Your Health & the Environment

NEWS FROM THE UNIVERSITY OF ROCHESTER
ENVIRONMENTAL HEALTH SCIENCE CENTER • SUMMER ISSUE 2004

Was Napoleon poisoned by arsenic in his wine?

Could it be that one of the most dramatic deaths of the nineteenth century, that of Napoleon Bonaparte, was a poisoning that went undetected?

In 1955, Dr. Sten Forshufvud, a Swedish dentist and amateur toxicologist first posed the question of how Napoleon actually died. He read the journal that Napoleon's valet kept during the exile on St. Helena. He also studied the memoirs and was struck by the account of the recurrent illnesses that Napoleon suffered before his death. Napoleon suffered alternating periods of decline and recovery inconsistent with the course of cancer, the most commonly suggested cause of his death. Forshufvud began to see a pattern leading him to believe that Napoleon had been poisoned with arsenic. A book, published in 1978 by David Hapgood is a scientific detective story entitled *"The Murder of Napoleon".*

In 1915 Napoleon was a source of disquiet to the rulers of Europe and was banished to the South Atlantic island of St. Helena after the disaster at Waterloo. At that time he was deeply involved in the political science and his death would certainly calm the nerves of his countrymen, however, his death had to be convincingly natural. What easier way to kill a Frenchman than to dissolve some arsenic in his wine? With this in mind, Forshufvud hit upon the idea of analyzing Napoleon's hair for evidence that would support his premise. Forshufvud was aware that public figures of the time often gave gifts of their hair as souvenirs and he set out to locate some of Napoleon's hair. After an extensive search, he was able to locate a strand of the emperor's hair clipped the day after his death. He was also able to track down Hamilton Smith, of the department of forensic medicine at the University of Glasgow. Smith had described in a recent paper a technique for measuring the arsenic content of a single human hair by neutron activation analysis. Forshufvud, Smith and Anders Wassen, of the University of Göteborg, published the results of their research in *Nature* in 1961. The publications incited a flurry of responses and most of them were disputing the conclusions. An editorial in *The Lancet* noted other possible sources of arsenic on St. Helena, such as cooking pots, drinking water and rat poison. But the editorial also admitted that perhaps the speculation was correct and they felt it necessary to determine if other residents of St. Helena suffered a similar fate.

Today, the mysteries of toxicology and medicine rarely concern such romantic events as the death of Napoleon. Rather, they revolve around the evaluation of hazard and risk - determining the increased incidence of cancer that may be attributable to living in certain areas or the threat of birth deformities. Such puzzles are on a larger scale and more subtle than Forshufvud's, but, like his, their solutions often depend on determining how much of a substance is in the tissues, where it is localized, and when it got there. The last is often the most significant, but unless the exposure is recent, it cannot be measured in the urine or blood.

Now, consider the evidence for Forshufvud's reconstruction of Napoleon's last weeks: a few strands of hair, journals, memoirs, historical accounts, and knowledge of prevailing medical practices. Are we any better equipped to solve our own toxicological mysteries? Even modern cases turn on little more than locks of hair. So, how did Napoleon really die?

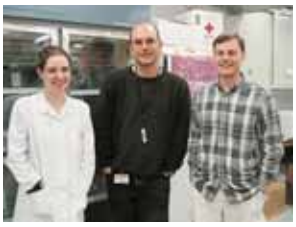
*This was originally written by Dr. Bernard Weiss as a review that was published in the book "The Murder of Napoleon" by Ben Weider and David Hapgood published by The New York Academy of Sciences.

McCabe Lab Does it All: Lead & Arsenic

Michael McCabe, Jr. , Ph.D.
Assoc. Professor
of Environmental Medicine

Research in the lab of Michael McCabe, Jr., Ph.D. focuses on identifying specific cellular and protein targets for metal immunotoxicity and on discovering the mechanisms whereby these metals alter immune function. Immuno-toxicology is the branch of environmental medicine concerned with examining the influences of drugs, chemicals and xenobiotics (a drug or chemical that is foreign to the body) on the immune system. The immune system is the body's "Department of Defense" charged with protecting against foreign invaders such as pathogens. When the immune system is suppressed, this can increase the body's susceptibility to pathogenic challenges. The long term goal is to understand whether and how metals contribute to immune system dysfunction including immuno-suppressive states, but also autoimmune diseases and even cancer. In collaboration with Environmental Health Science Center faculty, the McCabe lab actively investigates the effects of the metals mercury and lead as well as the metalloid arsenic. The work is conducted, in large part, by graduate students supported by the Toxicology Training grant. Two of these graduate students, Geniece McCollum (4th year) and David Farrer (3rd year), provide a description of their research projects below.

Geniece's work is uncovering the complexities of arsenite's mechanism of action as a chemotherapeutic agent. The aim of this work is to pinpoint the cellular proteins targeted by low levels of arsenite. The complexity of the system lies in the fact that the effects of arsenite are cell cycle dependent, and therefore likely mediated by unique protein targets that are active in distinct cell cycle compartments. Understanding how arsenite differentially affects these functional targets might shed light on the paradox of how arsenic can be both anti-carcinogenic (i.e., chemotherapeutic) as well as a pro-carcinogen (an agent that promotes cancer).



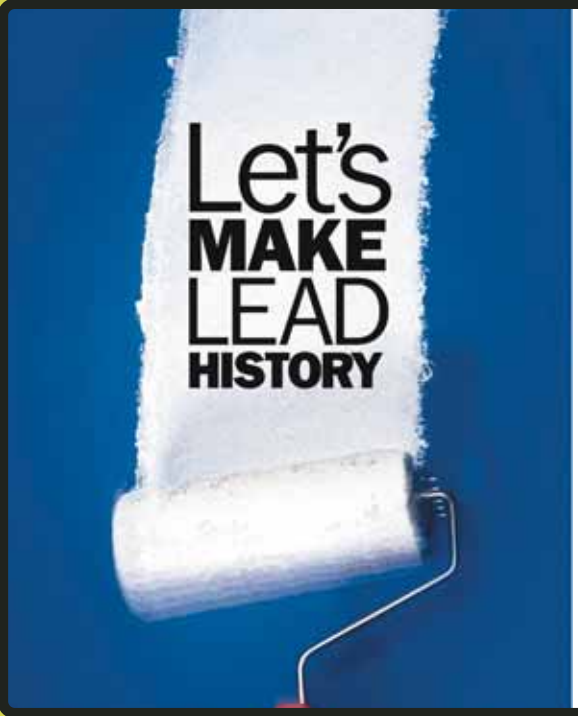
David's work aims to understand a mechanism underlying the immuno-toxicity of lead (Pb). Animal and human studies indicate that Pb is immunosuppressive; however, a mechanism explaining Pb immunotoxicity remains to be elucidated. David's data suggest that Pb targets a specific cell type called an antigen presenting cell (APC). These are cells that process and degrade foreign pathogens, and then present certain fragments (called antigens) to another cell type called helper T cells. Helper T cells are the major cell types that regulate immune function. David's work shows that Pb modifies the interaction and communication between APCs and helper T cells, which may be the basis of Pb immunotoxicity.

Life Sciences Learning Center Home School Science Club

Amanda Genaux
LSLC Technical Associate

Amanda Genaux joined the Life Sciences Learning Center (LSLC) in June 2003 as a technical associate. She has been affiliated with the LSLC for many years, first as a high school student in our Summer Science Academy. She returned each summer to assist us in the lab, and she also assisted us with many of our Saturday Morning Science programs. Amanda graduated from the University of Buffalo in May 2003 with a B.S. degree in biological sciences. Amanda has developed many new activities for LSLC students.

This past fall Amanda started a science club program at the LSLC to bring hands-on lab experience to middle school age home school students. Twelve students ages 11-14 met twice a month in our new teaching lab and participated in activities covering a range of life sciences topics, including a forensics day where students investigated a mock crime scene set up in the lab. Students also participated in a day trip to Montezuma Wildlife Refuge to learn about ecology and water quality testing. Each student also carried out an independent science investigation, along with a lab partner. This program gave home school students a chance to use high tech lab equipment they normally wouldn't have access to at home and the hands-on laboratories allowed students to get involved in actively doing science that was exciting to them. The fall program wrapped up with a science fair where our students' families had a chance to tour the lab, watch science demonstrations presented by the students and view students' posters describing their independent projects. We received positive feedback from the home school families and are currently running a second semester of this program with twice as many students (two sections of home school science club now meet twice a month). New activities include constructing model rockets followed by a launch where students will learn to triangulate the altitude of the rockets. Students will also participate in a field trip to Quest for Knowledge at Laser Quest (an entertainment center for kids of all ages to play laser tag) and where they will learn about lasers .



A Community Lead Summit was kicked off with a "virtual town meeting" on Wednesday evening June 9, 2004 on local PBS channel WXXI-TV. The program was centered around audience questions. Banks of local and national experts responded by phone and e-mail both off and on the air. The hour-long program also included video clips, live interviews and remote broadcasts from several small group gatherings.

On June 10, 2004, over 400 members of the community gathered at the Clarion Hotel to hear national and local experts participate in small workshops, visit exhibits and demonstrations. The opening session began with a welcome by Coalition Co-chair Ralph Spezio. Mary Jean Brown, Lead Poisoning Prevention Branch Chief for Centers for Disease Control and Prevention talked about the national perspective on the 2010 goal to end childhood lead poisoning. Dr. Bruce Lanphear, Sloan Professor of Children's Environmental Health at Cincinnati Children's Hospital Medical Center discussed the role of regulation in ending lead poisoning. Don Ryan, Executive Director of the Alliance for Healthy Homes, discussed strategies for achieving the goal of lead safe housing by 2010.

Graduate Student News

Environmental Health Sciences Center News

At the 43rd Annual Meeting of the Society of Toxicology held in March, 2004 in Baltimore, MD, Gary Minsavage won 2nd place for the Carl C. Smith Graduate Student award for meritorious research.

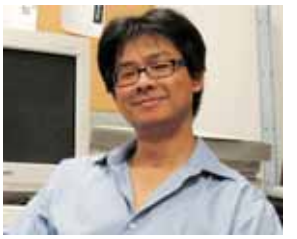
The following students will be defending their Ph.D.'s in the coming months—they are: Gary Minsavage, Christine Hammond, Christopher Helt and Amber Wyman.

Geniece McCollum was recently been notified that she is the recipient of a Pharmacology/Toxicology predoctoral fellowship award from the PhRMA Foundation. The fellowship is to be used to cover costs incidental to her training and is for a minimum of one year and a maximum of two years.

The annual Toxicology Training Program retreat took place on Friday June 4, 2004. The students participated in a poster session and also in workshops on presentation skills, manuscript writing skills, job hunting and networking and lastly, grant writing. During the retreat, our keynote speaker, Dr. Patrick Wier, Vice-President of Safety Assessment at GlaxosmithKline Pharmaceuticals spoke about "Applications of molecular biology in drug development; Predicting and understanding drug teratogenicity". An awards banquet was held that evening at a local resturant, with over 85 students, faculty and guests in attendance. Receiving the prestigious Kodak Diversity Award was Rosemarie Marchan. Mrs. William Neuman presented the Neuman Award to Geniece McCollum for academic, scientific and personal qualities which exemplify the imagination, enthusiasm and excellence that were characteristic of the life of Dr. William Neuman. This year, for the first time, two students, Christine Palermo and Jason Roper were awarded the Robert N. Infurna Award. This award is given to the student(s) who has/have published the best research paper as first author, in a peer-reviewed journal. The final award, the Harold C. Hodge Award, was given to Gary Minsavage for meritorious research as represented in his thesis.

Dr. Günter Oberdörster recently was notified that he has received a $5.5 million dollar grant to investigate whether the tiny particles of carbon and other materials made in the field of nanotechnology pose a health threat. The preliminary data for the study that Dr. Oberdörster is doing was published in the May issue of the *Journal of Inhalation Toxicology*.
Dr. Oberdörster will be collaborating with researchers from the University of Minnesota and Washington University at St. Louis. The study will use a team approach, involving biologists, material scientists, and physicists as well as experts in environmental medicine.

Much of our faculty efforts, over the past few months, were concentrated on preparation for our Center grant site visit that was held on Wednesday May 12, 2004.



Meet our newest faculty member: Dr. Kim Tieu. Dr. Tieu joined the department of Environmental Medicine on May 1st as an assistant professor after completing a postdoctoral fellowship at Columbia University, Department of Neurology. Dr. Tieu's major focus is in neurodegeneration and neuroprotection in Parkinson's Disease and in Huntington's Disease. In particular, he is interested in the role of mitochondrial dysfunction and in developing neuroprotective strategies for these disorders and, in addition, is also investigating the interaction between environmental toxins and genetic makeup.

At the University of Saskatchewan, Canada, Dr. Tieu received his Ph.D. in the Department of Neuropsychiatry. During Dr. Tieu's tenure at Saskatchewan, he was also employed as a practicing pharmacist.

We enthusiastically welcome Dr. Tieu to our Center and to our Department.

"A Small Dose of Toxicology" written by former graduate student, Steven Gilbert (Ph.D. 1986), provides a useful introduction to the principles of toxicology, written in everyday terms. Many of the examples used emphasize how toxicology fits into everyday events and life choices. The focus of the book is on the practical application of toxicology and applying the principles of toxicology to bigger issues.

A number of toxic agents are discussed, such as, alcohol, caffeine, nicotine, pesticides, lead, mercury, arsenic, metals solvents, radiation animal and plant toxins and persistent environmental contaminants. Also discussed are toxic agents that can be found in the home, such as: radon, lead in paint, indoor air, second-hand smoke, mold and mildew, household waste and many household products.

As Arsenic

Geniece McCollum

4th yr. Graduate student
Toxicology Ph.D. Program
B.A. Biology 2000
St. John Fisher College
Advisor: Dr. Michael McCabe, Jr.

Arsenic is worthy of much attention as a toxin and carcinogen, because every human population is exposed to some form of it. Arsenic toxicity manifests itself in a variety of ways. Ingestion of arsenic-tainted drinking water has been associated with cancers of the skin, liver, bladder, kidney and lung, as well as with cardiovascular and neurological effects. On the other hand, although arsenic can be very toxic, it has been an active ingredient in folk remedies for more than 2400 years. In the 1970's, investigators in China confirmed that arsenic trioxide had therapeutic value for the treatment of malignancies, especially acute promyelocytic leukemia (APL). Clinical studies were initiated in the United States, and the U.S. FDA approved arsenic trioxide for the treatment of relapsed or refractory APL in 2000.

Despite long-standing knowledge of arsenic's effects on humans, its mechanisms of action: toxic, carcinogenic and chemo-therapeutic, remain a mystery. My research is designed to increase understanding of arsenic's chemo-therapeutic mechanisms by studying the ways in which arsenic is able to inhibit growth in a myeloid leukemia cell line. I am using flow cytometry to measure arsenic's effects on cells at different stages of cell division. Cells in different phases of the cell cycle respond to arsenic in different ways. Actively dividing, or mitotic, cells are particularly susceptible to arsenic-induced cell death. Cells treated with arsenic in earlier stages of the cell cycle tend to grow more slowly and to become resistant to arsenic-induced cell death. I am exploring the possibility that arsenic induces some protective factor in these cells that allows them to avoid death, but slows their growth. It is useful in chemotherapy to inhibit the growth of cancer cells, but if normal cells are changed in such a way that they become resistant to cell death, they may be more prone to malignant transformation. Although it may sound paradoxical, it is conceivable that arsenic's ability to inhibit the growth of cancer cells is closely related to its ability to induce carcino-genesis. Therefore, an understanding of arsenic's chemotherapeutic mechanism may add considerably to our understanding of arsenic's carcinogenic actions.

Michael J. McCabe, Jr., Ph.D. presented data from this project at the 2004 Society of Toxicology Annual Meeting in a symposium talk entitled "Cell Cycle Dysregulation by Arsenite: Implications for its Chemotherapeutic Actions."

Pb Lead

David Farrer

3rd yr. graduate student
Toxicology Ph.D. Program
B.S. 2001 - Animal Science
Brigham Young University
Advisor: Dr. Michael McCabe, Jr.

Lead is a toxic heavy metal that is widespread and persistent in the environment. The most common source of exposure in the U.S. is lead-based paint in older houses. When most people think of lead poisoning, they think of children with learning disabilities and brain damage. However, lead is harmful to other body systems as well, including the immune system.

My project has focused on identifying specific targets for lead within the immune system. Central to the proper function of the immune system are communications between two specific types of immune cell. The first type, antigen presenting cells (APCs), train the second type, T cells, how to identify and combat specific disease-causing agents. Lead interferes with the APCs ability to give correct signals to the T cells. In fact, when lead is present, APCs instruct T cells to divide and proliferate more than they should. An overabundance of T cells can cause immune system-related health problems such as rheumatoid arthritis or decreased defense against invaders like bacteria and viruses. My project will continue to focus on lead's impact on the communications between APCs and T cells.

The results of my experiments should define APC as the nearest target of lead immunotoxicity and explain the mechanism by which lead alters T cell proliferation.