REGENERATIVE CAPACITY OF RAT OVARY AFTER COMPENSATORY HYPERTROPHY

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Regeneration of the ovary after resection has usually been brought about when the opposite organ is extirpated at the time of resection [1-8]. This gives rise to the question of whether the reaction of the ovary to injury in these conditions should not be regarded as compensatory hypertrophy rather than regeneration, and what precisely is the response to extirpation of the opposite organ.

In order to discover if the ovary is capable of regeneration, i.e., of restoration after part of it is removed, we carried out experiments in which the compensatory reaction was ruled out beforehand. We studied the response to injury in an ovary which had already undergone compensatory hypertrophy. Moreover, we wanted to find out if the capacity of ovarian cells for proliferative activity was exhausted after the intensive restorative processes constituting the response to extirpation of the opposite organ.

Experimental Method and Results

The objects of study were white rats weighing 100-120 g each. Altogether, we carried out five series of experiments with 10-14 animals in each series.

The nature of the experiments and the results of weighing the ovaries are shown in Table 1.

From the animals in the first, second, and third series of experiments we extirpated the right ovary (unilateral castration) in order to induce compensatory hypertrophy of the remaining ovary. Six weeks after the operation, the animals of the second series were sacrificed. As was to be expected, the remaining ovary underwent compensatory hypertrophy. Its weight (absolute 57.4 mg and relative 0.33‰) was more than 1½ times the weight of the ovary (absolute 37 mg and relative 0.2‰) in the control animals (fifth series). To demonstrate the regenerative capacity of an ovary which had undergone compensatory hypertrophy, we extirpated half of the hypertrophied ovary in the animals of the first series six weeks after the first operation. The weight of half the hypertrophied ovary (absolute 24.8 mg and relative 0.13‰) was a little less than the weight of the whole ovary in the control animals.

For a comparison of the course of the regenerative processes after resection of an ovary subject to hypertrophy, and an intact ovary, we completely extirpated the right ovary and half of the left from the animals of the fourth series. With this type of operation we had previously observed regeneration of the ovary in mice, rats, and monkeys [1,2,3].

Six weeks after the second operation (resection of hypertrophied ovary), and three months from the start of the experiment, all the experimental animals (second, third, and fourth series), and the controls (fifth series), were sacrificed. Regeneration was discovered both in animals of the fourth series and in animals of the first series of experiments. The rate of the regeneration process was found to be roughly the same. The weight of the

TABLE 1

Regeneration of Hypertrophied Ovary in Rats

Series	At start of expt.			Six weeks after start of expt.					Three months after start of expt.				
	no. of animals	weight of right ovary (mg)	ovary-to-body weight ratio (%)	further interference	weight of ovary		ovary/ bodyweight ratio (in %)		end of expt.	weight of ovary		ovary/ body weight ratio (in %)	
					right	left	right	left		right	left	right	left
First – right ovary extirpated	14	8,7	0,08	Half of left hypertrophied ovary removed	—	24,8	—	0,13	Sacrifice	—	58,2	—	0,25
Second – right ovary extirpated	10	8,8	0,08	Sacrifice	—	57,4	—	0,33	—	—	—	—	—
Third – right ovary extirpated	12	9,6	0,08	—	—	—	—	—	Sacrifice	—	63,0	—	0,27
Fourth – no operation carried out	14	—	—	Right ovary and half of left removed	31,4	16,3	0,18	0,09	Sacrifice	—	51,2	—	0,23
Fifth-control	20	—	—	Sacrifice	35,5	37,0	0,18	0,20	Sacrifice	34,0	31,1	0,14	0,13

TABLE 2

Number of Generative Elements in Ovaries of Rats in Each Series

Series	Number per section				Total number	
	Corpora lutea	follicles			primordial follicles in whole ovary	generative elements per section
		primordial	ripening	atresic		
First – regeneration of hypertrophied ovary	12.3	1.4	4.2	4.0	67	21.7
Second – hypertrophy of ovary (6 weeks after unilateral castration)	14.0	1.7	8.3	4.0	80	28.0
Third – hypertrophy of ovary (3 months after unilateral castration)	13.6	1.8	6.5	5.1	81	27.0
Fourth – regeneration of ovary (right ovary and half of left removed)	10.2	1.5	5.6	3.7	77	21.3
Fifth – control (mean from two ovaries)	6.4	1.8	3.6	7.9	66	20.0

regeneration process was found to be roughly the same. The weight of the regenerated ovary in animals of the fourth series (absolute 51.2 mg, relative 0.23‰), and first series (absolute 58.2 mg, relative 0.25‰), was considerably increased, being approximately twice the weight of the whole ovary in the control animals (fifth series: absolute weight 31.1 mg, relative 0.13‰) sacrificed at the same time.

Thus, going by the weight data and the restoration of the normal form of the organ, we can speak of the ability of the ovary to undergo regeneration after compensatory hypertrophy.

In animals of the third series (with unilateral castration) compensatory hypertrophy effects were observed three months after the operation. The weight of the remaining hypertrophied ovary (absolute 63 mg, relative 0.27‰) was twice that of the whole ovary in the control animals (absolute 31.1 mg, relative 0.13‰).

If the weight of the ovary in animals of the third and second series is compared, it can be noted that, during the subsequent six weeks, the weight of the ovary in rats of the third series hardly changed at all (slight increase in absolute weight – 63 mg against 57.4 mg, but the relative weight was reduced – 0.27‰ against 0.33‰). Hence, the compensatory hypertrophy took place mainly during the six weeks after operation, and the later hypertrophy was slight.

We made a histological study of the ovaries of the experimental and control animals, and also counted the number of generative elements. The count was made in every fifth section of ovaries serially cut at 8μ. We determined the number of primordial follicles at different stages of development, and the number of atresic follicles and corpora lutea. We determined the mean number of these elements in a section. We noticed that each primordial follicle appeared on not more than three to four sections through the ovary and, hence, the total number of primordial follicles which we counted corresponded roughly to the total number of primordial follicles present in the whole ovary. The results of the count are given in Table 2. We subjected these figures to statistical treatment; below we analyze only those differences which were statistically significant.

As the data of Table 2 reveal, in the case of regeneration of half the resected ovary, in animals of the first and fourth series of experiments it was the specific structural components of the ovary which were regenerated. For instance, the total number of generative elements per section increased to 21.7 in the regeneration of the ovary of animals of the first series. This indicates the formation of structural ovarian elements during regeneration, since the half of the hypertrophied ovary ought to have contained approximately 14 (half of 28; see second series). The number of primordial follicles increased from 40 to 67, i.e., reached the number of primordial follicles in the control, nontraumatized ovaries (66). In the ovary of animals of the fourth series, there was approximately the same number of primordial follicles as in the ovary of the control animals, thus indicating that their number was restored. Judging from the number of ripening and atresic follicles per section, the maturation of

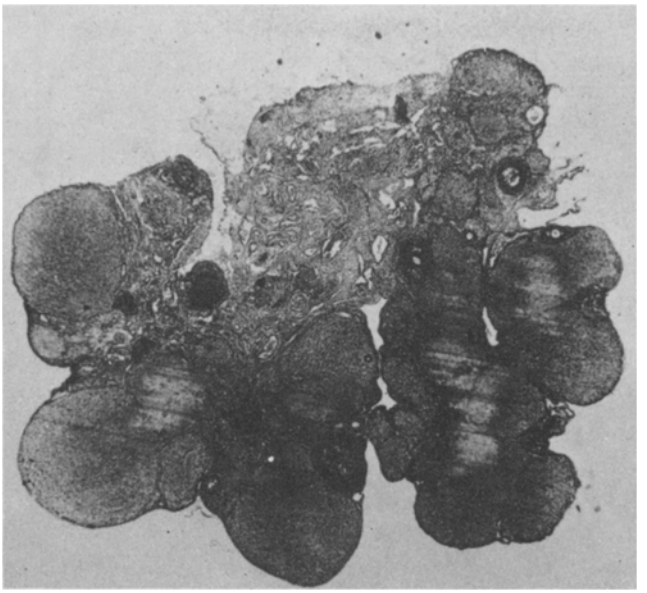

Fig. 1. Section through regenerated ovary which had previously undergone compensatory hypertrophy (first series of experiments). Recovery of normal shape of organ. Photomicrograph. Magnification 23 ×.

the follicles in the regenerating ovaries of rats of the fourth group (5.6) and first series (4.2) was a little more rapid than in the ovaries of the control animals (3.6), and the atresic of the follicles was almost twice as pronounced in ovaries of the control animals (7.9) as in the regenerating ovaries of animals of the fourth (3.7) and first (4.0) series.

We should also note that during regeneration of the ovary – both the uninjured ovary and the ovary which had undergone hypertrophy – the number of corpora lutea increased considerably; there were almost twice as many as in the controls. Similar changes were also noted in hypertrophy of the ovary after unilateral castration. The number of corpora lutea was greatly increased. Six weeks after operation there were 13.6, i.e., more than twice as many as in the ovary of control animals (6.4). In the case of hypertrophy, we also noted some intensification of the maturation processes in the follicles, and atresia took place at a somewhat lower level than in normal animals.

A very interesting feature was the increase in the number of primordial follicles in the case of compensatory hypertrophy of the ovary (both the total number and the mean number per section) in comparison with their number in intact animals. For instance, six weeks after unilateral castration, the total number of primordial follicles in the hypertrophied ovary was 80, and there were 1.7 per section; three months after operation, the total number of primordial follicles was unchanged – there were 81, and there were 1.8 per section, whereas in control animals the total number of primordial follicles in the ovary was only 66, with 1.8 per section. The total number of generative elements in compensatory hypertrophy was also greater (28 after six weeks, and 27.2 after three months) than in the controls (20.0).

Thus, an analysis of the information obtained indicates that the ovary in which hypertrophy had previously taken place was capable of regeneration after its resection. The normal shape of the ovary was restored, and the weight of the ovary was considerably increased by the specific structural components of the organ (Fig. 1). In this case, we observed normal functioning of the ovary (restoration of regular sexual cycles, presence of pregnancy, and so on).

The regeneration of the hypertrophied ovary was similar to the regenerative process after resection of half of the ovary and simultaneous extirpation of the opposite ovary. In the latter case, the initial shape of the organ was again restored, the weight of the remaining portion was considerably increased by specific structural components, and the relation between the generative elements was close to normal. The regenerated ovary functioned normally.

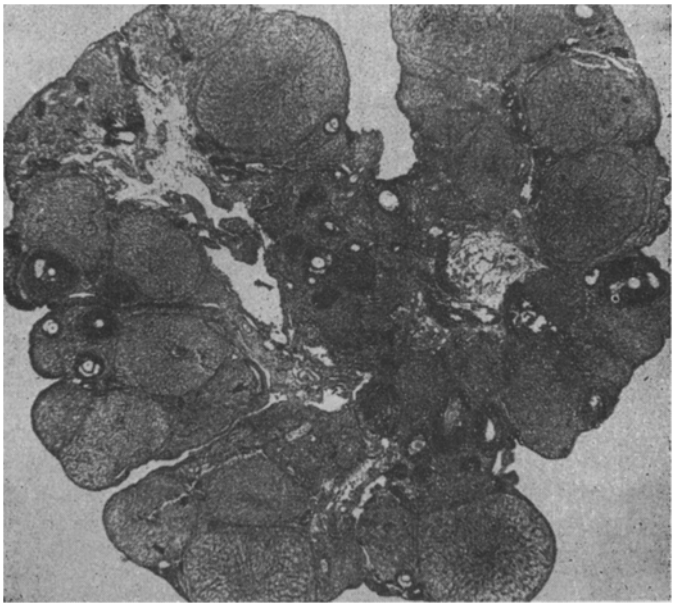

Fig. 2. Section through hypertrophied ovary after unilateral castration (third series of experiments). Photomicrograph.

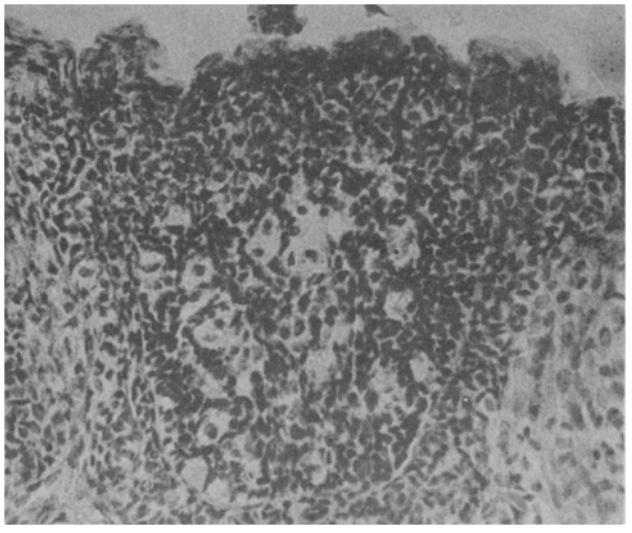

Fig. 3. Formation of primordial follicles at site of follicular epithelium in regenerating ovary (fourth series of experiments). Photomicrograph.

Thus, compensatory hypertrophy has features similar to those of the regenerative process. The considerable increase in weight of the hypertrophied ovary is due mainly to the increase in the number of corpora lutea; a similar situation was observed in the case of regeneration. In addition, we noted an increase in the total number of generative elements per section, and an increase in the number of primordial follicles (Fig. 2). Hence, formation of primordial follicles occurs not only in the case of regeneration, but in the case of compensatory hypertrophy too.

During regeneration of the resected ovary, we sometimes observed pictures indicating the formation of primordial follicles at the site of the follicular epithelium (Fig. 3).

The ovarian regenerative processes induced by removal of half of one ovary and the simultaneous extirpation of the other organ, as well as those induced by resection of a previously hypertrophied ovary, and also the compensatory hypertrophy of an ovary after unilateral castration, are undoubtedly regenerative processes arising in response to injury to the ovary, to the removal of some amount of functioning ovarian tissue.

When a large amount of ovarian tissue is removed, the proliferative processes are more rapid. The declining proliferative processes arising in response to injury can be enhanced again. For instance, after compensatory hypertrophy, rapid proliferative processes are observed when the remaining ovary is injured (resection of half), and these processes lead to the restoration of a normally functioning organ.

SUMMARY

Six weeks after unilateral castration in female rats weighing 120 g, half of the hypertrophied ovary was resected. A considerable increase in the weight of the ovary in $1\frac{1}{2}$ months was found. The weight of the ovary was 150% of that in the controls. The number of primordial follicles increased during the process of regeneration. The total number of generative elements reached the same value as in the control animals. The regenerative process ran a similar course to that observed in the resected ovary, provided complete removal of the paired organ was done.

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