

THE APPEARANCE OF ANGIOSARCOMAS IN RATS FOLLOWING  
ORAL ADMINISTRATION OF VINYL CHLORIDEPreliminary note

In a preceding paper (Maltoni, et al., 1974) we reported in detail the experimental plan and the results up through September 10, 1974 of a research series begun in sequence on the oncogenic action of vinyl chloride (VC) administered in various ways (inhalation, oral, subcutaneous, intraperitoneal), in different dosages and on different animals (rats, mice and hamsters).

In reference to that paper and in reports preceding it, the vinyl chloride administered via inhalation (the first studied) produces a whole series of tumors in which the spectrum varies, within certain limits, according to the type of animal. Of these tumors, the angiosarcomas, often localized in the liver, are among the most frequent, and are encountered in all three species of animals studied.

The experiment studying the effect of the compound under consideration when administered orally was begun on September 10. We have the results only for the first 33 weeks. There are no positive results yet.

In this experiment, the vinyl chloride was administered to Sprague-Dawley rats which were 13 weeks old. It was dissolved in olive oil and administered via gastric tube five times per week. The length of the treatment was programmed for 52 weeks.

The experiment included four groups of 80 animals each treated respectively with a volume of oily vinyl chloride solution at varying concentrations (20 ‰, 6.60 ‰, 1.32 ‰), to be administered in 50 mg, 16.65 mg and 3.33 mg per kilogram of the animals' body weight and with a volume of olive oil alone.

In order to make the quantity of the vinyl chloride increase sufficiently with the weight of the animals, the volume of the

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Cesare Maltoni\*, Adriano Ciliberti\*, Luciano Gianni\* and Pasquale Chieco\*: The appearance of angiosarcomas in rats following oral administration of vinyl chloride\*\* [Insorgenza di angiosarcomi in ratti, in seguito a somministrazione per via orale di cloruro di vinile]  
Ospedali della Vita, 2 (1), 65-66 (1975).

\*Institute of Oncology and Tumor Center - Bologna

\*\*Hospitals of Bologna, Regional Hospital Organization, In the Field of Research

UPL 14657

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Translated from Italian by The Ralph McElroy Co., Custom Division,  
2102 Rio Grande, Austin, Texas 78705 USA

Table I Experiment BT11: Study of the oncogenic action of vinyl chloride administered orally. Results after 50 weeks.

| Groups and treatments | Animals (Sprague-Dawley rats) |                        | Animals with tumors |                    |        |       |
|-----------------------|-------------------------------|------------------------|---------------------|--------------------|--------|-------|
|                       | Total                         | Surviving              | Angiosarcomas       |                    |        |       |
|                       |                               |                        | Liver               | Other localization | Others | Total |
| I<br>CV 50 mg/Kg      | 80<br>(40 ♀ e 40 ♂)           | 67<br>(34 ♀ e 33 ♂)    | —                   | 1 (2)<br>(Timo)    | —      | 1     |
| II<br>CV 16,65 mg/Kg  | 80<br>(40 ♀ e 40 ♂)           | 68<br>(37 ♀ e 31 ♂)    | 1 (1)               | —                  | —      | 1     |
| III<br>CV 3,33 mg/Kg  | 80<br>(40 ♀ e 40 ♂)           | 66<br>(39 ♀ e 27 ♂)    | —                   | —                  | —      | —     |
| Controls              | 80<br>(40 ♀ e 40 ♂)           | 75<br>(39 ♀ e 36 ♂)    | —                   | —                  | —      | —     |
| Total                 | 320                           | 276<br>(149 ♀ e 127 ♂) | 1                   | 1                  | —      | 2     |

(1) In the male. The tumor was encountered 49 weeks from the beginning of treatment. Pulmonary metastasis.

(2) In the female.

UPL 14658

solution administered was increased. The volume varied from 0.42 to 1.12 cc.

The plan of the experiment and the results 50 weeks after it had begun are shown in Table I.

Two angiosarcomas occurred as a result of the experiment in the two groups treated with the maximum dosages.

Though the number of these tumors is limited at the present moment, given the exceptional rarity of this type of tumor and on the basis of the effects of vinyl chloride administered via inhalation, it appears possible to conclude that these first results stand to indicate that vinyl chloride exercises an oncogenic action and in particular provokes hepatic and extrahepatic angiosarcomas when it is administered orally as well.

We report this first fact at this time, due to the fact that periodically we receive requests for information of such a kind from scholars and from health officials from many countries.

#### References

C. Maltoni, G. Lefemine, P. Chieco and D. Carretti: Environmental and occupational carcinogenesis: New views in the light of carcinogenesis caused by vinyl chloride "The Hospitals of Life", 1/5-6, 4-66 (1974).

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