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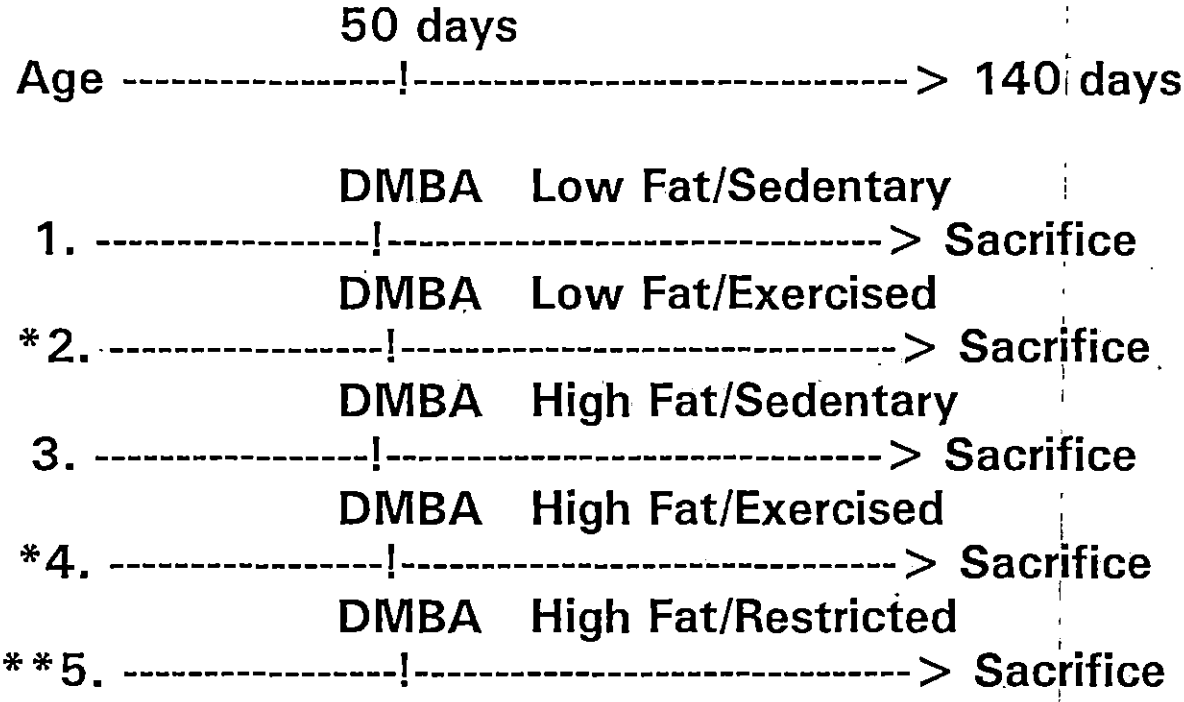
EFFECT OF EXERCISE AND CALORIC RESTRICTION ON DMBA-INDUCED MAMMARY TUMORIGENESIS AND PLASMA LIPIDS IN RATS FED HIGH FAT DIETS.

David Magrane. Morehead State University, Morehead KY 40351

Female Sprage-Dawley rats were given a single 10 mg dose 7,12- dimethylbenz[a]anthracene (DMBA) and grouped as follows: 1) low fat-sedentary (LF/SED), 2) low fat-exercised (LF/EX), 3) high fat-sedentary (HF/SED), 4) high fat-exercised (HF/EX), and 5) high fat-caloric restricted (HF/RES). Diets were isocaloric and contained 3.9% (LF) and 19.4% (HF) of corn oil. Group 5 was fed a 25% caloric restricted, but with a 24.6% fat content to equalize fat intake to group 3 (HF/SED). After 12 weeks of diet or treadmill exercise (15 minutes, 5 days/week, 0.33 m/sec.), tumor data and plasma lipid profiles were determined. Results showed that rats on HF/EX had more total tumors (21), a higher tumor incidence (71%) and a greater number of tumors per tumor bearing rat (2.1) than rats on HF/sed (12, 63%, 1.7). The effect of exercise was also evident in LF/EX rats (12, 63%, 1.7) when compared to LF/SED (6, 42%, 1.2). Average tumor size and volumes were not affected. The HF/RES group showed reduced tumor profiles compared to the HF/SED (6, 42%, 1.2). The mean tumor volumes (1.8 cm^3) were also reduced in the HF/RES as well as the mean tumor burden per tumor bearing rat (2.1 cm^3). HDL, LDL, triglycerides and total cholesterol were unaffected by HF or LF diets or exercise. These data suggest that tumorigenesis is increased by moderate and constant exercise. (Supported by MSU grant 1990)

Sixty female Sprague-Dawley rats received Purina Lab Chow and water ad libitum for two weeks until the age of 50 days when they were switched to semipurified diets. Table 1 shows the composition of the diets. At the age of 50 days, each rat was given a single 10 mg/cc dose of 7,12-dimethylbenz[a]anthracene (DMBA) in a 1 ml corn oil vehicle by gastric intubation. They were placed in one of the following five test groups.



*Groups 2 and 4 were exercised on a treadmill for 15 minutes, 5 days/week at a speed of 20 m/minute and a 1 degree incline.

**Group 5 was given a 25% caloric restricted diet but with an absolute fat intake equal to the calories of group 3. All rats were sacrificed 90 days after DMBA induction and the tumor size. volume and number were measured. Blood was collected at sacrifice and plasma lipid profiles were determined by Sigma kits 352-3 (HDL), 352 (Total Cholesterol) and 339 (Triglycerides).

Table 1. % Composition of Diets by Weight

Component	Low Fat*	High Fat*	Restricted High Fat **
Surcrose	57.0	21.9	21.9
Casein	21.7	21.7	21.7
Corn Oil	3.9	19.4	19.4
DL-Methionine	0.3	0.3	0.3
Cellulose	12.1	31.8	31.8
Mineral Mix	3.8	3.8	3.8
Vitamin Mix	1.0	1.0	1.0
Choline	0.2	0.2	0.2

* Low fat and high fat diets are isocaloric with each having 3.51 Kcal/g.

**Athough given at 75% of the quantity as the normal high fat diet, rats will recieve the same amount of calories from fat on the high fat diet.

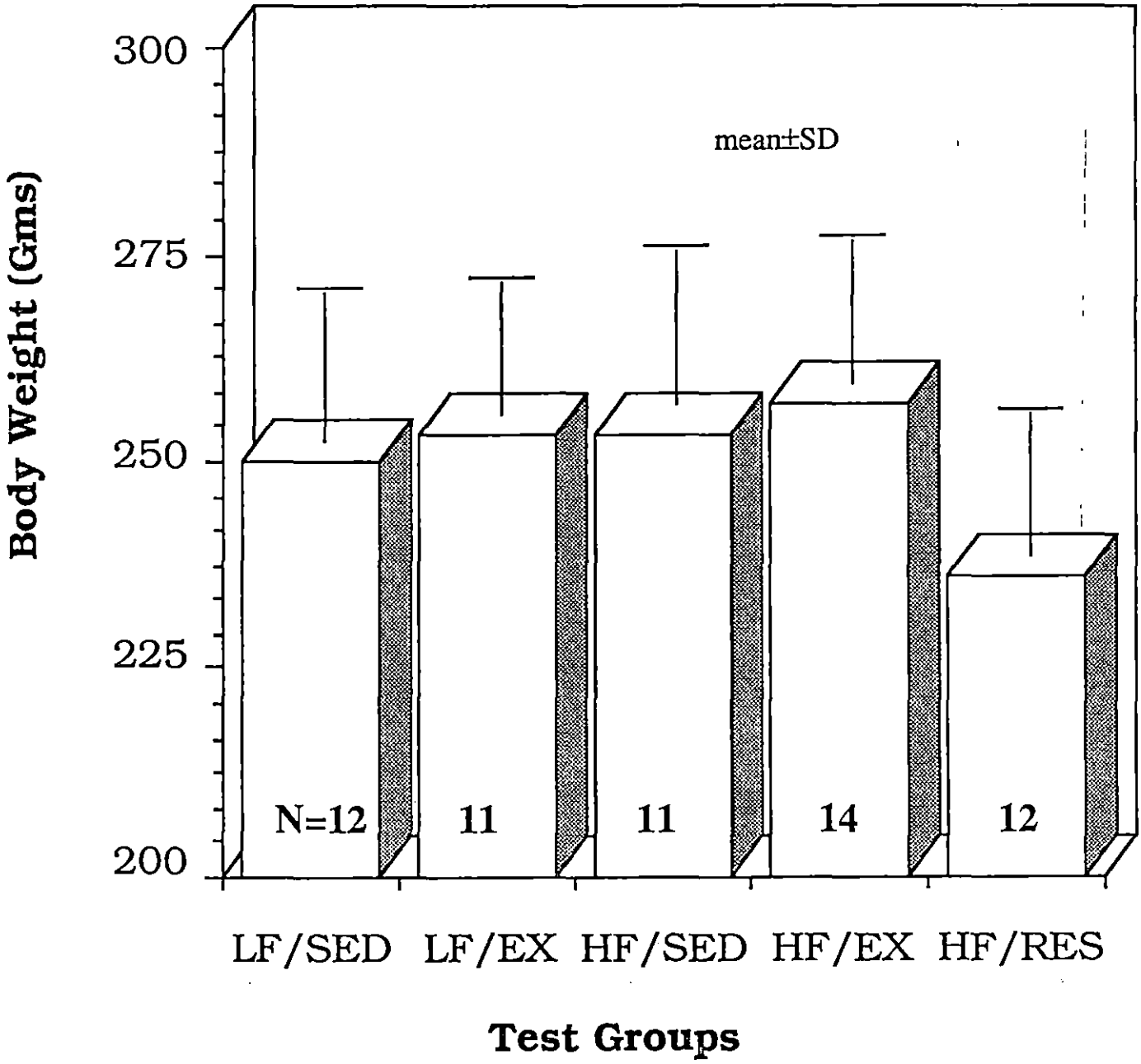


Figure 1. Effects of semipurified diets and exercise on body weights

Table 3. Plasma Lipid Profile (mg % ± SD)

Test Group	Triglycerides	Total Cholesterol	HDL	LDL
LF/SED	47.1 ± 14.2	62.8 ± 16.8	49.0 ± 9.0	4.4 ± 4.1
LF/EX	41.2 ± 11.5	70.6 ± 10.1	58.3 ± 12.6	4.1 ± 3.6
HF/SED	49.0 ± 15.8	75.5 ± 19.3	59.9 ± 11.0	5.8 ± 3.7
HF/EX	53.0 ± 12.8	81.2 ± 11.1	63.1 ± 9.6	7.5 ± 4.4
HF/RES	55.5 ± 8.1	70.2 ± 8.8	50.3 ± 11.5	8.8 ± 5.3

Table 2. Tumor Data

Test Group	N	Total Tumor #	Tumor Incidence = %		TBR*	Mean Tumor Volume (cc)	TVB/TBR**
LF/SED	12	6	5/12=	42	1.2	2.5 ± 1.3	2.9 ± 1.9
LF/EX	11	12	7/11=	63	1.7	2.2 ± 1.1	3.6 ± 1.3
HF/SED	11	12	7/11=	63	1.7	2.7 ± 1.5	4.5 ± 2.1
HF/EX	14	21	10/14=	71	2.1	2.7 ± 1.8	5.7 ± 2.5
HF/RES	12	6	5/12=	42	1.2	1.8 ± 0.8	2.1 ± 1.2

*Tumors per tumor bearing rat

** Mean tumor volume burden per tumor bearing rat

DISCUSSION

Rats fed semipurified diets containing high fat (19.4%) or low fat (3.9%) did not develop any significant differences in body weight after 90 days (Table 1). The effect of exercise was also not seen on body weights. Rats given a restricted diet with a 25% caloric reduction, but with an amount of calories from lipids equal to the intake by the HF groups, showed a non-statistical reduction in body weight. The analysis of tumor data (Table 2) demonstrated that constant and moderate exercise increased tumor incidence in both rats fed LF and HF diets. Tumors per tumor bearing rat and the mean tumor volume burden per tumor bearing rat were elevated somewhat by exercise. Compared to high fat-sedentary rats, rats given a 25% restricted diet showed a reduced tumor incidence, lower number of tumors per tumor bearing rat, reduced mean tumor volume and lower mean tumor burden per tumor bearing rat (Table 2). The plasma lipid profiles indicate that no significant differences were seen by dietary fat or exercise or caloric restriction (Table 3). Collectively, these data indicate that prolonged, moderate and unchanging exercise appears to increase DMBA induced mammary tumorigenesis in rats fed either low or high fat diets. The data corroborate data published by Thompson *et al* (Cancer Research 49: 1904 (1989).

CONCLUSIONS

1) Tumor incidence, tumors per tumor bearing rat, and mean tumor volume per tumor bearing rat were all increased by moderate treadmill exercise in rats fed either LF or HF diets. (Table 2)

2) Plasma lipid levels of triglycerides, total cholesterol, HDL's and LDL's were unaffected by lipid diets or exercise. (Table 3)

3) A 25% caloric restricted diet reduced body weight, tumor incidence, tumors per tumor bearing rat, tumor volume and total tumor burden per tumor bearing rat. (Table 2)

Data presented here supports previously published reports by Thompson *et al* (Can. Res. 49: 1904 (1989) that moderate exercise enhances tumorigenesis in rats whether they were fed low or high fat diets.