HAND DISEASE SUMMARY

This is a status report for the physicians of those plants of The B.F.Goodrich Company, where cases of "hand disease" among polyvinyl chloride manufacturing personnel have occurred. This information should be regarded as confidential and is not to be disseminated or discussed except to B.F.Goodrich Management personnel.

CLINICAL CASES

The basic characteristics of this disease have been described in an article by Wilson, McCormick, Creech and Tatum in the August 21, 1967 JAMA, a copy of which is attached. The major portion of the cases that have occurred exhibit osteolysis of the distal phalanges of the fingers and Raynaud's symptoms. We have observed a few cases with acroosteolysis and asymptomatic, and some with symptoms but without acroosteolysis. A few cases have shown suggestive lytic changes in other bones of the body. Currently, the best method of determining the presence of the disease is by x-ray. The B.F.Goodrich Company has been performing hand x-rays on all polyvinyl chloride personnel every six months. The recognition of early acroosteolysis from the x-ray requires the use of proper technique in producing the film, and expertise by the roentgenologist making the interpretation. Any Raynaud's symptoms that occur among polyvinyl chloride manufacturing personnel should be regarded as suspicious. Cases have been seen progressing from Raynaud's symptoms into marked acroosteolysis.

B.F.Goodrich Company

Positive and questionable cases exist at three B.F.G. plants: Avon Lake, Louisville and Niagara Falls. Some of the cases at these plants are asymptomatic and not too definite.

At three plants - Calvert City, Henry and Welland - the single cases reported are questionable. Including all positive and questionable cases, the totals are:

Avon Lake	18
Louisville	23
Niagara Falls	5
Calvert City	1
Henry	1
Welland	1

Acroosteolysis exists in one of the B.F.Goodrich's foreign affiliates.

Other Companies

Acroosteolysis has occurred in other polyvinyl chloride manufacturing companies in the United States and Europe. We believe that up to twelve other companies in the United States and Canada are involved, and at least three in Europe.

EPIDEMIOLOGICAL AND RESEARCH STUDIES

In the Fall of 1966 the B.F.Goodrich Company advised the U.S.A. and Canadian polyvinyl chloride producing companies holding membership within the Manufacturing Chemists' Association of the "hand problem". As a result, a research grant was made

to the School of Public Health at the University of Michigan by M.C.A. to conduct an epidemiological study. Nineteen companies agreed to participate by making hand x-rays and completing detailed work histories of their manufacturing personnel. This study is in the final stages of completion. The results should indicate the incidence of the disease in the Industry, and perhaps its possible causes.

The B.F.Goodrich Company has been pursuing the cause of the disease through its own research efforts. It has employed the services of the Kettering Laboratory, Cincinnati, Ohio, for both clinical studies and animal experimentation. Recently, this laboratory has reported that it has reproduced the disease in hamsters.

The B.F.Goodrich Company has sponsored research at the Brooklyn Polytechnic Institute on the effects of various chemicals on collagen tissue. These studies have not yielded any information as to the cause of the disease.

ETIOLOGY

The cause of acroosteolysis remains unknown. It probably is related to a chemical insult arising out of polyvinyl chloride polymerization. Any of the monomers or intermediate compounds produced could be the cause. In addition to the chemical insult, probably a physical insult and a personal idiosyncracy are necessary for the occurrence of the disease. Because of the low incidence of the disease even among polycleaners performing the same type of work and using the same chemicals, it is probable that the personal factor plays a very definite part. Individuals should not be used as polycleaners who have abnormal responses to temperature stress. The cold insult hand test introduced into our plants about a year ago, should be done prior to the assignment of any individual to polycleaning.

When the reports of hand x-rays are received by the plant physician from the Akron B.F.G. Medical Center, it is his responsibility to evaluate the case, discuss it with the affected employee, and decide on the necessity of reporting it to the proper state health authorities. However, no reporting to the state should be done without prior consultation with The B.F.Goodrich Company Medical Director,

Rex H. Wilson, M.D.

mj
6/24/68
cc: Mr. John Nelson
Mr. J.W. Miller, Jr.

were measured in the morning and again late in the afternoon exposure periods.

Subjective and neurological responses were measured before the subject entered the chamber, 15 minutes after entrance, and at 1-hour intervals thereafter. Flannagan Coordination and Crawford Manual Dexterity Tests were conducted at midmorning and again in the afternoon. Breath sampling began immediately after the subject left the exposure chamber. A 24-hour postexposure urine sample was collected and a blood sample was drawn the following morning for SGPT, LDH, alkaline phosphatase, BUN, creatinine, and bilirubin determinations.

Analysis of Breath Data

The decay curves for the breath vinyl chloride concentrations were constructed by stepwise multiple regression using a digital computer. An empirical relationship of the form Concentration = f (TWA, time) was selected from a choice of several terms, each based on TWA and/or time. The resulting regression equation best represents the ordered relationship between breath vinyl chloride concentration, time-weighted average exposures, and postexposure time.

Each breath decay curve has an associated standard error of regression which can be used to compute the confidence band for any chosen level of significance. The 95% confidence band for the mean of a group of observations was chosen in this case to describe the statistical error associated with the breath data and the regression technique.

Results

Experimental Breath Curves

A total of 13 men participated in the three experimental chamber exposures at nominal concentrations of 50, 250, and 500 ppm producing a total of 160 valid breath data points. Five of the six subjects exposed to 50 ppm were re-exposed at 500 ppm 2 days later. There was no measurable residual vinyl chloride detected on the breaths of the subjects prior to the second exposure. Serial breath sampling was initiated immediately after the subjects left the exposure chamber and continued up to 20 hours following the exposures.

TABLE I
Experimental Human Exposure to Vinyl Chloride

Chamber Concentration (ppm) $\bar{X}$	S.D.	Range (ppm)	TWA[a] (ppm)	Number of Subjects
59	2	65–53	48	6
261	8	289–243	248	4
493	7	518–471	459	4
491	5	525–475	491[b]	7

[a]Time-weighted average concentration based on 7.5 hours including a 0.5-hour lunch period in an uncontaminated area.
[b]Continuous exposure for 8.5 hours.

Table I shows the analyzed concentration to which the subjects were exposed. Calculations of the mean and standard deviation of exposure concentration are based on chart readings from the infrared spectrophotometer taken at 5-minute intervals over the two 3.5-hour exposure periods. The TWA is based on the total 7.5 hours which included a 0.5-hour lunch period in an uncontaminated area.

The final breath decay curves intended for use as an index to VCl exposures were adjusted to TWA concentrations of 50, 250,

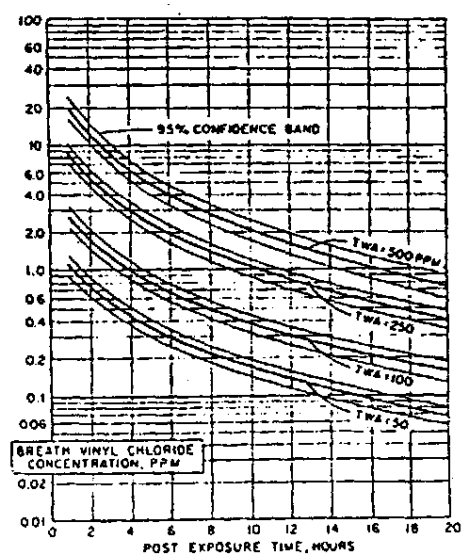

FIGURE 5. Breath decay curves based on experimental human exposures to 50, 250, and 500 ppm of VCl (7.5-hour TWA).

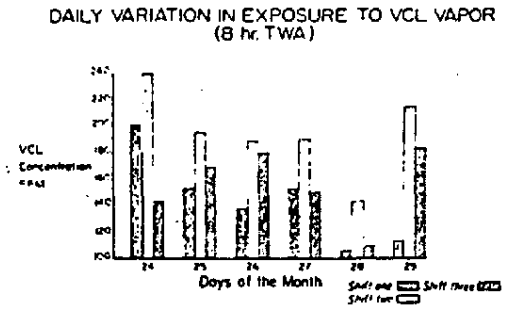

FIGURE 6. Variation in VCl vapor exposure for three shifts.

and 500 ppm (Figure 5). A 100-ppm decay curve was interpolated from the available data using regression analysis. These curves are presented with the calculated 95% confidence bands for the mean of a group of observations.

On-the-Job Breath Curves

Ten workmen participated in the on-the-job breath sampling program, producing a total of 91 usable sets of data. Ten percent of the breath samples collected were discarded because of pipet leakage or poor sampling techniques.

Absolute breath levels ranged from about 20 ppm in one sample taken less than 1 hour after an 8-hour TWA of 250 ppm, to barely detectable levels (<0.05 ppm) in samples taken after exposures at TWA's below 50 ppm.

The extremely broad variation in the TWA's experienced by workmen during one of the periods in which breath sampling was being conducted is demonstrated for three shifts of men bearing the job classification "coagulator operator" (Figure 6). Minute, hourly, and daily fluctuations in the concentration of a contaminant are most descriptively revealed by continuous monitoring. This method of sampling quickly points out the fallacy of judging TWA and peak exposure concentrations on the basis of spot sampling or periodic surveys of brief duration.

The remarkable correlation between breath concentration and corresponding TWA values made it possible to construct the series of breath decay curves shown in Figure 7, with confidence bands only slightly wider than those from controlled human experiments. The close similarity between these curves and those constructed from controlled exposure data are further illustrated in Figure 8.

Human Responses

From a subjective standpoint no significant untoward affects were noted at any of the exposure concentrations. The only complaints were those of two subjects who reported mild headache and some dryness of their eyes and nose during the 500-ppm exposure experiments.

No odor was detected by anyone entering the exposure chamber at 50 ppm. At 250 ppm all four subjects entering the chamber initially reported that they could detect a very slight odor of the chemical. Five of the seven subjects entering the exposure chamber at 500 ppm were able to detect the odor of VCl, but after 5 minutes of exposure those five were unable to detect it even with forced inspiration. Three of the four subjects re-entering the chamber after lunch were able

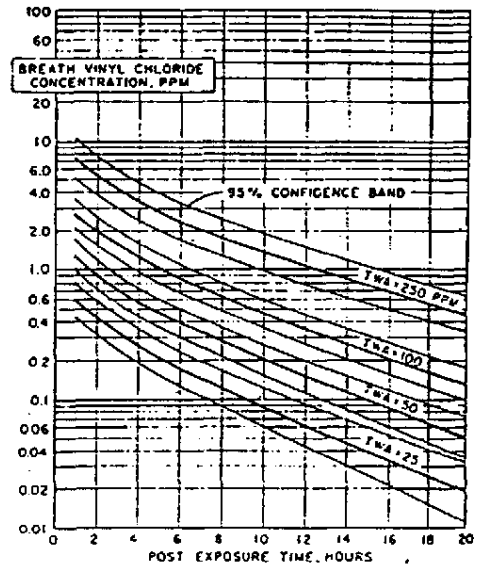

FIGURE 7. Breath decay curves derived from breath data collected from workers following on-the-job exposures to VCl vapor (8-hour TWA).

to detect a faint odor of VCl. One subject could detect a faint odor on deep inspiration for approximately 15 minutes after entering the exposure chamber.

The exposure had no noticeable effect on neurological responses, nor did it produce significant changes in the results of mental, coordination, or manual dexterity tests conducted during the exposure period. All clinical laboratory studies performed in the post-exposure period were normal and not significantly different from pre-exposure values.

Discussion

The object of the environmental health survey is to identify the atmospheric contaminant, determine the exposure level, and relate this to the health hazard it presents. If one is to judge hazard by ambient concentration measurements, then those measurements must accurately describe the exposure on a continuing individual basis. A carefully conducted survey combining continuous analysis of the work room atmosphere with a comprehensive job study will provide data valid for estimating time-weighted average exposure.

On the other hand, breath decay curves constructed from breath data collected during continuous plant monitoring are in close agreement with those obtained from exposure chamber experiments with VCl. These curves should therefore be useful as a second method for assessing exposure to VCl vapor.

The choice of whether one or both methods should be used depends on prevailing circumstances and on the thoroughness desired. For example, data useful in describing peak exposures are obtained from continuous monitoring. Concurrently, exposure trends and concentration gradients may help identify plant operational inefficiencies and equipment malfunctions by revealing specific sources of emission. Correcting these problems not only restores a healthful work environment but often results in bonus savings by reducing losses of raw material and product.

Continuous monitoring, however, is extremely costly both in time and in the equipment required. The scope of data acquired is limited by the number of sampling probes, and these probes are not always capable of accurately measuring the individual's daily exposure experiences, especially should these involve unusual incidences such as chemical spills or exposures outside the monitored area.

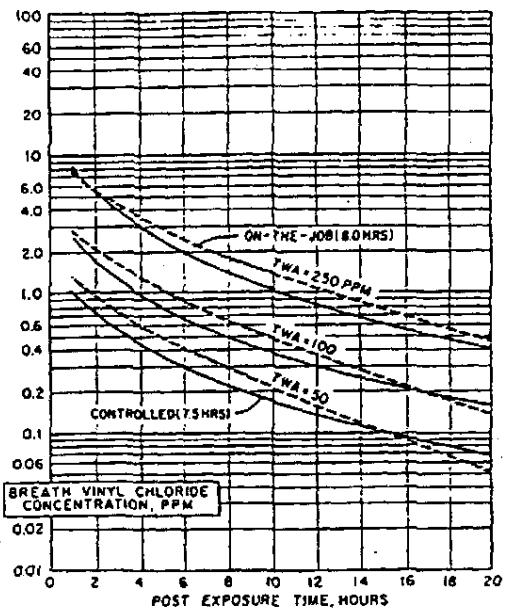

FIGURE 8. Comparison of breath decay curves derived from the on-the-job data and the experimental human exposure data.

Breath analysis has the advantage of individualizing each worker's integrated daily exposure. Breath decay curves, as an index of exposure, offer a means of estimating the average daily individual exposure on the basis of a few breath samples taken serially in the postexposure period. Consequently breath analysis can be used to diagnose as well as quantitate an exposure which has already occurred. It is a relatively inexpensive and simple method which can be put into operation without extensive and costly preliminary preparations.

However, postexposure breath analysis does not provide information on the daily fluctuations of exposure, and the peak exposure concentrations are not made evident by breath data. Finally, breath analysis is not applica-

ble to all chemicals, and breath decay curves established for one chemical are not useful as an index of exposure to any other chemical.

The decay curves presented here are intended to serve as an index of exposure to vinyl chloride vapor and are based on an exposure duration of 7.5 hours for the experimental exposures, and 8 hours for the on-the-job study. The close agreement between the two sets of curves and the narrow confidence bands obtained in each case demonstrate the usefulness and accuracy of both methods for estimating TWA exposures and indicate the importance of breath analysis and the need for expanding its use in evaluating exposures to other widely used volatile organic chemicals.

References

1. Peterson, J. E., H. R. Hovle, and E. J. Schneider: The Application of Computer Science to Industrial Hygiene. *Amer. Ind. Hyg. Assoc. J. 27:* 180-185 (March 1966).
2. Stewart, R. D., H. H. Gay, D. S. Erley, C. L. Hake, and A. W. Schaffer: Human Exposure to Tetrachloroethylene Vapor: Relationship of Expired Air and Blood Concentrations to Exposure and Toxicity. *Arch. Environ. Health 2:* 516-522 (May 1961).
3. Stewart, R. D., H. H. Gay, D. S. Erley, C. L. Hake, and J. E. Peterson: Observations on the Concentration of Trichloroethylene in Blood and Expired Air following Exposure of Humans. *Amer. Ind. Hyg. Assoc. J.23* 167-170 (April 1962).
4. Stewart, R. D., and V. K. Rowe: Quinze Ans d'Etudes sur le 1,1,1-Trichloroethane. *Arch. Maladies Profess. 28:* 194-201 (1967).
5. Stewart, R. D., H. C. Dodd, E. D. Baretta, and A. W. Schaffer: Human Exposure to Styrene Vapor. *Arch. Environ. Health 16:* No. 5 (May 1968).
6. Stewart, R. D., E. D. Baretta, H. C. Dodd, and T. R. Torkelson: Experimental Human Exposure to Tetrachloroethylene. *AMA Arch. Environ. Health. (In print).*
7. Stewart, R. D., H. C. Dodd, E. D. Baretta, A. W. Schaffer, and J. E. Mutchler: Chronic Overexposure to Benzene Vapor. Presented at the Sixth Annual Meeting of the Society of Toxicology, March 23-25, 1967, Atlanta, Georgia.

Received May 26, 1968

Notices and Deadlines

It is the policy of the AIHA Journal to accept and publish notices and short items of import and interest to our readers subject to the limitations of available space. This is done as a service to our profession and no fee is charged for such announcements.

Some notices are received too late to be carried to advantage in our Journal. Persons supplying announcements to us should keep in mind the time schedule of our publication. The Journal appears six times per year with the copies being mailed about the 20th of February, April, June, August, October, and December. While emergency or urgent notices can be inserted up to three or four weeks before the mailing date, such cannot be assured. Normally the announcements should be in the Editors hands at least two months or more before the issue in which they should appear. Perhaps these guidelines will aid you announcement generators.

Acute Inhalation Toxicity of Vinyl Chloride to Laboratory Animals

E. MASTROMATTEO, M.D., A. M. FISHER, Ph.D.,
H. CHRISTIE, B.Sc., and H. DANZIGER, M.D.

Division of Industrial Hygiene, Ontario Department of Health, Toronto, Ontario; Department of Physiological Hygiene, School of Hygiene, University of Toronto, Toronto, Ontario; and Welland County General Hospital, Welland, Ontario

Introduction

FIRST prepared in 1833, vinyl chloride has come into increased use in the last decade in the production of polyvinyl chloride resins. The fire and explosion hazard of the monomer and its narcotic properties on acute exposure are well known. As an industrial material, however, it has been regarded as of moderate toxicity. A Threshold Limit Value of 500 ppm was established by the American Conference of Governmental Industrial Hygienists.

No industrial fatalities associated with its use have previously been reported. It was therefore of special interest when two fatalities occurred in a plant handling vinyl chloride. This plant is engaged in the polymerization of the gaseous monomer with the aid of catalysts. One worker died while cleaning out a polymerization vessel and the other while working in a pit. Details of these two fatalities have been reported by one of the authors.[1]

Published information on the acute toxicity of vinyl chloride to experimental animals proved scanty. Patty, Yant and Waite[2] in 1930 reported on the acute response of guinea pigs to vinyl chloride. They found that exposure to 20 to 40 per cent in air killed guinea pigs in a short time; exposure to ten per cent was endured for several hours. Congestion and edema of the lungs with hyperemia of the liver and kidneys were noted.

Peoples and Leake[3] found the minimal anesthetic range of vinyl chloride in mice exposed for ten minutes was 8 to 12 per cent in air; 25 to 30 per cent was fatal in ten minutes. Dogs and rabbits were anesthetized within one minute when exposed to a concentration of about 18 per cent in air. Recovery was very rapid with no apparent untoward effect even after prolonged anesthesia.

Lehmann and Flury[4] noted that vinyl chloride was highly narcotic but had a wide margin between its narcotic and lethal concentrations. Its local irritating effect and its toxicity were described as very slight. Elimination from the body was very rapid. These authors quoted the work of Schaumann[5] with experimental animals. Mice, rats and dogs were able to endure repeated narcosis without any pathological evidence of liver or kidney damage. According to Schaumann, concentrations of seven to ten per cent in air would be narcotic to humans in a short time and 12 per cent would be dangerous.

Vinyl chloride has been studied as a possible anesthetic agent. Oster and associates[6] noted that incoordinated muscular activity of the extremities and cardiac arrythmias of a serious nature were observed in all six dogs used in their experiment. Carr and others[7] found that vinyl chloride produced sensitization of the myocardium in three of seven dogs in which it was administered as an anesthetic agent.

Two cases of vinyl chloride gassing occurred in a factory in Great Britain where polyvinyl chloride resin was being made. These were reported by the Chief Inspector of Factories.[8] In one case a process worker was standing outside a polymerization vessel and washing it with a water stream. After ten minutes of this he suddenly collapsed across the open manhole. Artificial resuscitation was successfully applied. Subsequent symptoms experienced by this worker were tightness of the chest, nausea, abdominal pain and headache. The second case occurred in a maintenance worker who was overcome while repairing a vinyl chloride leak. Both men were hospitalized. Another worker whose hands were accidentally sprayed with vinyl chloride liquid under pressure developed a burn. This latter case was reported by Hardy.[9] Such burns may occur with other highly volatile materials when sprayed onto the hands as a liquid under pressure.

Filatova and Gronsberg[10] in 1957 reported on hygienic conditions in a polyvinyl processing plant in the U.S.S.R. The plant was engaged in the polymerization of vinyl chloride by means

...catalyst. Air sampling was done and the concentration of vinyl chloride was found to vary ...om about 20 ppm to about 315 ppm. (U.S.S.R. Threshold Limit Value: 1 mg/liter or about 400 ppm). A spastic type blood vessel disorder was ...scribed in workers from this plant.

Because of the recent fatalities mentioned above it was decided to undertake acute inhalation studies in laboratory animals with commercially available vinyl chloride. This was done both for comparison with earlier work and to provide information on the acute response and pathological changes in more than one species of laboratory animal.

Experimental Materials and Procedures

Vinyl Chloride: The vinyl chloride was supplied in a metal cylinder under pressure. A commercial grade with the following specifications was used:

Specific gravity at 20°C	0.983-0.985
Water content	None
Boiling range °C	−11 to −0.5
Hydrogen chloride content	None
Acetylene	10 ppm maximum
Acetaldehyde	20 ppm maximum
Iron	Essentially iron free
Purity (per cent)	99.5 maximum
Impurities (per cent)	0.5 maximum

Pure vinyl chloride is a colorless gas at room temperature; its boiling point is −13.9°C. It has a sweetish odor. Its flash point is given at −78°C and its explosive limits in air from 4 to 22 per cent. It has the molecular formula CH_2:CHCl.

Animals: Mice, rats and guinea pigs were used in the study. Test and control animals were taken from the same laboratory stock. All were fed a standard commercial diet and housed in the same way. All were of the same stage of development.

Equipment: The inhalation chamber capacity was 56.6 liters. It was equipped with a viewing window and an inlet tube. Vinyl chloride was released in gaseous form through an adjustable valve on the top of the containing cylinder, then through connecting rubber tubing and a recalibrated Fisher flow-meter. Fresh air was pumped by motor at an adjustable controlled rate through a meter. The streams of air and vinyl chloride were combined at appropriate rates of flow by a glass Y-tube leading through further rubber tubing to the animal chamber inlet, to deliver a continuing stream in the desired proportions. Calculations and adjustments were made to produce the following flow concentrations of vinyl chloride in air for delivery: 10, 20, 30 and 40 per cent. All concentrations are expressed in this report as per cent by volume in air. No determinations of vinyl chloride concentrations were done in the test chamber during the experiments.

Experimental Procedures: Different groups of five mice, five rats and five guinea pigs were placed in the chamber and exposed for thirty minutes to concentrations of 10, 20 and 30 per cent vinyl chloride in air. Similar groups of control animals were maintained but not exposed to vinyl chloride. At the end of thirty minutes exposure the test animals were immediately removed to fresh air. An additional group of five guinea pigs was exposed to a concentration of 40 per cent vinyl chloride in air. In all 65 experimental animals were involved. Observations were recorded on the animals during and after exposure.

The animals which died either during the exposure or after a delay period were autopsied soon after death. Two weeks after the exposure surviving test animals and controls were sacrificed by a blow to the head with the exception of four control rats which were killed by exsanguination.

All animals were examined for gross pathological changes. Tissues were removed from all animals for microscopic examination. The lungs, liver, kidney and heart were removed in all cases. The brain, adrenal, spleen, trachea, lymph nodes, and the eye were removed from representative animals in each group for study. The tissues were preserved in formalin and sections made for staining with hematoxylin-eosin. Special stains were made where indicated.

Observations

Control Animals: No symptoms were exhibited by the 15 control animals and no deaths occurred.

Ten Per Cent Vinyl Chloride: The response of animals exposed to this concentration is recorded below in summary form:

Exposure Time (minutes)	Response
1	Slight irritation in mice and rats.
5	Increased motor activity first in mice, then rats and guinea pigs.
10	Increased motor activity in all species; twitching of extremities in mice.
15	Pronounced tremor, unsteady gait and muscular incoordination in all species.
20	Mice and rats in side position; muscular incoordination, tremors and twitching of extremities in guinea pigs.
25	Mice and rats unconscious, guinea pigs very unsteady but still standing.
30	Mice and rats in deep narcosis; guinea pigs in side position with tremors—one unconscious.

Exposure was stopped and the animals removed to fresh air. All recovered within five minutes.

Twenty Per Cent Vinyl Chloride: The response

of animals exposed to this concentration is recorded below in summary form:

Exposure Time (minutes)	Response
1	Immediate irritation in mice and rats.
2	Muscular incoordination in mice and rats.
5	Mice and rats on their sides with marked tremors and twitching of the extremities; unsteadiness and muscular incoordination in guinea pigs.
10	Mice and rats unconscious with rapid irregular breathing; guinea pigs unconscious but showing marked twitching.
15	All animals in deep narcosis; respirations irregular and rapid.
20	Deep narcosis; breathing slow and shallow.
25	Breathing ceased in one mouse; frothing at mouth and nostrils in mice and rats.
30	All animals in deep narcosis.

Exposure was stopped and the animals removed to fresh air. Mice and rats recovered faster than the guinea pigs and appeared normal within five minutes except for one mouse which was dead. The guinea pigs continued to show muscular incoordination, unsteadiness on their feet until 20 minutes after removal from exposure.

Thirty Per Cent Vinyl Chloride: The response of animals exposed to this concentration is recorded below in summary form:

Exposure Time (minutes)	Response
—	Mice showed irritation immediately and the rats showed irritation quickly thereafter.
1	Muscular incoordination in mice and rats.
2	Mice and rats in side position with marked tremors and twitching of the extremities; muscular incoordination in guinea pigs with developing paralysis of the extremities.
5	All animals unconscious; rapid irregular respirations in mice and rats with frothing about nose and mouth; twitching of extremities still occurred occasionally in guinea pigs.
10	Respirations stopped in mice; breathing slow and shallow in rats; guinea pigs still exhibited occasional twitching movements of the extremities.
15	Breathing stopped in rats; respirations slow and shallow in guinea pigs; twitching of extremities still present in guinea pigs.
30	Mice and rats still; guinea pigs in deep narcosis with slow shallow breathing.

Exposure was stopped and the animals removed to fresh air. The mice and rats were dead. The guinea pigs took 25 minutes to return to their normal appearance and activity. One guinea pig from this group died within 24 hours following exposure.

TABLE I

Number of Deaths in Different Groups of Five Mice, Rats and Guinea Pigs Exposed for Thirty Minutes to Varying Concentrations of Vinyl Chloride in Air

Vinyl chloride concentration (per cent by volume in air)	Laboratory animal			Total
	Mice	Rats	Guinea pigs	
10	0/5	0/5	0/5	0/15
20	1/5	0/5	0/5	1/15
30	5/5	5/5	1/5*	11/15
40	—	—	2/5*	2/5
Total	6/15	5/15	3/20	14/99

* A delayed death occurred within 24 hours following exposure.

Forty Per Cent Vinyl Chloride: Only five guinea pigs were exposed to this concentration. Signs of irritation were immediately apparent. Muscular incoordination appeared within seconds. After five minutes all the guinea pigs were unconscious with slow shallow breathing. At the end of the exposure period one guinea pig was dead and the remaining four were in deep narcosis. These survivors took 30 minutes to return to their normal appearance and activity, but one died within the following 24 hours.

The number of deaths occurring in different groups of five laboratory animals exposed for thirty minutes to varying concentrations of vinyl chloride in air is shown in Table I.

Pathological Findings

Gross pathological and histological studies were carried out. The findings are summarized below.

Control Animals: These animals showed no gross or microscopic evidence of damage.

Ten Per Cent Vinyl Chloride: All test animals survived this exposure. They were sacrificed two weeks later. On gross examination there was evidence in mice of slight hyperemia of the lungs. This was less marked in rats. Guinea pigs showed no difference from control animals. On histologic examination the mice showed very slight engorgement of the pulmonary vessels. One mouse showed degenerative changes in the tubular epithelium of the kidney with hydropic swelling. The rats showed slight congestion of the capillaries in the lung. Lungs in the guinea pig were also slightly more hyperemic than those of the control animals.

Twenty Per Cent Vinyl Chloride: One mouse died as a result of 30 minutes exposure to this concentration. Pulmonary congestion was evident on gross examination. Microscopically, there was

engorgement of the blood vessels in the lung with patchy areas of atelectasis and minimal edema. The kidneys showed minimal degenerative changes in the epithelium of the convoluted tubules.

The test animals surviving this exposure were sacrificed in two weeks. On gross examination, congestion of the lungs was present in all species, but it was more marked in the mice and rats than in the guinea pigs. Histologically, there was evidence of pulmonary congestion in exposed animals. Some fatty infiltration was present in the liver of one rat. All other tissues studied appeared normal.

Thirty Per Cent Vinyl Chloride: Gross examination of the animals which died as a result of this exposure revealed congestion of the lungs with hemorrhagic areas. The mice and rats in addition showed congestion of the liver and kidney. The one guinea pig death was delayed. In this animal there was marked congestion of the lungs with hemorrhages and the liver was distended and very friable. The microscopic changes in the animals which died included marked engorgement of the pulmonary blood vessels with edema and hemorrhages in the lungs. The trachea of one rat showed superficial desquamation of the epithelium. Congestion was also evident in the liver and kidney of the mice and rats. The liver of the guinea pig which had the delayed death showed severe fatty degeneration of the liver confirmed with frozen sections stained with Sudan III.

The four surviving guinea pigs were sacrificed two weeks later. Marked pulmonary congestion was present with hemorrhagic areas and edema. In one case there was evidence of secondary bacterial infiltration. The liver in these guinea pigs gave the appearance of fatty infiltration but no fat was demonstrated on frozen section.

Forty Per Cent Vinyl Chloride: One of five guinea pigs exposed to this concentration died during the exposure and another died within 24 hours. The two which died showed marked congestion of the lungs with hemorrhages on gross examination. This was also evident on microscopic examination. The liver of one of these gave the appearance of fatty infiltration, but no fat could be demonstrated on frozen section.

The three surviving guinea pigs were sacrificed two weeks later. Marked congestion of the lungs with hemorrhage was evident on both the gross and microscopic examination. In one guinea pig, the tracheal epithelium was completely absent.

Pathological studies which were made of the brain, heart, spleen, adrenals, lymph nodes and eyes showed no difference between controls and animals dying as a result of exposure or between controls and the surviving animals sacrificed two weeks after exposure. There was a tendency for the blood to remain unclotted in the animals dying during exposure. This feature was noted in the two human fatalities mentioned earlier but it is not a specific characteristic of vinyl chloride.

Discussion

The response of guinea pigs to inhalation of vinyl chloride was similar to that reported by Patty, Yant and Waite. The guinea pigs in our study, however, tolerated a greater exposure during the experimental period than either the mice or rats. The results in mice agreed closely with those reported by Peoples and Leake. Rats were similar to mice in their response.

The pathological changes in animals which died as a result of exposure were mainly those of vascular engorgement of the lungs with hemorrhages and edema. The severity of these changes varied with the severity of exposure. In the higher concentrations, pulmonary change was marked with severe damage to the tracheal epithelium. Congestion of the liver and kidneys also occurred in test animals. These changes are similar to those reported by Patty and associates.

Evidence of pulmonary congestion was still present in surviving animals sacrificed two weeks after exposure. Patty and associates reported that such changes had disappeared in about eight days.

Degenerative changes in the tubular epithelium of the kidney were noted in one mouse dying as a result of exposure and in one mouse sacrificed two weeks after being exposed. Such changes, however, were minimal and not shown by other animals in the group.

One of the guinea pigs with delayed death following exposure showed severe fatty infiltration of the liver. Changes suggestive of fatty infiltration were observed in other exposed animals but not confirmed by frozen sections stained with Sudan III.

Summary

Separate groups of laboratory animals comprising five mice, five rats and five guinea pigs were exposed in an inhalation chamber to concentrations of 10, 20 and 30 per cent vinyl chloride in air for 30 minutes. An additional five guinea pigs were exposed to a 40 per cent concentration for a similar period of time. The response by each of the three species to these concentrations is noted.

Inhalation of these relatively high concentrations produced narcosis and death. Mice were the most susceptible with guinea pigs considerably more resistant. Rats were similar to mice in their

response. Exposure to ten per cent vinyl chloride in air produced deep narcosis in mice and rats but no deaths; 30 per cent concentrations killed mice and rats. Exposure of guinea pigs to 20 per cent produced deep narcosis; but three of five guinea pigs survived exposure to 40 per cent concentration.

Animals dying as a result of exposure were autopsied shortly after death. Survivors and control animals were sacrificed two weeks later. Gross pathological and microscopic studies were done and these findings are described.

The principal pathological changes in animals dying from exposure were congestion of the lungs with pulmonary edema and hemorrhages in some, and congestion of the liver and kidneys. Failure of the blood to clot was also observed. One of the three guinea pigs which died following exposure showed severe fatty infiltration of the liver.

Survivors sacrificed two weeks after exposure showed little difference from the control animals. Pulmonary congestion was still evident but liver and kidney congestion was not.

References

1. Danziger, H.: Accidental Poisoning by Vinyl Chloride: Report of Two Cases, *Canadian Med. Assoc. J. 38:* 528 (May, 1960).
2. Patty, F. A., W. P. Yant, and C. P. Waite: Acute Response of Guinea Pigs to Vapors of Some New Commercial Organic Compounds V. Vinyl Chloride, *Pub. Health Rept. 45:* 1 (August 1930).
3. Peoples, A. S., and C. D. Leake: The Anesthetic Action of Vinyl Chloride, *J. Pharmacology 48:* 254 (1933).
4. Lehmann, K. B., & F. Flury: *Toxicology and Hygiene of Industrial Solvents*, Translated by E. King and H. F. Smyth, Jr., Williams & Wilkins, Baltimore (1943).
5. Schaumann, O.: Cited by Lehmann, K. B. and F. Flury.
6. Otter, R. H., C. J. Carr, J. C. Krantz, and M. J. Satenwald: Anesthesia XXVII. Narcosis with Vinyl Chloride, *Anesthesiology 8:* 359 (1947).
7. Carr, J., R. M. Burgison, J. F. Vitcha, and J. C. Krantz Jr.: Anesthesia XXIV. Chemical Constitution of Hydrocarbons and Cardiac Automaticity, *J. Pharm. and Exper. Therap. 97:* 1 (1949).
8. *Annual Report of the Chief Inspector of Factories for the Year 1951*, London: H.M.S.O. Cmd. 8772 (March 1953).
9. Harris, D. K.: Health Problems in the Manufacture and Use of Plastics, *Brit. J. Ind. Med. 10:* 253 (1953).
10. Filatova, U. S., and F. S. Gronsberg: Hygienic Working Conditions in Polyvinyl Chloride Tar Plants, *Gigiena i Sanit. 22:* 38–42 (January 1957). Abstracted in *Abst. of World Med. 17:* 69 (July 1957).

RN-Hodge-IC?
KHC Bernat - BP
A. Vittone Jr.
W C Hallenbeck
R W Strassburg
File - 10

THE NEW YORK ACADEMY OF SCIENCES

WORKING GROUP

ON

TOXICITY OF VINYL CHLORIDE-POLYVINYL CHLORIDE

analytical method
Coming -
Bill

"ENVIRONMENTAL CONCERNS BEYOND THE WORKPLACE"

Glenn E. Schweitzer
Director, Office of Toxic Substances
Environmental Protection Agency
401 M Street, S. W
Washington, D. C. 20460

20245001

Presentation to the Working Group on
Toxicity of Vinyl Chloride-Polyvinyl Chloride
The New York Academy of Sciences
New York City, New York
May 11, 1974

"ENVIRONMENTAL CONCERNS BEYOND THE WORKPLACE"

Glenn E. Schweitzer
Director, Office of Toxic Substances
Environmental Protection Agency
Washington, D. C.

During the past several months vinyl chloride has awakened [illegible] elements of the environmental community to the presence of the plastics industry. In some respects it is fortunate that we have been alerted in a rather dramatic fashion to the need for greater attention to this important segment of our industrial base which will surely continue to expand in the years ahead. While this symposium is directed to the existing and potential risks involved in the manufacture [illegible], and use of vinyl chloride monomer (VCM) and polyvinyl chloride (PVC), many of the types of considerations and uncertainties that punctuate these deliberations undoubtedly characterize a far broader swathe of concerns over chemicals in general. Hopefully, we can extrapolate from our current experiences with VCM and PVC in identifying problems with other potentially important commercial chemicals early in their embryonic stage and thus minimize the economic dislocations attendant to corrective actions.

Unfortunately, the proposed Toxic Substances Control Act has been lodged in a Joint Committee of the Congress for ten months thus, a very powerful tool for addressing the vinyl chloride problem and similar problems with other chemicals in an adequate manner is not available to the Federal Government. We must rely on other statutory authorities and on the power of persuasion in our efforts to insure that our population is not being unnecessarily exposed to concentrations of VCM and other chemicals used in connection with VCM. It is particularly distressing that until this statutory authority is on the books, the Federal Government will not be equipped - in terms of experienced personnel and supporting resources - to grapple with the intricacies of this type of toxic substance problem in a manner which will insure full attention to the balancing of risks and benefits.

Today I will report to you on the preliminary investigations undertaken by the Environmental Protection Agency during the past three months. We are still several weeks away from reaching even tentative conclusions as to what additional steps, if any, should be taken by the Agency concerning VCM/PVC activities. Our monitoring data are not yet