Absence of Carcinogenicity of a Cod Liver Oil Concentrate*

Paul E. Steiner, M.D.

(From the Department of Pathology of the University of Chicago, Chicago, Ill.)

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The possibility that cod liver oil concentrates might have carcinogenic activity and thus endanger their users was given consideration when a nonsaponifiable lipid extract of human liver injected into mice produced sarcomas (14). The preparation of this carcinogenic human liver extract involved saponification followed by extraction with a lipid solvent, a procedure not unlike that used in the preparation of cod liver oil concentrates [U. S. Patent 1,690,091] (9), some yellow bone marrow extracts [U. S. Patent 2,091,730] (8), some ovarian extracts, and some other biologicals used in medication. Since the possibility that the carcinogenic activity of the human liver extracts might be due to a chemical artifact was not at first excluded (although Schabad (12) prepared a human liver extract which had carcinogenic activity by a method which did not utilize saponification) it was not unreasonable to wonder whether similar artifacts might not be formed in the preparation of cod liver oil concentrates.

Accordingly a nonsaponifiable lipid extract was prepared from cod liver oil by procedures identical with those previously used in the preparation of a human liver extract (16). This was then tested for carcinogenic activity. While this test was in progress other reports appeared showing that the nonsaponifiable lipid fraction of human liver was carcinogenic (4, 6, 7, ii, i5). These results were additional justification for the experiments reported here.

It is also important to examine for carcinogenicity certain things present in the environment of Americans and North Europeans, and not present among some other peoples, which might explain differences in the incidence of cancer of various portions of the alimentary tract, particularly the stomach (1, 13). In contrast with the low incidence of such cancers in the Bantu of South Africa (2) is their common occurrence in the Afro-American (5, 10). The explanation might lie in differences in the environment, the genetic constitution presumably not having been totally changed.

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**PROCEDURE**

To 3,100 gm. (3,317 cc.) of a commercial cod liver oil was added 6,200 gm. of 95 per cent ethyl alcohol containing 775 gm. of commercial KOH. This was heated on the steam bath under a reflux condenser for 4 hours, after which it was extracted 3 times with ethylene dichloride. The extract was evaporated to dryness under reduced pressure at 50 °C. The residue was resaponified. The nonsaponifiable lipid fraction recovered after repeated extractions with ethylene dichloride was 9.1 gm.

This extract was tested for carcinogenicity by subcutaneous injection in mice. Each mouse received one injection consisting of approximately 250 mgm. of the extract dissolved in about 0.75 cc. of sesame oil. The mixture was heated to ~60 °C. to aid solution. The mice were 41 to 46 days old at the time of injection. They were of our own strain, previously reported as susceptible to sarcoma induction by crude extracts and hydrocarbons (13, 15). The number of mice of each sex and their survival to several time periods are shown in Table I. The sexes are given separately because their susceptibility to induction of sarcomas has appeared to differ.

**RESULTS**

No sarcomas have appeared at the site of injection although the experiment was begun with 37 mice, 19 of which are living at the end of 18 months, and 12 at 19 months. Tumors have appeared at distant sites in accordance with the approximate incidence for such
tumors in this colony of mice. The extract has been given a fair test for carcinogenicity as indicated by residues of the original extract at autopsy in many of the animals dying after 1 year.

SUMMARY

A cod liver oil concentrate prepared by saponification and extraction with ethylene dichloride has not been carcinogenic when injected into mice.

REFERENCES

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