REGENERATION OF THE KIDNEY IN NEWBORN RABBITS

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In newborn rabbits, in which growth and morphogenesis of the kidneys are incomplete, between one-fifth and one-sixth of one kidney was resected. Despite some rounding of the kidney at the site of injury, the organ did not acquire its typical shape, and the deficient part did not grow again. At the site of injury, a small, atypical focus of kidney tissue, consisting mainly of cystic structures, appeared.

After resection or injury of the kidney in adult animals, regeneration at the site of injury takes place only very slightly, and usually the end result is the formation of a connective-tissue scar [3]. Even if it is accepted that the atypical renal corpuscles and tubules, described by some authors at the site of injury a long time after the operation, are formed de novo, it must be borne in mind that this atypical tissue constitutes only a very small proportion of the total volume of the organ, and restoration of the kidney takes place predominantly by a mechanism of regeneration hypertrophy. However, it is not yet known how regeneration takes place after resection of the kidneys in newborn and young animals. Bakhromova [1] and Braun and Bakhromova [2], who studied regeneration of the kidneys in newborn rabbits, consider that this takes place through epimorphosis. This is the term they apply to the formation of fresh kidney tissue to replace the resected part as the result of an outgrowth of tissue from the wound surface.

Since this method of regeneration of a parenchymatous organ seemed unlikely, but the possibility of its occurrence could not be categorically denied, experiments were carried out in order to study resection of the kidney in young rabbits.

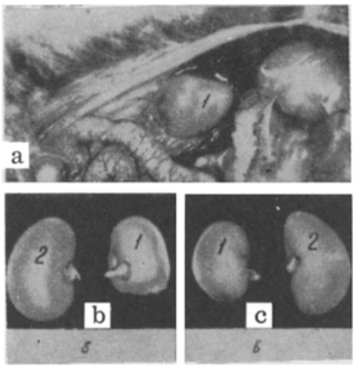

Fig. 1. Kidneys of young rabbits after resection on the 1st day after birth. Fixation 45 days after operation. a) resected kidney; b) typical shape of regenerated kidney; c) the only case of a uniformly rounded, regenerating kidney; 1) resected kidney; 2) intact kidney.

EXPERIMENTAL METHOD

In newborn chinchilla rabbits on the 1st or 3rd day after birth, from one-fifth to one-sixth of the right kidney was resected from the caudal pole under ether anesthesia. The experimental rabbits were sacrificed on the 7th, 11th, 12th, and 45th days after the operation, and at each time rabbits of the same litter were studied. The intact and partially resected kidneys were fixed in Carnoy's fluid. Paraffin sections, 7 μ in thickness, were stained with hematoxylin-eosin and by Van Gieson's method.

EXPERIMENTAL RESULTS

Complete restoration of the shape of the resected organ was not observed in any experimental animal. Where the injured part was adherent to surrounding tissues, the shape of the organ was considerably changed, the wound surface was readily distinguished, and it was covered by a connective-tissue scar (Fig. 1). In one case, in

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TABLE 1. Mean Weight of Kidneys of Experimental and Control Rabbits at Various Times after Birth

Age (in days)		No. of animals	Weight of kidney (in mg)		Ratio between weight of right and left kidney
at time of operation	at time of sacrifice		right (resected)	left (intact)	
1	7	3	527	623	0.84
1	11	2	1525	1750	0.87
Control	11	1	1650	1500	1.10
1	45	3	2466	3866	0.63
3	28	5	1700	2025	0.83
Control	28	1	1880	1860	1.01
"	14	1	1180	1160	1.01
"	35	3	1610	1566	1.00

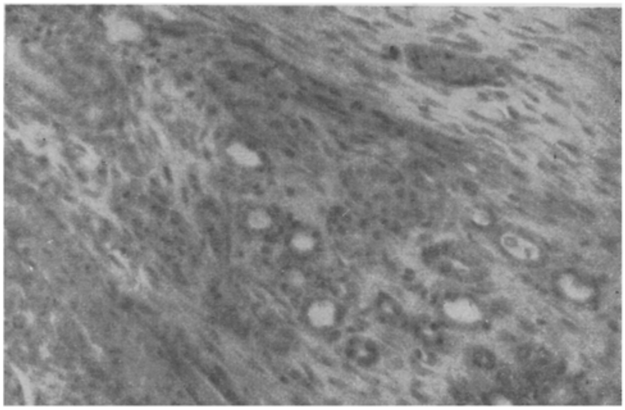

Fig. 2. Kidney of a rabbit 11 days after operation. Bottom left: intact area of kidney, remainder of field of vision shows proliferating connective tissue, in which isolated tubules can be seen; 420×.

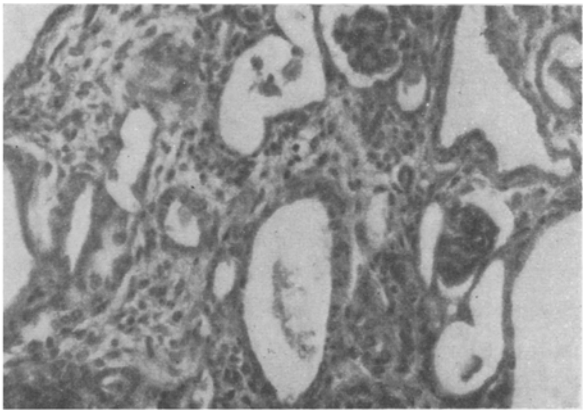

Fig. 3. Area of rabbit's kidney adjacent to site of injury, 45 days after operation. Proliferation of connective tissue, widely dilated lumen of tubules with flattened epithelium, renal corpuscles with enlarged cavity of Bowman's capsule; 210×.

which no adhesions between the kidney and surrounding tissues were present, the residual kidney was uniformly rounded in contour, but the kidney had not acquired its typical shape. In areas adjacent to the site of injury the renal capsule was thickened and did not strip easily from the inner layers, and in the kidneys of some animals very small, round structures resembling vesicles could be seen in these areas beneath the capsule. The resected kidney was shorter in every case than the control. This important finding showed that no regeneration of the resected area had taken place. In the control animals the ratio between the weight of the right kidney and the weight of the left was 1.00-1.10, while in the experimental rabbits this ratio was considerably reduced (Table 1).

Comparison of the weight of the intact kidneys of the experimental rabbits with the weight of the corresponding kidneys of the control rabbits revealed hypertrophy of the kidneys in the experimental animals.

Microscopic investigation showed that on the 7th day after the operation, a well-developed nephrogenic zone was present in the intact kidney and in the intact parts of the resected kidney, and in the latter it was in contact on both sides with the injured area. In the zone adjacent to the side of resection, an accumulation of young connective tissue was observed, and all that remained of the nephrogenic zone here were isolated islets of undifferentiated cells and structures of definitive form.

On the 11th day no accumulations of undifferentiated cells could be found in the nephrogenic zone, either in the intact kidneys of the partially nephrectomized rabbits or in the kidneys of the control animals, although the structures present there had not yet been definitively formed. In the resected kidney the nephrogenic zone was similar in shape, and at the site of injury a small area of atypical kidney tissue was found.

This focus consisted mainly of tubules, with a widely dilated lumen, lined by flattened epithelium, and with connective tissue growing between the tubules. Normal, unchanged tubules and renal corpuscles with enlarged cavities of their Bowman's capsules were visible.

In the later stages after the operation, the areas of atypical tissue still remained; the lumen of the tubules was dilated even further, until in some cases large cystic formations had appeared; the connective tissue between the tubules was abundantly developed; and the number of unchanged tubules was considerably reduced. The renal corpuscles present in these areas were of the ordinary size or slightly reduced, the outer layer of Bowman's capsule was thickened in some cases, and none of the tubules showed the characteristic open-work structure of the capillaries (Figs. 2 and 3).

These results show that after resection of the kidneys in newborn rabbits, in which the processes of growth and morphogenesis are not yet finally complete, the site of injury during regeneration of the organ is not so clearly demarcated as in adult animals, but the kidney had not acquired its typical shape by the end of the period of observation. The difference in weight between the resected kidney and the larger, intact kidney was mainly due to hypertrophy of the intact organ. In newborn rabbits regeneration evidently takes place also on account of hypertrophy, for the atypical part of the kidney amounted to only a very small part of the organ (2-4 fields of vision under a magnification of 56), and it consisted of functionally imperfect structures not producing a normal outflow of secretion. The possibility is not, of course, ruled out that new renal corpuscles and tubules could be formed at the site of injury, because a nephrogenic zone is present. However, the development of the connective tissue probably prevents the formation of perfect structural units. The question of the origin of the unchanged areas of the tubules in the atypical zones of kidney tissue remains unanswered. It is not known whether they are tubules formed before the operation, among which connective tissue subsequently proliferated strongly, or whether they are the result of further differentiation of intact areas of the nephrogenic zone among the proliferating connective tissue.

The possibility of regeneration of a deficient part of the kidney in newborn rabbits could not therefore be confirmed. Regeneration takes place by hypertrophy of the residual part of the organ just as in adult animals. No marked outgrowth of new tissue was observed at the site of injury, and the newly developed structures were atypical. Those workers who consider that regeneration in newborn rabbits takes place by epimorphosis evidently were confused by the fact that at the site of reaction the edges of the kidney are slightly rounded. However, this is not explained by growth of the tissues out from the wound surface, but by the rapid and, evidently, not absolutely uniform growth of the kidney.

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