

EFFECT OF AGE, ADMINISTRATION OF ESTRADIOL
DIPROPIONATE, AND OVARIECTOMY ON LIPID
DEPOSITION IN THE AORTIC WALL OF RABBITS

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Experiments on intact rabbits demonstrated the undisputed role of age as a factor in lipid deposition in the aortic wall. Ovariectomy of sexually immature and old rabbits, like injection of estradiol dipropionate into rabbits at the time of reaching sexual maturity and in the reproductive age, promoted lipid deposition in the aortic wall. Lipase was detected in the adventitia of the aorta in rabbits showing the most marked tendency toward deposition of lipids in the aortic wall.

* * *

The object of this investigation was to study deposition of lipids in the aortic wall of rabbits during aging and the role of estrogens in this process [1, 15, 17, 18]. It was also intended to compare lipid deposition with the lipolytic activity of the aortic wall [7, 16, 19].

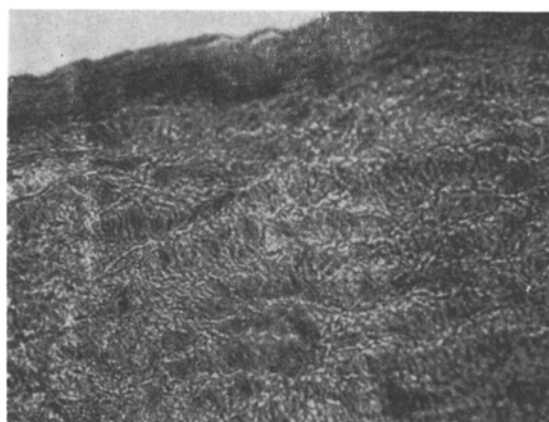


Fig. 1.

Fig. 1. Deposition of lipids in pale violet protein band on surface of intima of aorta in ovariectomized 4-year-old rabbit. Scharlach red, 200 \times .

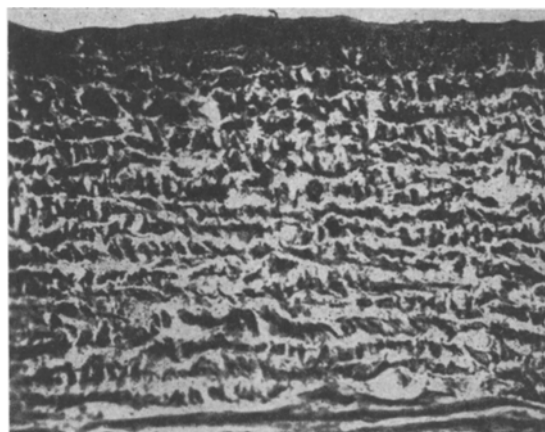


Fig. 2.

Fig. 2. Band of lipids on surface of intima of aorta in ovariectomized 4-year-old rabbit. Sudan black, 200 \times .

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EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on 76 rabbits of various ages (Table 1).

Pieces of the aorta taken from the margin of lipid plaques and from microscopically unchanged areas located proximally to the origin of the carotid artery were investigated. Sections were stained with Scharlach red and Sudan black. Sections from 43 animals (except those sacrificed at the age of 7 months) were investigated histochemically by the methods of Fischler and Baker and for lipase by Gomori's method with Tween-80 [17]. The liver lipase also was investigated.

The experimental results are given in Table 1.

In rabbits of reproductive age, sections stained with Scharlach red and examined under the microscope showed homogeneous palely or more brightly stained masses beneath the endothelium. Often homogeneous or finely dispersed granular lipid masses were deposited along the course of the intima, sometimes at the base of plaques composed of loose tissue, rich in cells of epithelioid type. In ovariectomized rabbits aged 4 years, the deposition of lipid varied in character from palely stained or pink masses located in a thin violet band on the surface of the intima (Fig. 1) to massive and brightly stained deposits throughout its thickness, with penetration of lipids into the subjacent layers of the media. Microscopically visible changes in the aorta were observed only in these rabbits.

In sections stained with Sudan black, lipids were distributed in the cytoplasm of the cells around nuclei stained with carmine. Only a few tiny granules and short bands, along the course of fibers of the vessel wall, were found in the ground substance. The intima was richest in lipids. Lipid masses stained with Sudan black were found as continuous bands of various widths (Fig. 2) on the surface of the intima in every case where deposition of lipids was found on staining with Scharlach red, and also in many cases where no lipids were detected by means of this stain. Baker's and Fischler's reactions were negative in every case, and the reaction for lipase with Tween-80 was negative in most animals. Lipase was found in the adventitia of only two control and one ovariectomized rabbit, aged 4 years, and also in one control and two ovariectomized rabbits sacrificed at the age of 1 year 8 months. In younger rabbits of reproductive age, no lipase was discovered in the adventitia of the aorta, but collections of lipase granules were found on the surface of localized thickenings of the intima in one rabbit receiving estradiol dipropionate and in one rabbit of the control group, receiving injections of peach oil. Numerous lipase granules were found in the liver of all animals. After injection of

TABLE 1. Changes in Lipid Content of Plasma and Microscopic Changes in Aorta of Rabbits of Different Ages

Age of rabbits	Character of experiment	Number of animals	Time of observation (in months)	Dose of estradiol dipropionate (in mg/kg)	Cholesterol (in mg%)		Phospholipids (in mg%)		Cholesterol phospholipids	
					before expt.	at end of expt.	before expt.	at end of expt.	before expt.	at end of expt.
					<i>M ± m</i>					
7 months	Ovariectomy Injection of estradiol dipropionate Control	8	6	—	60±2,3	101±5,5	116±7,4	130±15	0,5±0,03	0,7±0,09
		9	3	0,02	70±5,9	110±7,3	144±10,2	116±2,3	0,5±0,04	1,0±0,06
		5	6	—	59±2,0	95±2,4	115±3,9	124±1,2	0,5±0,06	0,7±0,05
From 10 months to 1 year 2 months	Ovariectomy Injection of estradiol dipropionate Control	8	6	—	56±3	91±5	142±7	134±5	0,4±0,04	0,7±0,06
		7	2	0,2	77±9,3	69±7	137±6,5	121±7	0,6±0,06	0,5±0,01
		5	6	—	62±5	69±13	138±	121±	0,5±	0,6±0,1
1 yr 8 months	Ovariectomy Control	10	6	—	50±3,9	58±4,4	90±6	80±6	0,6±0,05	0,9±0,1
		10	6	—	70±5,7	68±4,4	104±9	80±3,6	0,7±0,07	0,85±0,03
4 yrs	Ovariectomy Control	6	6	—	77±7,0	143±20	93±10	127±10	0,8±0,01	1,2±0,1
		4	6	—	73±13	68±11	109±8,5	128±10	0,6±0,02	0,6±0,1

estradiol dipropionate and ovariectomy and also in all ten 4-year-old rabbits investigated, there was a definite tendency toward accumulation of lipase around the central veins. This was not combined with deposition of lipids in these areas of the hepatic lobules and was observed when the serum cholesterol level was normal.

Changes corresponding to the "spontaneous disease of the aorta" described by Volkova [2] were found in the aortic wall of some rabbits of all ages. However, in the present experiments these changes were accompanied by deposition of lipids only if some other factor was present, facilitating their deposition in the vessel wall, such as: the age factor, administration of estradiol dipropionate, or ovariectomy, i.e., in cases when lipids could also be detected in the unchanged aortic wall. These observations are in agreement with data in the literature [15].

Deposition of lipids in the aortic wall is thus a regular feature of female rabbits over 1.5 years old. Ovariectomy and administration of estrogens promotes deposition of lipids in younger rabbits. Ovariectomy leads to massive deposition of lipids in old animals.

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