Society of Toxicology NEWSLETTER

SEPTEMBER/OCTOBER 1989

Hands-On Experience Opens Career Doors for SOT Summer Interns

The inaugural program of the Society of Toxicology Summer Internship was a resounding success!

Upon completion of the program, 31 graduate and undergraduate students renewed their studies with new levels of enthusiasm and a hands-on exposure to careers in toxicology. Students in the inaugural internship program were sponsored by 21 SOT members who realize the Internship Program is an investment in the future of toxicology as a strong and vital profession. Sponsors represented a cross section of toxicology including government, academic, and industrial organizations throughout the United States.

Andrea Zoumadakis, a biology and chemistry major from Westminster College in Salt Lake City, Utah, extracts DNA from tissues with SOT sponsor Michele Medinsky (right) at the Inhalation Toxicology Research Institute.

With the number of students choosing scientific careers in a general decline, the primary objective of the Society of Toxicology Summer Internship Program is acquainting science students with toxicology's abundant career opportunities. This active promotion of toxicology as a career choice may help avert a future shortage of trained toxicologists.

The national recruiting effort for the 1989 program included flyers and applications sent to biology, pharmacology, toxicology, zoology, chemistry, and biochemistry departments at colleges and universities across the United States and Canada. Over 150 students applied for intern-

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Reserve Space for Auxiliary Meetings

Enclosed with this issue of the Newsletter is a Request for Meeting Space for Related Groups during the 1990 Annual Meeting of the Society of Toxicology.

Specialty sections, committees, alumni organizations and others who wish to hold a meeting or social function in meeting space at the Fontainebleau Hilton Resort & Spa during the week of the Society meeting, February 12–16, 1990, should return the completed form to the Society headquarters as soon as possible, but no later than **December 15, 1989.** Space will be assigned on a first-come, first-served basis, once all of the SOT scientific and social programs have been accommodated.

For additional copies of the form, contact Stephanie Fox at the Society headquarters. ●

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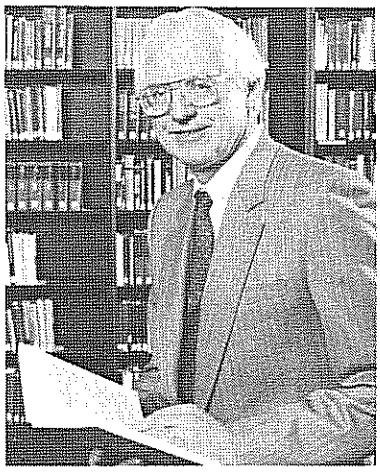

Society of Toxicology
1101 14th Street, NW
Suite 1100
Washington, DC 20005
(202) 371-1393
FAX (202) 371-1090

Deadline for next issues: January 8, 1990
March 8, 1990
May 8, 1990
July 8, 1990

1990 SOT Annual Meeting
February 12–16, 1990
Fontainebleau Hilton Hotel
Miami Beach, FL

President's Message

Dear Fellow Members:

The TOX-90's Commission indicated that "education, the foundation for future advances in toxicology, is the most important issue with which the Society must grapple." I strongly concur with the position stated by the Commission. The Society's concerns for education are broad, extending from how the Society of Toxicology can help recruit and train future generations of toxicologists to facilitating the continuing education of Society members to increasing public knowledge of toxicology. In this message I would like to highlight Society activities in the first two areas.

As the TOX-90's Commission reported, "the future of toxicology will depend on recruiting the most qualified students into the discipline." That task is being addressed by the "TOX-90's Educational Issues Task Force" in several ways. One of the exciting new initiatives developed in 1989 with major input from Task Force member **Michele Medinsky** was a highly successful Summer Internship Program. The 1989 program is described elsewhere in this issue of the Newsletter and information is also provided on plans for the 1990 program.

The importance of the Summer Internship Program can be readily personalized by asking yourself how you became interested in a career in toxicology? How was that interest nurtured? For many of us, contacts as students with toxicologists and biomedical scientists from other disciplines working in a research setting stimulated our interest in science. I can think of no better way to repay those who helped stimulate and nurture the present generation of toxicologists than to be certain we try to do the same for future generations.

It is my personal impression that today many students are receiving sound undergraduate training in the basic sciences. However, in many cases their classroom and laboratory experience is in very large classes and they have limited contact with research. Moreover, it is the exceptional situation when undergraduate students have direct contact with toxicologists. How then can students learn about career opportunities in toxicology? The Summer Internship Program is one avenue with the SOT serving as a "match-maker" between students and sponsors giving students the opportunity to gain firsthand experience in toxicology.

The membership of the Society can help assure the success of the 1990 Summer Internship Program in several ways. First, within your own organization promote the idea that it is in the best interests of your organization to sponsor one or more student interns during the summer of 1990 and then make certain your organization registers with the SOT. Second, go out of your way to call the Summer Internship Program to the attention of well-qualified students by direct contact or through faculty members. Urge interested students to contact SOT headquarters for applications. And third, if you are fortunate to have a student intern work with you, do everything you can to make it a stimulating and enjoyable summer and convey to them the exciting opportunities available today in toxicology. All of us will benefit from this kind of investment in the future.

The second educational topic noted earlier—the continuing education of Society members—is a major objective of our Annual Meeting. Elsewhere in this Newsletter you will find information on the outstanding array of Continuing Education Courses and Symposia to be presented in Miami. Take time now to read the brief summaries and note the speakers who will be participating. I am certain you will be impressed by the quality and diversity of the program. There is truly something for every member of the Society, whether your primary interest is conducting research on mechanisms of toxicity or assessing the potential health risks of exposure to specific toxicants. Make your plans now to attend the Annual Meeting from February 12–16, 1990 in Miami Beach, Florida. ●

Roger O. McClellan

Roger O. McClellan, D.V.M.

Hands On Experience Opens Career Doors for SOT Summer Interns

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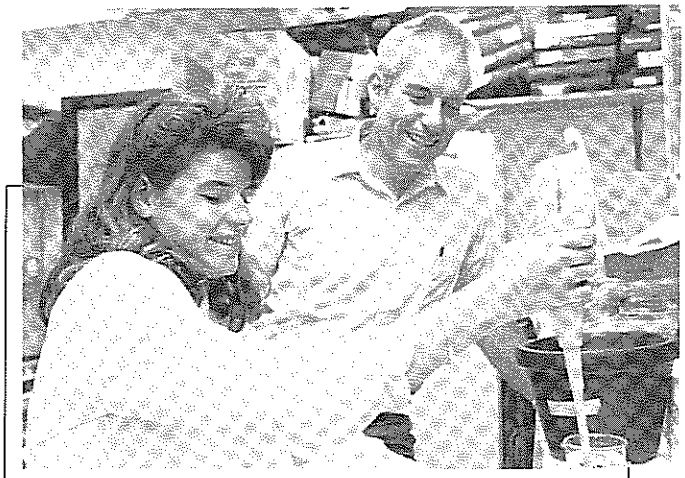
ship positions and 40 organizations responded with interest in sponsoring one or more students and provided criteria for student employment. The Tox 90s *ad hoc* Educational Issues Task Force matched students with potential sponsors and sent applications of prospective interns to participating organizations. Strong competition for the internship program let sponsors choose from among several qualified applicants for each position offered.

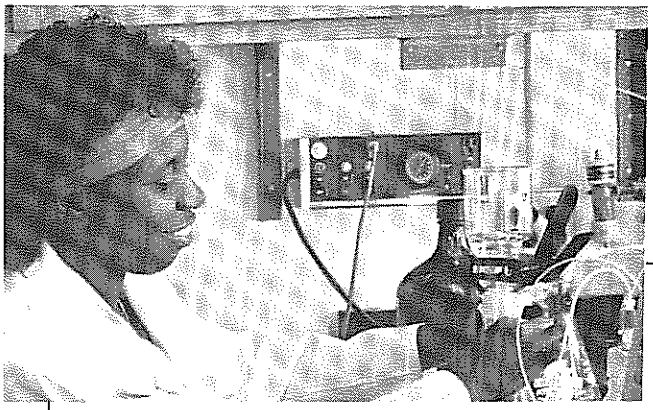
Due to the success of the program in its inaugural year, the Society of Toxicology is pleased to continue the internship program and looks forward to an expanded number of students and sponsors participating in the 1990 program. Fulfilling this goal requires earlier commencement of the recruitment/advertising process and earlier delivery of pertinent information from sponsors such as experience, compensation, housing arrangements if any, etc. SOT anticipates providing potential sponsors with applications of qualified students by mid-February. This will provide more time for sponsoring organizations to evaluate the applications they receive.

SOT members interested in supporting one or more interns during the Summer of 1990 should provide the information requested on the enclosed form. SOT also welcomes single page flyers or information sheets providing additional information on positions. In order to facilitate another successful program, responses must be received at SOT Headquarters by **January 15, 1990.**

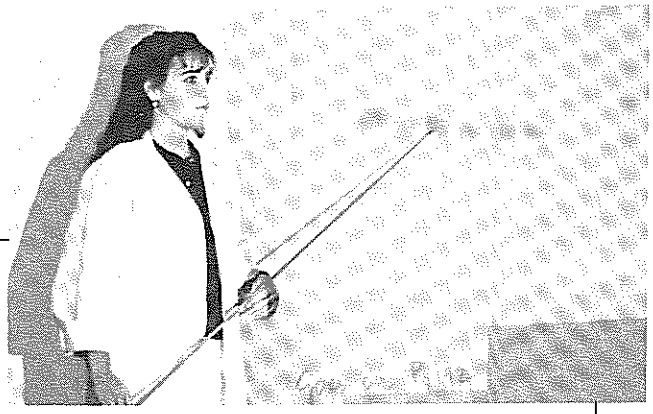
The Society of Toxicology and the Tox 90s *ad hoc* Educational Issues Task Force appreciate the support of sponsors of the 1989 program as well as the letters of encouragement and advice from potential sponsors for this program, which ultimately benefits the entire toxicology profession. SOT encourages these individuals to participate in the 1990 program and welcomes support from additional sponsors. ●



Christine E. Hughes of Ridgefield, CT, a sophomore at Marymount College in Tarrytown, NY, spent the summer as an SOT Toxicology Summer Research Intern at the University of Connecticut Toxicology Program. She assisted with ongoing studies of mechanisms of hepatotoxicity and nephrotoxicity in the laboratory of Dr. Steven D. Cohen.



Marylin Wilks, Senior, Mississippi Valley State University, completed the SOT Toxicology Summer Research Intern Program in the laboratory of Dr. H.M. Mehendale at the University of Mississippi Medical Center, Jackson, MS.



Christin Coulter, from Simon's Rock College in Maine, describes results of her research project at the Inhalation Toxicology Research Institute's Summer Research Symposium.

Christine M. Cicco (left), Wilkes College, one of nine interns selected from CIIT's 1989 Summer Intern Program, and Dr. Cheryl Walker, coordinator of the program, check on the progress of a gel electrophoresis separation procedure.

Society of Toxicology
Bulletin

1990 Burroughs Wellcome Award

The Burroughs Wellcome Fund offers a five-year Toxicology Scholar Award of $300,000, administered by the Society of Toxicology and awarded to an individual in a U.S. school. A commitment to Toxicology as a basic science by the individual and the institution is a major criterion. Selection is made by the guidance of a five-member committee and based on demonstrated ability and potential of the candidate and strength of commitment of the institution to program quality and the relative importance of the Award to the success of the program.

Applications are to be received by December 1, 1989 by the Chairman, Advisory Committee for the Burroughs Wellcome Toxicology Scholar Award, **Tom S. Miya,** School of Pharmacy, Beard Hall, Campus Box 7360, University of North Carolina, Chapel Hill, North Carolina 27599 (Telephone: 919/966-1121.) ●

Colgate-Palmolive Post-Doctoral Fellowship

The Colgate-Palmolive Company is sponsoring a post-doctoral fellowship, through the Society of Toxicology, directed specifically toward the development of *in vitro* alternatives to animal safety studies for assessment of dermal and ocular toxicity. The award is $33,500 annually for two years. Contact the SOT headquarters for more information and award application. Applications must be received by **December 1, 1989.** ●

SOT Headquarters Relocation

The Society of Toxicology has moved its headquarters office to 1101 14th Street, NW, Suite 1100, Washington, DC 20005. The new SOT telephone number is (202) 371-1393; fax (202) 371-1090. SOT's new offices are two blocks from the previous location, with the same convenience to Metro stations and other major Washington, DC landmarks. ●

SOT Ballot Process

The Society of Toxicology has developed a process for the election of officers, councilors and members of the Education and Membership Committees that ensures the confidentiality of members' votes and tallying of the results.

Members are provided a photograph and complete bio sketch of each candidate, which are mailed with the ballot to all voting members by February 1, as provided by the By-laws. Preparation of this package is no small task, as it occurs during the preparation of the Annual Meeting Program and *Toxicologist*. The cooperation of the candidates in providing this material to headquarters to meet this tight deadline is appreciated.

Two return envelopes are provided with the mailing: an outer envelope, which is addressed to SOT, and an inner envelope, which ensures the privacy of the members' vote. When the completed ballots are received in the SOT office, the member's name and signature is verified against the list of voting members. On the closing day for receipt of ballots, February 11, the unopened envelopes containing the ballots are sent to the independent accounting firm of Price Waterhouse & Company for tabulation. Price Waterhouse then provides the results to the President and the Executive Secretary, who notify all candidates of the results.

Although several members have questioned the need for two envelopes, the system works well and confidentiality is ensured. Please remember in completing your ballot to vote for the correct number of candidates for each category of candidates and to print and sign your name on the outer envelope. Envelopes that are not so marked will not be forwarded to Price Waterhouse for tabulation. ●

Air Force Grants

The Society of Toxicology is pleased to announce the availability of the Air Force Office of Scientific Research Toxicology Grants. They include: One Post-Doctoral Research Award consisting of a two-year grant of $40,375 per year (a new grant annually) and a New Investigative Research Award, a one-year grant (non-renewable) for $61,750.

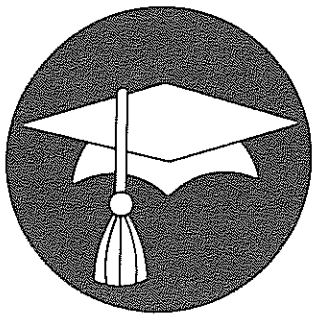
Interested parties should submit written requests for details and application to: Joan Walsh Cassedy, Air Force Grants Review Committee, c/o Society of Toxicology, 1101 Fourteenth Street, N.W., Suite 1100, Washington, DC 20005.

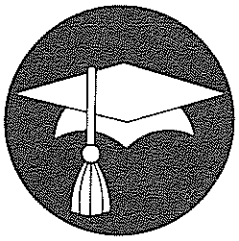
Closing date for grant submissions is **January 15, 1990.** Grant work begins in the 1990 Summer. ●

Continuing Education Courses for 1990 SOT Meeting

The Continuing Education Committees (**James Bond (Chairperson), Don deBethizy, Don Fox, Robin Goldstein, Gerald Kennedy, Ken Wallace**) is pleased to offer nine courses this year for the upcoming SOT meeting in Miami, FL. The course descriptions are given below. In selecting courses for this year, the Committee relied heavily upon suggestions from the membership who responded to last year's course questionnaires. For example, over 90 percent of the respondents were in favor of Advanced courses and having selected courses offered in both the morning and afternoon sessions. This year there will be two Advanced courses (Hepatotoxicity and Metabolism) and two courses that will be offered both in the morning and afternoon sessions (Concepts in Cell Biology and Carcinogen Risk Assessment). Advanced courses will focus on selected issues or current concepts and individuals signing up for these courses will be expected to have a basic understanding of the area being covered. We also received suggestions related to courses that might be oriented toward target organs and selected toxic agents. The Continuing Education Committee is pleased to initiate this year what will be the beginning of a series of courses related to Target Organ Toxicity and Toxicity of Agents. This year, two courses related to Target Organ Toxicity (Cardiovascular Toxicology and Respiratory Tract Toxicology) and one course related to Toxicity of Agents (Pesticides) will be offered.

The Committee would like to share with you some of the results of last year's questionnaires for the courses. Approximately 75 percent of the respondents rated the courses "good" to "excellent." Over 80 percent of the respondents were "somewhat" to "very much" pleased with slide quality, hearing speakers, and seating arrangements. The Committee found the responses valuable in terms of providing guidance for restructuring the course format; specifically, respondents wanted more time for a question and answer period. This year a new course format will include a 30-minute question and answer period after the completion of all lectures in a course. The Committee welcomes suggestions for potential courses that might be offered and would like to encourage everyone to contribute their ideas to members of the Committee. ●





Continuing Education

Concepts In Cell Biology

Chairperson: Glenn F. Rush, Toxicology Division, Eli Lilly and Co., Greenfield, IN

In this continuing education course we will attempt to cover a few selective topics that relate to the study of cell biology from a toxicologist's perspective. Thus, the course will be composed of sessions describing some of the fundamental biochemical and physiological processes that are often targets for a variety of drugs and chemicals as well as discussions on some of the new techniques available for studying these changes. To this end, five topics have been chosen. Cellular Energetics: This session will be focused on intermediary metabolism of the cell and how this function may be adversely affected by a variety of toxicants. In particular, the techniques used to detect metabolic changes as well as the consequences of disruption of intermediary metabolism will be discussed. Cell Growth and Differentiation: This session will cover how cells repair and regenerate from toxicant-induced damage. The majority of the discussion will be centered on the repair and differentiation of renal cells following proximal tubular injury. Signal Transduction and Control: In this session, new developments in our understanding of cellular signal transduction and control will be discussed. Emphasis will be placed on the role of phosphoinositide metabolism and protein kinase-C. Membrane Transport: This session will be focused on the different mechanisms involved in membrane transport and how changes in toxicological consequences of transport of drugs and chemicals will also be discussed. Fluorescence Image Analysis and Flow Cytometry: This session will describe the new techniques in flow and anchored flow analysis and fluorescence-activated cell sorting and how these techniques may be used to increase our understanding of the mechanisms of toxicant-induced injury.

Cellular Energetics. Glenn Rush, Eli Lilly and Co., Greenfield, IN.

Cell Growth and Differentiation. James Stevens, W. Alton Jones Cell Science Center, Lake Placid, NY.

Signal Transduction and Control. Susan Jaken, W. Alton Jones Cell Science Center, Lake Placid, NY.

Membrane Transport. Jeff Kasher, Eli Lilly and Co., Indianapolis, IN.

Fluorescence Image Analysis and Flow Cytometry. Debra Laskin/Jeffrey Laskin, Rutgers University/RWS Medical School, Piscataway, NJ.

Target Organ Toxicity: Cardiovascular Toxicity

Chairperson: Daniel Acosta, University of Texas, Austin, TX

This course will provide a foundation by which toxicologists and other scientists can better understand how the cardiovascular system responds to the toxic effect of xenobiotics. Lectures will be given on the normal physiology, as well as the pathophysiology, of the cardiovascular system. With these basic lectures as a foundation, an overview on the basic principles and mechanisms mediating cardiac toxicology and vascular toxicology will be given as individual lectures.

General Principles of Cardiovascular Physiology. Dr. Nicholas Sperelaris, University of Cincinnati, Cincinnati, OH.

Pathophysiology of the Cardiovascular System. Dr. Maximillion Buja, University of Texas, Dallas, TX.

Overview of Cardiac Toxicology. Dr. Eugene Herman, USFDA, Washington, D.C.

Basic Concepts of Vascular Toxicology. Dr. Paul Boor, University of Texas, Galveston, TX.

Developmental Toxicity: Changing Factors In Embryonic Susceptibility

Chairperson: Jeanne M. Manson, Merck Sharp & Dohme, West Point, PA

This course will emphasize general principles of Developmental Toxicology with specific emphasis on the rapid changes in embryonic susceptibility to prenatal insult. A unique characteristic of the field of Developmental Toxicity is that substantial qualitative and quantitative changes in embryonic susceptibility occur within relatively discrete time intervals, sometimes as short as a few hours to a single day. In the first lecture, a general overview of changing susceptibility with time and patterns of dose-response will be given. The second lecturer will provide a mechanistic underpinning for some of the changes in susceptibility, based on major shifts in intermediary metabolism during the organogenesis period of embryonic development. The third lecturer will describe these principles as they operate within craniofacial development and describe the underlying cellular and molecular processes that control palate morphogenesis. The final presenter will review the underlying

Continuing Education

principles of developmental neurobiology, with emphasis on the rapid changes in cell interaction and cell survival in the CNS during the perinatal period.

General Principles and Patterns of Dose-Response. Jeanne M. Manson, Merck Sharp & Dohme, West Point, PA.

Changes in Intermediary Metabolism During the Organogenesis Period. Thomas W. Sadler, University of North Carolina, Chapel Hill, NC.

Changing Factors in Cellular and Molecular Determinants of Craniofacial Development. Robert M. Greene, Jefferson Medical College, Philadelphia, PA.

Developmental Neurobiology: Changing Factors Determining Susceptibility to Maturation of the CNS. Patricia M. Rodier, University of Rochester, Rochester, NY.

Carcinogen Risk Assessment

Chairperson: Robert J. Moolenaar, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI

The course is devoted to discussing the use of experimental data for the assessment of risk to humans from exposure to chemical carcinogens. Various schemes devised to classify chemicals according to their potential to induce cancer will be presented and the rationale for selecting the preferred scheme discussed. Procedures for linearizing multistage dose-response relationships will be presented with emphasis given to the assumptions inherent to the model and examples of including experimental data in place of default assumptions. The session will conclude with detailed discussions of two modeling techniques for quantitative risk assessment. The purpose, design, and methods for constructing physiologically based pharmacokinetic models will be presented along with examples of the usefulness for certain aspects of risk assessment. The advantages of biologically motivated models for incorporating considerations of target organ growth and development, cytotoxicity, regenerative hyperplasia, and selective clonal expansion or regression in accounting for irreversible transformations will be discussed with emphasis on the high-dose carcinogenicity of nongenotoxic agents. The focus of the course will be to define the important considerations in assessing human carcinogen risk and to discuss the various modeling techniques available. Emphasis will be given to the assumptions and limitations inherent to the model design, data requirements and parameter estimation techniques. Examples will be included to demonstrate the utility and limitations of the variuos models presented.

Carcinogen Classification. Robert J. Moolenaar, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Quantitative Dose Response Assessment. Colin N. Park, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Physiologically Based Pharmacokinetic Modeling. Kenneth B. Bischoff, Department of Chemical Engineering, University of Delaware, Newark, DE.

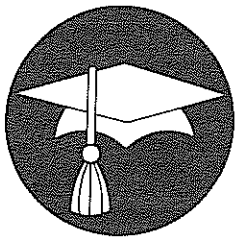
Biologically Motivated Models. Thomas B. Starr, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Advanced Metabolism

Chairperson: J. Donald deBethizy, Ph.D., R.J. Reynolds Tobacco Co., Winston-Salem, NC

Metabolism: A Determinant of Toxicity

New insights continue to develop on how the balance between detoxication and metabolic activation determines the toxicity of most xenobiotics. This course will provide updates in three rapidly developing areas in xenobiotic metabolism: Glutathione-dependent toxicity, the kinetics of metabolite formation and inactivation, and cytochrome P-450. The first lecture will discuss the role of glutathione conjugation reactions in the bioactivation of several classes of xenobiotics including vicinal dihaloethanes, haloalkenes, and bromobenzene. The second speaker will describe the rate limiting steps that are involved in the processing of xenobiotics and metabolites by the liver and kidney. The task will emphasize the role that heterogeneity in enzymic distribution, membrane barriers, and organ perfusion play in creating a concentration-in-space phenomenon that occurs in the direction of flow within the organ. The third presentation will continue to discuss the kinetics of metabolites by describing pharmacokinetic approaches used to classify metabolites according to their ability to leave the enzyme that generates their formation, and to leave the cells, the organ and the body in which they are formed. Procedures to relate blood concentrations of precursors of metabolites that fail to leave organs to enzyme activities in organs will also be described. The final lecture will provide an overview of the current understanding of the so-called super gene family, cytochrome P-450. The lecture will cover the multiplicity of P-450 genes and their products, mechanisms of induction and suppression, catalytic specificity and the relevance of these topics to metabolism and toxicity.



Continuing Education

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Overview. J. Donald deBethizy, Ph.D., R.J. Reynolds Tobacco Co., Winston-Salem, NC.

Glutathione-dependent Toxicity. Marion W. Anders, Ph.D., University of Rochester Medical Center, Rochester, NY.

Determinants of Metabolite Kinetics. K. Sandy Pang, Ph.D., University of Totonto, Toronto, Canada.

Methods Based on the Kinetics of Inactivation of Short-lived Metabolites. James R. Gillette, Ph.D., National Heart, Lung, and Blood Institute, Bethesda, MD.

Cytochrome P-450 Enzymes: Current Understanding of Basic Principles with Relevance to Metabolism and Toxicity. F. Peter Guengerich, Ph.D., Vanderbilt University, Nashville, TN.

Advanced Hepatotoxicity

Chairperson: James A. Popp, CIIT, Research Triangle Park, NC

Hepatotoxicity is a frequent response in rodents following exposure to xenobiotics. While entire textbooks are available on the subject, new advances are being routinely published. The purpose of this course is to provide the attendee with in-depth information on selected topics in hepatotoxicity. These topics have been chosen based on significant advances of in recent years. Studies of hepatotoxicity frequently consider only the role hepatocytes in the toxic response. In contrast, the first speaker will provide an overview of the role of the non-parenchymal cell in hepatotoxicity. Although the mechanism of hepatocyte toxicity has been evaluated for many years, our understanding of the biochemical mechanism of hepatocyte toxicity is continuing to evolve. The second speaker will describe the current and changing concepts in hepatocyte toxicity. Chemically induced hepatocyte proliferation is frequently suggested as an important toxic response in the liver. The third speaker will describe the current state of knowledge of the hepatocyte growth regulatory system and indicate how chemicals may alter this regulation to induce toxicity, including the development of cancer. The origin and lineage of the various liver cells are important in understanding the response of the liver to toxic agents. The function of hepatic oval cells and their response to toxic insults will be discussed.

Introduction. James A. Popp, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Role of Non-parenchymal Cells in Hepatotoxicity. Debra Laskin, Rutgers University, NJ.

Mechanisms of Hepatocyte Toxicity. Gregory L. Kedderis, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Regulation of Hepatocyte Proliferation. Randy Jirtle, Duke University, NC.

Free Radical Toxicology

Chairpersons: James P. Kehrer and Terrence J. Monks, Division of Pharmacology and Toxicology, College of Pharmacy, University of Texas at Austin

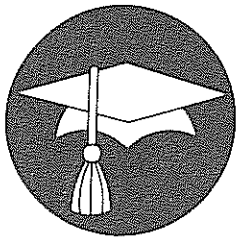
A free radical is any molecule that contains an odd (unpaired) number of electrons. Free radicals are generated in many metabolic pathways and the potential role of oxygen-centered free radicals in the pathology of several human diseases has stimulated extensive research. This course will review several important contemporary issues in free radical toxicology. The chemistry and reactivity of free radicals in biological systems will be introduced. The normal cellular sources of reactive oxygen species will be described and their reaction with vital cellular constituents presented. Current methods for detecting radicals and oxidative injury in biological systems will be discussed. Fortunately, through scientific ingenuity, many of these methods are relatively simple and straightforward. However, sophisticated instrumentation is required for the direct observation of free radicals. The mechanisms by which free radicals interact with biological systems and case tissue injury will be detailed. An elaborate arsenal of cellular defense mechanisms have evolved, that permit cells to thrive despite their continuous bombardment by reactive oxygen species. Despite these defenses, free radicals have been implicated in the injury produced by various xenobiotics (carbon tetrachloride, paraquat, quinones, etc.) and in the pathology of a variety of human diseases including rheumatoid arthritis (inflammation), atherosclerosis, reperfusion injury, cancer (initiation [?] and promotion) and pulmonary oxygen toxicity. However, because of the inherent reactivity of free radicals, the question of whether such species are a major cause of tissue injury and human disease, remains equivocal. Much work remains to be done. Free radical toxicology remains a fertile field for radical-minded scientist!

Overview. Terrence J. Monks, Division of Pharmacology and Toxicology, College of Pharmacy, University of Texas at Austin.

Chemistry of Free Radicals. Craig E. Thomas, Toxicology Department, Rohm and Haas Company, Spring House, PA.

Methodology for Detecting Radicals and Oxidative Injury In Biological Systems. Henry J. Forman, Division of Neo-

Continuing Education



natal/Pediatric Pulmonology, Children's Hospital of Los Angeles, Los Angeles, CA.

Mechanisms of Tissue Injury and Protection. Charles V. Smith, Department of Pediatrics, Baylor College of Medicine, Houston, TX.

Current Topics In Free Radical Mediated Tissue Injury. James P. Kehrer, Division of Pharmacology and Toxicoloyg, College of Pharmacy, University of Texas at Austin.

Target Organ Toxicity: Respiratory Tract Toxicology

Chairperson: James A. Bond, CIIT, Research Triangle Park, NC

The respiratory tract is an important portal of entry for inhaled toxicants and carcinogens and is also a target organ for non-inhaled materials. This course will provide an overview of the various mechanisms responsible for toxicant-induced injury in the respiratory tract. The first lecture will focus on cellular responses of the nasal tissue to inhaled intoxicants. This presentation will address the morphologic responses, both neoplastic and non-neoplastic, or nasal airway cells to a variety of chemical agents. In addition to providing a brief overview of the structure, function and cell biology of the upper airway in laboratory animals and humans, there will be a discussion of the intranasal sites of toxicant-induced lesions, emphasizing the nasal cells at risk. The second presenter will provide a brief overview of the structure and cell biology of the lung. Mechanisms of xenobiotic-induced lung injury, including direct and indirect injury, metabolic activation, and cyclic oxidation will be addressed. The major pathophysiologic responses of the lung will be covered, including edema, necrosis, inflammation, regeneration, fibrosis and emphysema. The third speaker will discuss the role of particles and fibers in including toxic responses in the respiratory tract. Mechanisms of particle translocation to the pulmonary interstitium, as well as mechanisms of lung inflammation and pulmonary macrophage clearance responses following particle deposition, will be reviewed. The role of cytokines and growth factors in the development of particulate-induced pulmonary fibrosis will also be discussed. The final presenter will focus on the neoplastic responses of the lung. Species differences in the carcinogenic response of the lung to toxicants will be addressed, with particular emphasis on differences between animal models for lung cancer and human lung cancer.

Overview. James A. Bond, CIIT, Research Triangle Park, NC.

Cellular Response of Nasal Tissue to Inhaled Toxicants. Jack R. Harkema, Inhalation Toxicology Research Institute, Albuquerque, NM.

Xenobiotic-Induced Lung Injury. Wanda M. Haschek-Hock, University of Illinois, Urbana, IL.

Current Concepts in the Pathogenesis of Particulate-Induced Lung Injury. David B. Warheit, Haskell Laboratory, DuPont, Newark, DE.

The Nature of Lung Tumors in Man and Animals. Implications for Toxicology. Hanspeter R Witschi, University of California Davis, Davis, CA.

Toxicity of Agents: Pesticides

Chairperson: James T. Stevens, CIBA-GEIGY Corp., Greensboro, NC

This course will emphasize several aspects of pesticide toxicology, including toxicity to humans, the environment, and the regulation and risk management of pesticides. The first lecture will provide an overview of the early use of chemical agents to control insect and weed pests, continue with the advent of organochlorine insecticides, and a discussion of more recent agents with pharmaceutical-like efficacy in the gram per acre range. The second lecturer will review the toxicology of pesticides, emphasizing the mechanism of toxicity for the different chemical classes. The third speaker will profile studies ranging from acute tests in marine and aquatic organisms, bees, non-target plants and birds, through mesocosm and avian field studies. The fourth session will evaluate the potential human exposure in food and drinking water following the application of pesticides to crops. A review of the Pesticide Tolerance Assessment system used by the Office of Pesticides Program, as well as procedures used by the Office of Drinking Water for calculation of HALS will be discussed. The final presenter will review the extent of toxicological testing required prior to registration of a new pesticide in the Federal Insecticide, Fungicide, and Rodenticide Act, as well as the requirements for the re-registration of older products. There will also be a discussion of the generation of new and revised guidelines for effecting the direction of toxicology testing under the guidance of the EPA.

Agricultural Chemicals: The Evolution of Pesticides. Wayland J. Hayes, Jr., Vanderbilt University, Nashville, TN.

Hazard Identification: Pesticide Toxicity to Humans. Donald J. Ecobichon, McGill University, Montreal, Canada.

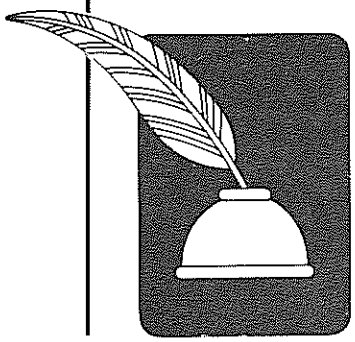
Hazard Identification: Ecotoxicity. Ronald Kendall, Clemson University, Clemson, SC.

Exposure Assessment: Quality of Food and Water Supply in the U.S., Christopher E. Wilkinson, Varsar, Inc., Springfield, VA.

The Regulatory and Risk Management Process. Penelope Fenner-Crisp, U.S. Environmental Protection Agency, Wilmington, DE.

SOT 1990 Annual Meeting Symposia

Participants at the 1990 Society of Toxicology Annual Meeting will want to reserve adequate time to attend Annual Meeting Symposia. An informative and diverse range of topics will be covered by this year's symposia. They reflect many of today's "hottest" issues in the field of toxicology and also anticipate the growing importance of other areas of research. Once again, members from SOT's full professional spectrum have contributed their time and talents to produce a slate of superior symposia. 1990 Annual Meeting Symposia begin on Tuesday, February 13 and run through Friday morning, February 16. ●



Cellular and Molecular Mechanisms of Learning and Memory: Interactions with Neurotoxic Chemicals

Sponsored by the Neurotoxicology Specialty Section

Chairperson: Hugh A. Tilson, USEPA, Research Triangle Park, NC

The advances made in the basic neurosciences in the last decade have provided a basis for understanding the mechanisms by which neurotoxicants adversely affect the structure and/or function of sensory, motor, and autonomic systems. Much less is known, however, about how neurotoxicants can affect cognitive processes such as memory and learning. This latter area is of great importance since it is well known that one of the frequent initial complaints following exposure to some neurotoxicants includes difficulty in remembering and confusion in thinking. It also has been suggested that a complete risk assessment of neurotoxicants should include an evaluation of cognitive processes, including learning and memory. The purpose of this symposium is to review, at four levels of neural organization, the processes of learning and memory. The talks will cover: 1) the cellular and molecular mechanisms of learning; 2) the location of the regions in the central nervous system associated with the storage, retrieval and processing of different types of memory; 3) the relative importance of specific neurotransmitter pathways in mediating learning and memory; and 4) measurement and quantification of learning and memory in humans. Speakers will not only explain basic principles involved at each level of neural organization, but also discuss potential sites of action for neuroactive chemicals. In this way, the symposium will provide a systematic presentation of material concerning this complex area of research. The fundamental information concerning the mechanisms by which learning and memory occur should help provide insight into potentially vulnerable sites of attack at which toxic chemicals may act.

Introduction. Hugh A. Tilson, U.S. Environmental Protection Agency, Research Triangle Park, NC.

The Cellular and Molecular Basis of Learning and Memory. Aryen Routtenberg, Northwestern University, Evanston, IL.

The Anatomical Substrates of Learning and Memory. Deborah Rice, Tox. Research Div., Health and Welfare Canada, Ottowa, Canada.

The Neurochemical Substrate of Learning and Memory. Hugh Tilson, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Cognitive Effects of Neurotoxicants in Humans. W. Kent Anger, Oregon Health Sciences University, Portland, OR.

Transplacental Transport of Toxic Metals and Fetal Effects

Sponsored by the Metals Specialty Section

Chairperson: Robert A. Goyer, University of Western Ontario

With increasing knowledge of potential health effects of metals during fetal life there is need for better understanding of the role of the placenta in the transfer of toxic metals from mother to fetus. There is also need to identify factors which influence or modify fetal toxicity.

The papers in this symposium concern placental transport and fetal effects of three toxic metals, lead, cadmium and mercury. When the three metals are compared it becomes evident that the mechanisms for placental transport for each of the metals is different. For lead and cadmium there is a close association with the transfer of an essential metal, lead with calcium and cadmium with zinc. The pathogenesis of the fetal effects differ. Whereas fetal exposure to lead and mercury is responsible for the observed fetal toxicities, lead and mercury are CNS toxins but the mechanisms responsible for toxicity and, perhaps, potential for reversibility, differ. Cadmium may reduce birth weight by indirectly depriving the fetus of the essential trace metal zinc in the fetus. And finally, metal toxicity may be modified by binding with specific proteins. Most is known about metallothionein but the mechanism for selective retention of cadmium and enhancement of zinc and copper transport is not known. Less is known about the lead inclusion body protein but there is some indication it may not be available in utero to sequester lead. Whether mercury forms protein complexes is not known.

Introduction. Robert A. Goyer, University of Western Ontario, London, Ontario.

Biokinetics of Lead During Pregnancy. Kathryn R. Mahaffey, National Institutes of Environmental Health Sciences, Research Triangle Park, NC.

Human Fetal Lead Exposure: Intrauterine Growth, Maturation and Postnatal Neurobehavioral Development. Kim N. Dietrich, University of Cincinnati, Cincinnati, OH.

Placental Transport of Mercury and Fetal Effects. Thomas W. Clarkson, University of Rochester, Rochester, NY.

Transplacental Transport of Cadmium and Fetal Effects. Robert A. Goyer, University of Western Ontario, London, Ontario.

Comparative Dosimetry of Inhaled Materials: Differences Among Animal Species and Extrapolation to Man

Sponsored by the Inhalation Specialty Section

Chairperson: Alan R. Dahl, Inhalation Toxicology Institute, Albuquerque, NM

Dose is a fundamental concept in the science of toxicology; yet, for all of its importance, the determination of dose for inhaled materials presents issues with which inhalation toxicologists are still grappling. Amid a myriad of lesser factors, the two major factors influencing dose for inhalants are the physicochemical properties of the inhaled materials and the animal species doing the inhaling. The speakers in this symposium will present the most recent advances in research describing dose for inhaled particles, particle-associated organic compounds, reactive vapors and metabolizable vapors. They will also discuss state-of-the-art methods for extrapolating to man inhaled doses measured in test animals and advances in the search for biomarkers for inhaled carcinogens.

The factors that affect the fate of inhaled particles will be reviewed and particle deposition and clearance patterns will be compared between experimental animals and man. Advances in determining dose for reactive vapors largely absorbed in the nose (exemplified by formaldehyde) and in the lung (exemplified by ozone) will be discussed in terms of relating experimental data to predictive models. The uptake of metabolizable vapors as affected by both the physicochemical properties of the vapors and the metabolic capacities of test animals and man will be explored using specific examples of vapors commonly encountered in the environment. Problems in making interspecies comparisons will be addressed. Finally, methods for indexing dose of inhaled carcinogens using toxic metablites, DNA adducts, hemoglobin adducts, oncogene activation, gene mutations and chromosomal changes as biomarkers will be reviewed with an emphasis on the use of such markers in risk assessments.

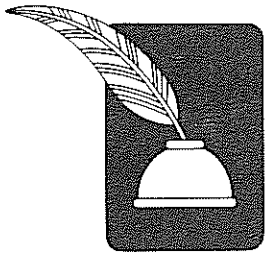
Introduction. Alan R. Dahl, Inhalation Toxicology Institute, Albuquerque, MN.

Comparative Deposition, Clearance and Retention of Particle-Borne Toxicants. Richard B. Schlesinger, New York University Medical Center, New Yoru, NY.

Comparative Dosimetry of Inhaled Reactive Vapors. Henry d'A Heck, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Comparative Uptake and Fate of Inhaled Metabolizable Vapors. Michele A. Medinsky, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Molecular Dosimetry of Inhaled Carcinogens: Implications for Epidemiology-Risk Assessment. George W. Lucier, National Institute of Environmental Health Sciences, Research Triangle Park, NC.



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Health Effects of Inhaled Fibrous Materials

Sponsored by the Inhalation Specialty Section

Chairpersons: Neil F. Johnson, Inhalation Toxicology Research Institute, Albuquerque, NM and David B. Warheit, Du Pont Haskell Laboratory, Newark, DE

Chronic inhalation of asbestos fibers has been associated with the development of fibrotic lung disease (i.e., asbestosis), bronchogenic carcinoma, and pleural mesothelioma. Inasmuch as the correlation between occupational exposure to asbestos and lung disease has been confirmed, it seems likely that the commercial use of asbestos fibers will be banned in the near future. To fill the void, a variety of non-asbestiform synthetic and mineral fiber substitutes are currently being promoted for commercial use in the insulating and composite industries. The potential pulmonary toxicity of many of these materials has not been fully determined, although the pathogenic effects of asbestos and other fibers have been attributed to their fibrous nature. It is widely accepted that fiber dimension is one of the most important factors in the pathogenesis of asbestos-induced lung disease.

Introduction. Neil F. Johnson, Inhalation Toxicology Research Institute and David B. Warheit, Du Pont Haskell Laboratory, Newark, DE.

Introduction to Fiber Toxicology. Gerald L. Kennedy, Du Pont Haskell Laboratory, Newark, DE.

Use of Mammalian Cells in Culture to Assess the Genotoxic and Carcinogenic Potential of Asbestos and Man-Made Vitreous Fibers (MMVF). Tom W. Hesterberg, Manville Technical Center, Littleton, CO.

In Vivo Assessments of Pulmonary Toxicity Following Exposure to Inhaled Fibers: Utilization of Bronchoalveolar Lavage (BAL) and Fixed Lung Tissue to Assess Fiber Deposition Patterns and Early Cellular Responses. David B. Warheit, Du Pont Haskell Laboratory, Newark, DE.

Assessment of the Biological Effects of Inorganic Fibrous Materials in Animal Experiments. Neil F. Johnson, Inhalation Toxicology Research Institute, Albuquerque, NM.

Human Exposure and Disease Associated with Inorganic Fibrous Materials. Jon L. Konzen, Owens-Corning Fiberglas Corporation, Toledo, OH.

Inhalation Risk Assessment: State-of-the-Art

Sponsored by the Risk Assessment and Inhalation Specialty Sections

Co-Chairpeople: Barbara D. Beck, Gradient Corporation, Watertown, MA and Judy A. Graham, U.S. EPA, Research Triangle Park, NC

Traditionally, quantitative risk assessment has focused on the risk of oral exposure to chemicals. However, inhalation presents additional complexities, such as issues of regional deposition in the respiratory tract or unique portal-of-entry effects. Part of the reason for the heightened interest in inhalation risk assessment is a result of the continuing efforts of the U.S. Congress to restructure the 1970 Clean Air Act, as amended in 1977, and the increasing recognition of the importance of inhalation exposures from volatilization of chemicals from a variety of sources, such as hazardous waste sites.

The goal of the symposium is to present five major approaches to the quantitative risk assessment of inhaled chemicals. The topics were chosen based upon their current and future use in risk assessment, their novelty to the scientific community, and their scope/approach to risk assessment. Studies of exposure to inhaled particles are being used to assess qualitative differences in response as a function of exposure level which indicate anomalous responses at levels frequently employed in toxicological studies. Physiologically-based pharmacokinetic models are being used to predict more accurately the dose of toxicologically relevant compounds in exposures to inhaled gases. These issues are critical in the development of risk assessment models. EPA has recently started to use the newly developed inhalation reference dose methodology for chronic exposures to toxic air pollutants and other inhaled pollutants related to pesticides and other hazardous wastes. The decision analytic approach is being applied by EPA to criteria pollutants such as ozone and SO_2. The Emergency Response Planning Guidelines represent a new approach to estimating risks from short-term exposures, frequently for chemicals with limited data bases on acute exposures.

Introduction. Barbara D. Beck, Gradient Corp., Cambridge, MA.

High Level Particle Inhalation Experiments: Possible Mechanisms and Extrapolation to Man. Gunter Oberdoerster, University of Rochester, Rochester, NY.

The Use of Acute Data to Set Exposure Standards. George M. Rusch, Allied-Signal, Inc., Morristown, NJ.

Use of Probabilistic Exposure-Response Relationships and Exposure Analysis in Risk Assessment for Criteria Air

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Pollutants. Harvey M. Richmond, U.S. EPA, Research Triangle Park, NC.

Inhalation Reference Dose (RfDi). Annie M. Jarabek and Judith A. Graham, EPA, U.S. EPA, Research Triangle Park, NC.

Predicting Target Tissue Dose for Inhaled Gases through Physiological Modeling Strategies: Melvin E. Andersen, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Metal-Induced Alterations in Gene Expression

Sponsored by the Metals Specialty Section

Chairperson: Carol T. Walsh, Boston University School of Medicine, Boston, MA

The purpose of this symposium is to present new findings on metal-induced alterations in gene expression and their significance to metal toxicity. The symposium will begin with a brief review of key regulatory components of gene expression including modifiers of DNA transcription and mRNA translation. An overview of known roles of essential metals such as zinc and iron and those of toxicological significance such as cadmium and mercury will be described. The regulatory DNA-binding proteins characterized by a zinc-containing region at the binding domain ("zinc finger-loop") will be explained. Current knowledge of the physiological significance of these proteins will be described. Hypotheses will be proposed for metal toxicity through interaction at the zinc-binding site. Findings on nickel-induced transformation of Chinese hamster embryo cells which suggest deletions of a tumor suppressor gene localized on the X chromosome will be presented. Approaches for chromosomal mapping of key sites in nickel-induced carcinogenesis will be described. Transcriptional induction by metals of the synthesis of metallothioneins, metal-binding proteins, will be discussed. Research will be presented, using yeast as a model eukaryotic system, which has demonstrated a regulatory gene encoding a metal-activated DNA-binding protein with a cysteine-rich metal-binding domain. Regulation by mercury in bacteria of the mer gene which codes for enzymes that detoxify the mercuric ion will be described. It will be explained how mercuric ion interacts with the transcriptional activator protein MerR, which together produce a distortion in the DNA promoter site for the mer gene facilitating its transcription.

Introduction. Carol T. Walsh, Boston University School of Medicine, Boston, MA.

Zinc Finger-Loop Domains in Gene-Regulating Proteins as Potential Targets for Metal Toxicity. F. William Sunderman, Jr., University of Connecticut Medical School, Farmington, CT.

Deletion of Heterochromatin and a Senescence/Tumor Suppressor Gene as a Mechanism of Nickel Carcinogenesis. Max Costa, New York University Medical Center, New York, NY.

Regulation of Metallothionein Gene Expression in Man and Yeast. Michael Karin, University of California, San Diego School of Medicine, La Jolla, CA.

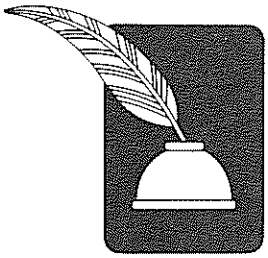
The merR Metalloregulatory Protein: Genetic Switch Controlling Expression of Mercurial Detoxification Genes. Thomas V. O'Halloran, Northwestern University, Chicago, IL.

Application of Pharmacokinetics in Developmental Toxicity Risk Assessment

Sponsored by the Reproductive and Developmental Toxicology Specialty Section

Chairperson: Robert J. Kavlock, U.S. EPA, Research Triangle Park, NC

Advancements in the art of performing risk assessments on suspected developmental toxicants will primarily occur as research progresses in four distinct areas: 1) better understanding of the relevance and biological significance of the manifestations of developmental toxicity; 2) application of pharmacokinetic information to assist in high-to-low dose and species-to-species extrapolations; 3) increased knowledge of mechanisms of dysmorphogenesis; and 4) better characterization of human exposure patterns. In the near future, it is likely that significant contributions to the risk assessment process will be derived mainly from the first two areas. The presentors will discuss the utilization of pharmacokinetic information to detect developmental hazards and to extrapolate develompental risk. The state-of-the-art in terms of pregnancy-related alterations in physiology that impact on pharmacokinetics, and the actual utilization of pharmacokinetic information in improving study design, study interpretation, and within and between species comparisons of adverse developmental outcomes will be discussed. Each speaker will highlight those research needs that when addressed will best facilitate the incorporation of pharmacokinetic information into the risk assessment process. While this research area is still in its infancy, sufficient progress has been made over the last five years to suggest that such efforts will be fruitful.



Symposia

Introduction. Robert J. Kavlock, U.S. EPA, Research Triangle Park, NC.

Physiological Alterations During Pregnancy: Impact on Toxicokinetics. Donald R. Mattison and Carol Cistola, University of Arkansas for Medical Sciences, Little Rock, AR.

Pharmacokinetic Considerations in the Design of Developmental Toxicology Studies. Heinz Nau, Free University, Berlin, F.R. Germany.

Correlation of Pharmacokinetic Data With Endpoints of Developmental Toxicity. John F. Young, National Center for Toxicological Research, Jefferson, AR.

Pharmacokinetic Considerations in the Extrapolation of In Vitro Test Data. Robert J. Kavlock, U.S. EPA, Research Triangle Park, NC.

The Application of Physiologically Based Pharmacokinetic Models to Adjust for Species Differences in Estimating Human Developmental Risk. John L. Gabrielsson, University of Upsala, Sweden.

Macrophage-Xenobiotic Interactions: Modulation of Toxicity and Macrophage Functions

Sponsored by the Immunotoxicology Specialty Section

Chairpersons: Lawrence Schook, University of Illinois, Urbana, IL and Peter Bick, Eli Lilly and Company, Greenfield, IN

This symposium was organized to present recent results on interactions between macrophages and xenobiotics and how such interactions affect either the nature and scope of the toxic response and/or changes in macrophage differentiation and function. The macrophage represents a cell which is central to the initiation and maintenance of an immune response. The cell is characterized by its resistance to pathogens and chemicals and is noted for its vast metabolic properties. These characteristics have permitted immunotoxicologists to study how the metabolic state of the macrophage may affect xenobiotic-induced toxicity and conversely how the xenobiotic may affect the functional state of the macrophage. This area of study has proven to be extremely rewarding since much knowledge has been gained in understanding the metabolism of xenobiotics, mechanisms of toxicity, regulation of macrophage differentiation and dissection of macrophage activation states. The development and use of xenobiotics which affect the immune system (e.g., recombinant hematopoietic growth factors and cytokines) will require that we continue to develop models to understand macrophage-xenobiotic interactions.

Mechanisms for Alteration of Macrophage Differentiation and Activation Following Chemically-Induced Toxicity. Lawrence B. Schook, Laboratory of Molecular Immunology, Dept. of Animal Sciences, University of Illinois, Urbana, IL.

Effect of Lead on Macrophage Growth and Function. M. Kowolenko, Bristol-Myers Co., Dept. of Investigative Toxicology, Syracuse, NY and D.A. Lawrence, Albany Medical College, Dept. of Microbiology and Immunology, Albany, NY.

Modulation of Chemically-Induced Hepatotoxicity by Altering Macrophage Function. Debra L. Laskin, Graduate Program in Toxicology, Rutgers University, Piscataway, NJ.

Activation of Macrophages and Xenobiotics. D.O. Adams, M. Klan, and J.G. Lewis, Laboratory of Cellular and Molecular Biology of Leukocytes, Departments of Pathology and Microbiology-Immunology, Duke University Medical Center, Durham, NC.

Genetic Determinants of Carcinogen Susceptibility in Rodents and Man

Sponsored by the Molecular Biology Specialty Section

Chairperson: Cheryl Walker, Department of Cellular and Molecular Toxicology, CIIT, Research Triangle Park, NC

Tumor induction is a multi-stage process, influenced by at least two types of genes: (1) cellular oncogenes and (2) tumor suppressor genes. Whereas oncogenes are activated by chemical carcinogens via mechanisms such as point mutations, tumor suppressor genes must be inactivated in order for neoplastic transformation to occur. Hereditary inactivation of a tumor suppressor gene is the strongest known risk factor for human cancer. Therefore, this class of genes can act as determinants of carcinogen susceptibility. This symposia will examine how such genetic determinants of susceptibility influence neoplastic transformation in rodents and man. In various rodent models, the role of tumor susceptibility genes in the process of chemical carcinogenesis has been examined in some detail. This area will be covered in the symposia by utilizing three rodent models as specific examples. First, an introduction to oncogenes and tumor suppressor genes will be presented in the context of a rat model for renal carcinogenesis. In this model, susceptibility to kidney tumors is due to the inactivation of a putative tumor suppressor gene, and the interation of this inactivated gene with activated cellular onogene(s) results in tumor formation. The second presenter will discuss how susceptibility to chemically induced lung tumors in inbred mice can be determined by at least three *Pas* (pulmonary adenoma susceptibility) genes, one of which may be the proto-oncogene K-*ras*. There are two alleles

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of this K-*ras* gene; strains with the 0.55 kb RFLP allele develop tumors, whereas those with the 0.70 kb RFLP allele are resistant. The last rodent model will indicate how a single gene, *Hcs*, that acts during the promotion phase of hepatocarcinogenesis has been found to be largely responsible for susceptibility to liver tumors in male C3H mice. The last two speakers will present information on how such genes act as a factor in human carcinogen risk. One will present work using normal human fibroblasts isolated from individuals with a hereditary predisposition to cancer that spontaneously transform to immortality in tissue culture and undergo complete transformation to tumorigenicity following transfection with a single activated H-*ras* oncogene. The final presenter will describe how information regarding specific tumor susceptibility genes can be utilized in the process of risk assessment by use of the two stage MVK model.

Introduction. Cheryl Walker, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

Tumor Suppressor Gene and Cellular Oncogene Interactions in a Rat Model for Renal Carcinogenesis. Cheryl Walker, Chemical Industry Institute of Technology, Research Triangle Park, NC.

Genetic Determinants of Chemically Induced Lung Cancer in Mice and Humans. Gary Stoner, Medical College of Ohio, Toledo, OH.

Genetic Control of Murine Hepatocarcinogenesis. Norman R. Drinkwater, University of Wisconsin, Madison, WI.

Human Cells *In Vitro:* Analysis of Cancer Susceptibility and Mechanisms of Tumorigenesis. Machael A. Tainsky, University of Texas, Houston, TX.

Genetic Determinants of Carcinogen Susceptibility: Implications for Risk Assessment. Thomas Starr, Chemical Industry Institute of Toxicology, Research Triangle Park, NC.

New Advances in Chemically-Induced Mitochondrial Dysfunction: Relationships to Toxicity

Sponsored by the Mechanisms Specialty Section

Chairperson: Glenn F. Rush, Eli Lilly and Co., Greenfield, IN

Within the last decade, there has been an increased awareness of the critical role that mitochondria play in homeostatic cell functions. Thus, toxicant-induced disturbances in functions such as mitochondrial calcium uptake, ATP synthesis, etc, may initiate a sequence of biochemical changes that can ultimately lead to cell death. Recent reports describe new methods for evaluating mitochondrial functon both in the intact cell and in isolated mitochondria. This symposium is designed to bring these new concepts in chemically-induced mitochondrial injury together in a single session. The symposium will be divided into two basic sections. The first three speakers will focus on the biochemical techniques and mechanisms involved in chemically-induced mitochondrial injury. The last two speakers will focus their presentations on specific toxicants that appear to target the mitochondia.

Introducton. Glenn F. Rush, Eli Lilly and Co., Greenfield, IN.

Direct Probing of Mitochondrial Function in Intact Cells. Rick G. Schnellman, University of Georgia, Athens, GA.

Overview of Mitochondrial Glutathione. Donald J. Reed, University of Oregon, Corvalis, OR.

Biochemical Alterations in Mitochondrial Function Leading to Lethal Cell Injury. Glenn F. Rush, Eli Lilly and Co., Greenfield, IN.

Biochemical Reactions Leading to Parkinsonian Symptoms Elicited by MPRP. T. Singer, University of California, San Francisco, CA.

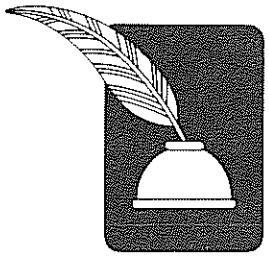
The Mitochondrial Toxicity of Cysteine-S-Conjugates: Studies with Pentachlorobutadienyl-L-cycteine (PCBC). A. Wallin, W. Alton Jones Cell Science Center, Lake Placid, NY.

Peroxisome Proliferation and Nongenotoxic Carcinogenesis

Sponsored by the Mechanisms Specialty Section

Chairperson: David E. Moody, Center for Human Toxicology, Department of Pharmacology and Toxicology, University of Utah, Salt Lake City, UT

First observed in 1965 as a causal factor in clofibrate-induced hepatomegaly, a number of diverse compounds have now been found to induce hepatic peroxisome proliferation. The identification of peroxisome proliferators is based upon predictable cellular changes, which include: 1) hepatomegaly accompanied by increases in peroxisomes and smooth endoplasmic reticulum; 2) increases in peroxisomal and non-peroxisomal enzymes involved in lipid and hydrogen peroxide metabolism; 3) induction of drug-metabolizing enzymes; and 4) hypolipidemia. The limited number which have undergone chronic bio-



Symposia

assays, 5) have also been found to cause hepatocarcinogenesis after long-term, relatively high dose, continuous treatment. This latter finding brings this class of compounds into the forefront of toxicological interest. Based on these criteria, greater than 50 chemicals have now been found to effect peroxisome proliferation. These compounds, of diverse commercial and environmental concern, include fibrate and non-fibrate hypolipidemic agents, other drugs, plasticizers with analogs of 2-ethylhexanol as the esters, selected pesticides, and certain halogenated hydrocarbons. First, an updated overview on the phenomenon of peroxisome proliferation, and their potential mechanism of carcinogenesis will be presented. Second, correlative *in vivo* and *in vitro* studies will be presented which address structure-activity relationships, species specificity, and mechanisms of proliferation. Third, some alternative avenues of carcinogenesis by these chemicals will be addressed. The formal presentations will close with comments on the regulatory perspective in regard to peroxisome proliferation and human cancer risk assessment, followed by a panel discussion on items of special interest.

Introduction. David E. Moody, University of Utah, Salt Lake City, UT.

Peroxisome Proliferation: An Overview. Janardan K. Reddy, Northwestern University, Chicago, IL.

Hepatic Peroxisome Proliferation: *In Vivo* and *In Vitro* Correlations. Brian G. Lake, BIBRA, Surrey, England.

Liver Tumor Promoting Effect of Chemicals that Cause Peroxisome Proliferation. James A. Popp, CIIT, Research Triangle Park, NC.

Peroxisome Proliferation: A Human Cancer Assessment Perspective. David H. Reese, USEPA, Washington, DC.

Roundtable Discussion.

Mechanisms of Hypoxic Cell Injury

Sponsored by the Mechanisms Specialty Section

Chairperson: James P. Kehrer, Division of Pharmacology and Toxicology, College of Pharmacy, University of Texas at Austin, Austin, TX

Hypoxic or ischemic tissue injury plays a major role in human pathology. This symposium will focus on some of the changes that occur in hypoxic cells and intact tissues which are currently believed to play a role in the mechanism of cellular injury and death. The most obvious and rapid change in hypoxia is the loss of ATP. Mitochondrial dysfunction appears to be a critical factor leading to hypoxic injury, but this dysfunction is heterogeneous, depending on regional oxygen availability, cell type, degree of differentiation and demand. In general, cells which have a relatively low density of mitochondria (such as fetal and transformed cells) can respire effectively at O_2 concentrations lower than those required for normal adult cells. However, all cells alter various functions during anoxia in order to preserve mitochondrial protonmotive force. These changes involve a loss of ionic homeostasis which may mimic damage as well as increase the cell's susceptibility to xenobiotic-induced injury. ATP depletion is a necessary but insufficient event preceding cell death. Other changes which have been observed during hypoxia include activation of plasma membrane bound phospholipase, increased membrane fluidity, increased permeability of the plasma membrane, rupture of surface blebs, increased cytosolic calcium, decreased mitochondrial potentials and decreased cytosolic pH. The relative importance of these changes in cell death has not been established. Recent evidence has suggested that intracellular acidosis suppresses the degradative processes activated by hypoxic and toxic injury. Restoration of normal pH accelerates cell killing by removing this inhibition suggesting cellular pH changes may be involved in reperfusion injury. The extensive regulatory role of calcium has focussed a great deal of attention on this cation as a mediator of hypoxic injury. However, increases in intracellular calcium during hypoxia do not correlate with the activation of phospholipase A and may be less important in mediating the cell injury than those changes evident at reperfusion. The generation of reactive oxygen species has been demonstrated in reperfused tissues and also postulated to be involved in some of the changes observed during hypoxia. Studies using isolated-perfused liver do not support this postulate. However, work in isolated-perfused heart tissue has revealed changes during hypoxia consistent with oxidative stress. Model and/or tissue related differences clearly are important considerations in studies on hypoxic injury. Decreased mitochondrial function appears to be central to the development of hypoxia-induced damage since there is no evidence that cells whose ATP content is not seriously depleted undergo hypoxic injury. The loss of ATP leads to ionic imbalances and the activation of various degradative processes which ultimately kill the cell. However, the specific degradative pathway, which is the critical determinant of cell death, remains unknown.

Introduction. James P. Kehrer, The University of Texas, Austin, TX.

Mitochondrial Function During Hypoxia. Dean P. Jones, Emory University School of Medicine, Atlanta, GA.

Digitized Videomicroscopy of Hypoxic Cell Injury: The Role of Intracellular pH. John J. Lemasters, University of North Carolina School of Medicine, Chapel Hill, NC.

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Irreversible Cell Injury in Liver Ischemia. John L. Farber, Thomas Jefferson University, Philadelphia, PA.

Oxidative Stress During Hypoxia in Isolated-Perfused Liver Tissue. Hartmut Jaeschke, Baylor College of Medicine, Houston, TX and Jerry R. Mitchell, The Upjohn Company, Kalamazoo, MI.

Glutathione-Conjugate Mediated Toxicities

Sponsored by the Mechanisms Specialty Section

Chairperson: Terrence J. Monks, Division of Pharmacology and Toxicology, College of Pharmacy, University of Texas at Austin, Austin, TX

Glutathione (γ-glutamyl-L-cysteinylglycine; GSH) is present in high concentrations in most living cells and participates in a variety of vital cellular reactions. In particular, GSH plays an important role in the detoxication of potentially toxic electrophiles by either reductive or conjugative mechanisms. Compounds that form GSH conjugates are usually readily excreted in urine as their corresponding mercapturic acids, which are S-conjugates of N-acetyl cysteine. However, in recent years evidence has accumulated suggesting that GSH conjugation plays an important role in the formation of reactive (toxic?) metabolites from a variety of chemicals. Thus, several classes of compounds are converted via conjugation with GSH into either cytotoxic, genotoxic or mutagenic metabolies. This symposium will highlight recent advances in our knowledge of: 1) the types of compound that undergo activation via conjugation with GSH; 2) the enzymology and regulation of GSH conjugate metabolism; and 3) the mechanism(s) and cellular toxicity of these GSH conjugates.

The halogenated alkanes were the first class of compounds for which conjugation with GSH was demonstrated to result in the formation of reactive metabolites. Vicinal dihaloalkanes form sulfur mustards upon GSH conjugation. Subsequent rearrangement results in the formation of highly reactive episulfonium ions that can react with cellular nucleophiles and are implicated in the cytotoxicity and mutagenicity of these comounds. In contrast, haloalkenal GSH conjugates require processing by the enzymes of the mercapturic acid pathway, and ultimately by cysteine conjugate β-lyase to give rise to various thiol containing reactive metabolites. The distribution and properties of the enzymes of the cysteine conjugate β-lyase pathway will be discussed. In particular, those factors that may regulate β-lyase activity and thus modulate β-lyase dependent activation will be presented.

Other compounds that require GSH dependent activation exhibit β-lyase independent toxicities. For example, oxidation of benzoquinols in the presence of GSH gives rise to multi-GSH substituted conjugates that are potent nephrotoxicants. The toxicity of these conjugates is dependent upon their metabolism by renal tubular γ-glutamyl transpeptidase but does not appear to require the involvement of β-lyase. Finally, several reactions of thiols with electrophiles are reversible. For example, benzyl or allyl isothiocyanate form GSH conjugates that are in equilibrium with the parent compound. The position of this equilibrium is influenced by conditions of pH and the concentration of the reactants. The conjugates of the isothiocyanates thus display a cytotoxicity similar to the parent compound. These conjugates thus serve as storage forms of the electrophile with initial detoxication being followed by release of the electrophile at sites where local conditions favor a shift in the reversible equilibrium.

In conclusion, several different classes of compounds have now been shown to undergo activation via conjugation with GSH. Differences in the processing of these conjugates results in a variety of toxicities, the mechanistic basis of which also varies.

Introduction. Terrence J. Monks, University of Texas, Austin, TX.

Glutathione-Dependent Bioactivation of Haloalkanes and Haloalkenes. Marion W. Anders, University of Rochester, Rochester, NY.

Genotoxicity of Amino Acid S-Conjugates. Wolfgang Dekant, University of Wurtzburg, FRG.

Enzymes of the Cysteine Conjugate β-Lyase Pathway. James L. Stevens, Alton Jones Cell Science Center, Lake Placid, NY.

Quinol-Linked Glutathione Conjugate-Mediated Toxicities. Serrine S. Lau, University of Texas at Austin.

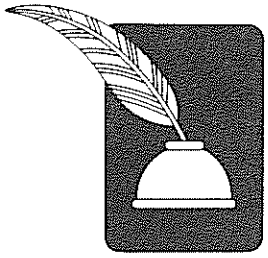
Reversible Glutathione Conjugation: Toxicological Implications. Peter J. van Bladeren, TNO-CIVO, The Netherlands.

New Directions in Cancer Risk Assessment: Modifying the EPA's Guidelines

Sponsored by the Carcinogenesis Specialty Section

Chairpersons: Theodore M. Farber, Science Regulatory Services International, Washington, DC and Penelope Fenner-Crisp, U.S. EPA, Washington, DC

The EPA's current cancer risk assessment guidelines have been actively employed by the agency for approximately five years. In that time the EPA and the scientific community have realized



Symposia

that certain aspects of these guidelines should be examined in light of new information and approaches regarding cancer risk assessment which have been developed within the discipline during this time-frame. The EPA in the last year has been very active in its reexamination of these guidelines utilizing the opinions of experts within and outside of the agency in its consideration of the modification of these guidelines. This symposium will deal with several aspects that have been discussed in this process. It is hoped that this symposium will allow the membership of the Society to suggest necessary and valid scientific changes that will assist the EPA in its deliberations.

Introduction. Theodore M. Farber, Science Regulatory Services International, Washington, DC.

Classifying Carcinogens by the Weight-of-the Evidence. Gary Flamm, Science Regulatory Services International, Washington, DC.

The Search for Adequate Bioassay Data. Crude Biology Versus Statistics. Gene McConnell, Raleigh, NC.

New Developments in Carcinogenic Risk Assessment. Dan Krewski, Health and Welfare Canada, Ottawa, Ontario.

Carcinogen Risk Assessment-Evaluation of the Process. Bill Farland, U.S. EPA, Washington, DC.

Annual Meeting Information

Annual Meeting Banquet

All meeting registrants may sponsor and prepay for tables of 10 at the Annual Meeting Banquet and Awards Presentation, which will be held this year on **Wednesday, February 14.** Registrants who purchase tables may choose their seating arrangements prior to the banquet by stopping by the SOT office at the Fountainebleau. Requests will be honored on a first come, first served basis. ●

SOT Accepts Visa and MasterCard

The Society of Toxicology now accepts Visa and MasterCard payments for Annual Meeting registration, payment of annual dues, and other Society expenses. Using your credit card is convenient and efficient. International members also avoid the problems of converting funds to U.S. dollars.

Please remember to complete the appropriate form (e.g., registration or dues renewal) and return it to headquarters to ensure proper credit. ●

Guest Hospitality Center and Program

Guests must be registered for the Annual Meeting to have access to the Hospitality Center and to be eligible for the discounted tour rates. Guests can register by using the Annual Meeting registration form.

The Hospitality Center will be open daily beginning Sunday afternoon.

The Center will be staffed Sunday through Wednesday with a representative from All Florida Adventure Tours. They will provide you with information on the city, register you for the tours offered through the Society, or distribute tour tickets purchased in advance of the meeting.

A special Guest Program has been planned for this meeting and will be printed in the Preliminary Program, to be mailed in early December. It will include a tour on Sunday, February 11 to the Florida Keys.

Social Evening

The social evening on Tuesday, February 13, will be a spectacular latin Fiesta in the heart of Little Havana, featuring continuous international music and dancing and a super all-u-can-eat Cuban dinner. IT'S HOT . . . IT'S COOL . . . IT'S EXCITING . . . IT'S MIAMI LATINO!

Post Tour Option

SOT is offering a special two-day cruise to Nassau following the Annual Meeting. The Cruise departs on Friday, February 16 and returns to Miami on the 18th. The SOT discounted rates range from $196 to $236 (plus $20 port charges). This includes entertainment on board and meals. The deadline for reservations is December 15, 1989. For more information contact: ALL FLORIDA ADVENTURE TOURS at 11137 N. Kendall Dr., Miami, FL 33176, or call toll-free 1-800-33-TOUR-3. ●

Register Early for the Placement Service

Placement Service registration will be somewhat different this year. The deadline for early registration was advanced because the Annual Meeting takes place earlier in the year. A new fee schedule was developed to cover the rising cost of expenses such as photocopying at the Annual Meeting. It is much more expensive to do these things at the Meeting, so the late registration fee increased. However, early registration fees are the same as in 1986.

If you register prior to **December 15, 1989,** you will receive a set of job openings/descriptions or resumes prior to the Annual Meeting; employers will also receive a computer search of the candidates who are preregistered. These will all be current openings/candidates (none leftover from last year). Those who register early will be two steps ahead of those who register at the Meeting and it is also much cheaper.

Changes in the Placement Service operations have been made to make it easier to match people with jobs. Candidates are asked to bring five copies of their resume to the meeting, and to bring them to the Placement Registration area as early as possible (preferably Monday). The Placement Service will be open Monday from 10:00 am to 3:30 pm for registration of

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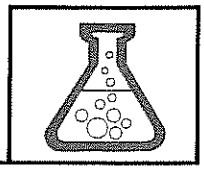
Placement Services



Associate Scientist/Associate Toxicologist

A position is available for a highly skilled and motivated associate scientist/toxicologist in a multidisciplinary Life Science Research group. Requirements include a B.S. or M.S. in the life sciences (preferably toxicology or nutrition) and at least 1 to 2 years of experience and *excellent technical skills* in conducting animal research studies. Experience in conducting GLP studies is desirable. Responsibilities include, but are not limited to, acting as study director and/or support contributor in challenging food safety and nutritional investigations and preparing technical reviews and reports. Send Curriculum Vitae to: Ms. Kathy Gibson, Human Resources Representative, Hershey Foods Corporation, 14 E. Chocolate Avenue, P.O. Box 814, Hershey, PA 17033 or call (717) 534-7829.

Research Associate Analytical Chemist/Toxicologist

Unique opportunity to work with scientific group designing life support systems for manned space flight: The Consortium for the Space Life Sciences, located at The University of Alabama in Huntsville, Huntsville, Alabama is recruited for a Research Associate. Qualifications include an advanced degree in Analytical Chemistry or Toxicology, with a strong background in instrumentation and risk assessment. Successful applicant will have working knowledge of EPA, NIOSH and related methodologies for the analysis of inorganic and organic constituents in air and water. Successful applicant will have experience using the following instrumentation: AA, ICP, UV/Vis, IR, FTIR, GC, GC/MS, LC, and TOC. Applicants should have demonstrated research experience by evidence of publication in the scientific literature. Candidate must be a U.S. citizen.

Respond to: Ms. Linda Kieffer
Staff Employment Office
The University of Alabama in Huntsville
Huntsville, AL 35899

An Equal Opportunity/Affirmative Action Employer

Assistant Professor of Toxicology

The School of Public Health, University of Texas Health Science Center at Houston, has reopened the search for a toxicologist in the position of Assistant Professor. Although a doctorate with research and teaching interests/experience in occupational/industrial toxicology is preferred, adequate doctoral training in environmental toxicology with some experience in industrial toxicology will be considered. Send curriculum vitae with three references to Dr. Ernst Davis, Convener of Environmental Sciences, School of Public Health, The University of Texas Health Science Center, P.O. Box 20186, Houston, TX 77225. The University of Texas is an Equal Opportunity Employer.

2-Year Postdoctoral Research Training Program

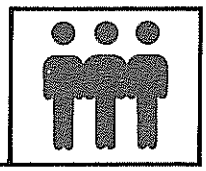
Chemical Industry Institute of Toxicology

The Chemical Industry Institute of Toxicology (CIIT) offers a 2-year postdoctoral research training program in toxicology for individuals who have recently earned a D.V.M., M.D., Ph.D. or other advanced degree in an academic discipline related to toxicology. Research programs stress elucidation of basic mechanisms of toxicity and chemical carcinogenesis, pharmacokinetics, disposition and metabolism, teratogenicity, development of in vitro tests for toxicity, cell biology, immunotoxicity, inhalation toxicology, epidemiology, biostatistics and quantitative risk assessment.

For further information, contact:

Human Resources Manager
Chemical Industry Institute of Toxicology
P.O. Box 12137
Research Triangle Park, NC 27709

Member News



Dr. **Ninfa Indacochea-Redmond** was appointed Manager of Toxicology and Metabolism with the Midwest Research Institute in Kansas City, Missouri. ●

Placement Service

continued from page 18

employers as well as candidates. No matching or files will be available until Tuesday morning. This year we will have confidential cards available for those who want to see what jobs are available but don't want to register; these can be obtained at the Placement Registration Office.

Make plans now to register early with the Placement Service to get the most out of your activity. Enclosed is a candidate registration form for your convenience; employer registration forms can be obtained from SOT headquarters. ●

Publications of Interest

Autoimmunity and Toxicology—*Immune Disregulation Induced by Drugs and Chemicals,* ed., M.E. Kammuller, N. Bloksma and W. Seinen, Elsevier Science Publishers, Biomedical Division, P.O. Box 1527, 1000 BM Amsterdam, The Netherlands.

Biological Markers in Pulmonary Toxicology, $22.50, The National Academy Press, 2101 Constitution Avenue, NW, Washington, DC 20418.

Biological Markers in Reproductive Toxicology, $27.95, National Academy Press, 2101 Constitution Avenue, NW, Washington, DC 20418.

Canine Research Environment, $30.00, Scientists Center for Animal Welfare, 4805 St. Elmo, Bethesda, MD 20814; (301) 654-6390.

The Consolidated Chemical Regulation Guidebook Federal/State/International Requirements, Andrew B. Waldo, $495.00, Executive Enterprises Publications, Executive Enterprises Building, 22 West 21st Street, New York, NY 10010-6904; (212) 645-8770, fax (201) 675-4883.

Digest of Education Statistics, $19.00, United States Department of Education, Superintendent of Documents, Washington, DC 20402-9325; (202) 783-3238.

The Environmental Litigation Deskbook, K.A. Touby, K.J. Smith, and J.T. Reilly, $75.00, Executive Enterprises Publications Co., Inc., 22 West 21st St., New York, NY 10010-6904; (212) 645-7880.

Elementary and Secondary Education for Science and Engineering, $7.00, U.S. Government Printing Office, Superintendent of Documents, Washington, DC 20402-9325; (202) 783-3238.

Environmental Risk Assessment, $8.00, Alliance of American Insurers, 1501 Woodfield Rd., Schaumburg, IL 60173; (312) 330-8500.

Environmental Quality, $13.00, Council on Environmental Quality, Superintendent of Documents, Washington, DC 20402-9325; (202) 783-3238.

Issues in Medical Waste Management, $2.25, U.S. Government Printing Office, Superintendent of Documents, Washington, DC 20402-9325; (202) 783-3238.

James Madison Elementary School: A Curriculum for American Students, $2.50, United States Department of Education, stock number 065-000-00350-3, Superintendent of Documents, Washington, DC 20402-9425; (202) 783-3238.

Radioactivity and Health: A History, J.N. Stannard, $71.00, Life Sciences Center, K4-14, Battelle, Pacific Northwest Laboratories, P.O. Box 999, Richland, WA 99352.

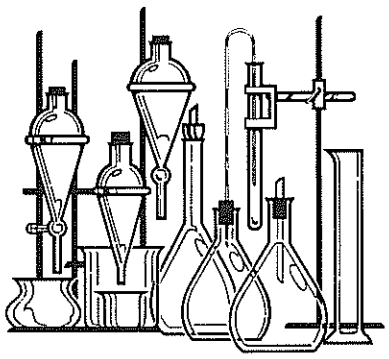
Science in Orbit: The Shuttle and Spacelab Experience: 1981–1986, NASA, $16.00, stock number 033-000-01039-7, Dept. 36-EX, Superintendent of Documents, Washington, DC 20402-9325; (202) 783-3238.

Toxic Substances Controls Guide, M.D. Worobec, G. Ordway, $35.00, BNA Books Distribution Center, 300 Raritan Center Parkway, P.O. 7816, Edison, NJ 08818-7816; (201) 225-1900, fax (201) 225-0812.

Toxicological Profile for Chromium, Agency for Toxic Substances and Disease Registry, U.S. Dept. of Health and Human Services, Public Health Service Centers for Disease Control, Atlanta, GA 30333.

Well-being of Nonhuman Primates in Research, $30.00, 4803 St. Elmo, Bethesda, MD 20814-4805; (301) 654-6390.

What You Need to Know to Live With Chemicals, R.I. Freudenthal and S.L. Freudenthal, $14.95, Hill and Garnett Publishing, Inc., P.O. Box 180, Greens Farms, CT 06436; (203) 222-3440. ●

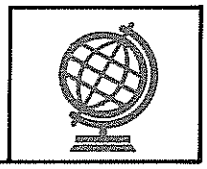


Animals in Research

By Loren D. Koller, DVM, Ph.D.

The SOT Animals in Research Comittee has been actively engaged in developing policy for use of animals in toxicological research. The Committee prepared, with subsequent Council approval, a document, "Comments on the LD_{50} and Acute Eye and Skin Irritation Tests," which has been submitted to *Fundamental and Applied Toxicology* for consideration for publication. A "Position Statement Regarding Use of Animals in Toxicology," and "Society of Toxicology Guiding Principles in the Use of Animals in Toxicology," was also approved by the Council and is enclosed with this newsletter. Copies will be available to the Society membership and to regional chapters. Another pamphlet, "Benefits of Animal Testing in Toxicology to Humans and Animals," is being developed by the Committee. The Committee is also in the process of preparing the proceedings of the 1989 SOT Meeting, "Refining Animal Experiments in Toxicologic Research Symposium," for publication. The Committee has identified a speaker. **Dr. Gerhard Zbinden**, to deliver a presentation at the 1990 SOT meeting on the benefits of using animals in toxicology/safety testing protocols. The Committee welcomes comments and suggestions from the membership regarding the documents, and other issues and topics, that the Committee should address. ●

Upcoming Conferences



Tenth Symposium on Pesticide Formulations and Application Systems, October 25–26, 1989, Denver Marriott City Center, Denver, CO. Contact: Anne McKlindon, ASTM 1916 Race Street, Philadelphia, PA 19103-1187; (215) 299-5490.

Toxicology for the 1990's in the Southwestern United States, November 10–11, 1989, San Antonio, Texas. Sponsored by Gulf Coast Society of Toxicology, Southwestern Association of Toxicologists and Southwest Environmental Mutagen Society. For more information, contact: Dr. John A. Dellinger, Manager, Toxicology and Applied Pharmacology, Southwest Research Institute, 6220 Culebra Road, San Antonio, TX 78228-0510; (512) 522-2569.

Third International Congress and Fair for Environmental Technology, November 21–23, 1989, Linz, Austria. For information, contact either the Austrian Trade Commission, or the organizer directly: Trend Commerz BmbH, A-4021 Linz/ Austria, P.O.B. 765, (tel) (732) 27 45 75.

Chemically Induced Cell Proliferation: Implications for Risk Assessment, November 29–December 2, 1989, Barton Crest Conference Resort, Austin, TX. For information, contact: Karen Engel, The University of Texas M.D. Anderson Cancer Center, P.O. Box 389, Smithville, Texas 78957.

Fourth International Meeting on Biological Reactive Intermediates, hosted by the University of Arizona Center for Toxicology, January 14–17, 1990 at the Double Hotel, Tucson, AZ. For further information, contact: Dr. I. Glenn Sipes, College of Pharmacy, University of Arizona, Tucson, AZ 85721, (602) 626-7123.

Second International Conference on Environmental Analytical Chemistry; Workshop on Identification of Problems, Methods and Monitoring Applications within the Pacific Basic Rim Nations, January 17–19, 1990, Honolulu, HI. For information, contact: Dr. S. Hanamura, The Center for Environmental Research, 468 Hollister Hall, Cornell University, Ithaca, NY 14853; (607) 255-6837.

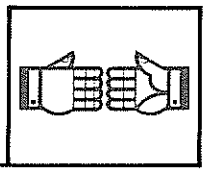
Biological Effects of Dietary Restriction, March 5–7, 1990, Ramada Renaissance Hotel, Washington, DC. For information, contact: Ms. Karen Taylor, ILSI, 1126 Sixteenth St., NW, Washington, DC 20036; (202) 659-3859.

Organophosphates: Chemistry, Fate and Effects, April 22–27, 1990. For further information, contact: ACS Meetings, 1155 16th St., NW, Washington, DC 20036, or Dr. Janice Chambers, Department of Biological Sciences, Mississippi State University, PO Drawer GY, Mississippi State, MS 39762; (601) 325-7572.

Association for Behavior Analysis, 16th Annual Convention, May 27–31, 1990, Opryland Hotel, Nashville, TN. For information, contact: ABA, Western Michigan University, 258 Wood Hall, Kalamazoo, MI 49008-5052. Telephone: (616) 387-4495.

Toxic Substances Control Act Management Workshop, December 4–5, 1989, Washington Marriott Hotel, Washington, DC. For information, contact: Executive Enterprises, Inc., 22 West 21st Street, New York, NY 10010-6904. ●

Committee News



RALA on the Move

By Carol M. Schiller, Ph.D., J.D., DABT

The Regulatory Affairs and Legislative Assistance Committee (RALA) is the focus for activities that aid and support the scientific activities of regulatory agencies and legislative bodies as well as keep Council abreast of new developments or legislation that concern(s) the regulation of chemicals. The Committee has made considerable progress in the last year in its efforts to facilitate communication of scientific information to the public(s).

As a first step, representatives of the specialty sections and technical committees met with the Committee during the annual meeting to discuss documents to be drafted in their areas of special expertise. These educational documents are being used as the scientific background for addressing legislative committees, public hearings, agencies and the PTA (any influential decision-making group) or just answering questions as institutions receive inquiring letters. The "A Look at Animal Use in the Science of Toxicology" document drafted by the Animals in Research Committee is an example of the kind of brochure that is useful in this manner. President McClellan has directed the Committee to work with the Animals in Research Committee to utilize this document in future direct contacts.

A second, more recent activity, involves concerns raised by the membership about the declining research funds for high calibre projects. The Council has written a letter endorsing the funding level of the House appropriations bill urging no further cuts. The Ad Hoc Group for Medical Research Funding is an advocacy group that will transmit that endorsement. Next year, the Society may draft a statement for presentation directly to the House subcommittee. The Committee is considering a lunch workshop at the annual meeting on "how to" contact public officials.

Further, an *ad hoc* subcommittee has been appointed to examine, evaluate and recommend avenues that the Society may pursue to encourage and facilitate the support of research projects through private funding mechanisms. This subcommittee will report on its activities at the annual meeting.

It has been suggested that the Committee provide a forum for the presentation of differing viewpoints on a particular issue at one of the future annual meetings. As always, the success of these projects depends on the continuing interest and support of the Committee members, Council and the Society. ●

Watching Washington

Animal Welfare Regs Finalized

Published in final form, Parts 1 and 2 of the Animal Welfare Act regulations have been rewritten and reorganized so that reporting and recordkeeping requirements are eliminated. Part 3 of the regulations is also final with a minor change eliminating the "veterinary care" section for each species and opting for an overall statement of veterinary care requirements contained in Part 2.

Although the finalized version of the Act reflects many of the changes suggested by the research community, a number of provisions still concern researchers and research organizations. Among them:

- Institutional Animal Care and Use Committee's (IACUCS) "review . . . of components of proposed activities related to the care and use of animals."
- Proposals to conduct activities involving animals must contain identification of species and number of animals, complete description of proposed use of animals, complete description of procedures to limit discomfort to animals, and any euthenasia method to be used.
- APHIS investigators would have access to research facility records and IACUC records making such information available under the Freedom of Information Act. APHIS also claims authority to photograph research facilities.
- Sources of Class "B" dealers are limited to other dealers, government owned and operated pounds or shelters and private animal pounds or shelters. Dealers may not obtain random source dogs and cats from individuals who have not bred and raised the animals on their own premises. The holding period for animals obtained from pounds becomes 10 days and additional information is required from persons selling animals to dealers. ●

New Regulation To Smooth Significant New Use Rules

EPA Administrator William Reilly's signing of the Expedited New Chemical Follow-up Rule, also known as the Generic Significant New Use Rule (SNUR), this summer is intended to make SNURs more timely, more predictable, and more uniform. The result of a series of informal and public meetings between EPA, the Toxic Substances Dialogue Group and others, the new procedural regulation applies to new chemicals for which EPA has issued orders and to new chemicals for which no orders have been issued but which meet criteria established in the rule. ●

Senate Approves Funding Legislation for Mouse Research Laboratory

Senators Ted Kennedy (D-MA) and Orrin Hatch (R-UT) this summer introduced a bill authorizing $25 million for a facility developing, producing and distributing inbred and mutant mice used in biomedical research. S. 1390 passed the Senate by voice vote and went to the House where very similar legislation was proposed by Olympia Snow (R-ME). If either bill is enacted, the actual funding must be provided in the Congressional appropriations process. Both pieces of legislation were introduced following a fire that destroyed part of Jackson Laboratory in Bar Harbor, Maine, one of the world's largest suppliers of genetically bred mice. ●

Metals Specialty Section

In recognition and support of excellence in graduate student research, the Metals Specialty Section invites graduate students to apply for two awards to be presented at the upcoming Society of Toxicology Annual Meeting in February of 1990. Each award will be based on work submitted in the form of an abstract to be presented at the annual meeting and will include a cash stipend of $500. Abstracts will be evaluated with the authors'/sponsor's names removed and will be judged on the basis of quality of study design and interest/importance of results, with additional consideration of quality/clarity of written presentation and relevance of the study to human exposures.

Each student applicant must be first author of the abstract, which must describe research performed while a student. Qualified applicants should send their name, address, abstract, and a letter of support from a full member of the Society of Toxicology to the address listed below. The letter of support should state that the work was done while a student and that this is the only specialty section award sought with this work. Abstracts may be submitted any time after October 6, 1989, with a deadline for submission of January 1, 1990. An awards committee will then select the winners, and awards will be presented at the 1990 Specialty Section Meeting in Miami Beach.

Send abstracts to: **Dr. Carol Walsh**, Secretary/Treasurer Metals Specialty Section, Boston University School of Medicine, 80 E. Concord St., L-603, Boston, MA 02118. ●