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Ovarian Cholesterol Levels During the Reproductive Cycle of the Rat.*

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Evidence that ovarian cholesterol may be a precursor of the ovarian hormones, particularly progesterone, has been by inference, both positive and negative. Comparison of results from previous studies on cholesterol variations during the ovarian cycle is difficult because of the lack of uniformity in presenting data, *i.e.*, some report the free cholesterol and others only the cholesterol esters. By histochemical methods, no changes were observed in ovarian cholesterol during the reproductive cycle in humans[1] although chemical analysis of human corpora lutea indicated a significant decrease in cholesterol esters only in the actively functioning corpus luteum of pregnancy.[2] In the pig, the cholesterol ester content of the corpora lutea was found to vary inversely with the activity of the gland.[3] Boyd[4] found that in the whole ovary of the rabbit, there was an increase in the free cholesterol during the first half of pregnancy followed by a decline while the cholesterol esters increased only during the last half of pregnancy. These results were interpreted as indicating that the rabbit corpora lutea reach a peak of activity about the middle of gestation. No change in free cholesterol was observed in the ovaries of guinea pigs during the course of gestation.[5] Based on histochemical studies of the corpora lutea of diestrum in the rat, Everett[6] strongly suggested that cholesterol serves as a precursor of progesterone.

A systematic examination of cholesterol in the ovary of the rat has been undertaken in this laboratory, and this report will show the changes in cholesterol level of the ovary in diestrum, pseudopregnancy, and at several intervals during pregnancy and lactation.

Methods. Total cholesterol was determined by the method of Chamberlain[7] which consists essentially in saponification of the lipids in alkaline alcohol, extraction of the lipids with ether, and determination of the cholesterol directly on the washed ether-extract residue by the Liebermann-Burchard reaction. A Bausch and Lomb colorimeter was used for color comparison. This procedure gave results which were comparable with those obtained by the digitonin precipitation method[8] both in recoveries of pure cholesterol from solution as well as from pooled ovarian tissue. For example, the average value of 3 determinations on an ovarian tissue sample yielded 0.39 mg by the digitonin method as compared to 0.37 mg for aliquot samples using the Chamberlain method.

The stages of the reproductive cycle at which the ovaries were analyzed are given in the table. Pseudopregnancy was induced by electrical stimulation of the cervix. The ovaries were trimmed of extraneous tissue under the binocular dissecting microscope and weighed to the nearest 0.1 mg.

Results. The cholesterol values are best compared on the basis of parts per thousand. It is noted in Table I that the highest levels were found on the 8th day of pseudopregnancy, 10th day of pregnancy and the 10th day of lactation. The cholesterol in the ovaries on the 15th day of lactation, while not as high as obtained above, nevertheless was significantly higher than that found at diestrum (P value between .05 - .02). The highest levels of cholesterol were found only at a time when it

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3 Bloor, W. R., Okey, R., and Corner, G. W., *J. Biol. Chem.*, 1930, **86**, 291.

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6 Everett, J. W., *Am. J. Anat.*, 1945, **77**, 293.

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TABLE I.
Cholesterol in Rat Ovaries During the Reproductive Cycle.*

	Period (days)	No. of rats	Body wt g	Ovarian wt mg	Total cholesterol mg	Cholesterol parts/1000	No. of fetuses or suckling young
Control	diestr.	10	223	62.5 (36.3- 94.8)	.45 (.30-.65)	7.3 (5.0- 9.0)	—
Pregnancy	10	7	223	60.9 (40.5- 66.9)	.64 (.53-.74)	10.6 (8.6-13.1)	7
	14	9	259	83.5 (73.5- 99.8)	.63 (.44-.79)	7.6 (4.8- 9.8)	9
	18	5	331	104.8 (100.0-105.2)	.80 (.72-.93)	7.7 (7.0- 9.3)	12
Pseudopreg.	8	6	218	43.5 (35.8- 53.8)	.47 (.36-.58)	11.0 (7.7-13.7)	—
Lactation	1	5	224	67.1 (60.0- 77.2)	.49 (.46-.51)	7.3 (6.4- 8.5)	9
	5	6	223	58.4 (41.4- 78.7)	.41 (.30-.51)	7.2 (5.1- 9.7)	8
	10	7	220	49.9 (42.3- 58.2)	.54 (.36-.68)	11.4 (6.2-14.3)	8
	15	7	245	52.0 (34.6- 71.3)	.44 (.30-.52)	8.6 (7.7- 9.7)	8

* All values are average, the range indicated by ( ).

is possible to demonstrate placentomata in the uterus and thus when there must be large amounts of circulating progesterone.[9] It is possible to demonstrate placentomata in the uterus on the 15th day of lactation provided an adequate number of young are suckling (8 or more).

The total ovarian cholesterol was found to be highest on the 18th day of pregnancy yet it is impossible to secure placentomata in the non-pregnant horn of a unilateral pregnant rat at this time.[9] Since functional corpora lutea or progesterone in the rat are necessary for the maintenance of pregnancy, it seemed odd that the cholesterol content of the ovaries in parts per thousand did not remain high throughout pregnancy. This suggests further studies on the ovaries of pregnant rats. It cannot be stated conclusively from these results that cholesterol acts a precursor of progesterone but in certain instances it appears that high ovarian cholesterol is associated with high levels of progesterone secretion.

[9] Burrows, H., *Biological Actions of Sex Hormones*, Cambridge Univ. Press, 1945, 419.

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Turnover of Serum Protein in Adrenalectomized Rats.*

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In previous experiments adrenal cortical activity was found to have no effect on the concentration of serum antibodies or on any other fraction of the serum proteins.[1] This finding, however, did not preclude the pos-

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