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Subject VAPOR TOXICITY OF ETHYLENE DICHLORIDE (DICHLOROETHANE, $C_2H_4Cl_2$) LITERATURE SURVEY

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Single Exposures

No doubt the work by Sayers et al (Public Health Reports 45, 225-239 (1930)) is by far the most extensive investigation that has been made. These workers determined the acute physiological response of guinea pigs exposed to air containing ethylene dichloride vapors. The concentrations of vapor and periods of exposure ranged from those which produced death in a few minutes to those that caused no apparent effect after several hours. In the order of occurrence the symptoms produced in these guinea pigs were eye and nose irritation, vertigo, static and motor ataxia, retching movements, semiconsciousness and unconsciousness accompanied by uncoordinated movements of the extremities, and death. The results may be tabulated as follows:

mg/l	ppm	Duration	Effect
400-800	100,000-200,000	Few minutes	Death
240	60,000	30 minutes	After 10 minutes eye and nose irritation, giddiness, ataxia, convulsions, loss of consciousness. Death in 30 minut s.
40	10,000	25 minutes	Same symptoms. Many delayed deaths.
24	6,000	30-60 minutes	Dangerous
14	3,500	60 minutes	No severe disturbance
4	1,000	Several hours	Very slight symptoms. Maximum amount without serious disturbances after several (8) hours.

Animal	mg/l	ppm	Time exposed	Result	Reference
Mice	11.5	(2,750)	123 minutes	Death after 1 day	Müller, J Arch. exper. Path. u. Pharmakol., 109, 276 (1925) (Cited by von Oettingen, J. Ind. Hyg. & Tox. 19: 349-448 (1937))
Mice	23	(5,500)	54 minutes	Death after 1 day	
Mice	23	(5,500)	70 minutes	Death during exposure.	
Mice	57	(13,700)	36 minutes	Death during exposure.	
Mice	114	(27,400)	15 minutes	Moribund within 1 day	
Mice	35	8,700	2 hours	Death of a majority of the mice.	Lazarew (1929) Pantelitsch (1933) (Cited by Browning, p. 162)
Mice	100	24,000	30 minutes	Death of a majority of the mice.	
Mice	15-20	3,700-5,000	?	Light narcosis	Lazarew (1929) (Cited by Browning, p. 162)
Mice	20	5,000	?	Deep narcosis	" "
Guinea Pigs	40	10,000	?	Deep narcosis	" "

Repeated Exposures

"No chronic symptoms arising from prolonged exposure to ethylene dichloride have been reported---" (Browning, 1937, p. 165)

Apparently no repeated exposures of laboratory animals to ethylene dichloride have been made.

Mode of Action

Müller (Arch. Exp. Path. Pharmak., 109, 276 (1925)) reported that ethylene dichloride produced severe effects upon the liver, however, these results are unconfirmed by more recent workers (Browning, p. 162).

In the acutely exposed cavies of Sayers et al the chief pathological lesions were found in the lung with secondary changes in the kidney.

Many investigators (See Browning, p. 163) have reported corneal opacity following inhalation of ethylene dichloride vapor. This opacity generally disappeared after several months.

Field Studies

No extensive field studies have been made in the case of ethylene dichloride. There has been one case reported following the drinking of two ounces of the material (Hueper and Smith, Fatal ethylene dichloride poisoning, Am. J. Med. Sci., 189, 778 (1935)). A case of acute, but not very severe, symptoms after exposure to the vapor of ethylene dichloride was reported in

England in 1932. The subject who was employed in a dye works complained of vomiting, diarrhea, giddiness and drowsiness, with slight breathlessness after recovery from the attack. (Cited by Browning, 1937, p. 165)

Smyth (Report of the Committee on Volatile Solvents to the Industrial Hygiene Section of the American Public Health Association, 1939, p. 6) in a survey of the literature for 1937 and 1938 listed five reported cases of ethylene dichloride poisoning but found no fatalities due to this material.

Toxicological Significance of Ethylene Dichloride

A direct quotation from Sayers et al (Sayers, Yant, Waite and Patty, Acute Response of Guinea Pigs to Vapors of Some New Commercial Compounds. I. Ethylene Dichloride. Reprint #1349. Public Health Reports 45, 225-259 (1930)) is of particular significance.

"A comparison of the results obtained for ethylene dichloride with those reported in the literature for other compounds indicates that for single exposures and periods of an hour or more the toxicity of ethylene dichloride is of about the same order as that of gasoline, benzene, carbon tetrachloride, and chloroform. For periods of less than an hour it is less toxic than these compounds.

"The odor of ethylene dichloride is distinct and noticeable in relatively safe concentrations. Also, it produces marked symptoms of dizziness in concentrations that will not cause permanent damage. If the odor or the first symptoms of dizziness are taken as a warning of the presence of vapor and the person retires from the contaminated atmosphere it is not likely that injury will occur from acute exposure. Serious effects might easily result, however, from forced exposure, involuntary exposure, or exposure to a high concentration of vapor which would cause unconsciousness before escape could be made.

"In conclusion, it should be stated that the investigation described in this report was designed to give information pertaining to the relative toxicity and effects of a single exposure to ethylene dichloride vapor. Accordingly the results can not be interpreted as applying to the possible effects of repeated exposure. There were, however, no indications that repeated exposure might cause a chronic type of poisoning of a nature other than the logical expectation of a possible accumulation of the effects noted and described for acute poisoning, when the daily exposure is sufficient to cause the latter. It is always a safe recommendation, however, that the manufacture, distribution, and use of new chemicals of this nature be accompanied by a period of observation of the effect on health, so that if poisoning occurs it may be detected in the incipient stage, thereby obviating serious results and permitting the design of a remedy for the situation.

Allowable Limits

On hundred ppm. has been suggested for Massachusetts as the maximum allowable concentration of ethylene dichloride. (Commonwealth of Massachusetts Department of Labor and Industries, Division of Occupational Hygiene, May 1938)

The U. S. Public Health Service, Connecticut Health Department, California Ind. Acc. Comm., and Wisconsin Ind. Comm. had not established definite limits for ethylene dichloride by May, 1938.

Note Concerning the Answer Given in the Queries and Minor Notes Section of the J. A. M. A. (1932) on the Toxicity of Ethylene Dichloride

Browning (Toxicity of Industrial and Organic Solvents, His Majesty's Stationery Office, London, (1937) p. 164) takes special note of the answer given in the J. A. M. A. (1932, p. 1401) in regard to the toxicity of ethylene dichloride. Quoting from Browning, p. 164: "An answer to a query in the Journal of the American Medical Association in 1932 would give the impression that dichloroethane is one of the most toxic solvents used in industry, but, except for the account of a fatal case from drinking the fluid (Heuper and Smith, 1935) and a case of not great severity reported to the Home Office in 1932, there is little information as to the symptoms and none to any organic lesions produced by its use.

The author of the 'Answer' above referred to evidently bases his statement on an analogy with carbon tetrachloride and on the evidence of animal experiments. He states: 'In addition to nausea, workmen with any considerable exposure, may develop headache, dizziness, diarrhea, hemorrhage into the intestinal tract, hemorrhage into the lungs or pleural cavity and irritation of the respiratory tract. Higher concentrations may lead to necrosis of the liver. It is believed that persons addicted to alcohol are especially susceptible to the action of the substance. At least this is true for carbon tetrachloride.' He gives no authority for these statements."

It should be noted that this "answer" is based entirely upon inference and that it is definitely misleading in the light of practical industrial experience with ethylene dichloride. One should notice particularly that the author of the "answer" gives no authority for his statements and was probably stating his personal opinion which, in all probability was based upon an exceedingly conservative analogy with the better known halogenated hydrocarbons.

Significant Articles and Reviews on the Toxicology of Ethylene Dichloride

(1) Sayers, R. R., Yant, W. R., Waite, C. P., and Patty, F. A., Acute Response of Guinea Pigs to Vapors of Some New Commercial Organic Compounds. I. Ethylene Dichloride. Public Health Reports 45, 225-239 (1930). Reprint No. 1349.

(2) Browning, E., Toxicity of Industrial Organic Solvents, His Majesty's Stationery Office, London (1937) p. 161-166.

(3) Smyth, H. F., Jr., Report of the Committee on Volatile Solvents to the Industrial Hygiene Section of the American Public Health Association, (1939) p. 6.

(4) von Oettingen, W. F., The Halogenated Hydrocarbons: Their Toxicity and Potential Dangers., J. Ind. Hyg. & Tox. 19, 394-397 (1937).

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December 10, 1937

S. B. Heath

E. M. Adams

Toxicity of dichloroethane, sym.

According to our information on animal experiments dichloroethane has a vapor toxicity of about the same order as that of carbon tetrachloride.

	$C_2H_4Cl_2$	CCl_4
Slight symptoms after several hours exposure.	0.1%	0.16%
Maximum amount that may be inhaled for 1 hr. without serious disturbance	0.35%	0.4-0.6%
Dangerous for 30-60 minutes.	0.4-0.6%	2.4-3.2%
Rapidly fatal	10-20%	4.8-6.3%

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