

STC

NEWS/NOUVELLES

OFFICIAL NEWSLETTER OF THE SOCIETY OF TOXICOLOGY OF CANADA

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***SOCIETY OF TOXICOLOGY OF CANADA INVITES INTERNATIONAL CONGRESS
OF TOXICOLOGY***

TO CANADA FOR 2004.

WAS OUR INVITATION ACCEPTED?

Read all about it on page 2

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FROM THE DESK OF THE PRESIDENT - Len Lillie

Well it was a wild and exciting ride. From the decision of the 1997 AGM on December 4, 1997 to submit a bid for the Tenth International Congress of Toxicology in 2004, to the decision of the General Assembly of the International Union of Toxicology to award ICT X to Tampere, Finland.

The vote was Finland 34, Canada 18, and Brazil 12. This was Finland's third bid for an International Congress of Toxicology and Brazil's second. And while we did not win, I do not feel in any way that we lost either. From a standing start in December we were able to prepare and present a highly credible and competitive bid. STC has been relatively quiet on the international front for some time. Through our efforts with the ICT X bid, we achieved considerable visibility and credibility within IUTOX on which we can build if we choose to do so.

But let me take you back to December and through at least part of the process. To reiterate, we had not planned to make a bid for ICT X because we had been told (in writing) that the National Research Council would not back our bid as they usually do for international scientific meetings held in Canada. We received word in late November that NRC's mandate had changed and that they would now support a bid. Based on that, the 1997 AGM decided that STC should submit a bid to hold ICT X in Montreal in July, 2004 and to spend up to \$20,000 of STC funds in doing so.

An ICT X Bid Committee was established under Co-chairs Gaston Chevalier and Gabbie Plaa and including Doug Arnold, Barbara Hales, and Bill Racz as well as the STC Board. The organizational meeting was held during the 1997 Symposium. We knew at that time that we had undertaken a very large commitment with a very short and inflexible deadline. What we did not know was just how short the deadline would be. We anticipated having to submit our bid package by the middle of March. We soon learned that the initial invitation package would need to be submitted to a meeting of the IUTOX Board in Eilat, Israel, January 8-11, 1998, approximately five weeks later.

At this point, I need to stop and introduce two non STC members of the team, Alain Carbonneau of le Palais des Congrès de Montréal and Laurier Forget of the National Research Council Conference Services Offices. Both Alain and Laurier are professionals in the organization and management of large national and international meetings. Without their advice and guidance we would not have been able to undertake and complete this project.

Our initial tasks were to confirm NRC's commitment and support, officially advise IUTOX of our intention to submit a bid for ICT X, prepare an initial bid (a first edition bid book), and organize a delegation to the January meeting of the IUTOX Board. Non of these were small tasks and the time frame was impossibly

short. However, all these things were accomplished, including preparation of a very handsome bound volume which constituted our invitation to hold ICT X in Montréal. Gaston Chevalier and Alain Carbonneau represented us at the Eilat meeting and the game was afoot.

What followed was a six month period of intense and continuous activity which included, refinement and resubmission of the bid, and notification of all national societies of Canada's intention to submit a bid (a letter from the President of STC to the Presidents of each of the 33 national societies). Lists of names, addresses and electronic contacts for the national societies and voting delegates to the 1998 IUTOX General Assembly were assembled and revised repeatedly, the final edition of the bid book was prepared and distributed, brochures were prepared, and an intense international lobbying effort undertaken.

The key members of the Bid Committee met each month and the STC Board met monthly by conference call (as well as our regular meeting in March) to monitor progress on the bid. Electronic communication flowed back and forth on a daily basis.

The final stage was the preparations for the presentation of the bid at ICT VIII in Paris in July. This included a full-page full colour advertisement for the summer issue of the IUTOX Newsletter. Each of you should have received a copy of the Newsletter, which also includes similar ads for Finland and Brazil as well as a two-page ad for ICT IX in Brisbane in 2001. A booth was set up at ICT X with poster sized versions of the ad and other promotional material, and a slide presentation prepared for the IUTOX AGM. A distinct highlight of our diplomatic effort was a reception for delegates at the residence of the Canadian Ambassador to France. This was a very elegant event with both the Ambassador M. Jacques Roy and Madame Roy in attendance.

Thanks are due to many people for the successful (in my view, at least) completion of this large project on time and in a very professional manner. To Alain Carbonneau and Laurier Forget, of course, to Gaston Chevalier and Gabbie Plaa for co-chairing our Bid Committee, to Doug Arnold for looking after our lobbying effort, to Tom Massey for serving with me as a delegate to the IUTOX AGM, and to the STC Board for many hours spent contributing to and reviewing all of the various activities associated with preparation of the bid and to anyone else that I may have inadvertently missed.

Where do we go from here? For one thing STC will have to decide if it wishes to resubmit our bid for ICT XI in 2007. If we decide to do so (and I think we should), I believe we will be the bid to beat. I do not want to take anything away from Finland's efforts this year. They worked very hard and had the courage and perseverance to make a third try. Their presentation was professional and well polished. However, on a straightforward basis, I believe our bid was at least as strong and certainly warrants another try. Most of the spadework has been done, the ground has been prepared and we would be very well positioned.

Beyond resubmission of the bid, we should prepare to submit credible nominations for positions on the IUTOX Board. Again, I believe we have achieved a degree of visibility and credibility, which would support the election of strong STC candidates. And finally there may be an opportunity for participation as part of the Scientific Program Committee for ICT X, an opportunity which, if offered, we should certainly

accept.

Finally, just a word on the costs of this project. STC is a small, lean organization and financial stability is always a concern for the Board. As I mentioned earlier, the 1997 AGM authorized the expenditure of up to approximately \$ 20,000 from our reserves (our reserves were approximately \$ 40,000.) We do not yet have a final accounting of the costs accruable to STC. However the majority of the costs will be covered from non-STC sources. These include promotional funds from Le Palais des Congrès, and a grant in support of bids competing for international meetings. STC costs will be limited primarily to travel costs for meetings of the Bid Preparation Committee to meet in Montreal and to approximately 25% of the costs of our delegates to the Eilat and Paris meetings.

A more detailed report and discussion of the ICT X Bid will be made to the 1998 STC AGM at which time we can decide whether to try again or not. While most other STC business has been on hold, we have not forgotten our own annual Symposium. Robin Walker, and his Scientific Program Committee have been working hard to organize our 1998 meeting - mark your calendars and plan to be in Montreal in the first week in December.



FROM THE EDITOR'S DESK - Michael Prior

AGING IS THE WAY OF ALL FLESH.

You are growing older as you read this! The percentage of Canadians over the age of 65 has doubled since 1901, and is predicted to rise to 12 per cent of the total population by 2001. Further, our expectancy of life at birth has increased by about fifteen years over the same period (Mark Novak, "Aging and Society: A Canadian Perspective" Nelson Canada: Scarborough, Ontario, 1993). Yet has our quality of life improved commensurately? According to the U.S. Public Health Service, the onset of those maladies which diminish our quality of life still arrive around the same age as they used to, despite our living longer. Our quality of life is not increasing at the same rate as life expectancy. This demographic shift increases the costs health care and pensions, politicizes grey power, and affirms geriatric medicine as a needed speciality. What are

the implications of an aging human population for toxicology?

In the 1980s, I took part in one of those serendipitous conversations that occur at toxicology meetings. The topic was the relevance of applying findings obtained from human and animal test subjects fed a well-balanced diet to teenagers, a group that often eats less than well. Could laboratory rats be fed a diet akin to the unbalanced diet of teenagers; a sort of fast-food chow? Yes they might, was the animal nutritionist's guarded reply. If this might be possible for teenagers, could we use aged rats as test subjects for older people?

According to Benjamin Franklin, nothing can be said to be certain, except death and taxes. Some businesses and citizens feel they are being taxed to death by the many small taxes that impede survival and growth. Is this a metaphor for apoptosis and human death? Aging humans and rats have declining plasma concentrations of growth hormone and IGF-I. Survival of bone marrow-derived haematopoietic progenitors of the myeloid and lymphoid series is caused by the ability of IGF-I to inhibit their apoptotic death. So declining IGF-I leads to involution of the thymus and, presumably, decreased immunocompetence (Kelley, KW, *et al*, Insulin growth factor-I inhibits apoptosis in hematopoietic progenitor cells. Implications in thymic aging. *Ann. NY Acad. Sci*, 840:518-524, 1998). One puzzling feature of heart failure is the progressive worsening of ventricular function over time despite the absence of clinically detectable concurrent adverse events. This may be due to cardiac myocyte apoptosis, which occurs after acute myocardial infarction, as well as in hypertrophied and aging hearts (Sabbah, HN & Sharov VG, Apoptosis in heart failure. *Prog. Cardiovasc. Dis*. 40(6): 549-562, 1998).

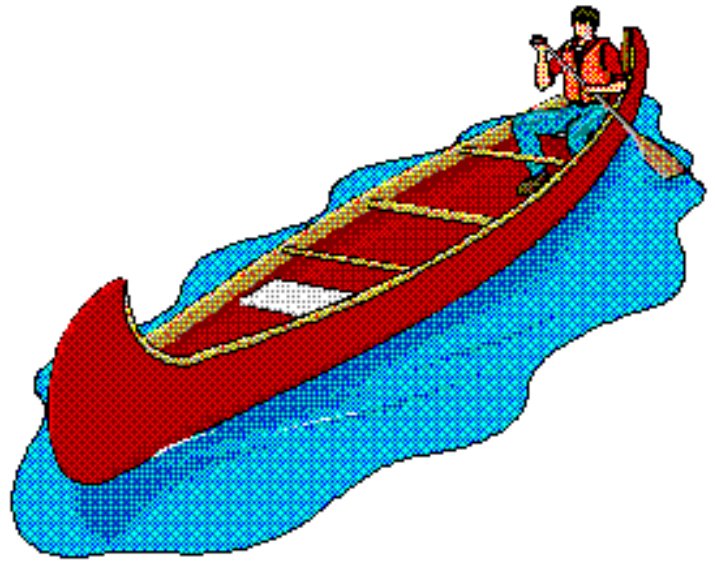
We all know that human erythrocytes have a circulating life span of some 120 days, before being phagocytized by macrophages. This is most emphatically *not* justification for a eugenics program. But just what is the critical signal that activates the resident macrophage to engulf the erythrocyte? Recent research suggests that cell surface sialic acid may be a determinant of erythrocyte life span, and that it is possible to characterize the senescent erythrocyte population (Bratosin, D, *et al*, Cellular and molecular mechanisms of senescent erythrocyte phagocytosis by macrophages. A review. *Biochimie* 80(2): 173-195, 1998). Can we characterize changes occurring with age in people, not just in their erythrocytes, from the pharmacological and toxicological perspective?

For example, does the incidence and site of apoptosis affect human response to xenobiotics? Do these changes affect pharmaceutical dosage and efficacy, or adverse effect level of exposure? Should we be thinking about reviewing regulations pertaining to human exposure to environmental toxicants? All to better reflect our aging human population. Who will do these tasks? Look around at your colleagues and note when they are likely to retire. Check the graduate schools for how new graduates to be available at the beginning of the next century. Indeed, will there be sufficient toxicological expertise available in the next millennium?

By the way, the elixir of eternal youth has not been approved by the necessary authorities for human consumption. In fact it's a myth!

THE VIEW FROM MY CANOE - Don Ecobichon

Spring has sprung. The ice is gone. The Canada geese have been flooding north in great gaggles for weeks. The memories of January's ice storm, 14 days without power, etc., are fading like a bad dream. Time to get out the kayaks and the canoe out, first, the flower garden and landscaping, much of which is the removal of limbs from damaged trees and cutting down those that won't make it. I have enough firewood ahead for some years if I can get to it before the insects do. So much for retired life!



A few years ago, biomedical sciences in Switzerland underwent the trauma of seeing a proposal to ban all animal experimentation being voted upon during elections in that country. This proposal was introduced by antivivisectionists, animal lovers, etc. It was defeated but led to severe restrictions being placed on animal research. Now a new proposal, the *Genschutzinitiative* (gene protection initiative) is to be voted upon in 1998 and, if accepted, will result in the constitutional prohibition of gene manipulation in any form. As described in an editorial in *Science* (Nov 14, 1997) by Dr. Rolf Zinkernagel (U of Zurich), the supporters claim that "*gene-modified plants cause allergies*" and that science is "*one step away from creating supermonsters*" and assert that scientists lack ethics, morals, sense of responsibility and have let the public down too often. While both houses of parliament have made a stand against the initiative, it will come to a referendum vote. The proponents are somewhat hypocritical in that the initiative does not prohibit the importation and use of drugs, foods and medical advances produced by gene technology. Whatever the result of the referendum, it will not solve the problem. Swiss companies involved in such research, and that must be most of them, will move their research facilities to more understanding climates, as they were prepared to do if the ban on animal research had been passed.

[*Editor's note: A report in the Manchester Guardian states Swiss voters overwhelmingly rejected curbs on genetic engineering in a national referendum. They voted two-to-one against the proposal to ban the genetic alteration and patenting of animals.*]

Some time ago, in an issue of the *STC NEWS/NOUVELLES*, I discussed one active ingredient in the neem tree, that bounteous tree that has uses for almost every medical eventuality. Now, it seems that a herbal, spermicidal contraceptive will make its appearance on the market in India in a couple of years, developed by scientists at India's Defence Institute of Physiology and Allied Sciences (DIPAS). To be used as a vaginal cream or suppository, the active ingredient, going by the code name NIM76, was found to be effective in killing sperm in mice, rats and rabbits. The compound is also a bactericide and clinical trial involving more than 2,000 woman is next, to expand upon the limited pre-clinical testing already done.

After eight years of supportive funding, the multi-campus research collaborative group, Neuroscience Network, part of Canada's Network of Centres of Excellence, fell victim to the federal government's budget cutting. The Unit, based at McGill University, will lose \$3.3 million in funding. Unfortunately, it would

appear to have been a bureaucratic decision by the 14-member selection committee since the external reviewers' report (the Lund Report) called it a "*model network . Giving Canada a world profile in this area while aiding biotechnology and conducting first rate research*". The chairman of the 8-member review committee, Raymond Lund of University College, London and a Fellow of the Royal Society, considered the government move bizarre, given the report submitted. The selection committee apparently based their decision on five performance criteria: scientific excellence, training, networking and partnerships, knowledge exchange and technology exploitation, and management. One wonders in which of these categories the group failed? Does it not sound familiar to all grant holders?

THE CONTROVERSY OVER ENVIRONMENTAL CHEMICALS AND BREAST CANCER - David Josephy

Many toxicological questions have political implications, but the public debate about breast cancer has recently reached an extraordinary intensity. Just a few days after Michael Prior asked me to write this column, the CBC TV Newsworld series "ROUGH CUTS" broadcast "Exposure", a documentary examination of environmental chemicals and breast cancer: (<http://www.newsworld.cbc.ca/roughcuts/docs/exposure.html>). CBC Radio's "Ideas" series (<http://www.radio.cbc.ca/programs/ideas/shows/epstein/index.html>) covered the same subject a few months ago, in a program featuring Prof. Samuel Epstein, Environmental and Occupational Medicine, University of Illinois School of Public Health. These are documentaries with a "point-of-view", and they presented their agendas very forcefully. Journalists insist on dramatizing these stories as romantic myths: "lone crusader takes on oppressive medical establishment".

In this short commentary, I want to consider why the identification of environmental causes of breast cancer has become so controversial. Then, I will comment on some of the evidence about the relationship between chemicals and breast cancer. My own viewpoint? I think that environmental chemicals play a significant role in human breast cancer - bigger than is accepted by most breast cancer researchers, but smaller than has been claimed by the journalists. Also, I suspect that the most important chemicals are not the ones usually indicted. But I'll return to my part of the story later.

Most of the major cancer sites (such as lung, colon, bladder, and prostate) are internal and, therefore, psychologically remote. But the female breast, our species' evolutionary masterpiece of sexual differentiation, is objectified like no other feature of human anatomy. Women's anger and frustration at the medical and scientific community's perceived arrogance, paternalism, and insensitivity is a strong theme in discussions of breast cancer. This emotion has been turned to positive action, as women demand that more support be given to breast cancer research. CBCRI, the Canadian Breast Cancer Research Initiative, was initiated as a result of this activism. However, little of the investment in breast cancer research by the major Canadian agencies has gone into the area of carcinogenesis and primary prevention; instead, genetics, molecular biology, and therapy have taken priority. For example, between 1994 and 1996, the CBCRI funded only three grants in the area of "Environmental Agents and Toxic Chemicals", out of more than eighty grants awarded.

In developed countries, the incidence of breast cancer has been climbing for decades. Other than those sites

which are clearly cigarette-related, breast cancer is the most obvious and increasing cancer threat to women in the USA, Canada, and Europe. The Canadian data can be viewed on the CBCRI Website: (http://www.breast.cancer.ca/english/e_frame.htm). The age-adjusted breast cancer incidence rate has increased by almost 50% since the late 1960s. The post-WWII rise in breast cancer incidence was roughly coincident with the widespread use of chemical pesticides and other suspect chemicals. But we should not lose sight of the fact that breast cancer was already a major killer of women even before the chemical industry began. Most or all of the increase has been in the post-menopausal, late-onset form of the disease, where we would expect environmental factors to have most impact, and genetic factors (such as BRCA1 and BRCA2 mutations) less.

It's less discouraging to look at the mortality rates (shown on the same WWW page). Mortality has held almost exactly constant, despite the rising incidence. The divergence between these two trend lines could result from improvements in therapy; or from improved early detection, resulting in timely treatment and higher cure rates; or even from a secular change in the biology of the disease.

An environment-breast cancer link is suggested by the great geographic variations in breast cancer rates, and studies of migrant populations (such as immigrants to high-risk North America from low-risk Japan) show that these differences cannot be explained away by genetic factors. Residence near chemical industries may be a risk factor for breast cancer, according to some studies. Still, "environmental" does not equal "chemical", and any number of nutritional, reproductive, or other lifestyle variables could be involved.

One book, more than any other work, has drawn media attention to the debate about the causes of breast cancer: "Our Stolen Future", by Colborn, Dumanoski, and Myers (Dutton, 1996). A foreword by the US vice-president gives their book extra cachet. To its advocates, "Our Stolen Future" is the most important contribution to environmental awareness since Rachel Carson's "Silent Spring". But to its detractors, the book is "junk science" -- alarmist nonsense. The Internet jangles with discussions and commentaries on "Our Stolen Future". (You can start your surfing at the "official" page, <http://www.osf-facts.org/index.html>).

"Our Stolen Future" is based on the theory that environmental estrogens ("xenoestrogens") are profoundly affecting wildlife and human reproduction and health. The adverse human health effects of these exposures are claimed to include decreased sperm counts and increased risk of breast cancer. Estrogen stimulates the proliferation of the mammary epithelium, and the effects of many breast cancer risk factors can be explained by their influence on lifetime exposure to estrogen. The recent much-publicized prevention trials with tamoxifen, in women at high risk of breast cancer, have proven that antiestrogen therapy can reduce breast cancer incidence. Whether most women will wish to inflict such a regimen on themselves is questionable.

Although most known environmental chemical carcinogens are genotoxic agents, it is, at least, plausible that hormonally-acting xenoestrogens could increase breast cancer risk. Experimental studies (such as *in vitro* analysis of binding to the estrogen receptor, and stimulation of the growth of estrogen-dependent

mammary tumour cells in tissue culture) led to the identification of many synthetic chemicals with xenoestrogen activity (Soto, A.M., *et al.*, p-Nonylphenol: an estrogenic xenobiotic released from "modified" polystyrene, *Environ Health Perspect.* 92: 167-173, 1991; Soto, A.M., *et al.*, The pesticides endosulfan, toxaphene, and dieldrin have estrogenic effects on human estrogen-sensitive cells, *Environ Health Perspect.* 102: 380-383, 1994). These chemicals include pesticides such as DDT, plasticizers, surfactants, and antioxidants (nonylphenol, bisphenol, phthalates); PCBs; and, of course, pharmaceutical estrogens.

The case against claims of xenoestrogenic toxicity has been made by Prof. Stephen Safe of Texas A&M University (Safe, S.H., Interactions between hormones and chemicals in breast cancer, *Annu Rev Pharmacol Toxicol* 38:121-158, 1998). Safe points out the major objection to the theory: the estrogenic potencies of organochlorine pollutants are exceedingly weak compared to natural estrogens.

Xenoestrogens were front-page news in 1996, when Prof. John McLachlan and colleagues, at Tulane University in New Orleans, claimed that "*Combinations of two weak environmental estrogens, such as dieldrin, endosulfan, or toxaphene, [are] 1000 times as potent ... as any chemical alone. ... The synergistic interaction of chemical mixtures with the estrogen receptor may have profound environmental implications.*" (Arnold, S.F., *et al.*, Synergistic activation of estrogen receptor with combinations of environmental chemicals. *Science* 272: 1489-1492, 1996). This seemed to explain how weakly-estrogenic chemicals could have potent biological effects. The *Science* paper was followed by four more articles from the same authors describing synergistic interactions of estrogens and xenoestrogens. But last year, following the failure of repeated attempts to reproduce this "discovery" in other laboratories, the entire report was retracted (McLachlan, J.A., Synergistic effect of environmental estrogens: report withdrawn, *Science* 277: 462-463, 1997). It remains quite unclear how the original data were obtained. As is usually the case, the retraction received less media attention than did the original report.

Prof. Safe also cites various molecular epidemiological case-controls studies of breast cancer which show no correlation - or even a negative correlation - between organochlorine body burden and breast cancer risk. Unfortunately, some journalists continue to cite only the few studies which show a positive relationship.

Could chemicals other than xenoestrogens be human mammary carcinogens? I have recently reviewed some of the evidence implicating genotoxic aromatic amines and polycyclic aromatic hydrocarbons (Josephy, P.D., Letter: Re.: Feigelson and Henderson (1996) Estrogens and breast cancer, *Carcinogenesis* 18: 1859-1860, 1997). ³²P-postlabelling analysis reveals carcinogen-DNA adducts in human breast tissue, and the Ames test detects mutagens in human mammary lipid.

Cigarette smoke contains many chemicals known to induce mammary tumours in rats. Is there any association between smoking and breast cancer? This is another controversial epidemiological question (Morabia, A., *et al.*, Re: "Smoking and breast cancer: reconciling the epidemiologic evidence by accounting for passive smoking and/or genetic susceptibility", *Am. J. Epidemiol.* 147: 992-993, 1998). Many case-control studies report that there is a link and many others do not. A recent study of BRCA1/BRCA2 carriers, from Prof. Narod's group in Toronto, actually reported a *protective* effect from smoking (Brunet, J.S., *et al.*, Effect of smoking on breast cancer in carriers of mutant BRCA1 or BRCA2 genes,

JNCI 90: 761-766, 1998). There are probably many factors operating here, and some of them are countervailing. For example, smoking may have antiestrogenic effects which counteract the presence of initiating carcinogens.

Differences in metabolic phenotype may account for differences in susceptibility. Ambrosone *et al.* reported a striking effect of the NAT2 N-acetyltransferase polymorphism (Ambrosone, C.B., *et al.* Cigarette smoking, N-acetyltransferase 2 genetic polymorphisms, and breast cancer risk, *JAMA* 276: 1494-1501, 1996; Shields, P.G. and Ambrosone, C.B., Smoking and breast cancer, *Women's Health, A Lifelong Guide: Scientific American Presents* 9 #2, 87-89, 1998). Slow acetylators were at greatly increased risk of breast cancer, whereas fast-acetylators were protected.

Another confounding factor is exposure to second-hand tobacco smoke. Morabia and colleagues, in Geneva, Switzerland, found that excluding passive-exposed "non-smokers" from the control group greatly increased the estimated breast cancer risk due to smoking (Morabia, A., *et al.* Relation of breast cancer with passive and active exposure to tobacco smoke, *Am. J. Epidemiol.* 143: 918-928, 1996).

Aromatic amines are mammary carcinogens in rats, and potentially mutagenic heterocyclic aromatic amines (IQ, MeIQ, PhIP, etc.) are found in grilled meats. North American diets high in fat and animal protein are also high in these carcinogens, and this diet seems to be associated with elevated breast cancer risk (De Stefani, E., *et al.*, Meat intake, heterocyclic amines, and risk of breast cancer: a case-control study in Uruguay, *Cancer Epidemiol. Biomarkers Prev.* 6: 573-581, 1997). PhIP, orally administered to nursing rats at low doses representative of normal dietary exposures, appears in the mammary tissue and milk, both as the parent compound and its metabolites (Mauthe, R.J., *et al.*, Distribution and metabolism of 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP) in female rats and their pups at dietary doses, *Carcinogenesis* 19: 919-924, 1998). My graduate student, Lillian DeBruin, has developed an analytical method for measuring monocyclic aromatic amine levels in human milk (DeBruin, L.S., *et al.*, Solid-phase microextraction of monocyclic aromatic amines in biological fluids, *Analytical Chemistry* 70: 1986-1992, 1998), and she is now applying this technique to samples which we are collecting from nursing mothers in Guelph and environs. We hope that determination of actual human mammary exposure to genotoxic chemicals can help us assess their carcinogenic risk. This research is supported by the Canadian Breast Cancer Foundation.

We know that occupational and environmental carcinogen exposures can cause human cancers in the lung, liver, bladder, and skin, and there is no evidence that the mammary gland is particularly resistant. It seems at least prudent for women to minimize exposure to potential mammary carcinogens, where this can be achieved by avoiding cigarette smoke, reducing dietary fat and grilled meat, avoiding pesticide exposure, and making other healthy lifestyle decisions.

NEWS FROM OTTAWA - Doug Arnold

The Health Protection Branch (HPB), more specifically, the Food Directorate, has been in the news again - but for all the wrong reasons. For several years, the managers and evaluators with the Bureau of Veterinary Drugs (BVD) have not seen eye to eye regarding a number of drug submissions. Bovine Somatotropin (BST) is the issue that brought the simmering



feud to a boil. The Bureau Director had just been replaced and the new Director had hardly been able to get the *lay of the land* before the story broke on the local CBC morning show. The crux of their story was that managers were purportedly about to approve the use of BST in Canada and evaluators did not agree with that decision. BST is definitely one of those hot button issues!

The Science Advisory Board (SAB) has now had several meetings. Since SAB has a limited amount of time to devote to HPB and its transition into the next millennium, there is a great deal of concern about who is providing the SAB with its information since Mr. Rock's attention is focussed on the contentious hepatitis C issue. The latest SAB meeting in early May dealt with the HPB animal/monkey colony. To date, there have been no announcements about the animal colony or the monkeys, especially the contentious matter of what to do with the monkeys that comprised the breeding colony. Rumour has it that a foreign country has initiated negotiations to buy some of the breeding colony monkeys.

Well, the new fiscal year has arrived and one of the items indicated as needing resolution has, in fact, been resolved. The 123 of us who received a letter (July, 1997) telling us that we were "...considered an 'affected' employee as defined in the Work Force Adjustment Directive..." were informed on March 9, 1998, that the 1997 letter had been rescinded. This was five months since Minister Rock announced in October, 1997, his moratorium on further changes to HPB.

When one looks at all of the side shows currently on-going within Health Canada, one is left to wonder if Mr. Rock was "assigned" the health portfolio because it would be a potential mine field for his political ambitions or if, for some reason, Mr. Rock thought that he could tame the Health Canada beast. If he could accomplish the latter, then being Prime Minister would be a walk in the park!

WELCOME TO NEW DEPUTY MINISTER OF HEALTH CANADA

The Globe and Mail, on their Web Site <<http://meds.queensu.ca/stcweb/<www.theglobeandmail.com/docs/news/19980717/>>> carried a "memo" from Hugh Winsor to David Dodge, Deputy Minister of Health Canada, welcoming him back from his sabbatical at the University of British Columbia. There is some irony in this, for David Dodge was the Deputy Minister of Finance when they introduced some draconian

financial cuts. Surely the Greeks had a myth about this? Hugh Winsor also gave publicity to "*Mad Cows and Mother's Milk, the Perils of Poor Risk Communications*" by Douglas Powell and William Leiss. Winsor notes that recent discussion papers about possible changes in the health-protection area, including a diminution of Health Canada's responsibility, "*if industry takes on more responsibility for product safety and standards.*" He closes by reminding readers that it was the Program Review under Dodge that reduced the annual budget in this area to \$136 million from \$237 million and that "*the Health Canada laboratories are already half closed.*" He suggests that more than the parable about the loaves and fishes is needed to explain this one.

BOOK REVIEW - Don Ecobichon

"Chemical exposures: low levels and high stakes" Second Edition. Nicholas A. Ashford and Claudia S. Miller. Van Nostrand Reinhold. New York, 1998. About \$75.

The first edition of this book appeared in 1991 at a time when multiple chemical sensitivity or chemical hyper-reactivity first broke on the medical scene. The authors presented, perhaps, the most rational approach to possible mechanisms by which this phenomenon occurred rather than indulging in the therapies in vogue, most of which smacked of quackery. If you missed reading this book, that is O.K. since you have a chance to redeem yourself.

Uniquely written, the second edition is divided into two parts. The first, containing six chapters (167 pages) is the first edition of the book in its entirety. The second part (four chapters, 269 pages) selectively updates the first edition and describes the evolving terminology, major workshops held, government interest and activity, and legal developments (Chapter 7); important new clinical findings and research on mechanisms of chemical sensitivity (Chapter 8); critical analysis of interpretative writings attempting to explore the nature and mechanisms of chemical sensitivity (Chapter 9); and a summary of the authors' current thinking on chemical sensitivity (Chapter 10). Appendices include a compilation of the results of laboratory/ clinical tests used for patients and a questionnaire used by one of the authors to collect a history form patients - an environmental exposure and sensitivity inventory (EESI).

The book has doubled in size but presents the same clarity in thought and writing. The authors present an excellent overview of this curious phenomenon. One can see the direction things have gone since 1991, the comparison being right there between the same covers. Having been involved with a number of chemically sensitive people, I was very sceptical until I read this book in 1991. As a matter of fact, my copy went wandering, never to return. I am pleased to have this book with its excellent update of the progress made since 1991. It is a book worth having on your shelf even if only for background information.

HIGHLIGHTS OF THE 1998 CFBS ANNUAL MEETING - Paul Hough

The 1998 Canadian Federation of Biological Societies (CFBS) Annual Meeting was held in the Shaw

Convention Centre in downtown Edmonton, Alberta. This is a fabulous centre, with an enormous hall where we had the poster sessions behind the exhibitors, and countless meeting rooms of all sizes on the level below the main hall. From a logistical point of view, this was a very smoothly run meeting, thanks to a well organized Local Organizing Committee chaired by Dr. Vern Paetkau, Chair of the Department of Biochemistry at the University of Alberta, and to the professional staff at the Shaw Convention Centre. This Committee did an amazing job of obtaining symposia sponsorship from the Alberta Heritage Foundation for Medical Research, so that many of the 11 symposia were co-sponsored by the Foundation. The University of Alberta also provided considerable support for the meeting.

The emphasis this year on nutrition, genetics, protein chemistry and muscle combined to make for a very good meeting with excellent science, good discussion and an environment that stimulated great interaction of graduate students, faculty, and exhibitors. From my perspective as a non-life scientist, I am always impressed with the focus on presentations by graduate students and young researchers, and by the unsolicited comments of senior researchers that the science described and the delivery by these young people is absolutely top-notch.

Besides the CFBS societies that normally participate in the Annual Meeting, the Genetics Society of Canada (a member of CFBS) meshed their annual meeting with that of CFBS; and the Canadian Society of Plant Molecular Biology (not yet a member of CFBS) did the same. In addition, the Protein Engineering Network Centre of Excellence sponsored a full day symposium on "Molecular and Cell Biology of Membrane Lipids". Satellite symposia on "Protein Design" and "Applications of Novel Peptide-Based Strategies" were built around this all day workshop.

Some real highlights of the meeting include:

Dr. Janet Thornton from University College, London, U.K. gave a beautifully organized and illustrated Plenary Lecture. Her talk, on "*From Genome to Proteome: the World of Protein Structures*", provided a clear summary of the work in her lab on the development of models to predict and represent protein structure.

Dr. Gilbert Schultz from the University of Calgary, gave one of the three PMAC Lectures on early stages of mammalian embryo genesis *in vitro* which has direct linkage to the agricultural industry and is now seen as an excellent model for studies of teratogens and toxicities.

The poster workshops went all the way from symposium format to reassembling posters linked by theme topic into one room for a walk through by each presenter and discussion afterwards. One in particular had a broad range of contractile mechanics of myosin head conformation and nutritional toxicities to NMR spectroscopy of muscle regeneration.

The symposia on lipid and protein metabolism gave a very thorough presentation of basic science aspects of cardiac and cardiovascular disease

The symposium on education included a number of stimulating concepts. One celebrated the teaching of

scientific methodology by using a cookie model of hypothesis development and testing in a graduate student class. Another was the use of a science hotline database of scientists that could be accessed by teachers at many levels, to answer specific questions in their curriculum. Still another involved the use of graduate student scientists teamed up with school teachers, so that one can be the resource on science for a few years continuity in a school, and the other can be the resource on teaching and education (like two-way mentoring).

No doubt many other equally important highlights could be mentioned, depending on specific interests. However, it was a very successful and relaxed meeting in a setting that worked very well indeed. The Annual Meeting is a very important activity for CFBS in that the revenues obtained from the meeting contribute significantly to the operating costs of the Federation, including the science policy function. Next year in Winnipeg, June 2-5, 1999, also promises to be a really interesting mix of themes, so I urge you to put those dates on your calendar.

Have a great rest of summer '98!

MMT - IS IT OR ISN'T IT A HEALTH HAZARD? - Michael Prior

Canadian refiners starting using methylcyclopentadienyl manganese tricarbonyl (MMT), in 1977, after tetraethyl lead was banned as a potent toxin. Both compounds are octane enhancers. The toxicological effects of tetraethyl lead are well documented. Concerns have been expressed that MMT, an organometal compound containing manganese (Mn), might adversely affect human health, especially the nervous system; and some in the auto-industry claimed it contaminated on-board automobile diagnostic equipment and reduced the efficiency of catalytic converters.

Three years ago the federal government introduced the Manganese-based Fuel Additives Act, prohibiting the importation and interprovincial sale of MMT, and the ban finally went into effect in June, 1997. In 1995, an appeals court ruled that the US Environmental Protection Agency (USEPA) had been wrong to continue to prohibit MMT's use based on health concerns, and allowed the use of MMT in some US states. No western European country allows use of MMT, and it is banned in California. The American manufacturer of MMT, Ethyl Corp., had requested a NAFTA dispute-panel ruling on the trade ban. Recently the Canadian government has decided to lift the trade ban on MMT.

What does some of the recent scientific literature have to say about MMT?

In assessing potential health risks of particulate Mn emitted from the combustion of MMT in gasoline, the USEPA considered not only the qualitative types of toxic effects associated with inhaled Mn, but also conducted extensive exposure-response analyses using various statistical approaches, and also estimated population exposure distributions of particulate Mn based on data from an exposure study conducted in California when MMT was used in leaded gasoline. The limitations in available data and the need to make several assumptions and extrapolations. The resulting risk characterization had inherent uncertainties that made it impossible to estimate health risks in a definitive or quantitative manner (Davis JM,

Methylcyclopentadienyl manganese tricarbonyl: health risk uncertainties and research directions. *Environ Health Perspect* 106 Suppl 1:191-201, 1998). This assessment may be instructive in identifying certain methodological issues of general relevance to risk assessment. A major feature of the inhalation health risk assessment was the derivation of Mn inhalation reference concentration (RfC) estimates using various approaches including benchmark dose and Bayesian analyses. This assessment used data from the Particle Total Exposure Assessment Methodology (PTEAM) study and other sources to estimate personal exposure levels of particulate Mn attributable to the permitted use of MMT in leaded gasoline in Riverside, California at the time of the PTEAM study (Davis JM, Jarabek AM, Mage DT, Graham JA, The EPA health risk assessment of methylcyclopentadienyl manganese tricarbonyl (MMT). *Risk Anal*, 18(1): 57-70, 1998).

Manganese oxides, primarily Mn_3O_4 , are formed during the combustion of MMT. Two sampling sites were selected on the island of Montreal, Quebec, based on their traffic density. Both respirable (MnR) and total (MnT) Mn were significantly higher at the high traffic site ($0.024 \mu g^{-3}$ and $0.050 \mu g^{-3}$ respectively) than at the lower traffic density site ($0.015 \mu g m^{-3}$ and $0.027 \mu g m^{-3}$ respectively). Temporal profiles at both sites were similar, and the period of the week was significantly related to MnR and MnT variations at both sites, with concentrations reflecting a positive relationship with traffic density. Average exposure by inhalation was 0.001 to $0.030 \text{ kg}^{-1} \text{ day}^{-1}$ for MnR and 0.001 to $0.05 \text{ kg}^{-1} \text{ day}^{-1}$ for MnT. However, the researchers found it difficult to attribute these results directly to the combustion of MMT in unleaded gasoline. On average, the MnR and MnT inhalation doses were 2 to 15 times lower than the RfC proposed by the USEPA for the general population (Loranger S & Zayed J, Environmental contamination and human exposure to airborne total and respirable manganese in Montreal. *J Air Waste Manag Assoc* 47(9): 983-989, 1997).

Researchers at the Département de médecine du travail et d'hygiène du milieu, Université de Montréal, found that the predicted air, soil, plant, surface water and sediment concentrations of Mn using GEOTOX, an environmental fate/exposure model, values were similar ($\pm 50\%$) to values measured in the Montreal region. The ingestion route was the main absorption route for adults ($>99\%$) (Loranger S & Zayed J, Environmental contamination and human exposure assessment to manganese in the St-Lawrence River ecozone (Quebec, Canada) using an environmental fate/exposure model: GEOTOX. *Environ Res* 6(1-2):105-119, 1997).

Inhalation exposure to Mn in garage mechanics in Montreal was 0.010 - $6.673 \mu g^{-3}$ (mean $0.45 \mu g m^{-3}$) and for a non-automotive worker control group 0.011 - $1.862 \mu g m^{-3}$, mean $0.04 \mu g m^{-3}$. The results suggested that less than 10% of the Mn exposure of the garage mechanics was due to MMT (Sierra P, Loranger S, Kennedy G, Zayed J, Occupational and environmental exposure of automobile mechanics and non-automotive workers to airborne manganese arising from the combustion of methylcyclopentadienyl manganese tricarbonyl (MMT). *Am Ind Hyg Assoc J*, 56(7): 713-716, 1995). The average whole blood Mn concentrations were similar for the two groups (0.67 - $0.76 \mu g DL^{-1}$); but the average hair Mn concentrations were significantly higher for the garage mechanics ($0.66 \mu g g^{-1}$) than for the blue collar workers ($0.39 \mu g g^{-1}$). As judged by the governmental standards or criteria for occupational and non-occupational environments, the current Mn levels in food, water and air may not cause any problems for workers (Loranger S & Zayed J, Environmental and occupational exposure to manganese: a multimedia

assessment. *Int Arch Occup Environ Health*, 67(2): 101-110, 1995). Beverages absorbed MMT from gasoline vapours for up to 16 hours (Forsyth DFS & Dusseault L, Determination of methylcyclopentadienyl manganese tricarbonyl in beverages by solid-phase microextraction. *Food Addit Contam*, 14(3): 301-307, 1997).

The October 1995 court decision allowing Ethyl Corporation to offer MMT for sale to refiners for introduction into unleaded gasoline as an octane enhancer is likely to result in an increase in fine (PM_{2.5}) Mn concentrations in ambient air. The results from three monitoring networks (one rural, one urban and one urban in Canada) and one USEPA study of personal exposure were analysed. Results suggest that some of the fine Mn observed in the USA during the 1986-1992 period was contributed by automobiles using leaded gasoline, for which MMT was a registered fuel additive. However, the near-disappearance of leaded gasoline has resulted in a very small portion of fine Mn being attributed to automobiles in the years since 1992. A source apportionment analysis suggests that crustal contributions to ambient fine Mn are in the order of 1-2 ng⁻³ in both the USA and Canada (Wallace L & Slonecker T, Ambient air concentrations of fine (PM_{2.5}) manganese in US national parks and in California and Canadian cities: the possible impact of adding MMT to unleaded gasoline. *J Air Waste Manag Assoc*, 47(6): 642-652, 1997).

It has been estimated that MMT use would result in only a small incremental increase in most people's Mn exposure. However, certain populations might be disproportionately exposed, e.g. foetuses, and other selected sub-populations. The critical question for two researchers at the Rollins School of Public Health, is whether the additional population exposure to Mn that would result from widespread MMT use would lead to toxic effects. They stated that currently available evidence does not permit firm conclusions (Frumkin H & Solomon G, Manganese in the US gasoline supply. *Am J Ind Med*, 31(1): 107-115, 1997).

One gets the impression that the evidence is not overwhelming one way or the other. Is there scientific evidence that low level exposure to airborne Mn is linked to nervous system problems and attention-deficit disorder among children? What percentage of the total Mn load is demonstrably attributable to exposure of people to Mn arising from the combustion of unleaded gasolines? Does the toxicokinetics of inhaled Mn predict toxic exposure of systems, organs or cells? Is it valid to use occupational health guidelines as the standard to protect susceptible human sub-populations?

By the way, I didn't have a copy of the 1994 Health Canada assessment of MMT to quote. As a toxicologist, what are your views about the potential health effects of MMT? Let the editor know and we'll publish them in a future issue.

STC ANNUAL MEETING, DECEMBER 3 - 4, 1998 - MARK YOUR CALENDARS!

The STC annual meeting will be in December again this year, on the 3rd and 4th. The meeting program committee is progressing well and has organized an interesting list of speakers.

The theme of the meeting this year will be "*Advances in the Scientific Basis of Safety/Risk Assessment*".

Topics to be covered include the following: New Approaches to Risk/Safety Assessment, Use of Carcinogenicity Data From Transgenic Animals in Toxicology & Safety Assessment, Biomarkers in Safety Assessment, and Safety Assessment of Non-genotoxic Carcinogens. The Henderson Award Winner will also be giving a presentation at the symposium in Montreal.

CANADIAN INSTITUTE OF HEALTH RESEARCH

The MRC has presented a new concept, the "Canadian Institutes of Health Research", to the Minister of Health. The plan is to develop a cross-Canada network of medical research facilities centred around the existing medical schools. Clearly, MRC intends this proposal to

be the centrepiece of efforts to increase government funding on the next few years. Further details are given in the "MRC Communique", vol. 2, June 1998.

CONFERENCES, MEETINGS AND WORKSHOPS

1998

Aug 12 - 15 The Forensic Science Society and the Canadian Society of Forensic Science, Acadia University, Nova Scotia. Contact: Dr. Peter Mullin, Meeting Coordinator, Kemic Bioresearch Labs, PO Box 878, Kentville, Nova Scotia B4N 4H8, Canada. Tel: 902-678-8195 Fax: 902-678-2839, e-mail: pmullen@fox.nstn.ca

Aug 16 - 19 3rd International Conference of International Federation of Societies of Toxicologic Pathologists, St. John's College, Cambridge, England. Contact: Meeting Voice, 4 Beckside, Little Urswick, Ulverston, Cumbria, England LA12 OPY Tel: 44 (0) 1229 869110 Fax: 44 (0) 1229 869049.

Aug 17 - 21 18th Symposium on Halogenated Environmental Organic Pollutants, Stockholm, Sweden. Contact: dioxin '98, Swedish Environmental Protection Agency, S-106 48 Stockholm, Sweden; e-mail: dioxin98@environ.se

Sept 10 - 15 1998 North American Congress of Clinical Toxicology, Hilton at Walt Disney World Village, Orlando, FL, USA. Contact: Registrar, Contemporary Forums, 11900 Silvergate Drive, Dublin, CA 94568-2257, USA. Tel: 510-828-7100 ext 0, Fax: 510-828-2121. E-mail: hlth@cforums.com Web Site <http://meds.queensu.ca/stcweb/www.cforums.com>

Sept 14 - 18 Tenth International Workshop on In Vitro Toxicology (INVITOX98), Winchester, Hants, UK. Contact: Caroline Sumner, INVITOX98 Secretariat, Meetings Management, The Chestnuts, 1st Floor 18 East Street, Farnham, Surrey GU9 7SD, UK. Fax: 44-1252-723303 or e-mail jherriot@meetsmgmt-u-net.

[com](#)

Sept 20 - 22 British Toxicology Society Autumn Meeting, University of York, UK. Contact Dr. T. J. B Gray, Meetings Secretary, Sanoff Research, Willowburn Avenue, Ainswick, Northumberland NE66 2JH England. Tel:44-1665 607302 or Fax 44-1665 607510

Sept 21 & 26 Meeting of the PanAmerican International Society of Toxinology Section, LagunaMar Hotel and Resort, Margarita Island, Venezuela. Contact their Web Site: cbb.ivic.ve/nfc.labspa.html/nfclab.html

Sept 28-Oct 1 Accidents due to venomous and poisonous animals, epidemiology, biology, medical management, prevention. Basel, Switzerland. Contact: Swiss Tropical Institute (STI), Course-Secretariat. PO Box GH-4002, Basel, Switzerland. E-mail: sticourses@ubaclu.unibas.ch. Web Page: <http://meds.queensu.ca/stcweb/www.wb.unibas.ch/STI/>

Oct 5 - 9 Society of Forensic Toxicologists (SOFT) & International Association of Forensic Toxicologists (TIAFT), Albuquerque, NM, USA. Contact SOFT/TIAFT 1998, PO Box 40711, Albuquerque, NM 87196-0711, USA Fax 714-642-2852. E-mail TIAFT98@aol.com.

Oct 10 - 13 7th International Symposium on Particle Toxicology, Maastricht, The Netherlands. Contact: Conference Agency Limburg, P.O. Box 1402, 6201 BK Maastricht, The Netherlands. Tel: +31-(0)43-361-91-92 Fax: +31-(0)43-361-90-20 e-mail: cal.conferenceagency@pi.net

Oct 12 - 16 14th International Symposium on the Forensic Sciences, Adelaide, Australia. Contact: 14th ANZISFS Plevin and Associates, PO Box 54, Burnside, South Australia 5066 e-mail: plevin@camtech.net.au

Oct 23 - 26 Joint Conference of Scandinavian Society of Cell Toxicology and Estonian Society of Toxicology, Tallinn, Estonia. Contact: Anne Kahru, Institute of Chemical Physics and Biophysics, Akadeemia tee 23, Tallinn EE0026, Estonia. Fax 372 6 398 382, e-mail: anne@kbfi.ee

Nov 15 - 19 19th Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC), Charlotte Convention Centre, Charlotte, North Carolina, USA. Contact: SETAC Office, 1010 North 12th Avenue, Pensacola, FL 32501-3367, USA. Tel: 850-469-1500.

Nov 23 - 28 X Congreso Latinoamericano de toxicologia IRA Reunion de directores de centros de toxicologia de america latina, Cuba. Contact: Lic Zosima Lopez Ruiz, Organizadora Profesional de Congresos, Palacio de Convenciones de la Habana, Apartado postal 16046, Cuba.

Dec 3-4 Thirty-First Annual Symposium, Society of Toxicology of Canada, Montreal, Quebec, Canada.

Dec 7 - 8 IACUC Responsibility for research animal well-being, San Antonio, Texas. Contact: Scientists Centre for Animal Welfare, 7833 Walker Drive, Suite 340, Greenbelt, MD 20770, USA

1999

March 14-18 Society of Toxicology Annual Meeting, New Orleans, Louisiana. For information or registration, contact: SOT, 1767 Business Center Drive, Suite 302, Reston,, Virginia 22090-5332, USA. HQ, Tel: 703-438-3115 or Fax: 703-438-3113

May 9 - 11 Health Effects Institute Annual Conference, San Diego, California. See <http://meds.queensu.ca/stcweb/www.healtheffects.org>> for more details.

June 13 - 17 18th International Symposium of the Society of Toxicologic Pathologists "Toxicologic Pathology of the Central Nervous System", Washington, DC, USA. Contact: STP Registration, 19 Mantua Road, Mt Royal, New Jersey 08061, USA. Tel: 609-423-7222 ext 360, Fax 609-423-3420.

June 27 - 30 Eurotox '99. 37th Congress of the European Societies of Toxicology, Oslo, Norway. Contact: Erik Dybing, National Institute of Public Health, Dept of Environmental Medicine, PO Box 4404 Torshov, -0403 Oslo, Norway. Fax: +47 22042686.

July 4 - 10 7th International Neurotoxicology Association Meeting (INA-7), University of Leicester, UK. Contact: Dr. David Ray, MRC Toxicology Unit, Hodgkin Building, Lancaster Road, Leicester LE1 9HN, England. E-mail: der2@le.ac.uk

Sept 28-Oct5 1999 North American Congress of Clinical Toxicology, La Jolla, CA, USA. Contact: Registrar, Contemporary Forums, 11900 Silvergate Drive, Dublin, CA 94568-2257, USA. Tel: 510-828-7100 ext 0, Fax: 510-828-2121. E-mail: hlth@cforums.com Web Site <http://meds.queensu.ca/stcweb/www.cforums.com>

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Nov 6 - 10 4th Congress of Toxicology in Developing Countries, Antalya, Turkey. Contact: Prof. Dr. Semra Sardas (4th CTOX-DC), Gazi University - Faculty of Pharmacy (Eczacilik), Toxicology Department, 06330, Hipodrom - Ankara, Turkey. Fax: 90+312 222 2322. E-mail: ek03-k@tr-net.net.tr

December Thirty-Second Annual Symposium Society of Toxicology of Canada

2000

March 13-16 Society of Toxicology Annual Meeting, Philadelphia, Pennsylvania. For information or

registration, contact: SOT, 1767 Business Center Drive, Suite 302, Reston., Virginia 22090-5332, USA. HQ, Tel: 703-438-3115 or Fax: 703-438-3113

June 24 - 28 19th International Symposium of the Society of Toxicologic Pathologists "Reproductive Biology/Endocrine Disrupters", Phoenix, Arizona, USA. Contact: STP Registration, 19 Mantua Road, Mt Royal, New Jersey 08061, USA. Tel: 609-423-7222 ext 360, Fax 609-423-3420.

Sept 17 - 20 38th Congress of the European Societies of Toxicology, UK. Contact: Alan Boobis, Imperial College, London W12 ONN, England. E-mail: aboobis@rpms.ac.uk

December Thirty-Third Annual Symposium Society of Toxicology of Canada

2001

Mar 25 - 29 Annual Meeting of the Society of Toxicology (SOT), San Francisco, CA, USA. Contact: SOT, 1767 Business Center Drive, Suite 302, Reston., Virginia 22090-5332, USA. HQ, Tel: 703-438-3115 or Fax: 703-438-3113.

June 24 - 28 20th International Symposium of the Society of Toxicologic Pathologists, Orlando, Florida, USA. Contact: STP Registration, 19 Mantua Road, Mt Royal, New Jersey 08061, USA. Tel: 609-423-7222 ext 360, Fax 609-423-3420.

July 8 - 13 9th International Congress of Toxicology, Brisbane, Australia. Contact: ASCEPT Secretariat, 145 Macquarie Street, Sydney, NSW 2000, Australia.