Atherosclerosis in the Rat. Effect of X-Ray and a High Fat Diet.* (27865)

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A previous report(1) dealt with the effects of irradiation of the thorax (with X-rays) on development of atherosclerosis in the aorta, pulmonary arteries and coronary arteries of rats fed a high fat diet (35.5% lard) with 2% cholic acid and 2% cholesterol added. In rats killed 8 to 15 weeks after completion of the irradiation, marked atherosclerosis was observed in 26.6% of the coronary arteries and 46.1% of the pulmonary arteries, but no significant atherosclerosis was noted in the arteries of unirradiated rats fed the same diet.

In the present study essentially the same diet was used, but propyl thiouracil was added in an attempt further to elevate the blood cholesterol, and the experimental period was lengthened.

Materials and methods. Forty-five male Wistar rats, average weight 133 g (range 97 to 160 g) were divided into 3 groups. Two groups were given a high fat diet (Table I). One group of 20 rats, on the high fat diet, was irradiated at weekly intervals, so that a total of 2500 r was given to the thorax, as described previously(1). A group of 22 rats fed the same high fat diet was not irradiated. The third group consisted of only 3 rats fed Friskie pellets and not irradiated. The number of rats in the last group was not increased because of known similar findings from previous experiments.

The rats were killed 20 to 28 weeks after completion of the irradiation. Sections were examined as in the previous study(1).

Results. The irradiated group was reduced to 18 rats by the early death of 2 animals. The average gain in weight in the same period, from onset of irradiation to termination of the experiment, was 106 g for irradiated rats, 120 g for those on the high fat diet but not irradiated, and 288 g for those fed Friskie pellets and not irradiated. The average terminal blood cholesterol(2) was 316 mg/100 cc for the irradiated group, 341 mg for the group on the high fat diet alone, and 98 mg for the controls. The corresponding values for uric acid(3) were 2.17 mg/100 cc, 1.84 mg and 1.45 mg.

TABLE I. Composition of High Fat Diet.

Casein	20.0
Alpha soya protein	5.0
Drackett protein	4.5
Lard	35.0
Sucrose	20.0
Celluflour	6.0
*Salt	3.0
†Vitamin	1.0
Alpha tocopherol acetate	.035
Cod liver oil concentrate	.015
Choline chloride	.750
Methionine	.500
Cholesterol	2.0
Cholic acid	2.0
Propyl thiouracil	.2
	100.000

* Salt mixture U.S.P. XIV (Nutritional Biochemicals Corp., Cleveland, Ohio).
† Vitamin diet fortification mixture (Nutritional Biochemicals Corp., Cleveland, Ohio).

Examination of the blood vessels disclosed the same changes observed previously(1). The intima was thickened and characterized by an infiltrate of lipophages as well as an accumulation of mucopolysaccharides. There was a slight deposition of mucopolysaccharides in the inner portion of the media. The lumen of some of the coronary arteries was almost occluded, but no thrombi or myocardial infarcts were noted (Fig. 1 to 4).

Table II gives the incidence of lesions in the arteries. The number of marked lesions was increased in the ascending aorta, thoracic aorta, coronary arteries and pulmonary arteries of the rats in the irradiated group, compared with those on the high fat diet alone. No significant lesions were encountered in rats fed the normal diet.

Discussion. Addition of propyl thiouracil to the diet did not increase blood cholesterol levels above those noted in rats on the same diet in the previous experiment(1). Although cholesterol levels of the 2 groups fed the high fat diet were elevated considerably above nor-

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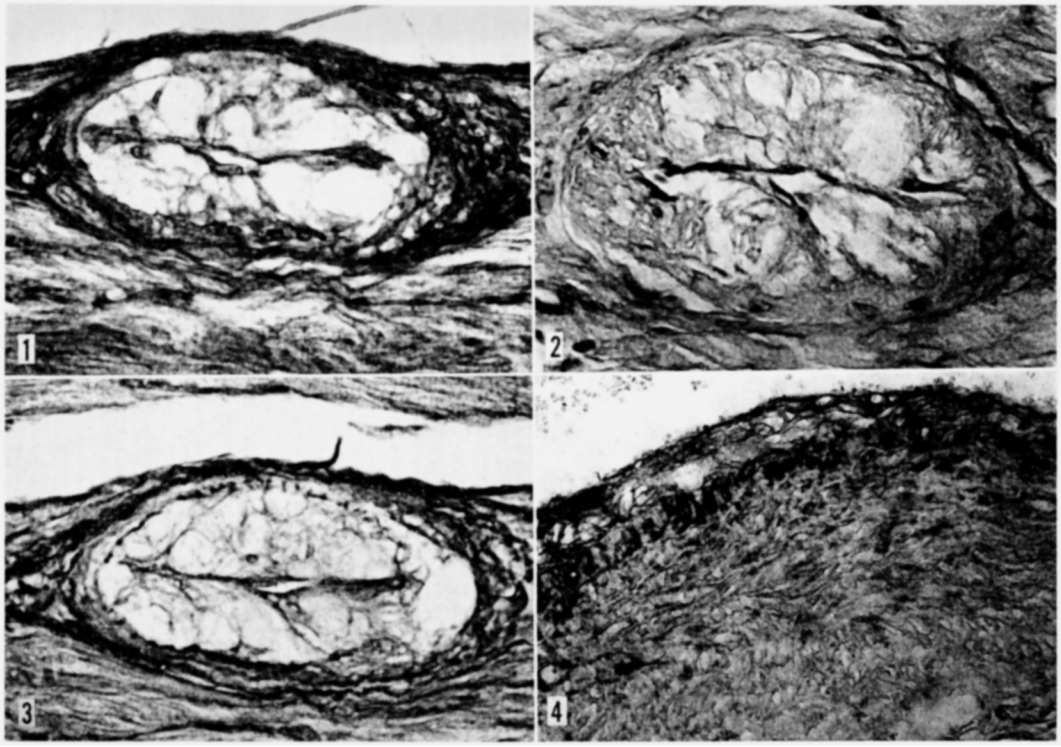

FIG. 1. *Coronary artery*—lumen almost occluded by lipophages and blue staining ground substance. Heidenhain's aniline blue—×185.

FIG. 2. *Coronary artery*—lumen almost obliterated by lipid and mucopolysaccharide accumulation. Alcian blue stain—×185.

FIG. 3. *Coronary artery*—thickened intima with disruption of internal elastica. Weigert's elastic tissue—×185.

FIG. 4. *Pulmonary artery*—intima thickened by mucopolysaccharide and lipophages. Alcian blue—×93.

mal, there appeared to be no evident relationship between degree of atherosclerosis and level of the blood cholesterol in any individual animal. Uric acid levels have been related to the development of coronary sclerosis (4), but there was no obvious relationship between the mean level or the individual level of uric acid and degree of atheroma in the rats.

The general effects of ionizing radiation on the cardiovascular system have been reviewed (1,5). It has been shown that irradiation depolymerizes the large molecular polysacchar-

TABLE II. High Fat Diet and Irradiation.

	No. of Rats	No. with lesions	No. with marked lesions	% with lesions	% with marked lesions
Ascending aorta	18	17	12	94.4	66.6
Thoracic "	18	18	4	100.0	22.2
Abdominal "	18	14	1	72.2	5.5
Coronary arteries	18	8	7	44.4	38.8
Pulmonary "	16	13	4	81.2	25.0
			High fat diet		
Ascending Aorta	22	22	9	100.0	40.9
Thoracic "	21	21	3	100.0	14.3
Abdominal "	19	17	2	89.5	10.5
Coronary arteries	22	6	5	27.2	22.7
Pulmonary "	19	13	0	68.4	0

ides into lower molecular dialyzable compounds, with a decrease in viscosity(6,7). Recently, aortic arteriosclerosis was produced in the dog after localized irradiation with X-rays(5) and by irradiation with electrons(8). It has been proposed that the naturally occurring process and sequences in which aging and possible nutritional factors were etiological had been accentuated and accelerated by irradiation(5). The present study shows that in the period of 20-28 weeks after completion of the irradiation, the rats fed the high fat diet and treated with X-rays showed pronounced coronary atherosclerosis in 38.8%, while those fed only the high fat diet developed atherosclerosis in 22.7%. In the previous study, however, in a period of 8-15 weeks post-irradiation, 26.6% of the irradiated rats had marked coronary atherosclerosis but there was none in the unirradiated group(1). This indicates that time is a necessary factor in the development of marked coronary atherosclerosis as a result of a high fat diet, and that irradiation accelerates the process.

Summary. Forty-two albino Wistar rats, average weight 133 g, fed on a supplemented high fat diet, were divided into 2 groups. One group was treated with 2500 r (X-rays) to the thorax, and the other kept on the high fat diet, but not irradiated. The rats were killed 20 to 28 weeks after completion of irradiation. Marked atherosclerotic lesions were observed in the coronary arteries of 38.8% of the irradiated group and in 22.7% in the group on the high fat diet alone. In the pulmonary arteries similar changes were noted in 25% of the irradiated group and none in the unirradiated group. Previous studies showed that in 8-15 weeks post-irradiation marked coronary lesions were present in 26.6% of the irradiated group and none in the unirradiated. It is suggested that X-irradiation accelerates the process that develops with diet and with time.

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Effect of Steroidal Anti-Progestins on Implantation of Fertilized Eggs of Rats and Mice.* (27866)

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The implantation of fertilized mammalian eggs is one of the most vulnerable steps in the processes of reproduction. An exact, harmless way of preventing implantation of eggs by interfering with the necessary preliminary changes in the uterus is still under investigation in many laboratories. The progestational proliferation or preparation of the endometrium, necessary for implantation of eggs, depends upon a delicate balance between estrogens and progesterone(1). The possibility of preventing implantation by altering estrogen levels or inducing adequate hormonal imbalance has been raised by Hartman(2). Investigations on the mechanism of implantation of fertilized eggs and the hormonal requirements of the process(3,4,5,6,7,8,9) lead to the general conclusion that either anti-estrogens or anti-progestins may effectively inhibit implantation. Estrogen in adequate dose prevents the action of progesterone, and

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