

CANCER HAZARD FROM EXPOSURE TO SOLVENTS

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Cancer accounts for a third to a quarter of all deaths in our time (Am Cancer Soc) and hence it is important to take adequate steps to prevent the disease as well as to direct efforts to its early diagnosis and cure. Prevention can only be applied if the environmental causes of cancer can be identified and a considerable effort is being directed at the moment towards this end. There are two principal methods available for assessing the carcinogenic hazard to man, firstly the identification of a chemical as a carcinogen and secondly the monitoring of human exposure to it.

The methods available for the detection of chemical carcinogens are limited to two or possibly three approaches. The first approach is the epidemiological one, the second is animal experimentation and the third method, which is likely to acquire more importance in the future, is the in vitro group of tests known generically as short-term tests for carcinogenicity and mutagenicity.

In this talk we shall touch briefly on some of the epidemiological studies employed to discover the carcinogenic activity of solvents but attention will be mainly paid to animal experiments and particularly to the pitfalls that may be encountered in assessing the carcinogenic risk from the results of such studies.

Let us first of all have a look at the reasons for using animals in the detection of carcinogens. The animals employed are mainly of the mammalian species -

non-mammalian species (eg, fish) have occasionally been employed but experience with them is very limited. For logistic and cost reasons, mice and rats are the species of choice but where the situation demands it, higher species, including primates, are used as well.

Experience shows that all mammals develop cancer towards the end of their life-span. In this respect they resemble man. The tumours that develop in animals may run a benign or malignant course as in man and, as in man, they may arise in any cell type. Histologically, tumours resemble also the human ones in architecture although but the histological appearance of the tumour is not necessarily associated with the same type of biological behaviour in animals and in man (Turusov, 1976, 1979). Furthermore, it has been repeatedly shown that substances which are carcinogenic to man are also carcinogenic in one or more species of laboratory animals. In Table 1, I have summarised some well known causes of human cancer. All of these chemicals and products (with one or two exceptions) have been tested in rodents or in dogs and gave a positive result when tested in animals.

This experience has served to indicate that animals are useful models for detecting substances that are likely to present a carcinogenic hazard for man and over the years many chemicals (including some solvents) have been tested by one or more route and found to be carcinogenic. Unfortunately, however, several pitfalls have been encountered in extrapolating animal data to the human and in discussing the carcinogenicity of solvents, some of these pitfalls will be mentioned.

Although epidemiological studies have been conducted on a number of solvents, a reasonably firm connection between solvent exposure and cancer was only obtained in the case of benzene. It is interesting to trace the historical background which led to the acceptance of benzene as a human carcinogen since it typifies the way in which human evidence is collected and analysed.

More than half-a-century ago D lore and Bø gomano

TABLE 1. CHEMICALS THAT ARE CARCINOGENIC IN RODENTS AND EXPERIMENTAL ANIMALS

Chemical	Man	Rat	Mouse	Rabbit	Dog	Other Species
4-methoxyphenyl	Bladder	Mammary gland Intestine	Bladder	-	Bladder	Rabbit - Bladder
Asbestos	Lung, pleura Gastrointestinal tract	Lung, pleura Intestine	Lung, pleura Intestine	Lung, pleura	-	Rabbit - Lung, pleura
Benzene	Bone-marrow	-	-ve	-	-	-
Ben-zene	Bladder	Liver Spleen gland Colon	Liver	Liver	Bladder	-
BONE	Lung	-	Lung Nasal cavity	-	-	-
Chromium (chromate production)	Lung Nasal cavity	Lung	-	-	-	-
Hexamethylenimine	Lung	-	-ve	-ve	-	Guinea-pig - Intestine
Mustard gas	Lung Larynx	-	Lung Mammary gland	-	-	-
2-naphthylamine	Bladder	-	Liver	Bladder	Bladder	Monkey - Bladder
Nickel (refining)	Nasal cavity Lung	Lung	-	-	-	-
Soot, tars and oils	Lung Skin	-	Skin	-	-	Rabbit - Skin
Urethane	Liver Lung	Liver Lung	Liver Lung	-	-	-

Note: Dash (-) means no relevant information available. From IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Supplement 1, IARC Lyon 1979.

(1928) drew attention to a possible association between leukaemia and occupational exposure to high concentrations of benzene. A few years later, Emile-Weil (1932) made similar observations. With one exception, all these cases had occurred in workers occupationally exposed to high concentrations of benzene vapour, usually of the order of 150-1,000 ppm. Many "quasi-epidemiological" studies have been reported on hospital patients in whom a diagnosis of leukaemia has been correlated retrospectively with an occupational history of exposure to benzene while examination of groups of workers with known high exposures to benzene revealed a higher than usual incidence of leukaemia (Van Raalte and Grasso, 1982). Since then the levels of benzene have gradually been lowered and the current exposure seldom exceeds 5-10 ppm but well-conducted epidemiological studies carried out on workers who had been exposed to benzene before current hygienic measures were enforced have demonstrated a higher than expected incidence of leukaemia: the cases of leukaemia were found to have occurred amongst those workers whose jobs involved a very high (>1,000 ppm) exposure to benzene (Van Raalte and Grasso, 1982). Further epidemiological studies have been carried out on workers whose exposure was much less than the "heroic" concentrations encountered fifty or so years ago. As far as can be judged at the moment, there is no convincing evidence that exposure to concentrations of benzene below 100 ppm have been causally connected with leukaemia.

I think there is a point worth making in considering the carcinogenicity of benzene. It is usually assumed in these epidemiological studies that the only mode of human exposure was by inhalation and yet it is inconceivable that some skin absorption had not taken place from the exposed parts of the body such as the hands and face, so that in reality, the actual dose of benzene absorbed is probably considerable higher than the epidemiological studies suggest. Although this consideration may provide some additional degree of reassurance that benzene is not as potent a carcinogen for man as some studies would suggest, there is no room for complacency and efforts should be made to reduce exposure to the lowest practicable level.

Benzene appears to be an exception to the rule that human carcinogens are also carcinogenic to animals. Several attempts have been made in the past to reproduce in

animals the bone-marrow effects seen in man. Although bone-marrow depression and aplasia have been produced readily in experimental species (Van Raalte and Grasso, 1982), it has not been possible to produce leukaemia in these species. Recently, however, Maltoni has succeeded in inducing ear duct tumours (Zymbal gland carcinomas) in Sprague-Dawley rats, by excessively high doses of benzene given orally. Although this brings benzene into line with other human carcinogens in their ability to induce tumours in animals as well as in man, it does not explain why rodents are refractory to the leukaemogenic effect of this chemical.

There is hardly any epidemiological work to speak of on the carcinogenicity of other solvents (See IARC, 1979) so that the animal carcinogenicity data are the only source of information on which to base an assessment of carcinogenic hazard to man. In fact very few of the 300 or so solvents in current use have been tested for carcinogenicity. One assumes that these few were selected either because of a history of heavy exposure and/or because of extensive industrial use.

The commonly used solvents that have been tested for carcinogenicity in rats and mice are listed in Table 2 and all of them produced a statistically significant increased incidence of tumours and by definition they are therefore, carcinogenic to experimental animals. Eight of these solvents produced liver tumours, one produced tumours in the stomach and mammary gland and one produced tumours in the urinary bladder. Only three solvents, acetone, toluene and dichloromethane have been tested with negative results (Van Duuren et al, 1978, Coombs, 1978, Theiss et al, 1977).

Most of these solvents have been in use for a considerable number of years and one suspects that exposure of workers to many of them was not much less than that to benzene and yet there is no indication that any of them have produced cancer in man. It is, therefore, essential to examine critically the results of the carcinogenicity tests in order to determine the relevance to human hazard of the type of tumours induced in rodents by these solvents.

Liver Tumours in Rodents

Tumours of the liver are induced more frequently than tumours in any other organ of the rodent by chemical carcinogens (ECETOC, 1982). A large proportion of hepatocarcinogens in rodents are non-genotoxic and include most of the chlorinated hydrocarbon carcinogens and substances such as phenobarbitone (Schulte-Hermann, 1974), BHT (Olson et al, 1983) and selenium (Wilbur, 1980). The solvents that induced liver tumours are either non-genotoxic or weakly mutagenic. Seemingly they produced mutations only in bacteria, [with the exception of 1,2-dichloroethane which induced mutations in *Drosophila* as well] (See IARC, 1979). It is relevant to examine briefly some of the mechanisms by which non-genotoxic chemicals induce liver tumours.

Most, if not all, genotoxic hepatocarcinogens either produce hepatocellular necrosis or some type of sub-cellular change such as SER hypertrophy, peroxisome proliferation or increased lysosomal activity (ECETOC, 1978, Schulte-Hermann, 1974, Cohen and Grasso, 1981). Hepatocellular necrosis stimulates a reparative process which involves active cell proliferation. Continued damage to the liver leads to a cycle of cell necrosis and regeneration. It is generally considered that cells in an active phase of division are more prone to transformation than normal cells (Coombs and Bhatt, 1978) either because they are more sensitive to damage from environmental carcinogens or else because there is a greater chance of an error in DNA replication if cells are forced to proliferate more frequently and over a much longer period than under conditions of "fair wear and tear" (ECETOC, 1982). The increased turnover rate of hepatocytes probably accounts for the development of cancer when repeated cycles of necrosis and regeneration are provoked.

The sub-cellular changes in the liver mentioned in the previous paragraph are almost invariably associated with liver enlargement, a process which involves an initial phase of hyperplasia. If the liver is maintained in an enlarged state by the continued administration of the chemical a subsequent and gradual increase in ploidy levels occurs (Schulte-Hermann, 1974) by a process of endonuclear reduplication. This process is considered to be the counterpart of hyperplasia (Brodsky and Uryvaeva, 1977).

The continued replication of DNA which endonuclear reduplication entails would appear to be as prone to lead to the development of transformed cells as the replication that takes place prior to cell division since the majority of compounds that cause liver enlargement also cause tumours (Schulte-Hermann, 1974, Cohen and Grasso, 1981). At current levels of exposure of man to solvents it is most unlikely that liver cell necrosis would occur.

Furthermore, the phenomenon of liver enlargement so common in the rodent, does not appear to occur in man (Cohen and Grasso, 1981), so that the risk of cancer development in the liver of man from hepatocarcinogenic non-genotoxic solvents at current levels of exposure is negligible.

Solvents have induced other types of tumours apart from liver tumours (See Table 2). For example, 1,2-

dichloroethane has induced squamous cell carcinoma in the stomach, haemangiosarcomas and uterine tumours in rats and mammary gland tumours, lymphomas and pulmonary tumours in mice, while diethylene glycol has induced tumours of the bladder.

Significance of Stomach Tumours

The stomach in rats is made up of a squamous (forestomach) and a glandular portion which are anatomically divided by a ridge of tissue known as the limiting ridge. The tumours induced by 1,2-dichloroethane were squamous cell carcinomas and therefore arose in the forestomach. The stomach of the mouse has a similar type of anatomical structure as that of the rat.

Earlier work, particularly in the mouse, has shown that this portion of the stomach is sensitive to tumour production by polycyclic aromatic hydrocarbons and other classes of carcinogens given by the oral route (Odashima, 1979). Furthermore, naturally occurring tumours are exceedingly rare in this region (Odashima, 1974) so that any tumour induction here has a much more clear relationship to the inducing agent than tumours induced in other tissues where the natural incidence is high (eg, 5% or more).

On this basis, the induction of tumours of the forestomach by 1,2-dichloroethane is clear evidence of its carcinogenicity. The significance for man of tumour

Table 2

SOLVENTS TESTED FOR CARCINOGENICITY WITH POSITIVE RESULTS

Solvent	Route of administration	Species	Site of carcinogenic action	Ref
Carbon tetrachloride	Oral inhalation and subcutaneous	Mouse, rat and hamster	Liver	1
Chloroform	Oral	Mouse and Rat	"	2
1,4-Dioxane	"	Rat	"	3
Hexachloroethane	"	Mouse	"	4
1,1,2-Tri-chloroethane	"	"	"	5
1,1,2,2-Tetrachloroethane	"	"	"	6
Trichloroethylene	"	"	"	7
Tetrachloroethylene	"	"	"	8
1,2-Dichloroethane	"	Rat	Forestomach Mammary glands Haemangio-sarcoma	9
"	"	Mouse	Mammary glands Liver, Lung Uterus	9
Diethylene glycol	"	Rat	Bladder	10

in the induction of this EORTC's, however, debatable. It has been shown that propionic acid (Mori, 1953) and butylated hydroxyanisole (BHA) (Ito et al, 1983) can induce tumours in this region. Propionic acid is a product of intermediary metabolism, while BHA had been tested previously for carcinogenicity mixed with the diet with negative results (Deichmann, 1955). Studies of the early changes with BHA (P Grasso's personal observation) have revealed marked hyperplasia in the squamous epithelium suggesting an increased turn-over rate of the cells in this tissue. As discussed in the previous section this increased turn-over rate could be the principal factor in cell transformation in this epithelium as in liver.

Mammary Tumours in Mice

1,2-dichloroethane induced also mammary tumours in mice. Mammary tumours in this species are now held to be caused principally by the mammary tumour virus (MTV) (originally known as the Bittner agent) since most strains of mice are infected by it (Grasso et al, 1977). The production of tumours by this agent, however, is influenced by two other factors: genetic tendency and hormonal status. The interplay of these three factors determines the background incidence of tumours in most of the mouse strains used in conventional carcinogenicity screening tests and accounts for strains with a low incidence as well as strains with a high incidence of tumours. Administration of carcinogens, eg, polycyclic aromatic hydrocarbons, by the oral route can increase considerably the incidence of these tumours but there is no evidence that these compounds are acting solely on the genome (Grasso et al, 1977). Since oestrogenic hormones, both the synthetic and naturally occurring ones increase considerably the incidence of these tumours (Nandi and McGrath, 1973) the carcinogens could be exerting some hormone-like action on the mammary gland tissue. Thus, the induction of mammary gland tumours is an uncertain index of carcinogenicity and cannot be advanced in support of any claims for the carcinogenic activity of 1,2-dichloroethane.

Significance of the Tumours in Mice

These were induced by 1,2-dichloroethane and there was also a marginal increase in these tumours in mice treated with dichloromethane.

The factors responsible for the induction of tumours in mice were discussed in detail in a review by Shinkin and Storer (1975). These authors cited evidence which indicates that these tumours are predominantly benign and are genetically determined. It would thus appear that some of the lung cells in the mouse are prone to undergo neoplastic transformation. This subject is discussed in detail in IARC Mono 20 and the conclusion reached was that induction of these tumours provides only a limited evidence for carcinogenicity so that on their own, they are unsuitable for assessing hazard to man.

Carcinomas of the Uterine Bladder

These tumours were reported in the results of carcinogenicity tests of diethylene glycol (Weil et al, 1965). This chemical was at one time extensively used in the pharmaceutical industry and to a more limited extent as a solvent in the food industry. It may occur as a contaminant of polyoxyethyleneglycol, an emulsifying agent used in food and may, therefore, be ingested by a wide section of the population as well as presenting some hazard to those handling the product.

Weil et al (1965), pointed out that stones were found in all the bladders bearing tumours and demonstrated that the bladder tumours did not develop in the absence of stones. Furthermore, they demonstrated that the stones produced tumours when implanted in the bladder of otherwise untreated rats.

Later experiments demonstrated that foreign bodies, such as paraffin wax or cholesterol pellets or glass beads, produced vesical carcinoma (Grasso, 1970). Attempts were made to explain these tumours on carcinogenic contaminants, but even glass beads that were carefully washed with soap and water and then rinsed in several changes of distilled water produced carcinomas. A study of the early changes produced by foreign bodies implanted in the vesical lumen revealed that a marked hyperplasia developed soon after implantation and that a strong correlation exists between hyperplasia and the later development of carcinoma (Grasso, 1976).

This correlation was established more firmly following the publication of the results of an experiment on

ethyl-sulphonyl naphthalene 1-sulfonamide (ENS) by Flaks et al, (1973). This compound is a potent bladder carcinogen in mice and a number of experiments have shown that it also produces pronounced hyperplastic changes as well as calculi in this organ. The calculi are thought to result from the alkaline urine produced by the administration of ENS. When the urine was acidified by the addition of ammonium chloride to the drinking water, neither calculi or tumours of the bladder were produced by ENS administration (Flaks et al, 1973).

The sum total of these observations indicate that if the compound produces bladder calculi then no conclusion can be drawn on the carcinogenic properties of the compound.

Significance of Lymphomas in Mice

It is now acknowledged that most mouse strains that are used in carcinogenicity testing harbour a variety of lymphoma viruses. This topic has been reviewed by Lilly and Pincus (1973) who concluded that two interrelated factors are responsible, namely the presence of a virus belonging to the C-type RNA group, a gene (or genes) that govern the likelihood of infection by lymphoma viruses and the host response to the transformed cell. The administration of a chemical may in some instances tip the scales against the host by, for example, interfering with the immune defence mechanism, allowing the virus to produce a tumour.

Because genetics and tumour viruses may play a major role in the induction of lymphomas, no reliance can be placed on an increased incidence of this tumour as evidence of carcinogenicity.

CONCLUSION

Of the solvents that have been investigated for their carcinogenic potential only benzene presents any real hazard. There is ample human evidence that exposure to levels of benzene of 100 ppm and over in ambient air carries a risk of producing leukaemia. None of the other solvents present any real hazard. As I have attempted to show, there are grounds for suspecting that the tumours observed when these solvents were tested in animals are not induced

as a result of damage to the genome (with the possible exception of 1,2-dichloroethane but by some other mechanism such an increase in cell turn-over rate or an increase in nuclear ploidy, viral infection, genetic factors or hormonal status. Although there are grounds for some reassurance that these chemicals are not carcinogenic for man every effort should be made to reduce human exposure to the lowest limit practicable.

1,2-dichloroethane deserves some special attention. This compound seems to have produced a galaxy of tumours, three of which (stomach, lung and mammary gland) have been commented upon. The other two tumour types (haemangiosarcoma and uterine tumours) are uncommon in control rats. For some unknown reason the haemangiosarcomas were found in a variety of tissues rather than in one organ as, say, vinyl chloride (liver) or propylene oxide (nasal mucosa). It could be argued that these tumours arise from the connective tissue and since this is diffusely distributed throughout the body the scatter of haemangiosarcoma is a reflection of the anatomical distribution of connective tissue. Although this argument is a sound one from the histogenetic viewpoint it must be kept in mind that the haemangiosarcomas were not dose-related and of a relatively low incidence. Only in the males did the tumour incidence reach statistical significance. The former comment applies also to the uterine tumours so that although the cited evidence provides a formidable array of tumours the hazard to man is not as great as the numbers and variety of the tumours might suggest. Nevertheless, the experimental findings with this solvent indicate that it is likely to present a greater hazard than any of the other solvents discussed in this talk, except for benzene.

REFERENCES

- American Cancer Society. Cancer facts and figures - New York. American Cancer Society 1974
- Brodsky WY and Uryvaeva IV (1977). Cell ploidy: its relation to tissue growth and function. *Int Rev Cytol* 50: 275
- Cohen AJ and Grasso P (1981). Review of the hepatic response to hypolipidaemic drugs in rodents and assessment of its toxicological significance to man. *Food Cosmet Toxicol* 19: 585-605
- Coombs MM and Bhatt TS (1978). Lack of initiating activity in mutagens which are not carcinogenic. *Brit J Cancer* 38: 148-150
- Deichmann WB, Clemmer JJ, Rakoczy R and Bianchini J (1975) Toxicity of di-tertiarybutylmethyl-pne ol. *Arch Ind Hyg* 11: 193
- Delore P and Borgomano C (1928). Acute leukaemia in the course of benzene intoxication: on the toxic origin of certain acute leukaemias and their relationship to serious anaemias. *J Med, Lyon* 9: 227-233
- ECETOC (1982). Hepatocarcinogenesis in laboratory rodent: relevance for man.
- Emile Weil MP (1932) La leucemie chez l'homme. *Bull Mem Soc Med Hop, Paris* 46: 193-198
- Flaxs A, Hamilton JM and Clayton DB (1973). Effect of ammonium chloride on incidence of bladder tumours induced by 4-ethylsulfonylnaphthalene-1-sulphonamide. *JNCI* 51: 2007
- Grasso P (1970). Carcinogenicity testing and permitted lists. *Chemistry in Britain* 6: 17-22
- Grasso P (1974). Reviews of tests for carcinogenicity and their significance to man. *Clinical Toxicology* 9: 745-760
- Grasso P, Crampton RF and Hooson J (1977). In "The mouse and carcinogenicity testing". BIBRA, Surrey
- IARC (1979). Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Some Halogenated Hydrocarbons 20: IARC, Lyon
- Ito N, Fukushima A, Hagiwara H, Shibata M and Ogiso T (1983). Carcinogenicity of butylated hydroxyanisole in F344 rats. *Cancer Res* 70. 343

- Lilly F and Vincous T (1973). Genetic control of murine viral leukemogenesis. *Adv Cancer Res* 21:1
- Mori K (1953). Production of gastric lesions in the rat by the diet containing fatty acids. *Gann* 44: 421-426
- Nandi S and McGrath CM (1973) Mammary neoplasia in mice. *Adv Cancer Res* 17: 353
- Odashima S (1979). Tumors of the oral cavity, pharynx, oesophagus and stomach. In "Pathology of tumors in Laboratory Animals" Vol 2 Tumors of the Mouse. Editor-in-chief VS Turusov. IARC Scientific Publ No 23 Lyon
- Olsen P, Bille N and Meyer O (1983). Hepatocellular neoplasms in rats induced by butylated hydroxytoluene. *Acta Pharmacol et Toxicol* 53: 433-434
- Pathology of Tumors in Laboratory Animals. Vol 1 parts one and two - Tumors of the Rat. IARC Scientific Publ 5 (1973) and 6 (1976). Vol 2 - Tumors of the Mouse. IARC Scientific Publ 23 (1979). Editor-in-chief VS Turusov. IARC Lyon
- Schulte-Hermann R (1974). Induction of liver growth by xenobiotic compounds and other stimuli. *CRC Critical Rev in Toxicology* 3: 97-158
- Shimkin MB and Stoner OD (1975). Lung tumors in mice: Application to carcinogenesis bioassay. *Adv Cancer Res* 21: 1
- Theiss JC, Stoner GD, Shimkin MB and Weisburger EK (1977). Test for the carcinogenicity of organic contaminants of United States drinking waters by pulmonary tumor response in Strain A mice. *Cancer Res* 37: 2717-2720
- Van Duuren BL, Loewengart G, Seidman I, Smith AC and Melchione S (1978). Mouse skin carcinogenicity tests on flame retardants tris(2,3-dibromopropyl)phosphate, tetrakis(hydroxymethyl)phosphonium chloride and polyvinyl bromide. *Cancer Res* 38: 3236-3240

Van Raalte HGS and Grasso P (1982). Haematological, myelotoxic, clastogenic, carcinogenic and leukemogenic effects of benzene. *Regulatory Toxicology and Pharmacology* 2: 153-176

Wilbur GC (1980). Toxicology of selenium - A review. *Clinical Toxicology* 17: 171-230

REFERENCES (Table 2)

- 1 NIOSH (1976). Criteria document. Recommendations for carbon tetrachloride standard. *Occupational Safety Health Report* 5: 1247-1253
- 2 National Cancer Institute (1976). Report on the carcinogenesis bioassay of chloroform, Bethesda, MD, Carcinogenesis Program, Division of Cancer Cause and Prevention
- 3 IARC (1976). Monographs on the evaluation of carcinogenic risk of chemicals to man. Vol II, Lyon
- 4 NIOSH (1978). Current Intelligence Bulletin No 20
- 5 National Cancer Institute (1978). Bioassay of 1,1,2-Trichloroethane for possible Carcinogenicity (Tech Report Series No 74). DHEW Publication No (NIH) 78-1324. Washington DC, US Dept of Health, Education and Welfare
- 6 National Cancer Institute (1978). Bioassay of 1,1,2,2-Tetrachloroethane for possible Carcinogenicity. DHEW Publication No (NIH) 78-827. Washington DC, US Dept of Health, Education and Welfare
- 7 National Cancer Institute (1976). Carcinogenesis Bioassay of Trichloroethylene (Tech Report Series No 2). DHEW Publication No (NIH) 76-802. Washington DC, US Department of Health, Education and Welfare.
- 8 National Cancer Institute (1977). Bioassay of Tetrachloroethylene for possible Carcinogenicity (Tech Report Series No 13). DHEW Publication No (NIH) 77-813. Washington DC, US Dept of Health, Education and Welfare

- 9 National Cancer Institute (1978). Bioassay of 1,2-Dichloroethane for possible carcinogenicity (Tech Report Series No 55). DHEW Publication No (NIH) 78-1361. Washington DC, US Dept of Health, Education and Welfare
- 10 Weil OS, Carpenter CP and Smyth HF (1965). Urinary bladder response to diethylene glycol. Calculi and tumours following repeated feeding and implants. Arch Envir Health 11: 569

APPLICATION OF PSYCHOMETRIC TECHNIQUES IN THE ASSESSMENT OF SOLVENT TOXICITY

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INTRODUCTION

Many hypotheses have been formulated and tested in empirical investigations concerning the nature of the effects to be expected in solvent exposure. These hypotheses cover a wide spectrum of impairments of the functional capacity of the nervous system. They range from a transitory depressant action on arousal, to serious irreversible organic brain dysfunctions.

The choice of the behavioral performance tests should depend on the hypothesis to be tested. A slight transient effect on arousal during short-term exposure to low solvent concentration could probably only be detected by means of a very sensitive and reliable vigilance task. In the case of serious organic brain damage, on the other hand, almost any behavioral performance test would probably reveal a deficit in mental capacity. In the latter case, the sensitivity of the tests to detect solvent-induced performance changes would be of secondary importance. More important would be to evaluate the extent and nature of the damage, which would require the use of a comprehensive and differentiated battery of behavioral tests.

The present paper presents a short review of the main results obtained from the application of behavioral performance tests in the study of solvent toxicity and is based on a paper presented at the International Conference on Organic Solvent Toxicity held in Stockholm 1984 (Gamberale, 1985). The studies reviewed have been divided into