VASCULAR AND TISSUE CHANGES IN THE OVARY IN RABBITS AFTER UNILATERAL OVARIECTOMY

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Many descriptions have been given of the compensatory hypertrophy of the ovary arising after removal of its fellow organ [2,5,8]. Controversy exists, however, regarding the subsequent fate of the residual organ [1,3,4,6,7]. The object of the present investigation was to determine the changes taking place in the residual organ and in its vascular system. Ovaries from the same animals were compared.

EXPERIMENTAL METHOD

The investigations were carried out on sexually mature rabbits of roughly the same weight. The animals were segregated from males for a preliminary period of 3 weeks to 1 month, to prevent the possibility of ovulation and pregnancy. During operation on the rabbits under ether anesthesia one ovary was removed and its neurovascular bundle ligated. The residual and excised ovaries were measured with a sterile slide caliper. The animals were sacrificed at various intervals after operation and the ovary measured. The blood vessels and lymphatics were injected. Thick, cleared (100-150 μ) and thin (10-20 μ) sections were cut and the latter were stained by Van Gieson's method.

EXPERIMENTAL RESULTS

The results of the measurements are given in Table 1. By approximately the 35th-40th day the residual ovary had grown in size by 0.11-0.28 mm, and on the 52nd day by 0.6-0.72 mm. By the 90th-175th day the organ had diminished in size by 0.06-0.75 mm. No similar changes were observed in the ovaries of 10 control rabbits.

TABLE 1. Changes in Size of Ovary (in mm) after Unilateral Ovariectomy

Time after operation (in days)	Size of ovary at operation						Size of residual organ					
	right			left			right			left		
	length	height	width	length	height	width	length	height	width	length	height	width
27	2,02	0,45	0,34	2 22	0,35	0,35		—		1,98	0,44	0,34
35	1,04	0,46	0,17	1,10	0,44	0,17	1,15	0,44	0 32		—	
36	1,00	0,27	0,2	0,95	0 29	0,30	1,50	0,67	0,47			
36	1,88	0,54	0,3	1,72	0 65	0,34	1,84	0,56	0 39		—	
38	1,17	0,42	0,25	1,12	0,36	0,19	1,24	0,37	0 24		—	
40	1,38	0 30	0 17	1,41	0,32	0 21	1,66	0,76	0,55		—	
44	1,30	0,58	0,29	1,28	0 47	0 37		—		1,55	0,64	0,70
52	1,22	0,34	0,29	0,97	0 29	0,30		—		1,82	0,54	0,36
52	1,55	0,52	0 43	1,24	0,46	0,47		—		1,03	0,41	0 31
52	1,25	0,22	0,20	1,56	0,41	0 24		—		1 97	0,63	0,44
55	1,21	0,25	0 24	1,39	0 28	0,22		—		1,20	0,39	0,32
60	1,23	0,42	0 37	1,24	0,35	0,40	1,43	0,72	0,66		—	
75	1,91	0,35	0,26	1,97	0 33	0 29	1,14	0,35	0,21		—	
75	1,51	0,31	0 24	1,42	0,38	0 29		—		1,00	0,24	0,20
90	1,35	0,29	0,16	1,29	0,22	0 18	1,00	0,41	0,29			
175	1,96	0 48	0,34	2,00	0,47	0,36		—		1,04	0,31	0,18
175	1,71	0,38	0,29	1,75	0,34	0,34	0,96	0,36	0,19		—	

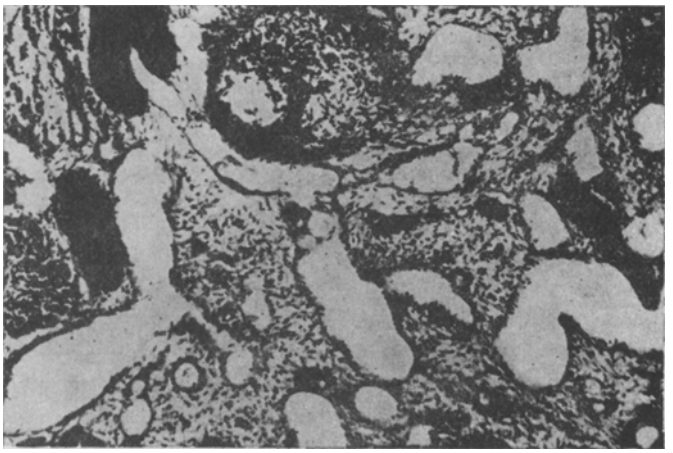

Fig. 1.

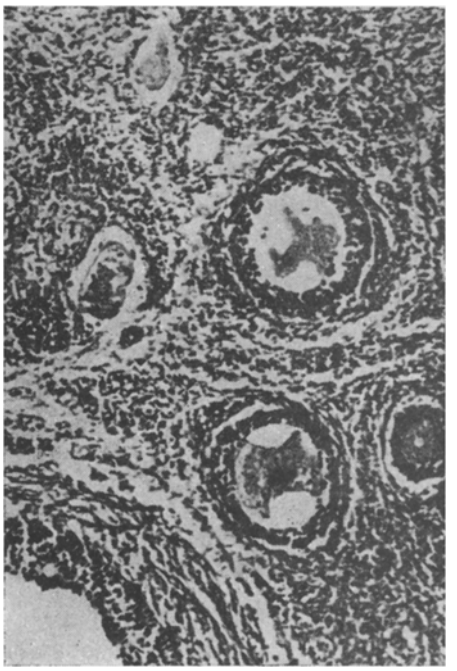

Fig. 2.

Fig. 1. Sharply dilated blood and lymphatic capillaries and vessels of the medullary layer of the rabbit's ovary. Lymphatic system injected. Van Gieson. × 48.

Fig. 2. Massive degeneration of oocytes of the cortical layer of the ovary during atrophy of the organ. Van Gieson. × 60.

Hence, the processes of compensatory hypertrophy in the residual ovary were clearly apparent for a period of 2.0-2.5 months. After the 3rd month there were signs of atrophy. It should be noted, however, that the reaction of the rabbits to the operations were individual in character, as reflected by the variations in the measurements of the residual organ.

The changes in the size of the organ were the result of morphological and functional adaptation. During the development of hypertrophy, proliferation was particularly intensive among the interstitial cells, surrounded by dense plexuses of blood and lymphatic capillaries. The vesicular ovarian follicles present at the time of the operation grew in size and reached the stage of the Graafian follicle. The enlarged ovaries were characterized by marked dilation of the blood vessels and lymphatics of the medullary layer (Fig. 1).

A more variegated morphological picture was observed when compensatory hypertrophy gave way to signs of atrophy. Some areas of fibrosis were seen in the stroma, at first localized in character and situated at the site of actively functioning generative elements. Atresia of the follicles into cysts or by obliteration essentially altered the structure of the organ. The foci of fibrosis merged with one another, replacing the interstitial cells and compressing the remaining generative elements. Corresponding reorganization took place in the blood and lymphatic system of the ovary. Individual capillaries became deformed and empty. Many corpora fibrosa were devoid of capillaries and had only large blood vessels at their periphery.

Particularly marked changes took place in the follicular apparatus of the ovary. Massive degeneration of oocytes and primordial follicles was observed 2.5-3 months after operation in the residual organ, and instead of round, they were now irregular and polygonal in shape. The oocytes were wrinkled and appeared to undergo gradual liquefaction (Fig. 2).

Stresia of the follicles of middle and large size developed initially against the background of a normal structure of the s "oma of the organ, while the system of blood and lymphatic capillaries and vessels was still relatively well developed. The fibrosis subsequently developing in the stroma, however, acclerated atresia of the follicles, and the well developed vascular system atrophied.

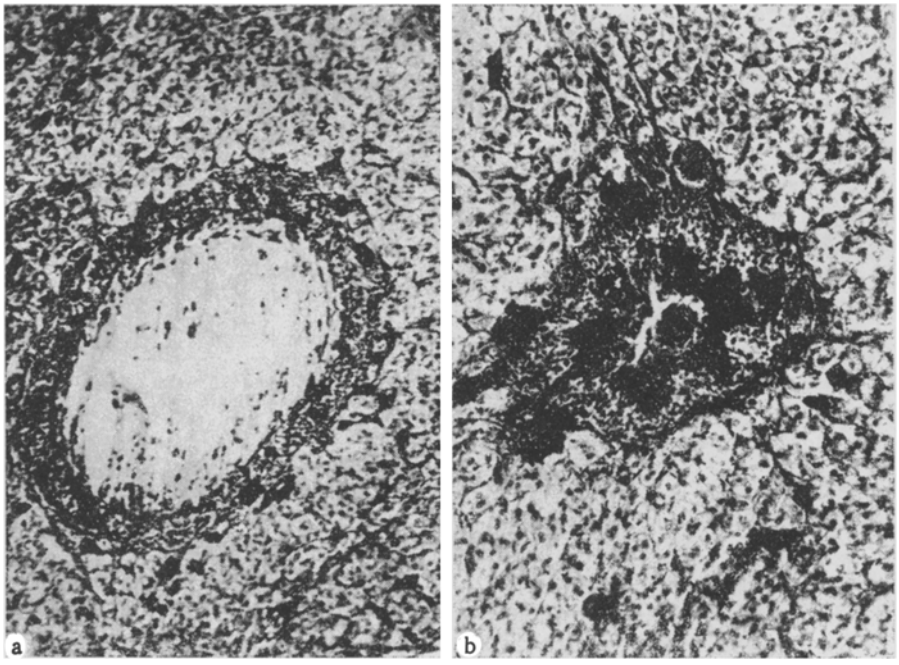

Fig. 3. Hypertrophy of the thecal membrane of the ovary. a) in the cystic form of atresia; b) in the obliterative form of atresia. Blood vessels injected. Van Gieson. × 48.

In some cases the blood and lymphatic capillaries (sometimes deformed) remained in the strongly hypertrophied specific membrane of the atretic follicles—the so-called "thecosis" of the ovaries (Fig. 3). From time to time hemorrhagic follicles and other signs of weakness of the capillaries in the wall of the atretic follicles appeared in the ovaries, leading to rupture during injection under minimal pressure and to escape of dye into the tissue.

Remarkable changes took place in the granular epithelium of the atretic follicles. In the early stages of atresia individual granulosa cells were arranged as rosettes at the periphery of the tiny cavities. The latter increased in size and joined together. In the larger follicles, undergoing atresia with cyst formation, these oval cavities gradually and completely replaced the whole of the granular epithelium.

The corpora lutea underwent much the same process. At the site of the ordinary lutein cells appeared small, round cavities, from 1.5 to 2.0 times larger than the corpus luteum cells. The apparent "liquefaction" of the cells was observed everywhere in the corpora lutea of the ovary, and led in turn to atrophy of its lymphatic and, more especially, its blood capillaries surrounding each lutein cell.

Anatomical changes in the capillaries also appeared in the form of a proneness to tear during injection, even at low pressure, and of permeation of groups of cells with blood.

These results show that hypertrophy (and, in particular, hyperfunction) of the ovary was superseded by atrophy, possible resulting from functional exhaustion.

Some authorities consider that the removal of one ovary leads to "overloading" of the residual organ and to a deficiency of ovarian hormone [1,4,7,10]. Disturbances of menstrual function, the premature appearance of a climacteric symptom-complex, and a marked lowering of fertility have been observed as a result of functional ovarian insufficiency.

Our experimental observations, made at a relatively late period (over 3 months) after operation, confirmed the clinical findings. The processes actually observed in the ovaries included fibrous degeneration of the stroma, death of the interstitial elements, cystic degeneration of the follicles and corpora lutea and hemorrhages into these structures, and regression of the corpora lutea. In association with this background of obvious hormonal deficiency and complex morphological reorganization (with compression), not only the growing generative elements (the vesicular follicles) but also the oocytes and the intact primordial follicles died. Acceleration of all these processes was brought about

TABLE 2. Successive Stages of Transformation of Residual Ovary after Unilateral Ovariectomy

Structural elements of ovary	Stages of transformation		
	I	II	III
Primordial follicles	Intact	Degeneration, atrophy	Almost indeterminable
Vesicular follicles	Intensified growth	Absence of growth	Atresia
Graafian follicles	Intensified growth	Atresia, persistence	Atresia, cystic changes, hemorrhages into cavity
Atretic follicles	No special change	Intensified growth and persistence	Fibro-cystic changes, hemorrhages into cavity
Corpora fibrosa	Usual growth	Intensified growth	Intensified growth, hemorrhages into corpora
Interstitial cells	No special change	Gradual replacement by fibrous connective tissue	Absent
Fibrous tissue	Weakly represented	Intensified growth	Hyalinosis
Vascular system	Intensified development	Atrophy of capillaries in cortical layer, hemorrhages, disturbances of permeability	Universal atrophy of blood and lymphatic capillaries and vessels
General results	Hypertrophy	Atrophy	Sclerosis and cystic changes

by the loss of individual segments of the vascular system described above, especially in the cortical layer of the organ. Frequently the primordial follicles were trapped between the stroma, undergoing fibrosis, and the thickened tunica albuginea. Interference with metabolism led to growth of connective tissue, and to fibrosis and sclerosis of the organ.

Death of a large number of the hormone-producing generative elements may explain the hypertrophy of the thecal membrane of the atretic follicles (see Fig. 3). The latter are known to be capable of producing sex hormones; the connective-tissue membrane of the follicles is a specific "thecal gland" [9]. All these considerations suggest that at a certain period, against the background of general atrophy of all the structures in the ovary, a temporary compensatory hypertrophy affects the hormone-producing formations, still to some extent preserved. Hence the abundance of blood and lymphatic capillaries which we observed in the hypertrophied theca, both ot the atretic follicles and of the frequent follicular cysts, may be regarded as functionally justified.

In experiments to reproduce an increase in the pressure inside the blood vessels of the ovaries, rupture of the capillaries was observed mainly in the growing follicles and less often in the corpus luteum, while no ruptured capillaries could be seen in the corpora fibrosa. This may presumably be explained by the fact that in ordinary conditions the process of formation of corpora fibrosa takes place relatively slowly, stretching over several months, and reduction of the vascular system likewise takes place slowly. On the other hand, in the ovaries of the unilaterally ovariectomized rabbits ruptured capillaries were also observed in the more rapidly formed corpora fibrosa.

The appearance of the cavities described above at the site of the lutein cells of the corpora lutea may be attributed to general atrophy of all the generative structures and to atrophy of the blood and lymphatic capillaries.

Following the operation a series of changes took place in the residual ovary of the rabbit, provisionally subdivided into three successive stages: stage 1–hypertrophy, stage 2–atrophy, and stage 3–sclerosis and cystic degeneration (Table 2).

SUMMARY

Unilateral ovariectomy was performed in 17 rabbits; the size of the remaining ovary was measured at the same time. The animals were killed 35 to 175 days later and the ovary was then measured again. Then the ovarian blood and lymphatic capillaries were injected and the section stained after Van-Gieson.

Compensatory hypertrophy processes were distinctly manifested in the remaining ovary for 2-2.5 months, being replaced about 3 months later by atrophic phenomena, 4-5 months later—by sclerotic-cystic degeneration of the organ. Development of a network of blood and lymphatic capillaries along the periphery of Graafian follicles testified an intensified hormonal activity of the organ. On the contrary, atrophy of capillaries and blood vessels pointed to the functional ovarian insufficiency. In the end unilateral castration in rabbits caused morphological (and evidently functional too) changes in the remaining ovary.

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