

September 5, 1974

Mr. Hiroshi Ochi
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200 Park Avenue
New York, New York 10017

Dear Mr. Ochi:

My people in Union Carbide have asked me if I would comment on certain medical questions raised at a meeting with the Japanese PVC Association. I will comment first on Reference IV on page 43 of the papers distributed at the meeting.

The Temporary Standard for Medical Surveillance I find to be essentially the same as that recommended by NIOSH for medical surveillance of workers in the United States. If in "2 (2) past exposure to hepatotoxic agent" you include drugs as well as industrial chemicals, this part is fairly complete. In our history form we list all drugs which are taken on a continuing basis as a separate item to make sure they are not overlooked.

I agree that there is no need to x-ray the hands more often than every three years, and I predict that if the environment is controlled below 50 ppm there will be no cases of acroosteolysis found.

We plan to do essentially the same history and physical on our people also. However, we will broaden the scope of the surveillance such that every other examination will be a complete physical examination adding to the usual examination SMA-12 chemistries, electrocardiogram, chest x-ray, hearing tests, pulmonary spirometry and a complete history by systems. This we are doing because the work of Maltoni suggests that both lung and kidney may also be involved in the carcinogenesis problem, and it would be tragic to fail to recognize this until it was too late.

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By the Second Medical Screening I assume you mean the additional medical studies undertaken on those who were not normal in the first surveillance. In this case we plan to repeat the liver chemistries and if they are still abnormal, the man will receive a complete medical work-up including BSP, liver scans, additional chemistries like GGTP, total and fractional proteins, fractional alkaline phosphatases and blood studies like platelet counts. If these suggest the presence of a tumor, a biopsy will probably be done with the type determined by the man's personal physician. If the man has a tumor, he will continue under the care of his personal physician. If he is found not to have a tumor, he will be removed from further exposure to hepatotoxins and kept under continuing observation.

In reply to the series of questions asked on page 37 and 38 I will answer each as best as I can.

Question 1

The clinical picture of hemangiosarcoma has varied widely with the state of advancement of the disease when it is found. In its early stages it has no symptoms and even the blood chemistries appear almost normal. The alkaline phosphatase seems to be the chemistry most profoundly altered but only late in the disease. Associated liver fibrosis may bring on first symptoms which are the same as would be seen with cirrhosis. We hope that a complete report on symptoms, findings and pathology will be available sometime in the future.

I believe the appearance of splenomegaly is a warning of severe liver disease in these cases. I think the splenomegaly is secondary to the portal hypertension resulting from fibrosis.

Question 2

I am not at all sure that these diseases are related except for the common etiologic agent, vinyl chloride. If there is a common pattern it is that vinyl chloride or some metabolite of vinyl chloride acts as stimulant to fibrous tissue. This would explain scleroderma and liver fibrosis and some of the splenic changes. It might explain acroosteolysis if we assume that proliferation of fibrous tissue encroaches on the blood vessel spaces and eventually occludes them leading to impaired oxygenation of the

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phalangeal tuft. I do not believe the carcinogenic part of the syndrome is caused by vinyl chloride itself but by some metabolite of vinyl chloride which is normally, quickly detoxified and thus cannot exert a carcinogenic action. When the dose of vinyl chloride is very large the mechanism for detoxifying the metabolite is overwhelmed and the metabolite is now free to exert its carcinogenic action. At this time this is all theory but there is some beginning work on the metabolism of vinyl chloride which suggests it may be correct in some degree.

Question 3

I believe this may be true in part as far as the fibrotic part of the disease is concerned but as noted above I am not sure that vinyl chloride itself is the guilty agent. It may be a metabolite.

Question 4

The epidemiological study of VC workers conducted by Tabershaw-Cooper Associates suggests that there may be some tumors in the lung, brain and lymphomas present in excess amounts but the numbers were not statistically significant.

Question 5

We are much concerned about determining a normal level for liver tests. For example, if the laboratory performing the test says that normal for bilirubin is 0.2 to 1.2 and the test report on a patient is 1.4, is that a cause for concern? We don't have an answer to this now but we suspect answers to be forthcoming in the next few years as we gain experience in the surveillance examinations.

Question 6

I'm not sure I understand what you mean by this question. If possible we have a post mortem examination. This is done by a pathologist and I have nothing to do with it. If you are speaking in reference to epidemiologic studies, we use the death certificate and investigate all cases of liver disease. We have no forms for this.



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Question 7

We don't have our data on computers so I have no opinion.

I hope this information is helpful.

Very truly yours,

Associate Medical Director

C. U. Dernehl, M. D.

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cc: Dr. W. B. Ackart

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