Using their feedback, the National Scientific Program Committee has prepared a draft of the scientific program. This framework will be revised and refined, and the detailed design of the sessions will be completed soon. Letters of invitation will be sent to speakers early in 2006.

Representatives of the Organizing Committee presented a progress report to the IUTOX Executive, at the EUROTOX meeting in Krakow, Poland, focusing on the planning of the Scientific Program. A meeting of the ISPC was also held during EUROTOX-Krakow. Throughout the year, there are many toxicology and related scientific conferences taking place where it would be valuable to promote ICT XI. However, it is not possible for ICT XI Organizing Committee members to attend all of these relevant meetings; therefore, we are looking to the members of the IUTOX Executive Committee, the International

The Local Arrangements Committee (LAC) is planning the social aspects of the Congress, which will include the Opening Ceremonies, President's Reception,

Advisory Committee to ICT XI and the ISPC for help in our promotional efforts by distributing information brochures at these meetings. Of particular note is the assistance of Drs. Tohru Inoue and Wallace Hayes in distributing ICT XI brochures at the Annual Meetings of the Japanese Society of Toxicology, the Irish Society of Toxicology, the American College of Toxicology and the upcoming Indian Society of Toxicology.

If you are planning to go to a toxicology related scientific meeting and would be

willing to take along some ICT XI brochures for distribution, please contact Doug Arnold (doug_arnold@hc-sc.gc.ca).

In closing, I would also like to acknowledge excellent assistance and support of our Congress Secretariat, Messrs. Laurier Forget and Pierre Lamoureux of the National Research Council.

Malle Jurima-Romet
President, ICT XI



Trivia Corner

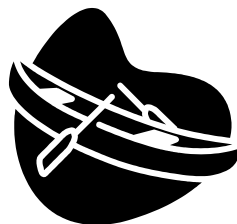
Bill Racz

What is the most toxic substance known to mankind in terms of fatalities per gram?

Read the answer in the next edition.

THE VIEW FROM MY CANOE

The summer has come and gone, the first flock of high-flying, migrating geese being seen around Sept. 20th. It was a peculiarly hot summer with little rain, and the flower gardens gave out early in August. With the recent rain, the plants have perked up again, so they are safe but have had few blooms. My “Aggie” expert tells me that plants shut down above 27^oC. – too true! I did not use the canoe much this summer, the hot temperatures not being conducive to paddling or fishing. We had lots of various biting “bugs” including the longest deerfly season that I can remember. The deer were really stressed by them and, on one occasion, a doe was seen running out of the woods into the field across from us screaming loudly. There have been lots of single and twin fawns born this year so we will be deluged with deer this fall. Some are already into the hostas that they can reach



Don Ecobichon

without actually invading the gardens. Max, our Labrador, has his work cut out for him

this autumn.

Perhaps the most interesting feature in the recent literature has been the Sept. 10th survey of higher education done by *The Economist*, covering primarily the problems of European universities which have progressively surrendered their lead in higher education to the U.S.A. In the year 2000, European officials proclaimed that the European countries would become the world’s premier “knowledge economy” by 2010. However, this has not progressed very far due to the strapped-for-funding situation, the fact that the state demands that universities process more and more students without permitting fees or any increases to the present low fee structure (where it exists), and the problem that professors are

considered to be civil servants. The U.K. is undergoing dramatic, painful changes in restructuring and introducing fees, much to the anger of students and parents – no free ride anymore! Continental universities are far behind in this reorganization, both from rigid practices in current use, a dearth of funding and meddling micromanagement attempts. All of this requires a drastic alteration in policies, something governments appear reluctant to do.

Currently, according to this survey, the U.S.A. boasts 17 of the world's top 20 universities (global ranking carried out by the Shanghai Jiao Tong University), currently employ 70% of the world's Nobel prize-winners, 30% of the world's output of articles on science and engineering and 44% of the most frequently cited papers. Many emerging countries are using the American "model": e.g., Singapore is turning itself into a "know-ledge island" with stem cell research being attracted by high level funding; India is increasing support to its institutes of technology; China is doubling the size of its university student population and pouring vast resources into specific, elite universities. This is an excellent review of future education and well worth reading with lots of facts and figures therein.

In the same issue of *The Economist* (Sept. 10th) is an interesting report on the status of California farm workers. Despite Cesar Chavez's work with the United Farm Workers' Union (UFW) in the mid-1970s (remember the strike of the grape-pickers and boycott of California grapes), little improvement has occurred - \$7.00 US/hr

and a 10-to-14 hr day. Farmers do not hire their own migrant workers but go to labour contractors who supply workers as and when they are needed. The U.S. Department of Labour claims that 53% of America's farm workers are "undocumented" foreigners but, in California, most estimates are as high as 90%. This all boils down to abuse of the system –poor wages, poor housing, poor food and deplorable working conditions. The biggest problem is the poor performance of farm workers' unions. The UFW has between 8,000-27,000 members (80,000 in the 1970s) while the International Teamsters and the Food Workers unions represent only 7,000 labourers. In California, only 2 out of every 100 migrant workers are represented by a union. As we all know, most of these workers are illegal Mexicans who cross the border looking for a better life. However, we should not sit complacently by, since the plight of our "own Mexican workers" in the greenhouse and fruit industries in southwestern Ontario is little better as was illustrated by a documentary presented by TV Ontario on workers in the Leamington region.

Returning to the plight of European universities, the U.K. is attempting to solve their problems by financial aid from the taxpayer to the tune of 1.15 billion pounds/year. Poor students, who currently only get a fee waiver, will be means-tested for grants of up to 2,700 pounds/year and a further means tested loan of up to 3,555 pounds/year, such loans being interest free though inflation-linked. Loans not repaid after 25 years are to be written off.



“Selling Sickness. How The World’s Biggest Pharmaceutical Companies Are Turning Us All Into Patients” by Ray Moynihan and Alan Cassels. Greystone Books, Douglas and McIntyre Publishing Co., Toronto, pp. 254, \$32.95 CDN.

Recently, before the CBC lockout, a piece of medical “news” was featured, the “discovery” of a pill that eliminated the female monthly period based on the argument of why should a woman have to put up with this. You only “need” three cycles/year or even none. It is the old story of “got a problem, we have a chemical solution for you”. Shortly afterwards, the *Globe and Mail* Books Section reviewed the above title.

The gist of the text is that drug companies “brand” not just their drugs but the diseases that go with them and, if there is no such illness, create one.

Selling Sickness makes it quite clear that drug companies want to play a role in health systems by defining who is sick. Canada’s laws prohibit the direct-to-consumer advertising of prescription drugs, but the advertising laws in the U.S.A. were changed in the mid-90s to permit this approach. We have all seen adverts on U.S. television suggesting that you ask your doctor about “drug X”. Meanwhile, physicians are being deluged by detail men, free samples, luncheons accompanied by a speaker glorifying the successes achieved with “drug X”, golf tournaments, cruises, etc., all designed to get the physician to prescribe their new product. The extent to which the pharmaceutical giants go is appalling as are the marketing/promotional costs.

There are ten chapters, each dealing with a particular, seemingly important health issue: e.g. high cholesterol, depression, menopause, attention deficit disorder, high blood

pressure, pre-menstrual dysphoric disorder, social anxiety disorder, osteoporosis, irritable bowel syndrome and female sexual dysfunction. Do these “problems” sound familiar?

The common complaints of life are being transformed into frightening conditions, with the unsuspecting and fearful public being turned into patients ready to take any medication to avoid “getting” the problem(s).

Each chapter has been thoroughly researched pro and con with lots of reference material listed in a 40 page addendum. There is a good index. Obviously, each topic cannot be reviewed here, but I would like to illustrate the tone of the approaches by looking at high cholesterol levels and increased risk of heart disease. Panels of cholesterol experts have revised the dangerous “level” of high cholesterol downward at least three times, each change placing more and more people at risk. Of course, the panels were loaded with expert physicians tied financially (partial salary, research funding, stock gifts, etc.) to the statin manufacturers. One “expert” received money from 10 such companies. The credentials of the “expert” physician, conference speaker, etc. always extol his/her university affiliations, NOT the financial association in promoting a particular drug. In contrast, other physician and public groups rightly claim that cholesterol is only one parameter in a complex situation and, by itself, most likely plays little role, the statin group of drugs having little effect on heart disease without

serious considerations of diet, smoking, exercise, etc.

The other chapters are presented in the same format, making it very clear that the game is to sell drugs to everyone, not just to sick people, thereby broadening the base of sales and profits. This, of course, reverberates back on the overburdened health care programs with increased costs for diagnoses and prescription drugs over the past decade. Where does it all end?

This is an interesting book, well worth reading and placing on your bookshelf despite the obvious approach of the authors who have extensive credentials in health care policy and drug policy research. It certainly opened my eyes to practices that, in my naivety, I thought had disappeared from the days when I was a pharmacist. They have not “gone away” but have become more subtle, to all our cost.

Bill Racz

News Items

I read with interest the plans to expand The Toxicology Centre at the University of Saskatchewan. According to the article in the Green and White, the U. of S. alumni magazine, The Toxicology Centre will triple its current space. In addition the University’s last two Canada Research Chairs are in the area of toxicology. One new appointee is described as a river systems toxicologist and the other an expert in persistent organic pollutants. The other piece of good news is that the graduate program in toxicology is also thriving.



A recent article in the Whig Standard, Canada’s oldest daily newspaper, caught my attention and I thought I would share it with you. Marv Shepherd, a researcher with the College of Pharmacy at the University of Texas, Austin, while speaking to the National Press Club in Ottawa, warned about the importation of prescription drugs from Canada to the United States. As more and more legislation is enacted in the U.S. there will be greater and greater pressure on the Canadian drug supply to the point that there will be shortages in Canada. He strongly advised that Canada outlaw the exportation of prescription drugs intended for the Canadian market. A sobering thought as the threat of bird flu is a real, if remote, possibility.

News items about your program or toxicology in your institution or any item of interest to the membership of STC would be appreciated.



Education Corner

Bill Racz

I have not had many responses to my questions in “Education Corner”, but there are issues that STC could address, perhaps after ICTXI.

Brain Teaser

Bill Racz

What modern day toxicant, toxin or drug would be appropriate for the purpose described in Shakespeare’s Romeo and Juliet Act IV, Scene I.?



Shakespeare

Friar Lawrence to Juliet:

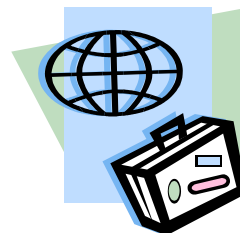
*“Take thou this vial, being then in bed,
And this distilled liquor drink thou off:
When presently, through all thy veins shall
run*

*A cold and drowsy humour; for no pulse
Shall keep his native progress, but surcease;
No warmth, no breath, shall testify thy liv’st
The roses in the lips and cheeks shall fade*

*To paly ashes; thy eyes’ windows fall,
Like death, when he shuts up the day of life:
Each part depriv’d of supple government,
Shall, stiff and stark and cold appear like
death:*

*And in this borrow’d likeness of shrunk
death
Thou shalt continue two-and forty-hours
And then as from a pleasant sleep” ...*

CONFERENCES, MEETINGS and WORKSHOPS:



2005

December 5-6 STC Annual Symposium “The Impacts of Toxicants on Child Health”
Montreal, Quebec
www.stcweb.ca

2006

January 4-7: 7th International Symposium on Biological Reactive Intermediates
Tucson, Arizona, USA
<http://swehsc.pharmacy.arizona.edu/bri>

March 5-9: Society of Toxicology Annual Meeting
San Diego, CA.
USA
<http://www.toxicology.org/ai/meet/am2006/index.asp>

July 2-7: The 15th World Congress of Pharmacology (IUPHAR 2006)
Beijing, China
<http://www.iuphar2006.org/>

Sept. 20-24: Eurotox 2006 / 6th CTDC Congress
Cavtat / Dubrovnik, Croatia
www.eurotox2006-6ctdc.org

Oct. 22-26: 14th North American ISSX Meeting
Rio Grande, Puerto Rico
USA
<http://www.issx.org/>



2007

July 15-19: 11th International Congress of Toxicology, ICT-XI,
Montreal, Quebec
<http://www.ict2007.org/>

2008

July 27 - August 1: The IXth World Conference
on Clinical Pharmacology and Therapeutics
Quebec City, Canada
<http://www.cpt2008.com/>