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Chulabhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

CRI's ICEIT has been designated as a
"UNEP Centre of Excellence for Environmental and Industrial Toxicology".

International Training Courses Organized by the International Centre for Environmental and Industrial Toxicology (ICEIT) of the Chulabhorn Research Institute in Collaboration with the Asian Institute of Technology (AIT)

7 November – 2 December 1994

The two training courses, the third series in a program directed by Professor Dr. Her Royal Highness Princess Chulabhorn, President of CRI, addressed the important need for human resource development and capacity building through interdisciplinary training in the specialized areas of toxicology and environmental engineering and their application to urgent and vital concerns in the management and prevention of health and environmental problems.

A total of 50 trainees from some 12 countries participated in the training courses prepared and presented by a faculty of internationally renowned experts in the areas of environmental engineering, environmental and industrial toxicology, pollution control and risk assessment.

Interviews with faculty and trainees are featured on pages 4-5.

The training course in Environmental Toxicology encompassed the fundamental principles of toxicology from exposure to chemicals in the environment, entrance of chemicals into the body, toxic responses in a variety of organ systems, to excretion from the body. The application of toxicology in risk assessment and management was emphasized through a number of exercises and case studies.

The courses, therefore, addressed the training needs of both engineers and health scientists in the vitally important area of chemical toxicity in relation to safety evaluation and assessment, management and planning, and policy formulation.

Trainees from some 12 countries participated in the training courses prepared and presented by a faculty of internationally renowned experts in the areas of environmental engineering, environmental and industrial toxicology, pollution control and risk assessment.

Identifying Chemicals with Adverse Health Effects

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Of the 70,000 chemical substances in commercial use, adequate toxicological data are available for only 10-20%.

The US National Toxicology Program (NTP) has invited members of the public, unions, industry groups, state and local governments, environmental organisations and academia to nominate chemicals or other agents to be studied by the NTP.

NTP studies will be made in the following categories:

1. Chemicals found in the environment that are not closely associated with a single commercial organization;
2. Biological or physical agents that may not be adequately evaluated without federal involvement;
3. Commercial chemicals with significant exposure that were first marketed before current testing requirements or those that generate too little revenue to support further evaluations;
4. Potential substitutes for existing chemicals or drugs that might not be developed without federal involvement;
5. Substances that occur as mixtures for which evaluations cannot be required of industry;
6. Chemicals or agents that will aid our understanding of chemical toxicities, or our understanding of the use of test systems to evaluate potential toxicities;
7. Chemicals that should be evaluated to improve the scientific understanding of structure-activity relationships and thereby help limit the number of chemicals requiring extensive evaluations;
8. Emergencies or other events that warrant immediate government evaluation of a chemical or agent.

The NTP will assess the specific needs for studies, evaluate existing literature and testing data, assess ongoing evaluations in the government and private sector, and also determine how the chemical fits into an overall plan for improving the test systems before committing to specific studies. The selection of a chemical or agent by the NTP Executive Committee does not automatically commit the NTP to evaluate that chemical or agent. The priority of the chemicals and the proposed

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Excitotoxins

Excitotoxins have been implicated in neurological disorders that range from the effects of eating contaminated shellfish in the North Atlantic or the grass pea plant in Asia and Africa to the causes of Huntington's and other neurodegenerative diseases.

Neurotoxicologists are increasingly focusing their attention on excitotoxins. These substances flood brain synapses to the point that they excite nerves to destruction.

Using molecular tools, neurotoxicologists are now studying changes in the brain that can turn endogenous excitatory amino acids, such as glutamate, into cellular destroyers.

Interest in excitotoxins was aroused by the outbreak of disease caused by domoic acid. This natural excitotoxin was found in diatoms consumed by blue mussels in the waters off Nova Scotia where, in 1987, it passed into the food chain, causing an outbreak of disease in the human population. Currently, neurotoxicologists are attempting to discover ways to detect domoic acid in seawater, while continuing to research the mechanisms of domoic acid excitotoxins in order to uncover the basic science of the glutamate system and receptor sensitivity.

Some researchers have proposed that chronic neurodegeneration, as seen in amyotrophic lateral sclerosis, Huntington's disease, and Parkinson's disease, may also result from increased sensitivity to endogenous glutamate toxicity.

Metals in the environment and excitotoxins may also act in concert. The theory that aluminium, a known toxin, helps promote Alzheimer's disease is still being explored.

The next level of research will involve the study of how genes may make some people susceptible to toxic, and excitotoxic damage. It may be that a missing or defective gene leads to the disease caused by environmental toxins.

Source: Environmental Health Perspectives, Vol. 102, Number 11, November 1994.

Identifying Chemicals with Adverse Health Effects

(Continued from page 2)

studies are assessed during the selection of contractors to conduct the studies. During any of these phases the chemical or study may be withdrawn if higher priority studies are found, or if the study proves to be impractical.

NTP to study 22 chemicals. The following chemicals are being considered for short- and long-term toxicology and carcinogenesis studies. The NTP welcomes comments on these chemicals and relevant information including ongoing toxicological studies, current or future trends in production and import, use patterns, human exposure levels, environmental occurrence, and toxicological data.

Riddelliine. This substance is a pyrrolizidine alkaloid found in plants of the genus Senecio in the western United States. Riddelliine and other alkaloids in these plants can cause the death of livestock if ingested at high levels, or may contaminate meat as a residue. Riddelliine may also contaminate commercial grains, milk and honey.

Urethane/ethanol mixture. Urethane and ethanol are by-products of fermentation and commonly found in alcoholic beverages and in many food products.

Dichlorodiphenyl sulfone. This chemical is a component of high temperature plastics. It is a known inducer of cytochrome P450s and was shown to cause marked hepatomegaly in NPT prechronic studies. Other studies have shown facile oral absorption and a relatively simple metabolite pattern, as well as self induction of metabolism with repeated administration.

Elmiron. This is a pentosan polysulfate used as an experimental drug in the United States for the treatment of cystitis and is used in Europe to prevent thrombosis and hyperlipidemia.

Benzophenone. A substance found in many consumer products, e.g., as a fragrance and flavor enhancer, photoinitiator, ultraviolet curing agent and polymerization inhibitor, benzophenone is also used in the manufacture of pesticides and various pharmaceuticals.

2-Hydroxy-4-methoxybenzophenone. This substance is a UV stabilizer used in cosmetic, pharmaceutical, and plastic products.

Methacrylonitrile. An industrial chemical widely used in a variety of organic processes related to the manufacture of polymers, it is a highly reactive unsaturated aliphatic nitrile found in cigarette smoke and is known to liberate cyanide *in vivo*.

Acrylonitrile. This chemical is extensively used in the manufacture of synthetic fibers, resins, elastomers, rubber and plastics. There is limited evidence for the carcinogenicity of acrylonitrile in workers and it has been shown to produce chromosome damage in the blood cells of exposed workers.

m-Nitrotoluene. The nitrotoluenes are high production volume chemicals used in the synthesis of agricultural and rubber chemicals and in various dyes. There are differences in the patterns of metabolism of nitrotoluenes. The *ortho*-isomer undergoes a series of microflora-mediated reactions leading to an intermediate with high capacity to bind to hepatic DNA and induce unscheduled DNA synthesis.

m-Cresol. The cresols are monomethyl derivatives of phenol, and are found as constituents of coal tar, in various industrial solvents and resins, and in some essential oils. There are currently no adequate chronic toxicity and carcinogenicity studies of the cresols.

2, 4-Decadienal. Decadienal is one of the class of dienaldehydes that occur naturally in a variety of foods as by-products of the peroxidation of polyunsaturated lipids. Ingested lipid oxidation products and oxidized fats have been reported to cause damage to the liver and kidneys, increased cellular proliferation in the gastrointestinal tract, and other nonspecific tissue injury.

Dipropylene glycol. This chemical substance is a component of antifreeze, air fresheners and sanitizers, and is used as a stabilizer in cosmetics, as a component in polyester, alkyd resins, plastics, as a plasticizer and as a solvent.

Arsenic trioxide. This is a by-product of copper and lead smelting operations and is used in pesticides, in the manufacture of glass, pharmaceuticals and other industrial chemicals.

Tamoxifen. Conjugated estrogens are listed by IARC as human carcinogens causing endometrial cancer. Estrogens are prescribed for prevention of osteoporosis in postmenopausal women and are used as oral contraceptives. Tamoxifen is a mixed estrogen agonist/antagonist known to be effective in the treatment and prevention of estrogen sensitive breast cancer. Tamoxifen also causes endometrial cancer in humans.

MX. MX [3-Chloro-4-(dichloromethyl)-5 hydroxy-2-furanone] is a mutagenic by-product of water and wood pulp chlorination and has been determined to account for about half of the mutagenic potency of finished drinking water. The EPA has nominated MX for carcinogenicity studies with the expectation that the outcome could influence U.S. drinking water contaminant standards.

Source: Environmental Health Perspective, Vol. 102, No. 11 Nov. 1994.

Interjecting Science into Regulatory Decisions Involving Environmental Pollutants

The fifteenth annual meeting of the Society of Environmental Toxicology and Chemistry took place in Denver from 30 October to 3 November 1994 and was attended by more than 2,500 environmental scientists. The theme of the meeting was how to interject science into regulatory decisions involving environmental pollutants. One topic that was given particular prominence was that of dioxins.

New data presented at the meeting suggests that paper mills can greatly reduce their release of dioxin – resulting from the use of chlorine as a bleaching agent – by substituting chlorine dioxide for chlorine.

A spokesperson for the American Forest and Paper Association reported that paper mills began switching voluntarily to chlorine dioxide in 1988 and the industry has promised to reduce dioxin levels to below detection in 1996. A group of prominent environmental scientists that included EPA's chief of research reported that using chlorine dioxide as the sole bleaching agent in paper production not only brings dioxin emissions below current detection limits, its use also dramatically cuts production of another class of compounds – phenols containing two or more chlorine atoms – that are harmful to fish.

Source: Science, Vol. 266, 18 Nov. 1994.

Insights into the gains and the demands of interdisciplinary training courses: the experience of the international training courses in pollution control and management and environmental toxicology, organized by the Chulabhorn Research Institute in collaboration with the Asian Institute of Technology

7 November – 2 December 1994

"From our experience in organizing training courses for government, industry and academia over a number of years, it has become increasingly evident that the training priorities of personnel from developing countries are somewhat different from the priorities in developed countries which have specialists to deal with health and environmental problems in a highly specific way. Developing countries we believe, need personnel with broader background knowledge in both health science and environmental management to cope with emerging environmental toxicological problems (often the result of rapid industrial development) which, if not addressed and resolved, will impede sustainable development and undermine national efforts to improve the quality of life of present as well as future generations". – Dr. Mathuros Ruchirawat, Vice-President for Research at the Chulabhorn Research Institute and a course coordinator.

During the second of the two training courses, the Editor interviewed both faculty members and trainees to get their views on the demands made by a interdisciplinary approach to training and the ensuing gains of such an approach; and also to obtain an insight into the function and management of the case studies, a means of highlighting the importance of interdisciplinary applications in problem solving, which were an essential feature of the Environmental Toxicology training course.

The scientific program of the Environmental Toxicology training course was an arduous undertaking for all participants, making a level of demand that matched their level of commitment. In a ten day period, it included a total of 37 lectures grouped under 6 headings: Introduction to Environmental Toxicology; Principles of Toxicology; Chemical Carcinogenesis; Target Organ Toxicology; Pesticides and Industrial Chemicals; and Risk Assessment and Risk Management. An important feature of the course, and one that was greatly appreciated by all participants, was the assignment of case-studies in which participants worked in groups of seven, with the support of a well-briefed resource person, to find a solution to a given problem involving the use of chemicals and their impact on the environment. The members of each case-study group had been selected on the basis of their scientific background and research interests to cover the interdisciplinary range of scientific knowledge from environmental engineering, applied medicine and toxicology necessary for identifying and resolving the problem area posed by the assignment.

The case-studies provided the opportunity for trainees to apply the knowledge and concepts of the lectures given on the training course to resolving an actual problem. This involved sharing expertise and using all available resources - data banks, registers of industrial chemicals, international guidelines, risk assessments – many of which represented new sources of information and new tools for the participants.

The five case-studies – Environmental PCB Contamination in an Urban Area; The Leadbury Site; Kepone: A Chemical Disaster; The Waterville Municipal Landfill; Ballast Water Disposal – were presented on the final day of the training course and were recorded on video to provide, in themselves, a future training resource.

Views of Faculty Members

Prof. R.C. Shank

Professor Ronald C. Shank, **Director of the Environmental Toxicology Program at the College of Medicine, Department of Community and Environmental Medicine at the University of California, Irvine, U.S.A.**

Professor Shank, has had a central role in the planning of CRI's training program. He has taught on the two previous courses in 1988 and 1991. In summing up what he considered to be the main areas of success of the Environmental Toxicology training course, he emphasized the high calibre of the trainees who had participated in this course. Their comprehension and use of English, in particular, was appreciably higher than that of trainees on past courses and this meant increased confidence and assimilation of information.

Asked about future improvements in the content and structure of similar training courses, Professor Shank expressed the opinion that lectures might be shorter, leaving time for individual questions immediately following the presentations, rather than the group discussion format that had been used on the present course. He also saw the need to expand the ecotoxicology aspect of the scientific program, perhaps with two additional lectures, and to add a component on the immune system in toxic response, which has not previously been covered. Overall, he was delighted with the way the course had been organized.

Prof. D.J. Ecobichon

***Dr. Donald J. Ecobichon*, Professor of Pharmacology and Therapeutics at McGill University, Montreal, Quebec, Canada.**

The task of designing the case-studies for the Environmental Toxicology training course was the responsibility of Dr. Ecobichon who had also taught on the two previous international training courses of the current program, in 1988 and in 1991. The present course was, however, the first on which case-studies were used as an integral component in the training, and Dr. Ecobichon was delighted at the success of the innovation and at the high standard of work that was achieved.

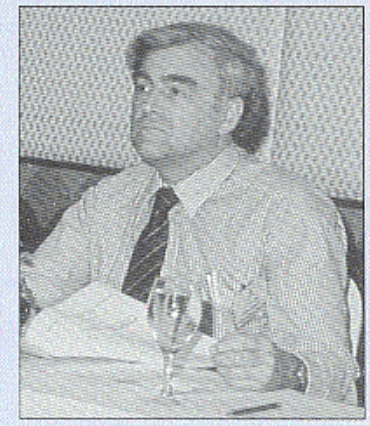
I asked Dr. Ecobichon for his opinion on the main problems in environmental toxicology faced by countries in the region. "Currently the most widespread problem is the uncontrolled use of pesticides. In most countries in South-East Asia, chemicals can be bought over the counter. Farmers are not trained in the way to use pesticides safely and this leads to the exposure of whole families in agricultural communities to harmful toxic effects of misuse. What is urgently needed is more training in environmental toxicology and a common code for the use of pesticides in South-East Asian countries".

Dr. Ecobichon considered that the current training courses had been particularly successful, essentially because of the interdisciplinary approach that had been taken. To solve environmental problems, engineers and toxicologists need to understand each other's work and know the kind of questions that need to be asked in order to identify the cause of environmental contamination.

Dr. G.C. Hard

***Dr. Gordon C. Hard*, Senior Toxicologist and Pathologist of the American Health Foundation, New York, U.S.A.**

Dr. Hard's areas of speciality, on which he lectured in the training course, are cellular responses to toxic injury, nervous system toxicity, and pulmonary and renal toxicity. This was the first occasion on which he had contributed to the training program and his impressions were highly positive. "The quality of the participants is outstanding and the diversity of their backgrounds, both in terms of nationality and professional training has been as essential aspect of the course, bringing about a common denomination of genuine understanding. The way in which medical material has been dealt with on the course in relation to toxicology in an interdisciplinary approach has produced a new dimension of understanding".



Prof. J.H. Duffus

***Professor John H. Duffus*, Director of the Department of Biological Sciences at the Edinburgh Centre for Toxicology, Heriot-Watt University, Edinburgh, Scotland, U.K.**

Professor Duffus endorsed the advantages of a interdisciplinary approach and of having trainees from a diversity of backgrounds taking part in the same course. In his preparation of lectures and the accompanying lecture notes for participants, he had been especially aware of the communication difficulties that arise when trainees have not only different areas of specialization but also come from different cultures. This can pose special problems, for example, when attempting to define the concepts of "risk" and "hazard", since these are understood differently in different cultures and societies. In Professor Duffus' opinion, addressing the needs of developing countries in environmental toxicology involves ensuring as wide an understanding as possible of the potential toxic effects of chemicals.

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Dr. R.A. Becker

Dr. Richard A. Becker **of the Department of Toxic Substances Control, State of California, Environmental Protection Agency, Sacramento, California, U.S.A.**

Similar concerns were expressed by Dr. Becker. He considers that the most important need is to increase the scientific components of Risk Assessment to make it a more rigorous discipline able to quantify more exactly levels of risk involved in, for example, the transport of contaminants. Risk communication should be part of an education and awareness raising process, not alarmist in intent but providing information to address major risks and place minor risks in perspective. There are gleams of hope for the future: government, industry, and academia are now working more closely together in focusing more attention on risk assessment with the, result that the private sector is less apprehensive than formerly and is beginning to accept risk assessment as an important tool in industrial operations. An important aspect of the current training course has been providing information to reduce catastrophies that can occur because of insufficient knowledge.

Views of the Trainees

Increasingly, CRI serves as a center for regional training. The importance of this regional role was evident in the selection of trainees on the current training courses, with representatives from Cambodia, Lao, Vietnam, Philippines, Myanmar, India, Indonesia, Malaysia, Indonesia, Papua New Guinea, as well as from Thailand.

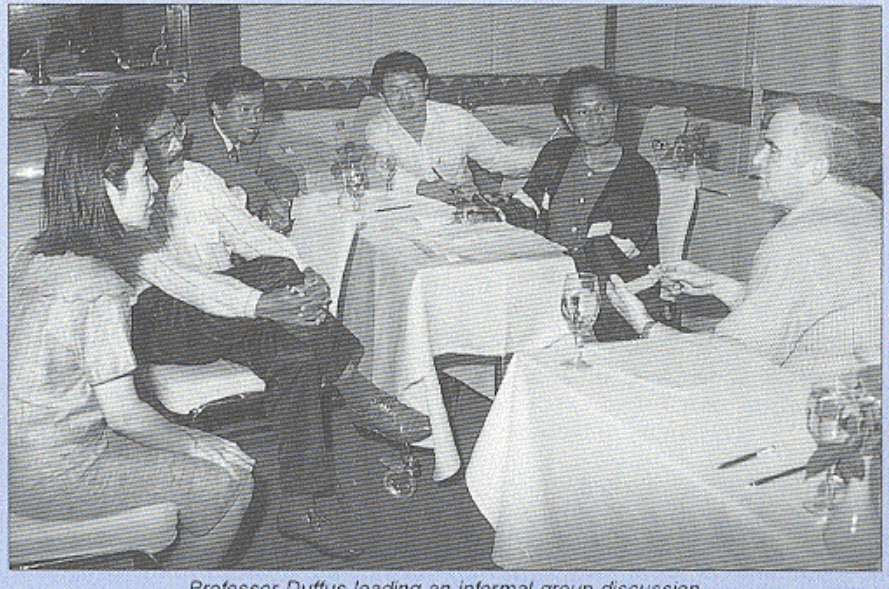
What kind of problems did trainees face, in interdisciplinary courses of this nature, given that their academic training was in only one of the two main areas that the program embraced? The Editor sought the opinion of six of the thirty seven trainees who took the course in Environmental Toxicology.

Dr. Phone Saing, a medical doctor by training, currently responsible for occupational medicine in the Ministry of Public Health in Myanmar: "For me these courses have been a totally new experience. I found no problem with the engineering component in the training, even though I have no background in this area. I think this is due to the high quality of the teaching and the way in which we, the participants, have helped each other in sharing information on our individual specialties. There has been an excellent, supportive atmosphere on the courses and no one has been made to feel deficient because of lack of prior knowledge".

When asked what specifically he has gained from the training courses, Dr. Phone Saing expressed: "Environmental concern is a new issue in Myanmar. What I have learned here will enable me to tackle problems before they become too serious. Part of my work has been on lead poisoning in the dye and glazing industries. From this course I have discovered new resources to deal with this problem through control and safety measures".

Although applicants for places on the training courses are carefully screened with regard to the level of their professional qualifications and the nature and responsibilities of their work to ensure that the training received will have the greatest possible multiplier effect, there is no specified English language level required for entry on the courses, which are taught through the medium of English. Did the language of instruction pose a difficulty leading to problems of communication, I asked ***Dr. Le Van Nai,*** a lecturer in Environmental Pollution from Hanoi University of Civil Engineering. Dr. Le Van Nai had studied for his bachelor degree in Atmospheric and Meteorological Physics at the University of Bucharest, where he had to learn Romanian, before he returned to Vietnam to take his Ph.D. in Environmental Engineering. "Yes, English is a problem for me. I cannot always express what I want to say. But the teaching here has been very good. Also the content of lectures has been good. The faculty all prepare written notes on their lectures. This has helped me a lot. For me the course on pollution control was not difficult because of my background in engineering; but environmental toxicology is a new field for me".

In Vietnam, Dr. Le Van Nai is Scientific Secretary of CEETIA, the Centre for Environmental Engineering of Towns and Industrial Areas and his research work focuses on air pollution in urban and industrial areas. In his research he samples and measures levels of air pollution in order to create maps showing the type and density of pollution prevalent in different areas.



Professor Duffus leading an informal group discussion.

The trainee who had furthest to travel to attend the course was ***Ms. Margaret Gabut*** a Biology graduate currently studying for her M.Sc. in Environmental Science and Environmental Pollution Control at the University of Papua New Guinea. When asked for her assessment of the value of the training courses to her present studies and her future career, Ms. Gabut was effusive in her praise. She had gained far more from the courses than she had expected. The AIT course had given her the first awareness of the importance of engineering in pollution control, and the methodology of toxicology studies presented on the CRI course had opened for her a new vista on the vital importance of toxicology in industry and in environmental health. "Papua New Guinea has very few toxicologists at the moment, and they concentrate their work on the use of pesticides. Only in recent years has there been an awareness of the importance of environmental toxicology in all areas of industrial development and public health".

In her future career, Ms. Gabut would like either to teach Environmental Science at the university (where, in Papua New Guinea, it is very much a new subject-Ms. Gabut is the first student to enrol for an M.Sc. in this area) or to work in the government sector in environmental protection.

Ms. Gabut was not alone in finding the area of environmental toxicology to be an eye-opening experience. ***Dr. Phyrun Ung,*** Deputy Director General of the State Secretariat for Environment in Phnom Penh was equally emphatic in stressing the importance of this area of scientific research and application.

A medical doctor who previously worked in the Ministry of Health, Dr. Ung is now responsible for the disaster control program and is very much aware of the problems caused by man-made pollution, particularly those problems arising from rapid industrialization. Such problems are now being experienced in Cambodia with the upsurge of new factories and industrial plants. In the absence of adequate control and planning, not only natural disasters but man-made disasters will be the future focus of disaster control programs. Of current industrial development in Cambodia, Dr. Ung says: "We have a lot of foreign experts who give us advice. But now, thanks to this training I have received in environmental toxicology, I can solve some of my own problems".

Some of the participants engaged in a workshop activity.

Dr. Roy Cuison, doctor of medicine and Associate Professor of Pharmacology at the University of Santo Thomas, in the Philippines, explained that the training course on Environmental Toxicology had been different from what he had expected. In particular, he found risk management an enlightening area. In the Philippines, he sees the most important need as raising awareness, both in the general public, and in government, of the importance of risk management in all areas of industrial development. "There is an urgent need for in-country training courses to attract decision makers, industrialists, and also industrial physicians. The volume of chemicals produced in the Philippines is very high, but no training is available to make managers and physicians aware of the dangers of chemical exposure in the workplace and in the ambient environment, and of the ways to deal with problems when they occur. Toxicity is not classified as one of the ten leading causes of morbidity in the Philippines, thus it is not given high priority and a concerted effort is needed to raise awareness of its importance".

Although international in scope and regional in focus, the environmental concerns of Thailand were very much on the agenda of the two training courses. Thai developmental interests were indeed well represented by some twenty participants whose professional backgrounds covered areas of environmental engineering, food engineering, pharmacology, environmental technology, agriculture, crop protection, medical technology and public health.

The work of one Thai trainee, ***Ms. Jaruwan Viriyahirunpiboon*** of the ERA (Regional Medical Sciences Center in Chiangmai) will serve as an example of the importance of the training courses to industrial development and health care in Thailand.

ERA is frequently used as an advisory institute due to the lack of personnel in both private and government sectors who can analyse the causes of environmental toxicological problems, particularly in the provinces. As part of her routine work, Ms. Viriyahirunpiboon has been asked to advise on the health problems resulting from lignite burning as well as those arising in industrial plants in Lampang Factory Estate. With her strong background in chemistry, the training courses have helped her to see environmental problems in a global way necessary for correct assessment to ensure appropriate management. The practical nature of the training courses with problem solving activities in the form of case study assignments requiring interdisciplinary approaches is a feature of the training that Ms. Viriyahirunpiboon and all the other trainees I spoke to found most important.

Changes in Serial Blood Lead Levels During Pregnancy

The first step in modeling lead kinetics during pregnancy includes a description of sequential maternal blood (PbB) during pregnancy and the factors controlling it. Researchers at the National Institute of Perinatology, Mexico City, Mexico and the Department of Anesthesiology, Charles R. Drew, University of Medicine and Science, Los Angeles, U.S.A. analyzed PbB of 105 women living in the Valley of Mexico from week 12 to week 36 of pregnancy and again at parturition. They also used data from all women contributing blood at any stage of pregnancy to determine antecedents of PbB. Pregnancies were uneventful and offspring were normal. Although geometric mean PbB level averaged around 7.0 µg/dl (0.34 µmol/1), with a range of 1.0-35.5 µg/dl throughout pregnancy, analysis of variance revealed a significant decrease in mean PbB from week 12 to week 20 (1.1 µg/dl) and various significant increases in mean PbB from week 20 to parturition (1.6 µg/dl). Regression analyses confirmed the positive linear PbB trend from 20 weeks to parturition and additional contributions of dietary calcium, reproductive history, lifetime residence in Mexico City, coffee drinking, and use of indigenous lead-glazed pottery. Although decreasing hematocrit has been suggested to explain first-half pregnancy PbB decrease, the time course of hematocrit decrease in the present study did not match the sequential changes in PbB. While hemodilution and organ growth in the first half of pregnancy may account for much of the PbB decrease seen between 12 and 20 weeks, the remaining hemodilution and accelerated organ growth of the last half of pregnancy do not predict the trend toward increasing maternal PbB concentration from 20 weeks to delivery. Mobilization of bone lead, increased gut absorption, and increased retention of lead may explain part of the upward PbB trend in the second half of pregnancy. Reduction of lifetime lead exposure may be required to decrease risk of fetal exposure.

Dietary sources of lead, especially prominent in the study population, were associated with increased PbB during pregnancy. Mexico has a nearly 500-year history of using lead-glazed pottery for cooking, serving, and storing food and drink. Although lead in domestic articles was recognized in Mexico as a source of lead poisoning in children nearly two centuries ago, and despite repeated notice to public health authorities regarding lead in ceramic ware, little has been done to remedy the problem until recently. As a result, the more than 40% of the sample reporting use of lead-glazed pottery showed elevated PbB during the last 28 weeks of pregnancy.

Canned foods using lead-soldered seams were common in the Mexican marketplace until 1993, when seamless or welded-seam cans replaced all but a small fraction, represented by imported foods. Canned foods, associated with increased maternal PbB, were also related to higher lead in children born to mothers participating in this study in a preliminary report. As existing stocks of lead-soldered cans are reduced, it is expected that the contribution of this source to the national lead load will disappear.

All mothers entering the study were given basic information on the major sources of lead and on the effects of lead on the fetus and young child and were urged to discontinue habits leading to increased lead intake.

Several of the findings of this study suggest that the increasing PbB found in the last half of pregnancy derives in part from maternal bone lead in addition to increased gut absorption. First, the timing of the increase in the last half of pregnancy coincides with increased fetal need for and increased maternal provision of calcium. If some of the additional fetal calcium requirement is supplied from maternal bone, mothers with high bone loads of lead may transfer more lead to the bloodstream with the calcium.

Since no measurements of bone, environmental, or dietary lead were made, the sources for maternal lead changes during pregnancy suggested by the models can only be considered tentative. Although the increased PbB in the last half of pregnancy is small, on the average about 1.6 µg/dl (0.07 mol/l; approximately 20%) from 20 weeks to parturition, this increase is found in the face of hemodynamic, metabolic, and organ size changes, all of which act to reduce maternal PbB concentration. Thus the measured increase indicates that, whatever the source, the amount of lead put into circulation in the last half of pregnancy may be substantial and physiologically significant.

The preceding results suggest that women with higher lifetime exposures, and thus more bone lead, and calcium-deficient women may have higher circulating lead levels during the second half of pregnancy with consequent increased exposure to the fetus. The results imply that to gain maximum public health savings through lead reduction programs, our goal should be to reduce lead-exposure of women at the earliest age possible and maintain the reduction through their reproductive years. We might expect a time lag of a generation or more before the benefits of reduced environmental lead are fully passed on to the fetus.

Many kinetic models of lead in organisms have been developed, though none yet treats lead during pregnancy in humans. Any valid kinetic model of the maternal-fetal PbB system must not only account for the decrease in maternal PbB in the first 20 weeks of pregnancy, it must also account for the measured increase in the second 20 weeks.

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