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Brief Summary

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## TOXICOLOGY OF VINYL-CHLORIDE MONOMER

This paper was presented at the occupational health session of the C.I.C. Conference, London, Ontario, June 1, 1976.

The speaker from Occupational Health Protection Branch, Toronto, was responsible for setting the VCM level in Ontario at 10 ppm in the atmosphere. He stated that the 1 ppm level, commonly accepted by some regulatory agencies, is unrealistically low.

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## VINYL-CHLORIDE

Vinyl chloride (chloroethylene) is a chlorinated hydrocarbon. It is a colorless gas, heavier than air, its density being 2.16. It is flammable and explosive.

### SLIDE

boiling point - 13.9°C

vapour pressure 760 mm Hg (13.8°C)

It is slightly soluble in water, soluble in ethanol, very soluble in ethyl ether.

It is a colorless gas with a weak sweetish odor resembling chloroform.

Its TLV is 10 p.p.m. or 26 mg/m<sup>3</sup> with a C-level of 25 p.p.m. for 15 minutes.

Its sweet odor can be detected only in high concentrations.

All chlorinated aliphatic hydrocarbons have common toxic effects.

They are

### SLIDE

- 1) neurotoxic ----- depressant of the CNS
- 2) local irritant ----- respiratory tract, eyes, skin
- 3) systemic toxic ----- liver, kidneys.

With all chlorinated hydrocarbons, acute and chronic intoxication can be expected. The acute intoxications very often have a biphasic course. In the first phase, usually anesthesia prevails, whereas in the second phase, the systemic effects like liver damage develop. These can become chronic consequences of acute intoxications.

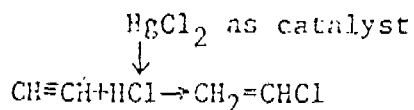
## VINYL-CHLORIDE (cont'd)

With chronic intoxications, the systemic effects are in the foreground. The chronic damage to the CNS manifests itself with behavioural changes, sleepiness and fatigue during the day and sleeplessness during the night, headaches and dizziness. With some compounds, the damage to liver and kidneys is in the foreground of the clinical picture. There have been many trials to predict the prevalence of the individual toxic effects of the chlorinated hydrocarbons by using the chemical structure such as number of chlorine atoms in the molecule or length of chains or double bonds. None of these trials was successful.

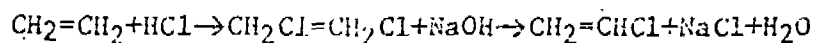
Vinyl chloride was industrially synthesized for the first time in 1912, but only after the huge development of the plastics industry and after the discovery of the polymerisation of VCM its production jumped and is today second only to the production of polyolefines. Its world production in 1970 was 6.2 million tons, almost one fourth of it in the U.S.A. It is used polymerised in many industries and last but not least in the production for medical appliances.

The gas vinyl chloride was industrially produced by hydrochlorination of acetylene using mercuric chloride as a catalyst. This process was the cause of Minimata disease - chronic intoxication with methyl mercury. At present, it is manufactured by thermal dehydrochlorination of ethylene dichloride.

### SLIDE



### II



## VINYL-CHLORIDE (cont'd)

### Health Hazards

Following the process of production is the easiest way to evaluate the hazard of VCM. The production takes place in enclosed systems and the employees are exposed to this substance only for short periods. However, leakages cannot be entirely prevented and in the U.S.A. up to one to two p.p.m. were found in the vicinity of the VCM plants.

After polymerisation, the film remaining on the vessel walls contains 3 - 8% of the monomer. Up to 50% of this is released during the cleaning of the reactors. Automatic cleaning of the reactor vessels by water jets and scrubbers has efficiently reduced the exposure of the cleaning procedure. Automatic cleaning, however, is not quite effective and has to be supplemented by hand-cleaning after every 20 - 30 polymerisation processes.

In 1955, Van Oettinger reviewed VCM and concluded that the gas had, in high concentrations, anaesthetic properties; however, its depressing effect on the circulatory system and its high flammability have prevented its use as a surgical anaesthetic.

In 1957, Filatova reported the occurrence of Raynaud's Syndrome among workers in a VC polymerisation plant in the USSR. The concentration of VCM in this plant was below the Russian TLV of 1 mg/l air or 400 p.p.m.

In 1960, Danzinger reported two cases of accidental fatal poisoning with vinyl chloride. These cases were investigated by Dr. Mastromatteo and one year later they published together the effects of acute exposure for vinyl chloride in animals. They quote results of Lehman and Flury who noted that VCM was highly narcotic, and that the margin between

## VINYL-CHLORIDE (cont'd)

irritating effect and its toxicity were considered to be very slight as elimination from the body was rapid.

## SLIDE

|                  |                                                                |                      |
|------------------|----------------------------------------------------------------|----------------------|
| 1955             | Van Oetringer                                                  | Narcotic properties  |
| 1957             | Filatova                                                       | Raynaud's Syndrome   |
| 1960             | Danzinger & Mastromatteo                                       | 2 fatalities (acute) |
| 1961             | Torkelson - animal experiments (50-500 p.p.m.) - TLV 50 p.p.m. |                      |
| 1966             | Acro-osteolysis reported                                       |                      |
| December<br>1973 | 3 cases of angiosarcoma of the liver reported                  |                      |

Mastromatteo and co-workers used VCM in concentrations of 10, 20, 30 and 40% for animal experiments. The animals, rats, mice, and guinea pigs, were exposed to these concentrations for 30 minutes. All animals were unconscious but recovered within five minutes after exposures to 10 and 20%. At 30%, all mice, rats and one guinea pig out of five did not survive. Congestion of lungs and liver, fatty degeneration of the liver and degenerative changes in the kidneys were found.

In an epidemiological study in 1971, Dinman and co-workers reported their experiences referring to Raynaud's Syndrome and to Acroosteolysis among VCM workers. They found:

1. Raynaud's Syndrome was the first manifestation noted and tends to antecede the bone changes of osteo-acrolysis.
2. All of the 25 afflicted workers had been reactor cleaners.

In unsuccessful attempts to produce acro-osteolysis, the carcinogenic properties of VCM were discovered. Rats, after inhaling VCM in con-

## VINYL-CHLORIDE (cont'd)

centrations of 50 to 2000 p.p.m. for four hours/day for five days/week during one year developed with the exceptions of the ones exposed to 50 p.p.m. malignancies of liver, skin, lungs and intestines. As a special case of liver cancers angiosarcoma was observed (Torkelson 1961) and a TWA of 50 p.p.m. was suggested.

Metabolism of VCM

VCM after being absorbed in the lungs is carried by the blood stream to the brain, where it exerts its depressant action and is mainly metabolised in the liver. Rannung of Sweden used *S. Typhimurium* (a bacterium causing a kind of paratyphus) to test VCM for its capacity of inducing mutations in these bacteria. He found that VCM became mutagenic only after liver cells were added to the cultures.

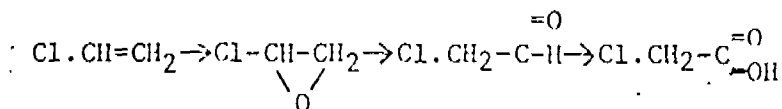
The liver metabolizes VCM to chlorethylene oxide which is further oxidized to chloracetaldehyde and lastly to chloracetic acid. This and the aldehyde are excreted in the urine.

Chloracetaldehyde competes with acetaldehyde produced in the metabolism of alcohol for the enzyme acetaldehyd-dehydrogenase. An excess of toxic acetaldehyde in the blood results. This is the reason why intake of alcohol shortly after VCM exposure is of special toxicologic importance.

Chloroethylene is an epoxide and an alkylating agent, furthermore, it could be during the metabolism oxidized to chloro-methyl-methyl ether which is a strong carcinogen in animals.

VINYL CHLORIDE (cont'd)

SLIDE



Chloracetic acid in the urine gives a positive result of the Fujiwara reaction. Maybe this reaction could help to evaluate the exposure of VCM workers.

The connection of human exposure to VCM with carcinogenesis was suspected in 1973, after three consecutive cases of angiosarcoma causing death in VCM workers were reported.

Angiosarcoma of the liver is a very rare tumor in man. According to the U.S. National Cancer institute, only 0.0014 cases per 100,000 population are expected to occur in one year.

In 1974, when the International Agency for Research of Cancer compiled 22 cases of angiosarcomas in VC-workers, 15 of them were reported in the U.S., 2 in Sweden, 1 in Norway, 1 in the U.K. and three in West Germany. The time of exposure in these cases ranged from 13 to 30 years.

There is, of course, the question of whether results observed in animal studies can be applied to man. In the case of VCM, these considerations are not important as similar health effects both acute and chronic have been observed in men. Besides signs resulting from damage to the central nervous system, Raynaud's Syndrome (white fingers), acro-osteolysis, signs suggesting chronic liver damage and angiosarcoma were seen in exposed workers.

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VINYL-CHLORIDE (cont'd)

Prevention must be both engineering and medical.

Medical prevention must start with a good pre-employment examination directed especially to the functional status of liver and kidneys.

Alcoholism is a contra-indication for employment in VC exposure.

Follow up examinations should include certain liver function tests, looking for Raynaud's syndrome and if this has been found, X-ray examination of the fingers of both hands.

People with pathological results of liver function tests and/or Raynaud's syndrome should be removed from exposure.

Contrary to the acute and chronic health hazards encountered in the production of VCM, the hazards of processing PVC are negligible. PVC when heated e.g. at the extruding nozzle, can give off small amounts of hydrochloric acid vapours and yet smaller amounts of chlorine gas, which may irritate skin, conjunctival and the upper respiratory tract. However, lately a case of pneumoconiosis was reported from Hungary. It occurred in a man who shoveled for one year PVC powder.

POSITION STATEMENT: VCM MORTALITY STUDY

The results of a study by Dr. Buffler and others of vinyl chloride monomer (VCM) plant employees in Dow's Texas Division show that the total number of observed deaths due to cancer (malignant neoplasms) was not substantially different from expected. The results of the study may raise a concern because a statistically significant difference is reported between observed and expected malignant neoplasms of the respiratory system.

However, the results must be viewed in perspective and considered with other available data. It is important to note several facts concerning the Buffler study:

- 1) The number of cases was very small.
- 2) There were five cases of cancer categorized as respiratory cancer by the ICDA coding system.
- 3) One of the five respiratory cancers was a type of tumor (mediastinal teratoma) which is not classified as lung cancer.
- 4) The mediastinal cancer occurred in a 21 year-old employee exposed for only one year to VCM (which is an unrealistically short latency period for development of any tumor due to VCM).
- 5) When this mediastinal cancer is deleted from subsequent analysis, there is not a statistical difference between observed and expected numbers of respiratory cancer.
- 6) Of the remaining four cases of respiratory cancer in employees with long-term exposure (greater than 5 years) to VCM, all had positive smoking histories.
- 7) Other studies of much larger populations with higher exposures have failed to show a definitive correlation between VCM and respiratory cancer.
- 8) The incomplete industrial hygiene data prior to 1970 necessitated subjective estimates of exposure levels.

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## POSITION STATEMENT - Page 2

- 9) The "initial exposure to vinyl chloride occurred in mid-career (34-43 years of age) for all four persons who died of lung cancer. In this regard, the lack of information on previous employment or occupational exposures for these individuals adds to the difficulty of interpreting the significance of these statistical findings."

We agree with the authors' conclusion that; "in view of our inability to detect a significant dose-response relationship, we cannot state that the observed excess in respiratory cancer deaths is due to VCM exposure. However, ...a relationship may exist." The authors also state that "the results of this study can only be considered in conjunction with other studies, both past and future. In view of inconsistent reports to date, more studies... are needed."

Dow will continue to closely examine employees exposed to VCM and to conduct and support additional studies aimed at determining and understanding any health risks that may be related to VCM exposures.

We do not believe that our employees are at any additional risk of lung cancer due to their current exposure to vinyl chloride.

# TRANSMITTAL SLIP

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| FROM | BUILDING |
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| <input type="checkbox"/> FOR COMMENT            | <input type="checkbox"/> PLEASE DO NOT RETURN |

☐

Two recent publications on vinyl  
are enclosed as well as some  
comments on The Buffalo paper.

The comments are not for publication  
but will give you our impression of  
the paper.

*JR Tablan*  
24 July, 1979

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