

A few introductory remarks

by Per Lundberg

Four parallel one-day workshops were held during each of the two days following the Conference. The form of the workshops differed, but they were all held in an informal mode.

Some of the workshops involved practical demonstrations, eg, inhalation chambers for human volunteers and experimental animals, computerized neurobehavioral testing systems, and psychological test batteries. Some of the workshops were dedicated to methodological questions, others discussed prevention of exposure to solvents, and others again dealt with different types of measurements, such as environmental and biological monitoring and clinical and biochemical measurements.

The variety of and the differences between the workshop programs are reflected to some extent by the divergency in the volume and wealth of the details in the reports from the workshops as presented. For those readers interested in further details it is advisable to contact the rapporteurs, or the scientists mentioned in the reports. The full addresses of the rapporteurs follow the last workshop report.

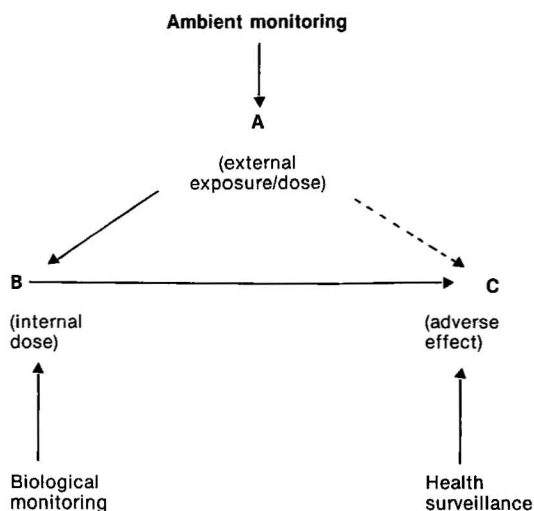
Environmental and biological monitoring

Rapporteurs: Carl Gustaf Elinder, Olof Vesterberg

Professor U Ulfvarson (National Board of Occupational Safety and Health, Solna, Sweden) gave a historical perspective. Gas chromatography became available in the late 1950s, and this technique made it possible to measure different organic solvents in air at comparatively low concentrations. Portable, battery-driven air pumps equipped with charcoal samplers which absorb organic solvents has made it possible to estimate the individual exposure of workers. With the use of these types of personal samplers it is nowadays possible to measure a worker's external exposure during a whole 8-h workshift. Professor Ulfvarson pointed out several pitfalls and errors, however, which can be encountered when air measurements from a limited period of time are used to calculate the exposure for longer periods. Different errors and bias types can result in large over- and underestimates of the true exposure (4). The general tendency is to overestimate exposure in most cases. This situation may lead to exposure limit values that are too high.

Professor R Lauwerys (University of Louvain, Brussels, Belgium) clarified the concepts of external exposure (A), internal dose (B), and adverse effect (C) as

follows:



[Modified from Lauwerys (3)]

The external exposure (A) is estimated from measurements of the substance under study in the workplace air. The estimate of dose does not take into consideration some inter- and intraindividual differences in uptake by different persons due to, eg, variation in physical activity, which influences the pulmonary ventilation. Biological monitoring may be used to assess the internal dose (B). This technique involves the determination of a workplace chemical or its metabolites in the body or, usually, in body fluids such as blood and urine. Biological monitoring may also entail measurements of biological effects, which should be nonadverse and preferably reversible. Biological monitoring aims at the prevention of adverse effects. Screening for adverse health effects (C) which may be the result of exposure should not be regarded as biological monitoring, but instead as a health surveillance program. It was pointed out that there is often a close association between internal dose (B) and the development of adverse health effect (C). This relationship has not been well established for solvents. Numerous data are available on the relationship between the external (A) and internal (B) dose. However, estimates are complicated by inter- and intraindividual variabilities.

Dr J Angerer (Central Institute of Occupational Health, Hamburg, Federal Republic of Germany) drew attention to the large and increasing industrial use of BTX-aromatic hydrocarbons (benzene-toluene-xylene). The biotransformation of these chemicals may entail hydroxylation of the aromatic ring structure. The major metabolic pathways of these chemicals in the human body are known. By use of sophisticated capillary gas chromatography, additional minor metabolites have been detected in some instances. More research remains to be done before such findings can be utilized for biological monitoring. It is important to accumulate enough knowledge on when samples should be taken in relation to the exposure and how to interpret the results. Determinations of substances in exhaled air and blood carry problems due to the rapid decline of the concentrations after the termination of exposure.

Professor M Guillemin and Dr PO Droz (Institute of Occupational Health and Industrial Hygiene, Lausanne, Switzerland) compared biological and air monitoring in assessing exposure to organic solvents. A few factors often cited in favor of biological monitoring were critically discussed. The influence of work load has been taken into account in field surveys thanks to a specially designed pump which regulates its flow rate according to the worker's heart rate (related in most cases to pulmonary ventilation). It has been shown that the work load does not explain the large interindividual variability of the biological monitoring results. It is suspected that interindividual differences in metabolic rate or renal clearance play a significant role in the dispersion of results, since this dispersion is smaller for solvents metabolized only to a small ex-

tent than for solvents extensively metabolized. The influence of life-style has been illustrated by the influence of ethanol, which inhibits styrene metabolism and makes reliable interpretation of biological monitoring results impossible. The influence of intra- and inter-day concentrations on biological indices was also stressed.

A cost-benefit approach as to whether ambient or biological monitoring should be used to assess occupational exposure to solvents was discussed in which the normalized variance of both indices (assuming they are lognormally distributed) is taken into account. For some solvents biological monitoring seems to be more cost effective than ambient monitoring.

Dr H Vainio [International Agency for Research on Cancer (IARC), Lyon, France] discussed the different possibilities available for monitoring exposure to mutagens and/or carcinogens. Some of the methods used are specific, such as the determination of the chemical itself or its metabolite in urine, blood, or exhaled air. Some are nonspecific, such as the determination of the mutagenicity of thioethers in urine. In addition to monitoring the chemical itself in the body, one can also measure the formation of adducts with macromolecules, such as the hydroxyethylation of hemoglobin with ethylene oxide. Some carcinogens require metabolic activation for their conversion to reactive intermediates. This necessity was exemplified by 4-aminobiphenyl and its reaction products with albumin and hemoglobin. Some carcinogenic compounds are known to induce sister chromatid exchanges and chromosome aberrations. Ethylene oxide was given as an example. The internal exposure, ie, formation of carcinogens in the body from the precursor compounds present, eg, in the diet, was also discussed by Dr Vainio. A method has been developed at IARC in Lyon which makes it possible to estimate potential *in vivo* nitrosation in humans. This method has the potential to be used in clinical and field studies to evaluate the role of endogenous N-nitroso compounds in the etiology of cancer at specific sites, such as the stomach or esophagus.

Dr K-H Schaller (Institute of Occupational and Social Medicine, Erlangen, Federal Republic of Germany) presented guidelines which have recently been published in the Federal Republic of Germany for the biological monitoring of organic solvents. Biologically acceptable threshold (BAT) values have been defined and implemented (2). There is a total of 16 such substances in the Federal Republic of Germany. Monitoring organic solvents constitutes about 10 % of the total surveillance program in that country.

Professor O Vesterberg (National Board of Occupational Safety and Health, Solna, Sweden) discussed the importance of good laboratory practice and quality control in connection with biological monitoring. Quality control exercises should preferably not only include one or two reference samples, but instead represent a concentration range similar to that of the

samples to be assayed. Experience is required to produce blood and urine samples stable enough for the substances to be analyzed. In laboratory control programs and proficiency evaluation, limits for acceptable results will have to be determined. Few such attempts have been published.

Dr L Lowry (National Institute of Occupational Safety and Health, Cincinnati, United States) presented experiences with regard to biological monitoring in the United States. It appears that the enthusiasm for biological monitoring has been less there than in Europe, but on the other hand interest has increased rapidly during the last few years. The American Conference of Governmental Industrial Hygienists (ACGIH) has recently proposed biological exposure indices (BEI) for six chemicals, of which five are organic solvents (1). Some of the values refer to group evaluation, whereas others may be used for assessing the exposure of individuals. The BEI values are intended to be used as warning levels of exposure to chemicals and are defined as bioequivalents to the threshold limit values under specified conditions (1).

In the final discussion some principal, legal, and ethical aspects of biological monitoring were discussed. At the present state of knowledge biological monitoring is suitable only for a quite small number of chemicals. This monitoring may have the principal advantage of being closer to the effect level than air monitoring. Interpretation of biological monitoring data often requires much experience and information

on sampling conditions. Many factors may influence the results. Preferably specially trained medical doctors should be involved in the interpretation of the results. It was a general consensus that data obtained in biological monitoring should become available to the examined worker. Data from biological monitoring should not, without agreement of the examined worker, be forwarded to the employer. Nevertheless, the employer should be informed if data from biological monitoring programs show that exposure is so high that it may constitute a health risk. Under such circumstances the employer should be advised to take actions to lower the exposure.

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Inhalation — Experimental techniques and toxicokinetics

Rapporteur: Gunnar Johanson

The first part of this workshop comprised lectures and discussions. Professor I Åstrand (National Board of Occupational Safety and Health, Solna, Sweden) gave a lecture on the factors influencing organic solvent uptake via the lungs, she summarized ten years of research. Some parameters that greatly influence solvent uptake are pulmonary ventilation, cardiac output, blood and tissue solubility, and solvent metabolism. Human exposure to various solvents has been studied. Pulmonary uptake during different work loads (rest, 50 W, 100 W, 150 W) was measured with the Douglas bag technique. Solvents can be roughly classified in two categories on the basis of their organ or tissue solubility. For the category of easily soluble solvents such as styrene and xylene, the uptake is almost proportional to the alveolar ventilation, or, in other words, the solvent uptake increases with increasing work load. The uptake of less soluble solvents, eg, trichloroethylene and methylene chloride, is approximately doubled during 50-W work as compared to rest, but it is constant or even decreasing when the work load is increased. Since solvents are generally fat

soluble, the content in adipose tissue is of great interest. Toluene levels in subcutaneous fat were found to be approximately ten times higher after 50-W work as compared to rest. This phenomenon is probably due to increased blood flow in subcutaneous fat because of increased fat metabolism. Styrene was found in subcutaneous fat up to two weeks after exposure. In conclusion, there is a risk of accumulation of fat-soluble solvents such as styrene, toluene, and xylene in occupationally exposed workers, especially when they are exposed to a high concentration during physical activity. The possible accumulation in other fat-rich tissues, such as the central nervous system, should also be considered.

The use of physiological models to simulate the toxicokinetics of solvents in different species was presented by Professor V Fiserova-Bergerova (University of Miami, Miami, United States). Data from the literature were presented to show that various transfer rates, eg, oxygen uptake, pulmonary ventilation, urine output, and creatinine clearance, in general obey the so-called "surface law," ie, they are proportional

to body surface rather than to body weight. As a consequence, transfer rates relative to body weight are higher, and thus equilibration times are shorter, in smaller animals. Another factor that influences the transportation rate of a solvent is its solubility. The tissue:air partition ratios for various organic solvents have been determined in man, monkey, dog, and rat. The variation between species is very small, with the exception of the blood:air partition ratio, which varies also within individuals. The blood:air partition ratio is increased after food intake. This effect is more pronounced for more fat-soluble solvents. The transportation rate of solvents to the tissues has been simulated for different species on the assumption that metabolic clearance equals hepatic blood flow. It has been shown that relative transportation rate is higher in smaller species. It has also been shown that with increasing blood solubility the transportation rate reaches a plateau level, the rate-limiting step being alveolar ventilation. Similarly, the effect of obesity on the uptake and transportation rate of lipophilic and hydrophilic solvents has been demonstrated.

Professor A Sato (Medical University, Yamanashi, Japan) gave a lecture on aspects of the absorption, distribution, elimination, and metabolism of solvents. Initially, a method to determine tissue : air partition ratios in vitro by the headspace technique was described. Data on water : air, oil : air, and tissue : air partition ratios for various solvents were presented. The influence of solubility properties and metabolic rate on the disposition of solvents was discussed. On the basis of in vitro data it was postulated that inhaled trichloroethylene is almost entirely excreted in urine after metabolic conversion, whereas 1,1,1-trichloroethane is almost exclusively exhaled unchanged. This postulate was supported by experiments with rats. In general there is an inverse relation between "toxicity" and the blood solubility of solvents, as was demonstrated by a logarithmic plot of threshold limit values (TLV) (as recommended by the American Conference of Governmental Industrial Hygienists) versus blood : air partition ratios. Exceptions are carbon tetrachloride, due to the metabolite's hepatotoxicity, and o-dichlorobenzene, which perhaps should have a lower TLV in the future. The toxicity of solvents can be divided into two categories, namely, parent compound-mediated and metabolite-mediated. While toxicity mediated by the parent compound decreases with increasing metabolic rate, the opposite might be the effect with metabolite-mediated toxicity. The caloric intake of the previous day has a marked influence on the metabolic rate of solvents in rat. Therefore the caloric intake should be standardized in in vivo experiments. Ethanol also has a marked effect on organic solvent metabolism.

Dr M Wallén (National Board of Occupational Safety and Health, Solna, Sweden) summarized her

investigations on the effects of ethanol and p-xylene on the kinetics of toluene. Volunteers were exposed to toluene (300 or 200 mg/m³), p-xylene (300 or 100 mg/m³), and toluene + p-xylene (200 + 100 mg/m³). Differences in kinetics were observed for both toluene and p-xylene when the high and low exposures were compared. These differences were interpreted as dose-dependent kinetics. No interactive effects between the two solvents could be seen. In another study, ethanol (15 mmol/kg body weight) was given orally in conjunction with toluene exposure. The total uptake, apparent clearance, and extraction ratio of toluene decreased significantly, while the maximum concentration in blood increased. The elimination profile of ethanol remained unchanged, when compared to that in non-toluene control experiments. In an additional study on isolated perfused rat liver, it was shown that the decreased metabolic rate of toluene obtained in the presence of ethanol is quantitatively comparable to that obtained in the human study. The results support the idea that the effect of ethanol is due to the altered metabolism of toluene rather than to altered hepatic blood flow.

Dr I Jakobson (National Board of Occupational Safety and Health, Solna, Sweden) presented an interaction study on trichloroethylene in female rats. The animals were exposed to trichloroethylene at 200–500 ppm for 6 h or at 100 ppm for 2 h in an exposure chamber. Jugular vein blood was obtained via a permanent polyethylene catheter implanted 2 d prior to the exposure. Isopropanol, disulfiram, pyrazol, and tetrachloroethylene given by gavage increased the steady-state blood levels of trichloroethylene significantly. Ethanol also had a significant effect but only at 100 ppm of trichloroethylene. The interactions obtained were discussed on the basis of the metabolic pathways of trichloroethylene.

The second part of the workshop was devoted to practical demonstrations at the Research Department, National Board of Occupational Safety and Health. At the first station Drs P Näslund and E Wigaeus demonstrated the exposure chamber and methods used while exposing a human volunteer. Station 2 was led by Professor B Holmberg and Dr I Jakobson. Rat exposure equipment and the technique of jugular vein catheter implantation were shown. The last station, led by Professor V Fiserova-Bergerova, presented personal computer-based simulation using physiological models. A commercially available program for teaching in anesthesiology, but equally useful for the understanding of the essentials of organic solvent uptake and distribution, was demonstrated. Different programs developed by Professor Fiserova-Bergerova and her co-workers illustrated various aspects of solvent disposition that can be investigated by simulation. Dr G Johanson described the advantages of DARE P, a simulation package intended for larger computers.

Neurophysiological methods

Rapporteur: Per R Nylén

Many neurophysiological methods can be used for investigations connected with solvent exposure; some of them could not be dealt with during the workshop. Three main types of recordings from the central nervous system (CNS) are electroencephalography (EEG), evoked potentials (EP), and cerebral blood flow (CBF). Electroencephalography has become more and more popular since computer analysis. For example, fast Fourier transformation (FFT) enables the investigator to obtain detailed electroencephalographic data from larger populations than when manual analysis only is available. Electroencephalograms can also be designed for studies of different functions, eg, the multiple sleep latency test (MSLT). Evoked potential recordings are often used clinically and can of course also be used for comparison between groups with different solvent exposures. Cerebral blood flow can be correlated to altered neuron function and changes in mood, motivation, and vigilance.

Event-related evoked responses (ERER) have been used for studies of, eg, senile dementia and might also be a tool for studies of groups occupationally exposed to solvents. The P₃₀₀-technique has the advantage of not being too sensitive to object cooperation, which is important for the correlation of motivation in group comparisons.

Sensory threshold or magnitude estimations are used for detecting abnormalities in the nervous system. Different sensory qualities can be tested, as vibration, temperature, pain, audition, or smell.

Computed tomography (CT), nuclear magnetic resonance (NMR), and positron emission tomography (PET) are methods suitable for studying morphological changes in the nervous system.

The peripheral nervous system (PNS) can be studied by different methods, eg, electromyography (EMG), single-fiber electromyography (sfEMG), and electro-neurography (ENeG). The different electroneurographic parameters can be averaged to a polyneurographic index.

Electromyograms provide information about muscular dysfunction, eg, denervation, motor-unit polyphasic potentials, increased fiber density, reinnervation, and sprouting.

Sensory neurography might be a sensitive test of the condition of the peripheral nervous system. Especially, a recording of sensory nerve action potentials (SNAP) and late components with needle electrodes can be useful in this context. Important parameters in these registrations are local body temperature, stimulating site, recording site, recording surface, and skin resistance.

Measurements of the refractory period can be performed by stimulation at two different distal distances. By varying the time interval between stimulation at the

two sites, one can get a spectrum of different nerve-fiber conduction velocities and refractory periods of the actual nerve.

In a following discussion it was pointed out that, in a neuropathy index, the balance between latencies and amplitudes might be important and that there might be a need for one type of index per solvent.

When groups are compared, it is often better to use rank tests of the employees instead of setting the level of electroencephalographic abnormality for each individual case.

Recordings of the vestibular system functions can give important information about functions in the brain. Studies of the vestibuloocular reflex, a well defined three-neuron reflex, has been performed in connection with the exposure of both humans and animals to different solvents. Nystagmus can be generated in many different ways, and the interpretation is dependent on the method of stimulation. The vestibulo-ocular motor function can be tested by the electronystagmographic technique, eg, sinusoidal swing in darkness, optovestibular stimulation in a lighted room, optokinetic stimulation, the saccade test, the smooth pursuit test, and the randomized swing test. Other tests of the auditory system used in connection with solvent exposure are cortical evoked potentials with frequency ramps as stimuli and interrupted speech tests.

Body sway is controlled mainly by vision, vestibular function, proprioceptors, and the corresponding cerebellar pathways. The test is rather complicated and therefore not suitable for field studies. The person being tested has to stand with his feet close together and with his eyes alternately closed and open. The signals from the platform are recorded by a computer.

If neurobehavioral tests are to be adapted to micro-computer designs, it is favorable to keep to existing methods. The advantage of computerization is improved efficiency in data collection, facilities for saving and processing data, guarantees for reproducible test conditions, and the minimizing of interviewer bias. Possible disadvantages are cost and availability; in addition some people are afraid of the possibility of changes in the nature of what is being tested and some people are not.

Neurophysiological methods can often be of great value in detecting effects caused by solvent exposure. Since the effects sometimes are small (even if significant), it is of great importance that the quantification of effects be as accurate as possible. The investigators are not only responsible for performing the actual neurophysiological registrations, but they must also watch for confounding factors that might bias the result. The numbers of confounding factors are so large in these types of measurements that some kind

of index might be necessary for an accurate comparison between groups with different solvent exposure.

Some of the mentioned techniques were demonstrated at the Section of Occupational Neuromedicine, National Board of Occupational Safety and Health. In the discussions and demonstrations the following persons participated: Dr AM Seppäläinen (Institute of

Occupational Health, Helsinki, Finland), Dr K Savolainen (National Public Health Institute, Kuopio, Finland), Dr E Baker (Harvard School of Public Health, Boston, United States), Dr LM Ödkvist (University of Linköping, Linköping, Sweden), Dr I Rosén (University Hospital, Lund, Sweden), and Drs A Wennberg, AC Hansson and P Nylén (National Board of Occupational Safety and Health, Solna, Sweden).

Skin permeability and disorders

Rapporteur: Jan E Wahlberg

Skin exposure to solvents might cause various kinds of side effects — both local and systemic. Dryness and skin irritation — in many cases developing into irritant contact dermatitis — are well known features of industrial exposure, while allergic contact dermatitis is a rarity today. Percutaneous absorption of solvents may lead to systemic effects and eventually mortality. There are a few case reports describing generalized skin rashes following exposure to trichloroethylene (1), as well as scleroderma (13).

The workshop dealt with factors that accelerate and retard the percutaneous absorption of solvents, local effects — erythema and edema — after topical administration, and the histopathology.

Dr M Lodén (National Defence Research Institute, Umeå, Sweden) presented results from *in vitro* studies on the penetration of four organic solvents (benzene, ethylene glycol, n-hexane, styrene) and formalin through excised human skin. The penetration rate was determined in three ways: (i) the diffusion flux at steady state, (ii) the total skin uptake, and (iii) the initial skin uptake. The penetration rates measured were higher when both steady-state diffusion flux and total skin uptake were taken into account. The distribution of substances in the skin showed a decreasing concentration with depth.

Dr A Boman (National Board of Occupational Safety and Health, Solna, Sweden) described an animal model in which absorption of three organic solvents (toluene, 1,1,1-trichloroethane, n-butanol) through injured or diseased skin were studied. Blood concentrations of the solvents were assessed by gas chromatographic methods (2). Chronic injuries showed an inhibitory effect on skin absorption of the lipophilic solvents, but no effect on n-butanol. Acute injuries showed also an inhibitory effect on the absorption of the lipophilic solvents and a marked potentiating effect on n-butanol absorption.

Dr G Mahmoud (University of Louvain, Brussels, Belgium) described an animal model in which normal skin sites and sites pretreated with barrier creams were

exposed to toluene and n-hexane. The effects were assessed by histopathological examination of biopsied skin sites, and clear differences between protected and unprotected sites were observed (6, 7). The finding implies that this method is a valuable tool for the evaluation of commercial barrier creams.

Professor JE Wahlberg (National Board of Occupational Safety and Health, Solna, Sweden) described two objective methods for the assessment of irritant effects after the topical administration of ten solvents to man and experimental animals. Laser Doppler flowmetry records the erythema, and skin-fold thickness measurement the edema (8, 9, 10, 12). Marked effects were observed from trichloroethylene, toluene, and dimethylsulfoxide, while propylene glycol, methyl ethyl ketone, ethanol, and water gave only marginal effects.

Dr T Kronevi (National Board of Occupational Safety and Health, Solna, Sweden) described the histopathological picture after epicutaneous administration of a number of solvents to guinea pigs. The animals were biopsied after 15 min, 1 h, 4 h, and 16 h, and the time course of the changes were described in detail (4, 5). The pronounced tissue reactions observed histologically for some of the solvents might reflect a defense reaction against penetrating toxic agents.

It was concluded that no simple relationship seems to exist between erythema and edema formation, the microscopic picture, percutaneous absorption rate (3), and the ultimate systemic toxicity after topical administration (11).

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Epidemiologic studies on neuropsychiatric disorders — Empirical and methodological aspects

Rapporteur: Christer Hogstedt

This workshop was organized in two sections. The first concerned diagnostic criteria for neurotoxic syndromes, while the second dealt with some epidemiologic studies on neuropsychiatric disorders among solvent-exposed workers.

In the section of diagnostic criteria for neurotoxic syndromes Dr G Struwe (University Hospital, Huddinge, Sweden) and Dr P Arlien-Søborg (Hvidovre Hospital, Hvidovre, Denmark) reviewed the concepts and methods for the psychiatric and neurological diagnosis of neurotoxic syndromes. The premorbid personality was especially emphasized. Brain cell affection was given as a plausible pathological mechanism rather than neuron death.

Dr C Edling (Karolinska Hospital, Stockholm, Sweden) reported on a diagnostic protocol used in the departments of occupational medicine in Sweden. This protocol requires specific information on solvent exposure, symptoms, clinical evaluation, psychological and neurological test results, consultant evaluations, and, finally, different diagnostic alternatives. It is aimed at producing a uniform diagnostic work-up among the different departments of occupational medicine and also at being a document for the baseline investigation of referred patients, the information from which could be used for future follow-up studies on the prognosis among patients with different diagnostic alternatives and exposures.

Professor S Hernberg (Institute of Occupational Health, Helsinki, Finland) started the second section with a review of four published articles concerning epidemiologic studies on neuropsychiatric disorders among solvent-exposed workers (1, 2, 3, 4, 5). Some

criticism was given to the studies, but the overall conclusion from Professor Hernberg was that there seems to be causal relationship between long-term exposure to organic solvents and an increased frequency of neuropsychiatric disorders of the presenile dementia type.

Comments on the studies and the review were given by Professor O Axelson (University Hospital, Linköping, Sweden), Dr S Mikkelsen (National Hospital, Copenhagen, Denmark), and Dr S Sabroe (Aarhus University, Aarhus, Denmark), as well as by Dr N Cherry (McGill University, Montreal, Canada). Four of the five author groups behind the discussed studies were represented by this panel. No major disagreement was revealed between the participants on the panel as to the evaluation of the studies or the overall conclusion suggested by Professor Hernberg. Neither was there any expressed disagreement from the audience of about 50 persons.

Warnings were raised against causal evaluations from studies of patient materials, as serious selection biases might appear. Several suggestions were given for study designs of future investigations. For example future studies should aim at better precision of the diagnostic entities, improved exposure categorization, and attempts to establish exposure-response relationships.

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Psychological assessment

Rapporteur: Anders Kjellberg

In the morning session general methodological questions were treated as a background for the afternoon demonstrations of specific methods.

Dr A Kjellberg (National Board of Occupational Safety and Health, Solna, Sweden), in his introductory presentation, discussed the different demands that may be put upon tests to be used in the evaluation of the effects of solvent exposure. The varying requirements in laboratory, field, and clinical contexts were stressed.

Dr K Ekberg (Department of Occupational Medicine, Linköping, Sweden) gave a brief outline of methods currently used in Sweden for clinical purposes and pointed out the problems of estimating premorbid level and making a differential diagnosis. She also noted the lack of well-developed methods for the assessment of functions more directly relevant for the person's life quality, eg, his social capacities.

Dr A Seeber (Central Institute for Occupational Medicine, Berlin, German Democratic Republic) presented performance and questionnaire data from large groups of workers that had been referred to his institute.

Dr H Hänninen (Institute of Occupational Health, Helsinki, Finland) presented a test-retest study (including 132 workers) made in order to evaluate the usefulness of a test battery as a screening tool in periodic health examinations. A significant, although often small, learning effect was seen for all the tests. The reliability coefficients were, however, adequately high for most of the tests.

Dr J Jeppesen (Institute of Occupational Medicine, Aarhus, Denmark) reported preliminary data from a study of 23 workers exposed to freon 113. A blind scoring of test results had shown an unexpectedly high percentage of cases with suspected brain dysfunction, especially among those exposed for the longest time.

As an introduction to the discussion of different test batteries, Dr Hänninen recounted the World Health Organization's (WHO's) recommendations for a core test battery to be used in the assessment of neurotoxic effects and explained the rationale behind the selection of the tests.

In the afternoon three computerized test batteries were presented. Drs A Fidler and E Baker (Harvard School of Public Health, Boston, United States) demonstrated a test battery developed for a portable computer (COMPAQ). The battery adheres rather closely to the WHO recommendations and has been designed primarily for large-scale field surveys. Data from three such studies were briefly reported.

Dr A Iregren (National Board of Occupational Safety and Health, Solna, Sweden) gave an account of the development of automatized test methods used at his institute from the start of solvent research in 1971 to the computerized test battery now adopted. The battery has been developed for research purposes, and some of the tests are applicable primarily to laboratory experiments. Data from field and laboratory studies demonstrating the sensitivity of some of the tests were presented.

Dr I Andersen (National Institute of Occupational Health, Hellerup, Denmark) described the computerized test battery developed at the Institute of Hygiene, Aarhus, Denmark. In this battery several of the paper-and-pencil tests were kept in their original form. However, having them fastened on a graphic tablet has enabled the scoring to be automatized. A standardization study comprising 1 000 subjects has been completed and will be reported in 1985.

Dr D Camerino (Institute of Occupational Health, Milano, Italy) demonstrated a computerized pattern recognition test.

Dr B Tvedt (Institute of Occupational Health, Oslo, Norway) reported preliminary data on a 10-word learning test, suggesting that it may be used to differentiate presenile dementia from dysfunctions due to solvent exposure.

The discussions covered a wide range of topics, some of the more important issues being (i) the lack of valid tests of memory functions, (ii) reliability testing, (iii) long-term versus acute effects, (iv) differential diagnosis and the specificity of solvent effects, and (v) the possibilities offered by test computerization.