CRI/ICEIT
NEWSLETTER

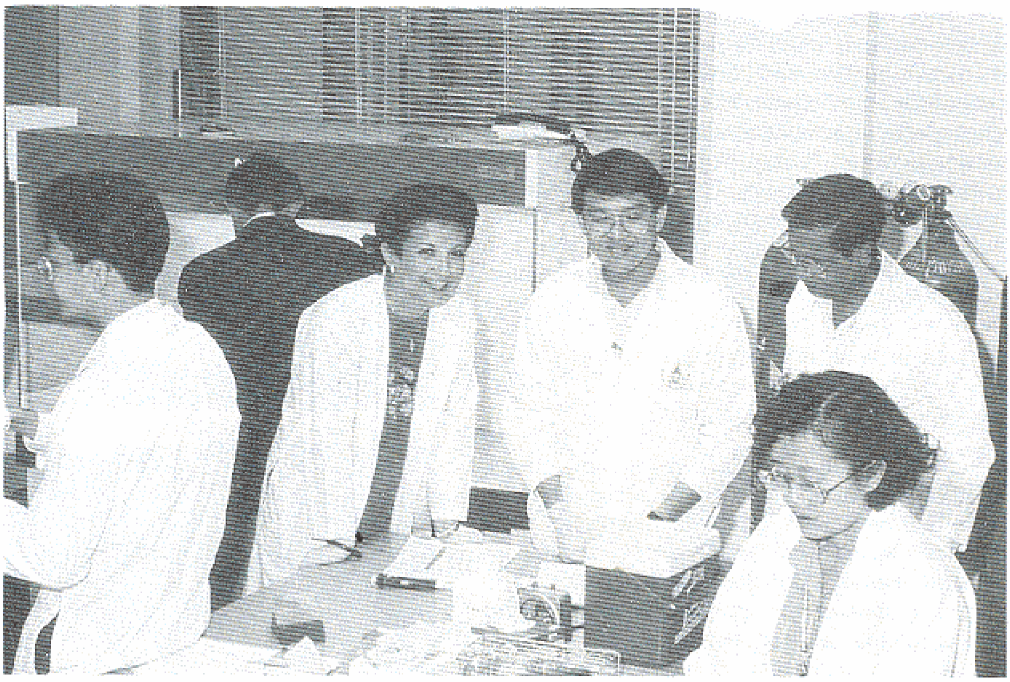
VOL. 4 NO. 1 – January 1994
ISSN 0858-2793
BANGKOK, THAILAND

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 COURSE



Chulabhorn Research Institute (CRI) hosted "The International Training Course on the Detection of Health Hazards in Human Populations Exposed to Mutagens and Carcinogens" in November, at its laboratories in Laksi, Bangkok. The training course was jointly organized by the International Agency for Research on Cancer (IARC), the WHO and CRI.

It attracted 36 high calibre participants from 13 countries. The organizers, Dr. H. Vainio and Dr. C. Wild of IARC and Dr. M. Ruchirawat of CRI were assisted by 10 faculty members who gave plenary presentations and acted as tutors in discussion groups.

(Continued on page 2)

INTERNATIONAL TRAINING COURSE

(Continued from page 1)

The programme of the training course was organized around morning lectures followed by practical sessions which provided opportunities for hands-on experience for all participants. This practical component contributed greatly to the success of the course.

The scientific programme covered the basic mechanisms in mutagenesis and carcinogenesis with emphasis on chemical and viral carcinogenesis, identification and assessment of hazards and cancer risks, dosimetry of chemical carcinogen exposures, markers of biological effects and assessing individual susceptibility to carcinogen exposure.

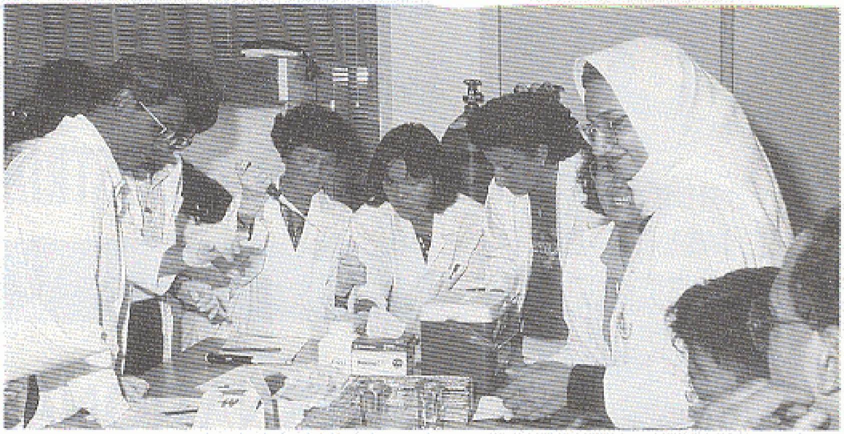
The practical sessions focussed on various methods used for detection of exposure to carcinogen(s) and analysis of damages induced by carcinogens. The three study groups which were run simultaneously with the practical sessions were: "Lung cancer cases among professional drivers in Bangkok", "Pesticide poisoning among antimalarial workers", "Field molecular epidemiology: feasibility of monitoring for workers potentially at risk for developing bladder cancer".

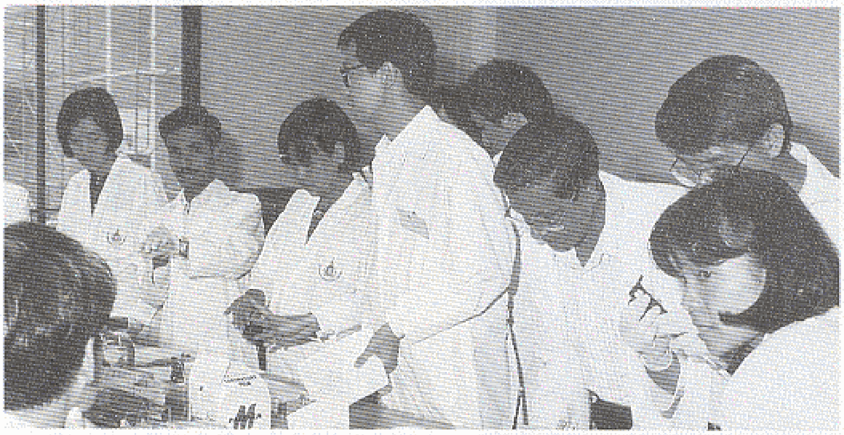
As a result of study group activity carried out on the training course, three project proposals/designs were detailed:

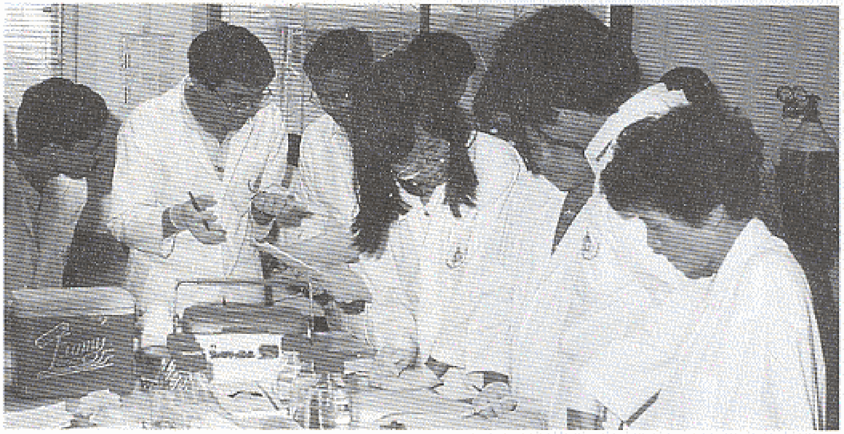
A preliminary proposal was drawn up for a research project on cancer risks associated with traffic-delivered air pollution involving biomarkers associated with exposure to air pollution among Bangkok Traffic Police. The project proposes to use methodologies and techniques that were presented on the training course and can be completed within a timeframe of 2 years.

Secondly, a study design was elaborated, based on a given scenario in which a medical officer recently appointed for a large malaria control programme learns that there has been a suspected increase in the number of pesticide poisonings soon after the beginning of the last spray season. The information on the poisoning and 5 deaths (2 mixers and 3 spraymen) is of particular concern because this is a large antimalaria programme involving 7,700 workers. The study design features procedures for surveillance of long-term toxicity and a proposal for long-term follow up.

Thirdly, a project design was drawn up that aims at critical evaluation of exposure to benzidine dye and the consequence of its toxic effect, viz bladder cancer, by the use of cellular and molecular methods in combination with medical and epidemiological support to identify risk factors in workers in a defined population.







TECHNICAL GUIDELINES ON HAZARDOUS WASTE FROM THE PRODUCTION AND USE OF ORGANIC SOLVENTS

Many organic substances exhibit solvent type properties. Whilst any attempt to estimate the number in regular or common use involves subjective judgement, it is suggested that some 60 substances fall into this category.

Solvents display a very wide range of properties and characteristics. Many are flammable, some highly flammable; many are volatile and evaporate quite rapidly to give off vapours. Such vapours may be toxic or flammable: flammable vapours in confined spaces can be explosive. Toxic properties can be very varied, and include being carcinogenic, narcotic, ecotoxic and may even be mutagenic or teratogenic. Solvents may be more or less dense than water, more dense substances sinking to the bottom of watercourses, vessels etc. Whilst some solvents are totally miscible with water, others are not and display barely any solubility in water.

Solvents have three principal areas of use; as cleaning agents, as a raw material or feedstock in the production and manufacture of other substances, and as a carrying and/or dispersion medium in chemical synthetic processes.

Users include many sectors of industry and commerce, not to mention some domestic applications. Particular industry user sectors are:

- Cleaning :

  Electronics, metal finishing, dry cleaning.

- Raw Material :

  Paints, resins, adhesives, plastics.

- Carrying Medium :

  Fire chemicals, pharmaceuticals, agrochemicals.

Solvent wastes embrace a broad range of physical and chemical characteristics. The solvent part of the waste may constitute a large or small portion of the total. The balance may be solid or liquid material, and may consist of inert/semi-inert substances or other hazardous constituents of an organic or inorganic nature. Consequently wastes may be highly mobile and pumpable at one extreme, or of a solid or virtually solid nature at the other.

Organic substances that exhibit solvent type properties are widely used in many different areas of industrial production. Since it is unlikely that their use will be eliminated in the short term, it is of particular importance that the toxic properties of solvents and solvent waste generated by industry be carefully evaluated.

The nature of solvents, and the uses to which solvents are consequently put, makes it unlikely that those uses can be avoided or eliminated altogether. However, substitution and improved efficiencies of use can affect the nature and quantity of waste, as can better separation of the components of waste streams at source. Such separation may avoid the creation of difficult mixtures, and result in separate streams more amenable to recovery/reuse.

Waste avoidance can be considered to include alterations to a process such that the waste generated is less dangerous and/or of reduced potential to harm the environment. Thus, waste avoidance may include the substitution of one solvent for another, where the use of a difficult or harmful solvent is avoided. Such practices are widely encountered in the projected phasing down of the use of chlorinated solvents, and are considered to have a major part to play in achieving real reductions in the potential for adverse environmental effects and overall environmental impact.

The avoidance of fugitive losses is a desirable objective in itself, but is unlikely to impact significantly on the quantity of waste requiring attention. It will however result in a reduced requirement for new material, and hence help reduce waste generation associated with the manufacturing process.

The table on p. 7 presents some examples of solvent waste generated by industry.

(Continued on page 7)

CRI hosted "The International Training Course on the Detection of Health Hazards in Human Populations Exposed to Mutagens and Carcinogens."

15-26 November, 1993

This course was jointly organized by the International Agency for Research on Cancer (IARC), the World Health Organization (WHO), and the Chulabhorn Research Institute at its laboratories in Bangkok. The ten day training course was attended by 36 participants from 13 countries.

At the end of the course, the joint programme coordinators, Dr. H. Vainio and Dr. C. Wild of IARC were interviewed by the editor.

Question:

What were your priorities when designing this training course?

Dr Vainio: We very much wanted to have a course in this part of the world because Southeast Asia is a region that is developing very rapidly at the moment. Societies are in transition: on one hand you have infectious diseases, parasitic diseases and other diseases of this nature leading to a high mortality rate; and on the other hand, you have societies that are rapidly becoming industrialized; that brings problems of urbanization and very quick changes in life style. For this reason what is happening in Thailand and other countries in this region is an interesting phenomenon. Moreover, people in this region, perhaps because of the rapid economic development, have a real interest in education and training.

We have run similar courses before in India in 1986,in Mexico in 1989, and the last one, before this present course, was in Zimbabwe in 1991, so it seemed a logical development to have a course in this part of the world.

The way in which we have run the course has changed on the basis of our experience of the needs of trainees. The first course, in Bombay, didn't have a practical hands-on component, but consisted of discussion and study groups. We developed the practical sessions in Harare and have now included them for the first time as a major course component at CRI.

The feedback has been very positive. It is quite evident that people really want to have hands-on experience and the opportunity to try out new techniques themselves and to decide how the techniques can be applied to their own research programs.

Question:

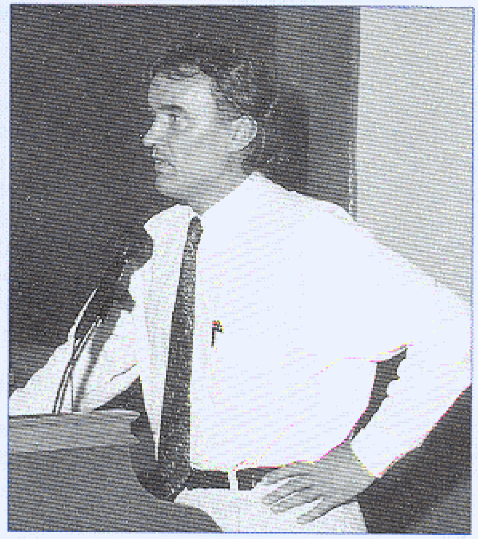
Dr Wild, this training course has clearly put a lot of emphasis on practical laboratory training sessions, would you give us some examples of specific techniques in identification of carcinogens that participants have been trained in on this course.

Dr Wild: What we have tried to do is to give examples of different laboratory approaches to detecting environmental health hazards because in the last ten years or so there has been what you might call an explosion in technology. As a result, there have been major advances in detection of hazards, and it is very important for people at all levels to know what is involved in these techniques and to know how they can be used in their own research projects.

We chose three areas as examples. The first was measuring exposure to chemical carcinogens by measuring the chemical in the body either bound to protein or DNA, or excreted in the urine, and these approaches allow a more precise measurement of exposure to carcinogens. The compound we specifically chose was aflatoxin which is a mycotoxin contaminating food supplies. We chose this partly because the method is relatively simple, and also because it is a problem that is of relevance to countries in this region.

A second area was looking at consequences of carcinogen exposure in terms of genetic alterations in the cell, detecting mutations in specific genes. This is one area where the technology has developed rapidly in the last few years, so the techniques are state-of-the art and people want

Dr. C. Wild



Dr. H. Vainio

to learn about them. And it's very important that people see the techniques for themselves.

Question:

Does this technique involve the use of new or expensive equipment?

Dr Wild: One piece of equipment needed is the polymerase chain reaction machine, the PCR machine, as it is known. This is relatively expensive, costing around $US7-8,000. But the techbique itself is comparatively simple, and the fact that the students perform the technique here in Bangkok helps to demystify the technology.

The area that we specifically looked at was ways to measure a person's capacity to metabolise carcinogens, and this involves mainly chromatographic techniques.

One thing that is, I think, important to mention with regard to the practical sessions on the course is that we provide examples of the technology, but we do not want to give people the impression that they should organise their research around these techniques. Rather, we attempt to awaken people to what is the best approach to a particular problem, and not to look for a problem to match a particular technique.

Question:

Dr Vainio, your opening lecture on the course dealt with the topic "Environmental Health: Populations vs Individuals." What are the main differences in these two perspectives?

Dr Vainio: This difference can be best illustrated by taking an example such as cigarette smoking. If everyone in a particular society smoked 20 cigarettes a day, then clinical and epidemiological studies would indicate that lung cancer was a genetic disease because there would be homogeneous exposure to the necessary agent among all the population so that the distribution of cancer cases would be wholly determined by individual susceptibility in this case. Whereas, if you look at the causes of the incidence of lung cancer, then it is clear that lung cancer is caused by smoking.

I think this relates to what Dr Wild was saying a moment ago. In a way, you can use many different techniques nowadays such as genotyping, for example, to find out what an individual is susceptible to, but at the same time we must not forget that the causes of the incidence are factors in the society which create the influence. When you consider public health, our emphasis should be on how to tackle the causes of incidence and secondarily to consider the genetic factors determining the individual susceptibility. These differences are not exclusive but interrelated.

Question:

Dr Wild, could you tell us what is involved in phenotyping?

Dr Wild: This comes back to the same issue. In a sense carcinogens are inactive in their native form and require some metabolism in the body to actually cause any toxicological outcome. So, one way in which this occurs is via the cytochromes P450 which are a group of enzymes that activate the carcinogen and enable it to bind to the DNA or to protein in the body. So, it would be very nice to look at the ability of the individual to metabolise a carcinogen, which is essentially the phenotyping, to look at differences between individuals and to identify individuals who are at a higher or lower risk from a given carcinogen due to their phenotype.

There are two ways to measure this. Either you can give people a drug which is metabolised by a specific enzyme and you can look at the metabolites of the drug in the urine. In this case you may

(Continued on page 6)

CRI hosted "The International Training Course on the Detection of Health Hazards in Human Populations Exposed to Mutagens and Carcinogens," 15-26 November, 1993

(Continued from page 5)

have logistical problems and in addition some ethical problems with regard to treating people with drugs simply to examine metabolism. So the method we chose, in fact, was where there is a substrate of the enzyme already in the body, an endogenous substrate, in this case cortisol. This compound is metabolised by a specific cytochrome P450 and you can then look at the cortisol and its metabolite, 6 ßhydroxy cortisol, in the urine. The ratio of these two tells you something about the metabolism of the individual and the level of enzyme in that individual. The less cortisol you see in the urine, then the more active that individual is in metabolising the carcinogen. The enzyme examined is one important in the metabolism of aflatoxin, so it thus tied in with other parts of the practical course where we looked at aflatoxin markers.

Question:

Can you tell us what are the toxins present in the environment in Thailand that pose the greatest risk?

Dr Vainio: Thailand is famous for the high incidence of a particular type of liver cancer. This liver cancer appears to be related to the occurance of liver flukes in some parts of Thailand. The other thing that is of particular interest in Thailand, is the exposure to mycotoxins, particularly aflatoxin, which can interact with hepatitis B viruses in the causation of liver cancer. So that is why some of the practical sessions were directed at measurement of aflatoxins. We have been struck by the level of industrial development in Thailand. One result is that now in Bangkok people seem to spend a considerable amount of their time sitting in traffic and so they are increasingly exposed to exhaust fumes. Therefore, one of the study groups was looking at problems related to air pollution in Bangkok and how to explore the situation effectively.

The group proposed a study to be carried out in Bangkok on traffic policemen because this is an occupational category which is highly exposed and so might serve as an indicator of the effect of traffic fumes on the population. The study utilizes the techniques that have been covered on this training course. Hopefully it will get the necessary funding.

Question:

The course participants all feel that they have benefitted greatly from the training they have received. In your view, Dr Wild, what are the factors that have made the course so successful?

Dr Wild: The first thing is the quality of the participants themselves; without well motivated participants, no course can be successful. On this course, both the participants from Thailand and from abroad have been very active and enthusiastic from the start.

The second factor has been the multidisciplinary backgrounds of the participants. Some come with very strict laboratory training right the way through to people involved in public health, so you get a very broad view, sometimes a conflicting view, which is a good way to synthesise ideas and translate modern techniques into something concrete.

The third factor that has really helped in contributing to the success has been the logistics of the course; that is CRI itself. For the laboratory practicals, we have had excellent human resources in terms of help to organize what we need for each laboratory session to set up the practicals; and of course, the availability of equipment that is necessary to perform the practicals.

There can be few laboratories that are better equipped than this one, which means that potentially it is an important resource not just for the institute itself but for scientists throughout Thailand.

Dr Vainio: Could I just endorse what Dr Wild has said. This has been an ideal instiute in which to organize this type of course – to have the laboratory facilities on hand for the study groups. In many countries this is just not possible.

Question:

One new facility that is of great interest to CRI is the IARC Cancer Database that you demonstrated this morning. Could you tell us something about the work that has gone into this, and when it is likely to be available.

Dr Vainio: This IARC Cancer CD-ROM is actually drawing on much of the work that has been carried out at the Agency for the last 25 years. It contains all the information from the published IARC monographs representing more than 20,000 pages of documentation. In addition, it also contains databases such as cancer incidence in 5 continents, and genetic activty profiles.

The purpose of having all this information on one CD-ROM is to make this large amount of data available in an easy, user friendly form, particularly for those who do not have the facilities of retrieving data from the existing sources.

The CD-ROM disc I demonstrated this morning will be available early in 1994. We hope it will be of special help to those people who are working on environmental cancer and on cancer prevention in developing countries. One of the special features of this disc is that it only contains evaluated data.

Question:

Thank you both very much. Are there any final points you would like to make?

Dr Vainio: I would like to end by saying how delighted we both have been to work with CRI. The assistance we have received from the local organizers has been really excellent, and so for both of us this has been not only a very productive course, but also a highly enjoyable one.

TECHNICAL GUIDELINES ON HAZARDOUS WASTE FROM THE PRODUCTION AND USE OF ORGANIC SOLVENTS *(Continued from page 3)*

Acetone	Chemical industry, textiles, plastics, photographic, printing industry.
Acrylonitrile	Petrochemical industry.
Benzene	Cleaning and degreasing of metal.
Butanol	Chemical industry, pharmaceuticals, textile, manufacture of coatings.
Butyl acetate	Chemical industry, printing.
Carbon bisulfide	Chemical industry, textile industry, plastics processing.
Cyclohexanone	Chemical industry, textile, manufacture of coatings, plastics.
Diethyl ether	Chemical industry, textile industry, plastics processing.
Dimethyl formamide	Chemical industry, textile, plastics.
Esters	Motor vehicle manufacture.
Ethanol	Chemical industry, therapeutic products, textile, extractive industry, printing, photographic.
Ethyl acetate	Chemical industry, manufacture of therapeutic and pyrotechnic products.
Glycol ether	Chemical industry.
Isopropanol	Extractive industries, food flavouring, cosmetics, toiletries, paint and varnish manufacture.
Kerosene	Cleaning and degreasing of metal, motor vehicle manufacture.
Methanol	Chemical industry, manufacture of therapeutic products.
Methyl ethyl ketone	Chemical industry, adhesives.
Propanol	Textile industry.
Pyridine	Chemical industry, plastics processing.
Styrene	Petrochemical industry.
Tetrahydrofuran	Chemical industry, manufacture of therapeutic and pyrotechnic products.
Toluene	Cleaning and degreasing of metal, motor vehicle, adhesives, chemical industry.
Xylene	Cleaning and degreasing of metal, coking plants, gasworks, chemical industry, motor vehicle printing industry.
Carbon tetrachloride	Plastics processing, chemical industry, manufacture of fluorocarbons, aerosol.
Chloro-benzene	Chemical industry, textile, dry cleaning, degreasing, manufacture of coatings.
Chloroform	Chemical industry, fluorocarbons, dyestuffs, pharmaceuticals, cosmetics, toiletries, textile, dry cleaning, degreasing, manufacture of coatings.
Dichloroethane	Chemical industry, vinyl chloride production, manufacture of paint, varnish and finish removers.
Ethyl chloride	Chemical industry, manufacture of tetramethyl lead.
Ethylene dichloride	Chemical industry, textile, dry cleaning, degreasing, manufacture of coatings.
Ethylene dibromide	Chemical industry, synthetic resins, pesticides, anti-knock agent in fuels.
Methylene dichloride	Chemical industry, pharmaceutical and food extraction, paint removers, degreasing.
Pentachlorophenol	Textile, wood, paint and biocide.
Perchlorethylene	Chemical industry, manufacture of fluorocarbons, textile industry, dry cleaning, degreasing.
1,1,1-trichloroethane	Wide range of solvent and degreasing applications, e.g. textile, rubber industry.
Trichloroethylene	Chemical industry, textile industry, dry cleaning, degreasing, manufacture of coatings.
Trichlorofluoromethane	Aerosol, refrigerant, plastic foam blowing agent, chemical intermediate.

Note: The technical guidelines summarized in this article were adopted provisionally by the First Meeting of the Conference of the Parties to the Basel Convention (December 1992) and reviewed by the Technical Working Group of the Basel Convention (June 1993).

Sources of Methylmercury Exposure and Poisoning in Infants

A longitudinal study of infants in the Faroe Islands reported in the January 1994 issue of Environmental Health Perspectives evaluated the possible transfer of methylmercury to infants via breast-feeding. Evidence from poisoning episodes indicates that methylmercury exposure may cause neurobehavioural damage to the fetus at exposures corresponding to a maternal hair mercury level above about 10 ug/g. In some fishing communities, this limit may be exceeded due to dietary reliance on seafood.

In the Faroe Islands, located in the North Atlantic between Scotland and Iceland, the population relies to a large extent on seafood, including pilot whale, which has a high mercury concentration. The study of 583 Faroese children followed the infants from birth. The duration of nursing was recorded and hair samples were obtained for mercury analysis at approximately 12 months of age.

The hair mercury concentrations were found to increase with the length of the nursing period, and infants nursed throughout their first year showed the highest geometric mean. It would seem, therefore, that human milk is an important source of methylmercury exposure in infants and in certain fishing communities, infants nursed for long periods may be at increased risk of developing methylmercury toxicity.

ALUMINIUM AND ALZHEIMER'S DISEASE

The theory that aluminium may play a part in the development of Alzheimer's disease has arisen as a result of a number of observations and findings over the last twenty years.

Alzheimer's disease, which is one form of senile dementia, usually is found in patients over the age of 65 but it can occur in people as young as 40.

The disease can only be diagnosed with certainty post mortem by the presence of increased levels of aluminium in the bulk brain tissue and the particular association of aluminium with the neurofibrillary tangles and neuritic plaques. However, it is still a debated question whether accumulation of aluminium is a causal factor in the development of Alzheimer's disease and other degenerative disorders or whether it only reflects impaired regulatory mechanisms in a diseased brain.

Probably the most controversial aspect of the aluminium/Alzheimer's debate is the data from epidemiological studies associating the disease with intake of aluminium from drinking water.

However, such studies need to be treated with caution. Results may merely reflect the influence of some other, as yet unknown, factor. Current data suggests that further epidemiological investigation is needed together with a better understanding of the factors that influence the absorption of aluminium.

Chemical Sensitivity Syndromes

Progress in understanding disorders caused by an individual's sensitivity to chemicals in the environment has in the past been hampered by the lack of an established mechanism to explain how exposure to concentrations of volatile organic chemicals that are well tolerated by most of the population can produce a range of symptoms in sensitized individuals.

However, recent studies indicate that neurogenic inflammation may play a key role in our understanding of a broad class of environmental health problems resulting from chemical exposures.

Neurogenic inflammation is now a well defined physiological mechanism by which mediators are directly released from sensory nerves to produce vasodilatation, edema, and other forms of inflammation. Future research should lead to ways of describing with some accuracy the role that neurogenic inflammation, triggered by specific environmental chemicals, plays in human health and chemical sensitivity syndromes.

Mercury Poisoning

Gold miners who use mercury to separate out the gold particles dredged from river beds have caused serious pollution to hundreds of kilometers of major rivers in Brazil's Amazon basin. Prospectors dredging for gold have left deposits of quicksilver which gradually are converted into methyl mercury entering the food chain through its high concentration in large fish.

It has been estimated that 200 tons of mercury escape into the Amazon waters each year. Some is burned off in the process of separating the gold, creating a toxic vapour that percolates back into the watershed via tropical rain.

In its most advanced form, mercury poisoning leads to Minamata disease, an affliction that causes brain damage and birth defects.

Source: Time Magazine, January 10, 1994

The ICEIT NEWSLETTER is published quarterly by the International Centre for Environmental and Industrial Toxicology of the Chulabhorn Research Institute, supported in part by the Asian Development Bank. It is intended to be a source of information to create awareness of the problems caused by chemicals. However, the contents and views expressed in this newsletter do not necessarily represent the policies of ICEIT.

Correspondence should be addressed to:

ICEIT NEWSLETTER
Chulabhorn Research Institute
Office of Scientific Affairs
c/o Faculty of Science,
Mahidol University
Rama 6 Road, Bangkok 10400,
Thailand
Telex: 84770 UNIMAHI TH
Telefax: (662) 247-1222
Tel: (662) 247-1900