LIVER REGENERATION IN BIRDS

V. F. Sidorova

From the Laboratory of Growth and Development (Head—Prof. L. D. Liozner) of the AMN SSSR Institute of Experimental Biology (Director—Prof. I. N. Maiskii)
(Presented by AMN SSSR Active Member N. A. Kraevskii)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 52, No. 12, pp. 88-92, December, 1961
Original article submitted February 4, 1961

Comparative experimental study of the regenerative processes can help both in solving the many controversial problems connected with analysis of internal organ regeneration and toward a better understanding of the evolution of the regenerative faculty. In particular, the processes of liver regeneration in vertebrates need further investigation.

The experimental investigations which we conducted recently on amphibians and mammals [4, 6], showed that liver regeneration is accomplished mainly through regenerative hypertrophy. In this type of regeneration, the resected portions, whether they be whole lobes or sections of them, are not restored. The proliferative and hyperplastic processes occur primarily all through the remaining part of the organ, causing the resected mass to be rather rapidly replaced, although the original shape of the operated organ is not restored. A scar forms on the wound surface, and no proliferations are observed in this area. Upon review of the literature data, however, we found that a rather significant degree of regeneration from the wound surface is possible, right up to total restoration of the resected portion of the liver [1].

This is particularly true of birds, in which a number of researchers have observed regeneration of one [1, 2] or both [5] lobes of the liver after amputation of the latter. If the literature data cited are to be believed concerning the regenerative ability of birds' liver, they evidently belong in a special group and should not be classed with the other vertebrate animals, in which hepatic regeneration does not restore the initial shape of the organ.

In this connection, we decided to conduct repeat experiments studying hepatic regeneration in birds. Besides cytohistological analysis of this regeneration, special attention was given to the changes in shape of the regenerating liver.

METHODS

The experiments were performed on roosters three months old. In the first series (17 animals), we resected the distal edge of the left lobe of the liver at the level of its bifurcation; in the second series (5 animals), we resected the distal edge of the right lobe at the gall bladder level (Fig. 1). When the operation was completed, a ligature was applied 3-4 mm above the level of amputation. The resected portion of the liver weighed 2.2-4.3 g, the total liver weight being 25-37 g. The animals were sacrificed 3, 14, 30 and 90 days after the operation, 3-6 experimental and two control animals being killed at a time. The liver was weighed and measured and the shape of its lobes traced. The material for histological study was fixed in Carney's fluid and 10% formalin. Paraffin sections were stained with hematoxylin and after-stained with eosin.

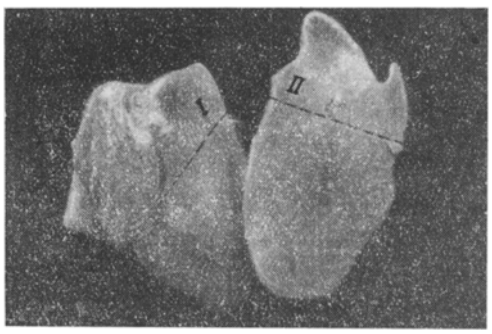

Fig. 1. Intact liver of a rooster. Dotted line—amputation level; I) with partial resection of left lobe of liver; II) with partial resection of right lobe.

RESULTS

At the earlier post-operative intervals (3-14 days), junction of the wounded surface of the operated lobe to the gastric wall or the carina muscles was often observed due to the development of inflammation at the trauma site. The following histogenous changes in the regenerating liver were observed, for the most part in the first series of experiments.

TABLE 1. Average Weight of Body and Liver of Roosters at Different Times during Regeneration

Experimental series	Animal group	Regeneration time (in days)	Weight of resected portion of liver (in g)	Weight of animal when killed (in g)	Weight of Liver	
					Absolute (in g)	Relative (in %)
First	Experimental	3	4	1061	37	3.7
	Control	-	-	886	24	2.6
	Experimental	14	2	1021	23	2.3
		30	3	1304	31	2.3
	Control	-	-	1061	27	2.6
	Experimental	90	3	1822	37	2.0
	Control	-	-	1562	30	2.0
Second	Experimental	90	4	1696	37	2.2

TABLE 2. Change in Certain Parameters of the Regenerated Left Hepatic Lobe Three Months after Excision of Its Distal Edge

Animal group	Animal No.	Height of lobe at base (in cm)	Length of linguiform process from base of lobe to amputation level (in cm)	Height of linguiform process at distal end (in cm)
Experimental	1	2	4.6	1.8
	2	2	4.4	2.4
	3	1.8	4.7	2.0
	4	1.9	4.5	1.8
	5	1.7	4	1.8
	6	2	4	1.8
Average		1.9	4.3	1.9
Control	1	1.2	4	1.3
	2	1	3.5	1
Average		1.1	3.7	1.1

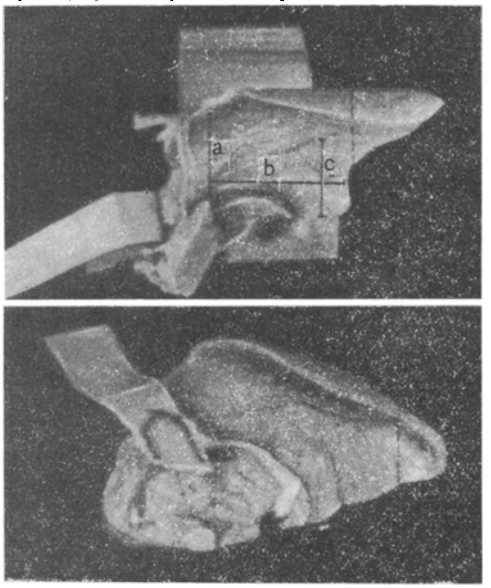

Fig. 2. Left lobe of liver viewed from side of its junction with right lobe. Top photo shows lobe of control animal's liver: a) height of lobe at base; b) length; c) height of linguiform process on dorsal side of lobe; bottom photo shows liver of experimental animal 3 months after operation. The hypertrophied linguiform process is seen protruding beyond amputation level.

The operated lobe reacted to the trauma by relatively slight parenchymal necrosis at the incision site, attended by leukocytic infiltration and followed by the formation of scar tissue on the surface of the wound. Profuse proliferation of the bile ducts and of the hepatic canals located along the very edge of the wound surface was typical of the early stage of hepatic regeneration. The differentiating cells of these canals often acquired a marked resemblance to the epithelial cells of the bile ducts. There was little change except for some hyperemia in the main mass of the hepatic parenchyma proximal to the amputation line. The growth of the hepatic parenchyma and the ducts was caused by mitotic division of their cellular elements. Mitoses were found in the hepatic cells located both near the wound surface and far from it, even in the uninjured lobes of the liver.

Hypertrophy of the hepatic cells was also observed soon after the operation (3rd day). At this time, the liver of the experimental animals weighed somewhat more than the liver in the control (Table 1).

Fourteen days after the operation, a scar began to form on the wound surface, and the healthy portions of the parenchyma were sharply separated from the portions in which the trauma had caused necrosis. Gradual degeneration

of the enlarged bile ducts was observed at this time; the nuclei of their cells became corrugated, and the ducts themselves collapsed and were replaced by the connective tissue growing rapidly on the wound surface. Subsequently, the scar which formed cut off the encapsulated portions of the necrotized parenchyma at the trauma site. From this time on, the weight of the regenerating liver approximated the control (see Table 1).

Starting the 30th day after the operation, small (5-8 mm long), peculiar protuberances of the parenchyma became evident, being particularly marked in the case of trauma of the left lobe of the liver. Examination of the anatomical features of the traumatized left lobe of the liver and the course of regeneration at later stages (90th day) led us to conclude that the small protuberances which formed on the wound surface were due to proliferation of the hepatic parenchyma, primarily from within the organ, and to constriction of the parenchyma by the scar. In the experimental animals, hypertrophy of the small linguiform process usually located on the dorsal side of the left lobe of the liver was also observed near the amputation level at this time (Fig. 2).

To obtain a clearer picture of the changes in the shape and size of the left lobe of the liver during regeneration, we made certain measurements in the control and experimental animals of both the lobe itself and the process on its dorsal side. We measured the height of the left lobe at its base on the side where it is attached to the right lobe and the length and height of its linguiform process (Fig. 2 and Table 2).

As Table 2 shows, regeneration of the liver after resection of the distal portion of its left lobe was accomplished by regenerative hypertrophy, with thickening of the traumatized lobe and enlargement of the process on the dorsal side. When the general shape of the left lobe of the liver in the experimental animals is compared with that of the same lobe in the control animals, this is even more apparent (Fig. 2).

It should be mentioned that the formation of protuberances on the wound surface was not observed after resection of the distal edge of the right lobe of the birds' liver (Fig. 3) because of the anatomical characteristics of this lobe (normally devoid of supplementary processes). The hypertrophy of the processes of the left hepatic lobe and the parenchymal proliferation at the wound surface may well have been wrongly interpreted by previous researchers as regeneration of the excised portions of the lobe. In actuality, however, as the material given above indicates, neither of the formations which develop at the trauma site during hepatic regeneration resembles the excised portions of the lobe in origin, location or shape.

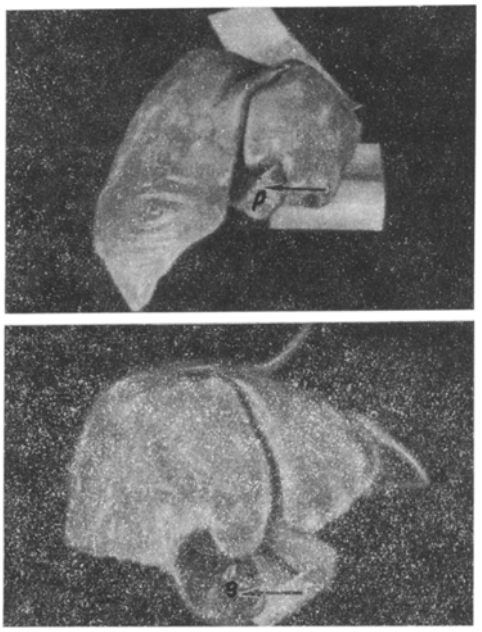

Fig. 3. Regenerated liver of rooster three months after partial hepatectomy. Top photo shows general view of liver after operation on left lobe. Small proliferations of parenchyma, linguiform process (p) visible below; bottom photo shows general view of liver after operation on right lobe. No parenchymal proliferations. Gall bladder (g) visible at amputation level.

The results of this investigation, therefore, lead one to conclude that in birds, as in the other vertebrates studied earlier, hepatic regeneration is accomplished by regenerative hypertrophy, and the original shape of the traumatized organ is not restored. Many attempts to detect regeneration of the excised portion from the wound surface have already been made by us [3] and other researchers [1, 2] studying liver regeneration in amphibians and mammals. Repeated investigations, however, have made us certain that any growth which does originate from the wound surface is negligible. As a rule, the impression that the resected portion of the organ regenerates is erroneous. It is usually based on the formation of various protuberances from or alongside the wound surface. This formation could be due to a number of reasons, the principal one being irregular growth of the remaining part of the organ. One must also consider the influence of: a) the animal's age (the intense growth processes in young animals promote regeneration of the organ); b) a ligature applied to the operated organ (which distorts the normal course of the regeneration processes); c) inflammatory processes, intensified at the trauma site due to the influence of various external or internal factors.

It is also possible that in experiments performed on adult roosters with no ligature applied to the lobe, there would not be even the slightest parenchymal proliferation which could be mistaken for growing tissue.

Therefore, the irregular growth of the remaining part of the organ, which causes the formation of protuberances and, sometimes considerable, hypertrophy processes, is responsible for the impression gained by a number of researchers that regeneration occurs from the wound surface.

SUMMARY

Experiments were conducted on roosters aged 3 months. In the first series of tests the distal edge of the left lobe of the liver was removed at the level of its bifurcation, in the second, the distal edge of the right lobe, at the gall bladder level. The removed part constituted from 1/8 to 1/10 of the total weight of this organ.

A study was made of the histogenetic processes, and the changes in the shape of the liver during its restoration, for 3-90 days. Hepatic regeneration occurs in birds by the process of regenerative hypertrophy, i.e., enlargement of the size of the liver is caused by the proliferative processes in the remaining part of the organ. The initial shape of the liver is not restored. After removing the distal edge of the left lobe there occur insignificant proliferations of the parenchyma at the wound surface and hypertrophy of the process located at the dorsal side of the operated lobe, which may imitate the growth of the excised part of the lobe. No such phenomena were observed in operations on the right lobe.

LITERATURE CITED

1. N. I. Grigor'ev, The reactivity of the epithelium of the small intestine, gall bladder and liver in vertebrate animals and in man. Doctor's dissertation [in Russian]. (Leningrad, 1955).
2. R. P. Zhenevskaya, Transactions of the Severtsov Inst. of Animal Morphology [in Russian] (Moscow, 1954) 11, 40.
3. L. D. Liozner and V. F. Sidorova, Doklady AN SSSR (1950) 72, 2, 425.
4. L. D. Liozner et al., in: Restorative processes in vertebrate animals [in Russian] (Moscow, 1959) p. 240.
5. V. N. Orekhovich, Transactions of the Inst. for Scientific Research in Experimental Morphogenesis [in Russian] (Moscow, 1938) 6, 293.
6. V. F. Sidorova, Byull. éksper. biol. i med. (1959) 8, 99.
