CHAPTER 6

SOLVENTS

Steven Markowitz
Philip Landrigan
Óscar Feo
René Mendes
Richard Letz
Rafael Moure

1 Mount Sinai School of Medicine; New York, New York; USA.
2 Faculty of Health Sciences, University of Carabobo; Maracay, Venezuela.
3 School of Medicine, Federal University of Minas Gerais; Belo Horizonte, Minas Gerais; Brazil.
4 Emory University School of Public Health; Atlanta, Georgia; USA.
5 College of Engineering, University of Lowell; Lowell, Massachusetts; USA.
HEALTH EFFECTS

1. Introduction

The organic solvents are a large and heterogeneous group of chemical compounds. They are simple organic substances that are liquid at room temperature, relatively nonreactive and are capable of dissolving many organic compounds. Most are quite volatile and lipophilic. Solvent exposure occurs primarily through the respiratory route. It typically occurs in operations associated with surface coating (paints, varnishes, and their removal), cleaning and degreasing, chemical and fuel production, mixing and transfer of industrial chemicals. They include alcohols, aldehydes, benzene, toluene, the glycol ethers, carbon disulfide, trichloroethylene, perchloroethylene, n-hexane, formaldehyde, and carbon tetrachloride.

Occupational and environmental exposures to organics solvents have been associated with a number of adverse effects on human health. These include leukemia and lymphoma in persons exposed to benzene; cancer of the lung and nasal sinuses in persons exposed to formaldehyde; male sterility in relation to the glycol ethers; liver and kidney damage in relation to perchloroethylene and carbon tetrachloride; peripheral neuropathy in relation to n-hexane and methyl-n-butyl ketone (MBK); chronic encephalopathy in relation to chronic exposure to a wide range of organic solvents; and ischemic heart disease, psychosis and suicide among workers exposed to carbon disulfide.

Although substantial information has been developed on the toxic effects of organic solvents, there are also great gaps in the current knowledge base. According to data presented by the US National Academy of Sciences, the toxicity of 80% of industrial solvents has never been assessed. Moreover, for most of the solvents that have been evaluated, data are available only on toxicity in relation to acute high dose exposure, but not in relation to delayed and chronic toxic effects at lower levels of exposure. Data are also lacking on the health effects of simultaneous exposure to more than one solvent.

In the nations of Latin America and the Caribbean (LA&C), occupational and environmental exposures to organic solvents are growing. Production of organic solvents is increasing year-to-year in the petrochemical industry of LA&C. Tens of thousands of workers and citizens are exposed daily to organic solvents in small business, home industries, consumer products and in the environment. The possible toxic effects of these exposures have largely been undocumented.

This report has several purposes:

a) to summarize the toxicity and human health effects of the major organic solvents;

b) to review recent studies of occupational solvent exposure and toxicity in LA&C;

c) to develop a listing of populations in LA&C who are of high risk of exposure to solvents and who may constitute priority populations for epidemiological studies;

d) to develop a strategic plan for the prevention of solvent exposure and solvent-associated health effects in populations exposed to solvents in LA&C.
Prevention of exposure is essential for the prevention of the toxic effects of solvents inasmuch as many of these effects respond at best only poorly to medical treatment. Leukemia and chronic encephalopathy are examples of diseases caused by exposure to solvents but can not readily be treated by medical means and that therefore should be approached through prevention.

2. Toxicity of Solvents

2.1 Nervous system toxicity

The organ most commonly impacted by a wide variety of solvents is the nervous system. Both the central and peripheral components of the nervous system have come under increasing scientific scrutiny over the past 15 years with respect to the untoward clinical, physiological, and pathological effects produced by a variety of solvents (Baker, 1985, 1986, 1988; NIOSH, 1987).

Clinical classification schemes for the effects of exposure to organic solvents have been proposed by the World Health Organization in 1985. A somewhat similar classification scheme was also proposed at a later workshop in the U.S. (Cranmer, 1986). The WHO scheme consists of two acute conditions (acute intoxication and acute toxic encephalopathy) and three chronic conditions (organic affective syndrome, mild chronic toxic encephalopathy, and severe chronic toxic encephalopathy).

Acute solvent nervous toxicity is demonstrated by central nervous system (CNS) depression, psychomotor impairment and narcosis. Less intense exposure may result in symptoms of dizziness, incoordination, paresthesias, headaches and drowsiness. Knowledge of severe acute toxicity is obtained from case reports of workers exposed to high levels of solvents and from individuals who have subjected themselves to volatile substance abuse. The mild clinical and sub-clinical effects produced at lower levels of exposure have been obtained from epidemiological studies and experimental chamber studies, where healthy volunteers are exposed to well-controlled low levels of solvents in the air (National Research Council, 1992).

The chronic effects of solvents on the central nervous system have been the best documented in relationship to the development of chronic toxic encephalopathy. Expression of this syndrome is variable in symptoms and severity and may include a dominant emotional component or principally intellectual impairment as demonstrated by decreased concentration, memory and learning capacity. Severe chronic encephalopathy is rarely seen in the occupational environment and more typically refers to the severe intellectual deterioration associated with individuals who abuse solvent-containing products deliberately for the associated euphoria. The clinical expression of severe chronic encephalopathy has been accompanied by documented pathological changes in the brain (Arlien-Soborg, 1992).

A milder variety of CNS derangement type associated with chronic solvent exposure is organic affective syndrome, which is characterized by mild changes of mood, irritability, fatigue,
and difficulty in concentration and memory. This is the more common syndrome resulting from occupational exposure to solvents (Arlien-Soborg, 1992).

In recent years, the most common means of studying the functional state of the central nervous system is through the application of neurobehavioural tests. Standardized batteries of tests have been developed, including the WHO and the neurobehavioural evaluation system test batteries, which utilize computer and manually administered tests. Such batteries are advantageous in that they are reliable, sensitive, increasingly utilized and feasible for field application. A number of studies employing these test systems have been published in recent years, principally of solvent-exposed painters and paint-manufacturing workers as well as fiberglass fabrication workers who are exposed to styrene. These studies generally show some impact of solvent exposure on the nervous system, though the specific abnormalities observed have not been entirely consistent with reference to the types of abnormalities found or the dose at which alterations have been observed. Limitations of studies to date include the inadequate control of confounding factors such as alcohol consumption, the relatively crude characterization of exposure to the solvents, the variability in the test batteries and the lack of the use of prospective study design that might separate the impact of solvents from other factors. More in-depth descriptions of the use of these testing systems are available in several references (Anger, 1990; Letz, 1991).

Exposure to selected organic solvents is also associated with a well-characterized peripheral neuropathy. This neuropathy is typically a distal axonal type that produces a symmetrical sensorimotor defect. This pattern has occurred in humans and in animals following exposure to n-hexane, methyl-n-butyl ketone (MBK) and carbon disulfide. Neuropathological alterations are characteristically axonal swelling and focal demyelination in the distal regions, principally affecting the larger axons. More severe cases are associated with complete degeneration of the axon distal to the site of initial swelling. Such changes have been seen both in humans and in animals. The recovery of patients is variable and seems to be proportional to the severity of the illness. The neuropathy have heretofore been fairly specific to n-hexane, MBK and carbon disulfide, though other agents such as methyl-isobutyl ketone have been shown to exacerbate the neuropathy produced by n-hexane (National Research Council, 1992; Baker, 1992).

Important research needs relating to the neurotoxic effects of solvents have been identified by the U.S. National Institute for Occupational Safety and Health (US DHHS, 1987), including:

a) improved correlation of effects with exposure;

b) better validation of quantitative tests used to assess neuropsychological function;

c) determination of the reversibility of neural toxic effects of solvents;

d) evaluation of the importance of the interaction of workplace solvents with alcohol or other drugs on the impact of nervous system of workers;

e) impact of solvent exposure on accidental injuries on the job;

f) improvement in methods of biologic monitoring of solvent exposure.
2.2 Cancer

A number of solvents have been shown to cause or are suspected to cause human cancer. The best known of these, benzene, was first associated with human leukemia in the 1920's and has since been shown to cause lymphoma. Numerous studies of benzene-linked leukemia, mostly case series, were published over the decades (Landrigan, 1992). The most important epidemiological study was that conducted by NIOSH in the 1980's. The risk of death from leukemia among rubber workers exposed to benzene in two plants in Ohio was examined (Rinsky, 1987). They had air monitoring data that allowed evaluation of the exposure-response relationship. The investigators found a 66-fold increase in leukemia mortality for workers who were exposed to 400 or more ppm-years, which corresponds to working 40 years at the prevailing threshold limit value of 10 ppm. This study played a key role in the subsequent regulatory reduction of allowable airborne benzene levels in workplaces to 1 ppm in the United States in 1989.

There are several additional solvents that are established animal carcinogens and, therefore, suspect human carcinogens (USDHHS, 1991). However, insufficient data is available to judge their capacity to cause cancer in human populations. Perchloroethylene causes liver cancer in mice and leukemia in rats. Limited studies of perchloroethylene exposure among laundry and dry cleaning workers show limited excesses in a number of cancer sites but these studies were judged to be inconclusive by International Agency for Research on Cancer (IARC) and the U.S. National Toxicology Program (US DHHS, 1991).

Carbon tetrachloride is a documented animal carcinogen, based on the excesses of liver cancer in rats and mice and reproductive cancers in female rats. Case reports of liver cancer associated with cirrhosis have been reported among workers exposed to carbon tetrachloride. These findings have not yet been supported by any epidemiological studies. The use of this agent has been restricted due to its potential to cause severe liver injury. International production will terminate over the next 5 to 10 years according to the recent Montreal Protocol agreement recently reached by participating nations.

Additional organic chemicals that have a primary use as raw materials or chemical intermediates but additionally have limited use as solvents have been shown to cause cancer in animals. These include formaldehyde, bis(chloromethyl)ether, chloromethyl methyl ether, and carbon disulfide. Bis(chloromethyl)ether and chloromethyl methyl ether are recognized human carcinogens (US DHHS, 1991). Limited epidemiological evidence currently exists in support of the human carcinogenicity of formaldehyde.

2.3 Kidney disease

A variety of solvents have been classically associated with the occurrence of acute tubular necrosis following high levels of occupational exposure or intentional inhalation (Gerr, 1992). Solvents associated with this syndrome include carbon tetrachloride, toluene, glycol ethers and others. This syndrome can cause acute renal failure, which is usually reversible at least in part with the assistance of renal dialysis.
Solvents have also been associated with injury to the glomerular or filtering apparatus of the kidney, that is, glomerulonephritis. Numerous case control studies have been strongly suggestive of a relationship between occupational exposure to solvents and subsequent development of glomerulonephritis. The responsible specific solvents have not yet been identified, and the dose-response relationship has not been characterized.

In recent years, subclinical kidney alterations caused by solvents have been evaluated through the monitoring of low molecular weight of urinary proteins. These include N-acetylglucosaminidase, retinol-binding protein and β2-microglobulin. The clinical significance of these changes are unclear at present, but this is an important area for future study.

2.4 Liver disease

Numerous of the halogenated hydrocarbon solvents are well-known hepatotoxins, causing acute necrosis of the liver and, in the case of carbon tetrachloride, hepatic cirrhosis. Solvents that are used more commonly at present, including trichloroethylene and 1,1,1-trichloroethane, are generally less hepatotoxic than the solvents used in the past, though they too can cause acute liver necrosis after a high exposure and liver inflammation following exposure on a recurring basis. There is limited evidence at present that chronic exposure to solvents such as toluene and styrene can lead to mild reversible inflammation. As with the study of other solvent-related effects, this has been a difficult area for research due to the prevalence of confounding exposures such as alcohol consumption, simultaneous exposure to mixed solvents, and the limited ability to quantify prior exposure to solvents.
EXPOSURE: POPULATIONS AT RISK FOR SOLVENT-RELATED DISEASE

Production and consumption of important solvents has increased considerably in LA&C in the past two decades. This is in part due to the tightened occupational and environmental regulations in developed countries without concomitant changes in regulation in countries in LA&C.

Despite the economic instability which has affected over the last decade the Latin America's development, the chemical and petrochemical industry continued its growth and expansion programs. In 1990, Latin America's olefins (ethylene, propylene and butadiene) capacity represented approximately 5% of the world's capacity and this participation is expected to increase to 6% by 1995. In the case of aromatics (benzene, mixed xylenes and styrene), the Latin America's capacity will also increase to about 6% of the total world output by 1995 (Quijada, 1990).

Figure 6.1 includes some data on the production capacity of basic petrochemicals for the years

![Figure 6.1](image)

Anticipated growth in production of selected organic compounds in Latin America, 1990 and 1995

1990 and 1995 (Quijada, 1990). The primary Latin American countries in this capacity are Argentina, Brazil, Mexico and Venezuela, which are trying to develop their national petrochemical industries to meet domestic needs and export any surpluses available.

An excellent example of this trend is benzene. In Venezuela, the annual consumption of benzene is approximately 36,000 metric tons, which until 1990 had been imported exclusively from the United States. A new benzene plant was constructed in the late 1980's and began producing 59,000 metric tons annually in 1990. With this new plant, Venezuela has now exceeded its own domestic demand and has begun exporting benzene to other Latin American countries. A second benzene-producing facility is current under construction to increase capacity. It should be noted that the existing permissible exposure level for occupational exposure to benzene in Venezuela is 10 ppm (10 times higher than the equivalent exposure limit in the USA), and there is no general awareness of its deleterious health effects.

Recent benzene production in other Latin American countries is shown in Table 6.1. Brazil and Mexico are the leading benzene producers with a significant increase in production during the past five years. These two countries now account for 3.5% of the world benzene production. The production of benzene in Brazil over the past two decades has increased dramatically from 259,000 tons in 1971 to about 650,000 tons in 1991.

An important non-industrial source of exposure to solvents is deliberate inhalational abuse, especially among poor youth. This topic is reviewed in the section below (Special Considerations).

<table>
<thead>
<tr>
<th>Country</th>
<th>Production 1986 (metric tons)</th>
<th>Production 1990 (metric tons) (export)</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>522,462</td>
<td>605,591 (94,254)</td>
<td>+16</td>
</tr>
<tr>
<td>Mexico</td>
<td>221,843</td>
<td>319,778 (0)</td>
<td>+44</td>
</tr>
<tr>
<td>Argentina</td>
<td>138,200</td>
<td>119,616 (35,338)</td>
<td>-13</td>
</tr>
<tr>
<td>Colombia</td>
<td>37,000*</td>
<td>34,300 (2,169)</td>
<td>-7</td>
</tr>
</tbody>
</table>

* 1987 production
STUDY REVIEW: CURRENT RESEARCH OF SOLVENT HEALTH EFFECTS

A review of the available published and unpublished reports and ongoing studies in LA&CoC over the past 10 years was made. Occupational studies fall into several categories: 1) cross sectional studies of health symptoms, neurobehavioural function and other major organ function, 2) biological monitoring of workers exposed to solvents, and 3) a cohort cancer mortality study of workers exposed to benzene at a petrochemical complex.

1. Cross-Sectional Health Studies

In Brazil, 680 foundry workers exposed to benzene through work in coke ovens in the early 1980's were studied (Augusto, 1984). Among these workers, 153 cases of neutropenia (defined as ≤ 4 000 neutrophils or < 5 000 leukocytes with < 2 500 neutrophils) were found. Of these 153 cases, the investigator attributed 93 cases to definite chronic benzene intoxication, most of whom were coke oven operators or maintenance personnel working near the coke ovens. Benzene exposure was not measured.

Thirty six workers from a variety of Mexican factories using a number of different solvents were studied (Durán, 1983). Nystagmus and other clinical evidence of cerebellar abnormalities among these workers were found.

In Mexico it was reported a case of a 47-year-old woman with long-term employment in a furniture making operation with exposure to a wide variety of solvents (Junco, 1988). She was diagnosed as having organic brain syndrome as demonstrated on neurologic and psychiatric examinations and through administration of psychological tests.

Graphic arts workers from Monterrey, Mexico, were studied (González, 1988). In the exposed group 60 workers were exposed to toluene, ethanol and ethyl acetate; eight were in the unexposed group. It was found an increased prevalence of mental symptoms in the exposed group, including difficulty in concentration, irritability, memory loss, insomnia and others. It was also found elevated levels of hippuric acid in the exposed workers.

In the one of the earlier studies of neurobehaviour and solvent exposure, 31 Cuban workers who were chronically exposed to toluene for more than one year were studied (Almirall, 1983). It was found a relationship between two measures of exposure -duration of exposure and urinary hippuric acid levels- to neurologic symptoms and impaired performance on a test of visual memory. It was also found a relationship between neurologic symptoms and urinary levels of hippuric acid.

In a later unpublished study, paint manufacturing workers were studied in Cuba (Cedillo, 1987). The investigator observed differences in neurobehavioural testing results between the exposed group and the control group, though these differences did not reach statistical significance. One specific measure in the nerve conduction velocity testing regimen was observed to be different in the exposed compared to the control group. No correlation was found in the investigation between air levels of toluene and urinary hippuric acid levels.

In a recent study from Venezuela, it was used the WHO Neurobehavioural Core Test Battery (NCTB) to assess neurobehavioural function among 82 workers exposed to organic solvents at an adhesive factory (Escañona, 1993). A group of 67 workers not exposed to neurotoxic chemicals were
used as a control group. The results show that the exposed group had a poorer performance than the unexposed group in 12 of 13 subtests. After controlling for the effects of age, sex and education, the exposed group demonstrated statistically significant reductions in the performance on the following tests: profile of mood states, digit symbol test and simple reaction time. The exposed subjects demonstrated an increase of frequency of the following symptoms: sleep disturbances, behavioral changes, and difficulties with memory and cognitive processing. The authors concluded that the test methodology was useful in the population studied and that the covariates, including age, sex and education, behaved as expected from other studies.

A study is currently being undertaken by M. Dávila from the Department of Accident Prevention and Work Illnesses of the Mexican Institute of Social Security. They are evaluating the neurotoxic effects of solvents among paint production workers following adoption of preventive measures.

In 1989-1990 in Santiago, Chile, there was an epidemic of clinical peripheral neuropathy induced by overexposure to n-hexane among female shoe manufacturing workers (Garcia, 1992). Ten women developed moderate to severe peripheral neuropathy of the arms and legs, necessitating hospitalization. Additional co-workers reported mild symptoms. The epidemic was investigated by the Chilean Security Association, which found that several factors at the factory led to the epidemic, including: inadequate ventilation; a recent increase in production; and a sharp increase in the n-hexane content (approximately 60%) of the glue used in the production process compared to the same product used in previous years. This epidemic prompted testing of a large number of adhesives in commercial use in Chile, which showed that most adhesives contained n-hexane and that the average content was 50%, with the maximum of 96% n-hexane. A recommendation was made to the Health Department and the Manufacturing Association of Adhesives that the maximum allowable concentration of n-hexane in adhesives be reduced to 30% or less.

In an unpublished study, 43 workers in a graphic arts plant with exposure to toluene and xylene were studied and showed mild liver function abnormalities (Mireles, 1991). It was also monitored urine for hippuric acid and higher levels in the urine of the 43 exposed workers were found when compared to a control group of seven unexposed workers.

2. Biological and Environmental Monitoring

Levels of urinary phenol among a group of 79 factory shoemakers and 65 additional shoemakers who worked at home were determined (Fernicola, 1976). The relevant occupational exposure was to benzene that was present in the shoe adhesives. Urinary phenol levels in the first group of shoemakers was elevated relative to a control group that was not exposed to shoe adhesives.

In 1991, the results of urinary phenol levels among 769 workers at a petrochemical plant in São Paulo were reported (Rodrigues, 1991). A number of 1606 urine samples during an 18 month period in 1989 to 1990 on all workers potentially exposed to benzene was obtained. It was found that 77 phenol workers were above the biological tolerance limits. Investigation of these 77 abnormal urinary phenol levels indicated that some of the high levels were due to obvious occupational exposure.
In Brazil it was described the use of monitoring inorganic and organic sulfate levels of urine as a means of assessing benzene among 885 exposed workers to industrial solvents (Mozes, 1982).

Exposure to benzene may be more widespread than generally believed. In Mexico, samples of 30 “thinner” solvent purchased from hardware stores and from industry were analyzed (García, 1983). An average of 25% benzene was found in these samples, two-thirds of which contained some level of benzene.

Thirty one samples of commercially available adhesives in Brazil in the mid-1970’s were studied (Wakamatsu, 1976). It was found that 1/3 of the samples contained more than one percent benzene and that the range of benzene content was zero to seven percent. It was also evaluated urinary phenol levels among workers exposed to these adhesives and found elevation in these levels.

In Chile, it was made a study on the exposure to a variety of solvents in several workplaces including furniture manufacture, leather article manufacture, and a fiberglass-using facility. Of 122 workers tested for urinary metabolites of benzene, toluene, and styrene, 33 (27%) showed a level above biological tolerance levels. An additional 11% of workers were exposed to ambient air levels of one or more of these substances higher than the maximum permitted ambient concentrations in that country (Jacial, 1991).

3. Cohort Mortality Study

A large study was recently undertaken in a large petrochemical complex in Camacari, Bahia, Brazil, by the “Fundação José Silveira”, under contract to the Union of the Petrochemical Industries of Bahia (Fundação José Silveira, 1992). Approximately one-third of the benzene that is produced in Brazil originates in this complex, which began production in 1978-1979. The main purpose of this study was to identify and quantify some medium and long term hematologic effects of occupational exposure to benzene on workers in this petrochemical plant. For this purpose, medical records of all workers hired from the beginning of the operation to present, were retrieved, in order to collect: a) information on the diagnosis of some selected hematologic diseases; and b) data of hematological examinations. For the first aim, 17,453 medical records were retrieved; for the second aim, data from 62,829 exams available in 11,948 medical records were retrieved.

A retrospective cancer incidence study was undertaken. Data sources included hematology clinics in the region, company medical records, local hospital records, and death certificate registries in the Salvador metropolitan area. This was extremely laborious, since death certificates are not computerized, and needed to be reviewed and catalogued by hand. An excess incidence of lymphomas and aplastic anemia was observed among workers exposed to benzene compared to the regional rates of these diseases. There was also excess mortality from leukemia and aplastic anemia among exposed workers.
The longitudinal evaluation of the hematologic data, studied by survival analysis and hazard rate function, showed the following results. The relative risk (RR) of leukopenia (white blood cell count ≤ 4,000 cells) varied from 1.2 to 4.5 for various groups of exposed workers at the end of the first year of exposure. The RR of leukocytosis (white blood cell count ≥ 10,000 cells) varied from 1.6 to 5.5 for the six groups of exposed workers. The RR of anemia (red blood cell count ≤ 4.6 million), was 1.3 to 2.8 for the exposed groups. The RR of polycythemia (red blood cell count ≥ 5.8 million) was 1.7 and 2.7 among the two groups of workers analyzed for this parameter.

This is a continuing study, aided by the fact that death certificate data is now computerized and additional health information has been integrated into the database. In addition, there is an ongoing air monitoring program established by industrial hygienists. It is to be noted that there are currently 4,500 workers in these six plants studied. Data currently in hand require additional analysis, but the cohort deserves further study.
SPECIAL CONSIDERATIONS

Apart from industry, the most important source of exposure to solvents is the deliberate inhalation of a variety of solvents for their psychotropic effects. This practice has been documented throughout Latin America, especially in Mexico (Medina, 1982, 1986). Few reports are available from some countries such as Chile and Argentina. Easily accessible solvents such as those contained in gasoline, glues, and thinners are the most popular, though other sources more easily hidden, such as perfumes and inks, have also been used. Typically, young (ages 10 to 14) homeless boys who are school dropouts abuse inhalational solvents as a regular practice. These children also abuse tobacco and alcohol when available, but tend to have limited access to marijuana and other drugs. Age at first use of inhalational agents is often as young as 8 to 10 years of age. Rates of abuse greatly depend upon the population studied but may be as high as 20 to 60% among street children (Medina, 1986).

Solvent abuse among older segments of the population also occurs. Teenage students in Mexico City in the late 1970’s were studied. It was found that four to five per cent admitted to use of solvent inhalants, which was more than for all other drugs except alcohol and tobacco (Castro, 1982). While older people with more access to income sometimes abuse solvents, use of other drugs such as marijuana, alcohol, and manufactured medicines (such as tranquilizers and amphetamines) is more common than among teenagers (Medina, 1986).
RECOMMENDATIONS FOR A PLAN OF RESEARCH AND PREVENTION OF SOLVENT-RELATED DISEASE

1. Neurobehavioural Research

The principal area in solvent-related research where a multidisciplinary research effort has been successfully initiated in LA&C is the study of the neurobehavioural effects of solvent exposure. For several reasons, this area is the most important research area to cultivate for the future. These include:

a) Investigators in Cuba, Chile, Mexico, and Venezuela have already acquired experience and have a successful track record of utilizing standardized neurobehavioural tests to perform research.

b) The relevant effects can be studied among relatively small groups of workers (40 to 80), due to the sensitivity and standardization of the tests themselves.

c) Occupational settings including glue-manufacturing and glue-using industries, paint manufacturing facilities, painters, and other medium-sized industries that use solvents are undoubtedly available for such study.

d) Many of the standardized tests have been translated into Spanish, if not Portuguese, and are ready for use.

2. Reproductive Damage

There has been little research examining the possible reproductive and developmental effects of solvent exposure in LA&C. This area needs to be studied. The majority of the women with occupational solvent exposure are of childbearing age. The impact on male fertility should be examined as well. This may be of special relevance to populations exposed to solvents as a narcotic, since the population engaged in inhalation abuse is young, with possible long term effects. Any broad studies of effects of solvents should include consideration of reproductive and developmental effects as possible endpoints.

3. Surveillance of Solvent Hazards

There is a clear lack of data regarding the production and uses of most solvents used in LA&C. Only minimal information regarding the quantities and types of uses of solvents could be identified for this report. This is due in part to the nature of the subject. Solvents are used broadly throughout many types of industries and workplaces. Some of the most important and potentially most
hazardous uses of solvents may be in small workplaces or in mobile occupations such as painters, where the systematic collection of information concerning quantities used and levels of exposure may be especially difficult to obtain.

A systematic study of solvent production, uses and exposures should be undertaken for selected solvents. This study should focus on the agents identified above as established carcinogens, neurotoxins, nephrotoxins, and hepatotoxins. Information should be gathered by country and should include the levels of production, the principal occupations and industries that use these agents, and levels of exposure that have been measured. Special attention should be paid to vulnerable populations such as children and pregnant women.

4. Sentinel Health Research

To assist physicians in the recognition of causal associations between toxic occupational exposures and diseases, Rutstein and colleagues developed the concept of the "sentinel health event (occupational)." This is defined as "an unnecessary disease, disability, or untimely, death which is occupationally related." A list is presented in Table 6.2 (Mullan, 1991).

By scanning the table of sentinel health events (occupational), physicians can identify work-related illnesses or exposures that may occur in their patients, and they can identify occupations and industries that may be pertinent to their practice populations (Landrigan, 1991; Mullan, 1991).

The sentinel health approach can also be used to develop research efforts. An example is the outbreak described above of peripheral neuropathy among shoe workers exposed to n-hexane in Santiago, Chile. In this example, cases of neuropathy were recognized clinically, and an alert physician recognized the association with occupational exposure. A study followed. Such opportunities can be used by physicians, industrial hygienists, and others to study exposure-response relationships and clinical manifestations of disease. The capability to translate such outbreaks into public health and clinical research depends not only on the ability to find sentinel cases but also upon the readiness of scientific investigators to respond on a short-term basis to outbreaks of disease. That is, there must be a team of environmental and occupational health professionals with the tools, skills, and ideas to exploit these opportunities for research.

Sentinel health events also offer a case-based approach to occupational health surveillance (Landrigan, 1991; Mullan, 1991). Because of the limited ability of medical treatment to reverse the effects of occupational exposure, the physician has a responsibility to participate in surveillance programs for work-related illnesses. The purpose of surveillance is to identify cases to target individuals and groups of workers at risk of developing the same disorder. Surveillance data also may be used to assess variations in the occurrence of occupational diseases between different industries or work sites, between different geographic areas, or over time.
### Table 6.2

**Examples of occupational health events:**

**Unnecessary disease, disability, and untimely death**

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>A&lt;sup&gt;a&lt;/sup&gt;</th>
<th>B&lt;sup&gt;b&lt;/sup&gt;</th>
<th>C&lt;sup&gt;c&lt;/sup&gt;</th>
<th>INDUSTRY/PROCESS/OCCUPATION</th>
<th>AGENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silicotuberculosis</td>
<td>P&lt;sup&gt;d&lt;/sup&gt;</td>
<td>P&lt;sup&gt;T&lt;/sup&gt;</td>
<td>P&lt;sup&gt;T&lt;/sup&gt;</td>
<td>Quarrymen, sandblasters, silica processors, mining, metal foundries, ceramic industry</td>
<td>Silica + Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Farmers, shepherds, veterinarians, lab workers, slaughterhouse workers, field officers</td>
<td>Brucella abortus, suis</td>
</tr>
<tr>
<td>Tetanus</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Farmers, ranchers</td>
<td>Clostridium tetani</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Day care center staff, orphanage staff, mental retardation institution staff, medical personnel</td>
<td>Hepatitis A virus</td>
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<tr>
<td>Leptospirosis</td>
<td>P</td>
<td>P</td>
<td>P&lt;sup&gt;T&lt;/sup&gt;</td>
<td>Farmer/laborer</td>
<td>Leptospira</td>
</tr>
<tr>
<td>Malignant neoplasm of nasopharynx</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Carpenter, cabinet maker, sawmill worker, lumberjack, electrician, fitter</td>
<td>Chlorophenol</td>
</tr>
<tr>
<td>Mesothelioma of peritoneum and pleura</td>
<td>P</td>
<td>-</td>
<td>P</td>
<td>Asbestos industries and utilizers</td>
<td>Asbestos</td>
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<td>Malignant neoplasm of bone</td>
<td>P</td>
<td>-</td>
<td>P</td>
<td>Radium chemists and processors, dial painters</td>
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</tr>
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<td>Myeloid leukemia acute</td>
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<td>P</td>
<td>Occupations with exposure to benzene</td>
<td>Benzene</td>
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<tr>
<td>Aplastic anemia</td>
<td>P</td>
<td>-</td>
<td>P</td>
<td>Explosives manufacture</td>
<td>Tetrachloroethylene</td>
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<td>Occupations with exposure to benzene</td>
<td>Benzene</td>
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<td>Radiologists, radium chemists and dial painters</td>
<td>Ionizing radiation</td>
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<tr>
<td>Toxic encephalitis</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Battery, smelter, and foundry workers</td>
<td>Lead</td>
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<td>Electrolytic chlorine production, battery makers, fungicide formulators</td>
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<tr>
<td>Cerebellar ataxia</td>
<td>P</td>
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<td>Chemical industry using toluene</td>
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<td>Electrolytic chlorine production, battery makers, fungicide formulators</td>
<td>Organic mercury</td>
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<tr>
<td>Cataract</td>
<td>P</td>
<td>P&lt;sup&gt;T&lt;/sup&gt;</td>
<td>-</td>
<td>Microwave and radar technicians</td>
<td>Microwaves</td>
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<td>Explosives industries, tetrachloroethylene workers</td>
<td>Tetrachloroethylene</td>
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<td></td>
<td>Radiologists</td>
<td>Ionizing radiation</td>
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<td>Blacksmiths, glass blowers, bakers</td>
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<td>Mould repellant formulators, fumigators</td>
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<td>Explosives, dye, herbicide and pesticide industries</td>
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<td>Ethylene oxide sterilizer operator, microbiology supervisors, inspectors</td>
<td>Ethylene oxide</td>
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<td>Noise effects on inner ear</td>
<td>P</td>
<td>P</td>
<td>-</td>
<td>Occupations with exposure to excessive noise</td>
<td>Excessive noise</td>
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<td>Acute or chronic renal failure</td>
<td>P</td>
<td>P&lt;sup&gt;T&lt;/sup&gt;</td>
<td>P&lt;sup&gt;T&lt;/sup&gt;</td>
<td>Battery makers, plumbers, solderers</td>
<td>Inorganic lead</td>
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<td>Electrolytic processes, arsenical ore smelting</td>
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<td>Battery makers, jewelers, dentists</td>
<td>Inorganic mercury</td>
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<td>Fluorocarbon formulators, fire extinguisher makers</td>
<td>Carbon tetrachloride</td>
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<td>Antifreeze manufacture</td>
<td>Ethylene glycol</td>
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<td>Chromate pigment production workers</td>
<td>Inorganic lead</td>
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<td>Infertility, male</td>
<td>P</td>
<td>P</td>
<td>-</td>
<td>Kepone formulators</td>
<td>Kepone</td>
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<td>DBCP producers, formulators, and applicators</td>
<td>Dibromochloroprene</td>
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</table>

<sup>a</sup> Unnecessary disease; <sup>b</sup> Unnecessary disability; <sup>c</sup> Unnecessary untimely death; <sup>d</sup> Prevention; <sup>T</sup> Treatment

5. Research Training: North-South Collaboration

One of the important rate-limiting steps in LA&C research productivity is the relative lack of trained researchers in the areas of occupational and environmental health sciences. This weakness limits the development of research relating to solvents as well as other areas.

We therefore recommend that consideration be strongly given to the initiation of an international fellowship program that would promote research training in disciplines essential to the study of occupational and environmental illness. It is possible to fashion a training experience that would combine meaningful research with enhancement of skills and knowledge in order to achieve two goals simultaneously: conduct of research and training of scientists. Both facets would be facilitated by close North-South collaboration.

Such a fellowship would combine didactic and experiential training in one or more of the following areas: environmental epidemiology, neurobehavioural sciences, clinical occupational medicine, toxicology, exposure assessment, and the surveillance of occupational and environmental diseases. The training program will consist of two sets of activities: an academic component and a research project. The academic component will be undertaken by the trainee from LA&C through an academic program established in collaboration with scientists in North or/and LA&C. This program component will be taught primarily through tutorials with individual supervisory faculty members. The curriculum will be individualized to suit the individual needs and expectations of each fellow.

The research project will originate in the ongoing work of the fellow in his or her position in the institution in the home country in LA&C. It will be developed as a result of the expressed need of the fellow and the home institution prior to or concurrent with the period of the fellowship. Specific research design and plan will occur primarily in collaboration with university scientists in North or/and LA&C. Project implementation will take place at the fellow’s country of origin in consultation with the fellow’s supervising faculty.

As an example of the structure of such a training program, the fellowship period would be two years in duration, during which the fellow works principally in his or her country of origin. At the beginning, middle, and end of the fellowship, the fellow spends four to six weeks at a university in North and/or LA&C. The academic component of the fellowship is completed during these periods, while the research project is completed over the entire two year period.

Once the training program is completed, follow-up activities will be planned to sustain and build on the completed research project and maintain communication with the fellow, either individually or inter-institutionally via long-term institutional agreements of cooperation. The continuity afforded by ongoing consultation to the fellow and his institution will allow building of collaborative research programs and will consolidate learning and builds capacity and expertise in the home institution in Latin America and the Caribbean.
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González RS. Efectos a la Salud Asociados a la Exposición a Disolventes Orgánicos en Trabajadores de la Industria de las Artes Gráficas. [Tesis]. Monterrey: Universidad Autónoma de Nuevo León; 1988.


