

COMMENTS ON VINYL CHLORIDE

Frank G. Standaert, M.D.

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Carcinogenicity, angiosarcoma: Vinyl chloride's capacity to induce angiosarcomas in animals is established. It has been shown in several laboratories, in several species (including fish, rats and mice) and at all concentrations tested so far.

Vinyl chloride's capacity to produce angiosarcoma in man has not been proven absolutely but the unusually high incidence of angiosarcoma among vinyl chloride workers and the similarity of the tumors in these workers to those produced in animals is as convincing evidence as it is possible to get without deliberate exposure of men. The few parts of the Record that question this conclusion point out that all of the cases have been concentrated in a few factories; seven of them occurred in the Louisville, Kentucky plant alone. This concentration raises the question of whether these workers received a greater exposure or whether other factors were operating in these individuals who succumbed. For instance, were there co-carcinogens present? Were there genetic predispositions to the disease in these individuals? Did regional dietary habits or environmental factors play a role? Was a latent or unknown infection or other disturbance a contributing factor? These are valid questions, but there is no way of knowing whether or not these possibilities influence the carcinogenic potential of vinyl chloride in man. Regardless, it should be

a variety of lesser lesions (Lange et al., Exhibit 183). The urgency of the angiosarcoma problem apparently has precluded careful study of other lesions in animals, but damage to brain, liver, kidneys, thyroid, bone, nerves and skin were noted by Viola some years ago and fibrotic changes in the liver are constant concomitants of the angiosarcoma. The Biotest data clearly show early and excess deaths among animals exposed to all concentrations of vinyl chloride tested. Studies of teratogenic effects in animals have not had positive results but hints of possible mutagenic effects in man can be found in the excess chromosome splitting seen in Selikoff's laboratory. The possibility of teratogenicity is raised by Maltoni's observation of angiosarcomas in newborn animals.

Conclusion: The attention that has been given to angiosarcoma of the liver should not encourage a narrow view of the hazard of vinyl chloride. Even the limited data that is available on human toxicity clearly shows the gas to cause changes in virtually every organ in the body. The animal data shows that angiosarcomas are less than one-third of the total number of tumors that can be produced and that other damage is commonplace. In short, the record is replete with evidence that vinyl chloride is a serious potential hazard to the health of man.

Polyvinyl chloride: The Record only touches on the toxicity of polyvinyl chloride, but there are suggestions that it may not be inert. At the least, it is a carrier of the entrapped monomer. In addition the particles are phagocytosed and enter many organs. There are suggestions that they may cause pneumoconiosis

It is even more difficult, if that is possible, to ascertain the amount of vinyl chloride that produces noncancerous lesions. There is virtually no quantitative information for either animal or man and there has been no attempt to quantitate the occurrence of these lesions, or the concentrations of vinyl chloride that cause them. This is a major gap in our knowledge. More workers may suffer from these effects than from the carcinogenic effect.

There is no clue to the villain in the toxicity produced by vinyl chloride. It could be the intact molecule or it could be a metabolite or a reactive intermediate. Several metabolites have been found and several potential routes of metabolism have been illustrated, but which of these, if any, leads to carcinoma and other changes is not known. There is also evidence that the metabolism of vinyl chloride is concentration dependent with one pathway predominating at higher concentrations and another at lower ones. These data obviously would be significant if it were known which route led to the deleterious material, but the critical insight is not available.

The Record contains many discussions of the dose-response relationship between vinyl chloride and its toxicity, but the data needed to establish the critical part of the relationship are absent. Every concentration tested so far has produced tumors and excessive rates of death in animals. Some scientists have taken numbers from these experiments, and have attempted to project the dose response curve below the observed values. Such projection is speculative, at best. Even at the high end of the curve, the data are scanty and give a poor basis for line fitting. They give no grounds for extrapolating to the unknown. More fundamentally,

to follow. As noted above, it is as clear as it is possible for it to be that a similar set of toxic effects occurs in man and experimental animals. It is also clear that among the experimental animals there is no great difference in the concentrations of the gas that produce effects in the various susceptible species. Under these circumstances, there is only one prudent course to follow: assume that man is at least as sensitive as the most sensitive mammalian species. This assumption is universally applied in assessing the toxic hazard of materials to man. The potential for disaster in any other course is apparent.

Time factors: There is a similar void in our knowledge of the time it takes to produce carcinomas. In animals the tumors do not appear soon after exposure. Instead, there seems to be an inverse relationship between concentration of gas and time to onset of tumors, and in some cases the time to onset approaches the lifespan of the animal. Much has been made in the Record of these facts and the fact that the human victims worked in the vinyl chloride industry for many years before their tumors were diagnosed. However, we have no way of translating these observations into practical guidance. We do not know if this long time to onset is an induction period; that is, a long, continuous exposure to the gas is necessary to produce the fatal change; or whether it is a latency period; that is, the tumor begins its inexorable course very soon after exposure but its initial growth is slow and its recognition is delayed.

The Record hints that the former may be the case. There is a suggestion in the recent Maltoni data that long continuous exposure is

effects have been produced by concentrations that existed in the work place in the past, but virtually nothing is known about the circumstances that produced them. The deficit in our knowledge is so great that there is no hope of getting adequate quantitative data in the foreseeable future and a full explanation of the hazard is probably several decades away. Since we do not and cannot know what concentration of vinyl chloride is dangerous for man, it will not be possible to set a standard on a solid basis of fact. The best that can be done is to try as hard as possible to reduce the potential medical risk without incurring unacceptable economic risk.

Recommended approach--Philosophy and tactics: An important factor is the special terror of cancer in our society. The risk of violent death or injury is accepted by workmen in many industries. The risk of chronic disease has also been accepted in certain industries, (e.g. "black lung"). Cancer is not and will not be viewed as sanguinely by the American public and workman.

The tactics for achieving a reduction in exposure are not in my area of competence, but the following observations may be helpful. To me, it does not seem likely that vinyl chloride can be banned without damage to our economy. It also does not seem likely that human exposure can be eliminated immediately. Therefore, some risk will have to be borne by some individuals. In my view, this risk should be as small as possible and it should be confined to the smallest possible number of people. Those at risk should be fully aware of the risk, accept it voluntarily, have the best means of protecting themselves against it, and be compensated for bearing

may be less stringent and, therefore, less costly than those imposed on American companies.

In this regard, the record suggests that little thought has been given to the technology for stripping the monomer. Therefore, this may be an area in which very large gains might be made with relative ease.

2. I suggest a reduction in the emphasis on ventilation as a means of reducing exposure in the monomer and poly plants. Ventilators perforce distribute the gas to the surrounding environment and the Record is filled with observations of significant concentrations in offices, laboratories, open areas and even beyond the fence line. Some of these concentrations are uncomfortably high. The public and unsuspecting workers should not be exposed in this way.

3. Following the theme that the area of risk should be as small as possible, I suggest different standards for different groups of people. I suspect that the general public and workers at end-product plants can be protected much more quickly and easily than those engaged in polymer production. I see no reason why a low concentration standard for these people has to be delayed until more difficult situations in the polymerizing plants can be solved.

I recognize that setting different standards for different groups may be taken by some as callousness, i.e. a different concern for one group of workers than for another. This isn't the case. The purpose of separate standards is to reduce the exposure for everyone at the rate that is possible in each area. Permitting exposure of some workers to high concentrations

limit is one that can be observed, monitored, and enforced. This means it must be within the capability of current analytic technology. The hearings were not specifically directed at this, but the consensus seems to be that the NIOSH recommendation is probably a good appraisal of the equipment that is available for routine field use today and that this equipment is capable of one ppm. Therefore, one ppm becomes the lowest reliably detectable and enforceable limit.

The term "no detectable amount" deserves comment. It has substantial appeal, but it is fraught with potential mischief because what is or is not detectable will vary from circumstance to circumstance and from time to time. The mere existence of such a term is a challenge to the analytic chemist to sharpen his tools and push the frontier downward, and the state of the art of organic analysis is such that major advances can be made in a short time. Thus a "no detectable amount" standard becomes infinitely elastic and subject to constant redefinition. The manufacturer who in good faith purchases and installs the best equipment available today may find himself challenged tomorrow by someone with a new technology. Even worse, the present wording is extremely ambiguous. Almost everyone at the hearing interpreted it to mean a standard of 1 ppm, but that is not what the document says. It says "no detectable amount, as determined by a . . . method capable of detecting . . . 1 ppm". Thus, this standard really doesn't specify a vinyl chloride concentration; it specifies the minimum sensitivity of the analytic equipment. This seems to me to be an illogical way to set a standard.

given to the major potential target organs, but it should not be limited to them.

History-complete; including previous illnesses, previous employment, exposures to toxic materials, alcohol intake and dietary habits.

Physical-complete; including skin; limbs; vascular system; lungs; heart; abdominal organs.

Laboratory; chest x-ray; complete blood count including smear for differential and estimation of platelets; urinalysis including microscopic examination; chemical analysis of blood, including SMA-12; liver function and serum enzyme determinations; hepatitis associated (Australian) antigen, and (where available) carcinoembryonic antigen and alpha fetoprotein; pulmonary function tests (FEV₁ and FVC).

The medical examination should be done by a licensed physician, preferably one experienced in industrial hygiene, and the laboratory work by an accredited and licensed laboratory. (Physicians familiar with the toxic potential of vinyl chloride should be available to all of the monomer and polymer manufacturers. They are not as likely to be available to the many processors of the polymer--another reason for trying to contain the monomer within the confines of the major plants.)

Annual examinations should be adequate. Abnormal findings should be checked as quickly as possible and appropriate additional examinations should be done to find the cause of abnormalities.

Records should be maintained at least for the lifetime of the employee, preferably for several years longer; it would be very helpful

skin. Therefore, I do not see any need for impervious suiting under anything except the most extreme conditions (prolonged exposure to many thousands of parts per million of vinyl chloride). The use of ordinary protective clothing to reduce the exposure to polymer and entrapped liquid vinyl chloride would be desirable.

The Record suggests that there is a fortuitous relationship between polymer and air such that a polymer containing, for example, 50 ppm of monomer can produce an air concentration that is also 50 ppm. This relationship should not be allowed to confuse the reader. A careful distinction should be made between gas concentration in air and monomer concentration in polymer. Both may be expressed in the same units, but their importance is entirely different. For example, an upper limit of 1 ppm of gas in air may be a necessary and attainable goal for major segments of the industry, but 1 ppm of monomer in polymer is probably neither necessary nor attainable. Therefore, if a purity standard for polymer is set, it should be different from that set for air. The Record suggests that plants handling polymer with 50-100 ppm of monomer are having little or no difficulty maintaining less than 1 ppm in the working area.

The Record suggests to me that area monitoring is feasible and desirable. It also suggests that personal monitoring should also be done, particularly for those whose jobs cause them to move from one area to another.

I am not competent to choose among the various types of respiratory protection equipment, but to me it seems that a strong case has been made

immediate medical attention. The "within twenty-four hours" requirement is not adequate.

I am sympathetic with those who object to the proposed signs and labels in that they are frightening without telling the individual what it is he should be frightened of, or how to avoid danger. The label should contain the name of the material, recognize that cancer is not the only (or even the most likely) form of health hazard, and give instructions or precautions for avoiding the hazard.

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