Some 35 years ago, Yoshida of Japan reported the appearance of liver cancers in rats maintained on diets to which "butter yellow" and related azo dyes had been added. The news was popularized by Kinosita, who was on a lecture tour in the United States. Practically all our cancer research laboratories existent at that time began to repeat the work. Liver was, and remains, a popular material for biochemical studies. Livers are easily identified, removed, and used as homogenates, slices or extracts. Normal livers, embryonic livers, livers regenerating after partial hepatectomy and livers obtained after timed exposure to carcinogenic chemicals, provided a rich spectrum of experimental material for identifying biochemical events related to carcinogenesis.

Surprisingly, rats placed on diets to which azo dyes were added refused to develop liver tumors in the United States. Consultations and investigations soon showed that the key discrepancy between Japan and the United States was in the diet to which the azo dyes were added. In Japan, the rats were maintained on a Spartan diet based on polished rice. In the United States, the animals were pampered on carefully balanced diets designed for optimum growth. Further investigations pinpointed riboflavin as the main protector against the carcinogenic effects of azo dyes. Rats on riboflavin-deficient diets to which azo dyes were added promptly developed liver tumors as described by Japanese workers.

These episodes in cancer research occurred during a period of intense interest in the relationship of diet to the initiation and growth of cancer.

The azo dyes and the hepatomas they induce in rats proved instructive to cancer research. The riboflavin protection against azo-dye carcinogenesis, however, appears to be related and limited to the metabolic conversion and detoxification of azo dyes. Riboflavin protection has not been demonstrated in the appearance of "spontaneous" hepatomas in mice, nor in the hepatomas evoked in rats by aflatoxin, a much more potent hepatocarcinogen than the azo dyes.

Richard S. Rivlin (Columbia University College of Physicians and Surgeons, New York, New York), provides a review on riboflavin and cancer in the September issue of Cancer Research. Rivlin points out that several studies indicate that riboflavin deficiency inhibits tumor growth in experimental animals and possibly in man. There are also provocative observations that certain patients with cancer excrete less riboflavin than do normal individuals. Following the methotrexate "model," riboflavin deficiency was demonstrated by Lane in six patients treated with galactoflavin, and in three there was some evidence of decrease in tumor growth rate. The field of vitamin analogues and inhibitors in the treatment of cancer, pioneered by the late Sidney Farber, seems far from exhausted.
At the same time, recent reports by Wynder indicate that riboflavin-deficient mice are more prone to develop skin cancer following application of a carcinogenic hydrocarbon, DMBA, than normal mice or mice on a high intake of riboflavin. Thus, adequate levels of riboflavin yield some protection against carcinogenesis with DMBA as well as the azo dyes. It would be useful indeed to ascertain whether riboflavin and other dietary deficiencies are related to increased risk of cancer among human populations exposed to environmental carcinogens.

Cancer research has moved, properly, into the arena of molecular biology. As examples, mention is made of two intriguing reports from New York in the October issue of Cancer Research. Bertrum Sheid et al. (State University of New York, Downstate Medical Center, Brooklyn, New York) describe that eight human ovarian carcinomas had 2-25 times higher tRNA methylase specific activity and tRNA methylating capacity than normal ovarian tissue. Nicole Suciu-Foca et al. (Columbia University College of Physicians and Surgeons, New York, New York) studied cellular immune responsiveness of lymphocytes, which was significantly lower in 60 patients than in 81 normal controls.

These forward thrusts, full of promise, should not obscure the perennial problems of diet in cancer and of anorexia and cachexia of neoplastic disease (cf. Cancer Research, 30: 2816, 1970). A systematic encouragement, under the expanded National Cancer Act of 1971, is desirable of further research on diet and cancer. Tannenbaum’s work of 20 years ago (cf. Advances in Cancer Research, 1: 451, 1953) would be a good benchmark from which to restart.