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## COVER LEGEND

Aflatoxin is a historical landmark in chemical carcinogenesis. It is a potent environmental carcinogen from "natural" sources rather than from industrial contaminants or synthetic chemistry.

In 1961, there occurred two epizootic outbreaks. In England, thousands of turkey poults, ducklings, and chicks died of hepatic necrosis. In the northwestern United States, rainbow trout, the favorite game fish of the region, died with hepatomas. Initially, there was no evident relationship between these outbreaks (*cf. Advan. Cancer Res.*, 8: 191, 1964).

The fowl epidemic of hepatotoxicity was traced quickly to food sources, then to peanut meal, and finally to the contamination of the food by a common fungus, *Aspergillus flavus*. M. C. Lancaster, F. P. Jenkins, and J. McL. Philp, of the Unilever Laboratories in England, fed rats with food containing the toxic material and, in 6 months, 9 of 11 survivors developed hepatomas (*Nature*, 192: 1095, 1961).

Two teams of chemists, one in England (*Nature*, 195: 1062, 1962) and the other in the United States (*J. Am. Chem. Soc.*, 85: 1706, 1963), isolated and identified the active chemicals, the aflatoxins (*A. flavus* toxins). These compounds, on a molecular-weight basis, are among the most active hepatocarcinogens in the rat; they produce sarcomas at the site of s.c. injection and have other carcinogenic effects.

Hepatomas in trout also were rapidly related to food sources. Fractionation of fish diets for the carcinogen was initiated by John E. Halver at the Western Fish Nutrition Laboratory of the United States Department of Interior at Cook, Washington. Isolation of aflatoxin from *A. flavus* contamination of poultry food kept under warm, humid conditions pointed to this possibility of a similar etiology of trout hepatomas.

To test this relationship, concurrent experiments were arranged. Hepatomagenic fish diets were sent to Gerald N. Wogan at the Massachusetts Institute of Technology, Cambridge, Massachusetts, for analysis for aflatoxin, and aflatoxin was likewise sent to Dr. Halver for feeding to trout. Crystalline aflatoxin B<sub>1</sub> prepared by Wogan produced hepatomas in rainbow trout, and there was an almost perfect relationship between the appearance of hepatomas in trout and the aflatoxin content in the food (J. E. Halver and I. A. Mitchell, eds. *In: Trout Hepatoma. Research Conference Paper 70*, United States Department of the Interior, Bureau of Sports, Fisheries and Wildlife, Washington, D. C., 1967). Hepatomas were later produced in the rat and duckling.

Epidemiological investigations in Africa by M. E. Alpert *et al.* (*Cancer*, 28: 253, 1971) and in Thailand by R. C. Shank *et al.* (*Food Cosmet. Toxicol.*, 10: 171, 1972) show correlations between the prevalence of hepatoma in man and the aflatoxin levels in the food. Aflatoxicosis thus appears to be an important environmental carcinogenic hazard in man.

The historical events and developments are presented in *Mycotoxins in Foodstuffs* (MIT Press, Cambridge, Mass., 1964).

Pictured are M. C. Lancaster, b. 1930 (*upper left*), John E. Halver, b. 1922 (*right*), and Gerald N. Wogan, b. 1930 (*lower left*), who are among the many key investigators of aflatoxin, especially its carcinogenic aspects. The structural formula of aflatoxin B<sub>1</sub> and a photomicrograph of a trout hepatoma are also included.