14567

Dietary Fat with Reference to the Spontaneous Appearance and Induction of Leukemia in Mice.*

F. Douglas Lawrason and Arthur Kirschbaum.

From the Department of Anatomy, University of Minnesota Medical School, Minneapolis, Minn.

Diets high in fat have been reported to increase the rate of formation of certain types of induced tumors.[1,2,3,4] The total number of induced tumors was also increased when threshold amounts of carcinogen were used.[4,5] The induction of some types of tumors has been found, however, to be unaffected by the amount of fat in the diet.[2,4,6] The external presence of fat at the site of percutaneous application of carcinogen was considered to be at least partially responsible for the accelerating effect in the induction of skin tumors.[3,7,8,9] For spontaneous mammary cancer in virgin Dba mice, the total tumor incidence was greater and the time of appearance earlier if the animals were fed a diet containing 12 rather than 3% fat;[4] food intake of animals in both groups was approximately isocaloric, although the mice were fed *ad libitum*. Lavik and Baumann[9] positively correlated caloric intake with number of induced skin tumors when animals were fed relatively high and low fat diets. The high fat animals consumed 12 to 30% more calories and developed more tumors than mice on the low fat diet. Recently dietary coconut oil has been found to exert an inhibiting effect on the genesis of induced hepatic tumors of rats.[10]

In the present experiments the effects of diets relatively high (32%) and low (3%) in fat were tested on (1) the appearance of spontaneous leukemia in the high leukemia F strain[11] and (2) the carcinogenic induction of leukemia in strain Dba. The diets used were modified from those described by Tannenbaum.[4] Each diet contained 250 parts of Purina fox meal, 100 parts skimmed milk powder, 30 parts brewers' yeast, and 8 parts of cod liver oil. The high fat diet contained in addition 180 parts of hydrogenated cottonseed oil,† and the low fat diet 405 parts, or an equicaloric amount, of cornstarch. Animals were fed *ad libitum*.

Strain F mice were placed on these diets shortly after weaning age. Litter mates were divided so that half were fed each of the diets. Growth rate was more rapid in mice on the high fat diet; progressively their caloric consumption became significantly greater. At one year of age the average weight of the high fat animals was 23 g as compared with an average of 18.4 g in the low fat group. Table I presents data indicating a slightly earlier appearance of leukemia in the high fat group, although the total incidence of leukemia has been approximately the same for both groups.

It is unlikely that the difference in age of onset of spontaneous leukemia in the two groups, if significant, can be attributed to the variable of fat content of the two diets. Dif-

* This investigation was aided by grants from The Jane Coffin Childs Memorial Fund for Medical Research and the Cancer Fund of the Graduate School of the University of Minnesota.

1 Baumann, C. A., and Rusch, H. P., *Am. J. Cancer*, 1939, **35**, 213.

2 Baumann, C. A., Jacobi, H. P., and Rusch, H. P., *Am. J. Hyg.*, 1939, **30**, 1.

3 Jacobi, H. P., and Baumann, C. A., *Am. J. Cancer*, 1940, **39**, 338.

4 Tannenbaum, A., *Cancer Research*, 1942, **2**, 468.

5 Lavik, P. S., and Baumann, C. A., *Cancer Research*, 1941, **1**, 181.

6 Miller, J. A., Miner, D. L., Rusch, H. P., and Baumann, C. A., *Cancer Research*, 1941, **1**, 699.

7 Morton, J., and Mider, G. B., *Pub. Health Rep.*, 1940, **55**, 670.

8 Rusch, H. P., Baumann, C. A., and Kline, B. E., Proc. Soc. Exp. Biol. and Med., 1939, **42**, 508.

9 Lavik, P. S., and Baumann, C. A., *Cancer Research*, 1943, **3**, 749.

10 Miller, J. A., Kline, B. E., Rusch, H. P., and Baumann, C. A., *Cancer Research*, 1944, **4**, 153.

11 Kirschbaum, A., and Strong, L. C., *Am. J. Cancer*, 1939, **37**, 400.

† The hydrogenated cottonseed oil (Kremit) was kindly supplied by the Armour Company.

TABLE I.
Age Incidence of Leukemia in Strain F Mice on High and Low Fat Diets.

	High fat (48 mice)			Low fat (48 mice)		
Age in days.	Leukemic	Non-leukemic	Living	Leukemic	Non-leukemic	Living
0-100						
101-200						
201-300	6			2	1	
301-400	6			6	1	
401-500	9	2	3	9	1	2
501-600	6	3	8	12	1	12
601-700		2	3		1	
Totals	27	7	14	29	5	14

ferences in caloric intake and growth of the two experimental groups could account for the results obtained.

In order to test the effect of dietary fat on the carcinogenic induction of leukemia, methylcholanthrene (0.5% solution in benzene) was applied percutaneously twice weekly to 49 strain Dba mice (subline 12) fed the high fat diet, and to 48 mice of the same strain and subline which were fed the low fat diet Mice of this subline are susceptible to the induction of leukemia with this treatment.[12] Administration of carcinogen was begun when mice were 8 weeks of age and had been fed their respective diets for 4 weeks. Of those mice on the high fat diet, 16 of 22 males and 14 of 27 virgin females developed leukemia after average latent periods of 143 and 135 days respectively. Of those on the low fat diet, 21 of 33 males and 12 of 15 virgin females were leukemic after average induction periods of 116 and 113 days. Food intake was approximately isocaloric and there was no appreciable difference in the weights of the high and low fat animals. Frequency distribution curves plotted from induction periods of individual mice on the two diets indicate that the delay in onset of carcinogen-induced leukemia of mice on the high-fat diet was statistically significant.

It would seem that although the leukemia incidence was the same for both dietary groups, the induction of the disease was significantly delayed when the diet contained a relatively high per cent of fat. The oil on the fur of the high fat animals might have retarded absorption of carcinogen, thus prolonging the induction period.

[12] Kirschbaum, A., Lawrason, F. D., Kaplan, H. S., and Bittner, J. J., PROC. SOC. EXP. BIOL. AND MED., 1944, in press.

14568 P

Prevention of Neuroma Formation by Encasement of the Severed Nerve End in Rigid Tubes.

EDGAR J. POTH AND E. BRAVO-FERNANDEZ. (Introduced by Chauncey D. Leake.)
From the Experimental Surgery Laboratory, Department of Surgery, University of Texas Medical Branch, Galveston, Texas.

Neuromata characteristically form at the proximal end of sectioned peripheral nerves. These tumors are frequently painful and represent a most troublesome problem in the handling of amputation stumps. The methods recommended in the Neurosurgical section of the Military Surgical Manual[1] to prevent such neuroma formation are: (a) the alcohol injection of the stump as suggested by Huber and

[1] National Research Council: Military Surgical Manual, Vol. 6, W. B. Saunders Co., Phila., 1943.