# FUNCTION IN A TRANSPLANTED REINNERVATED KIDNEY

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The work of G. M. Shpuga and her co-workers [7, 8, 9] has shown that in dogs the function of an autografted kidney is greatly reduced in comparison with the intact organ. These results have been confirmed by the work of Dempster and Joekes [11].

As a result of the work of our colleagues in this laboratory, it has been proposed that the reason for the reduced function is the deenervation which occurs inevitably during the transplantation. It has also been shown that if the autografted kidney is reinnervated from the vagus [7], its function then approaches that of the intact kidney [3, 7, 8].

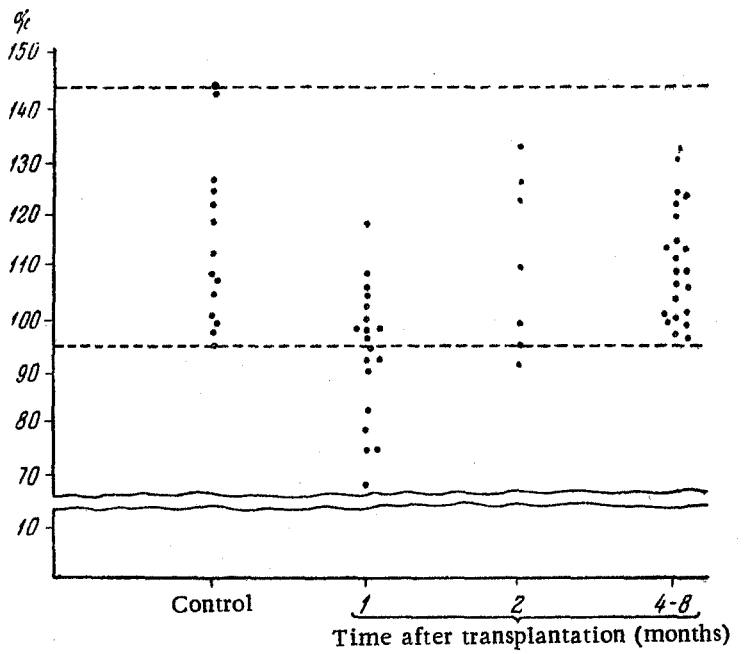


Fig. 1. Filtration of the right transplanted and reinnervated kidney in Al'fa, Mary, and Lyuks as a percentage of the left kidney, serving as control.

Here we have made an attempt to follow the changes in function of the transplanted kidney during regeneration and anastomosis of the vagus, and to investigate function after reinnervation.

## METHOD

A study was made on 10 dogs with an autografted reinnervated kidney. The right kidney was transplanted into the neck, and connections made between the renal vessels and the jugular vein and carotid artery. Reinnervation was established by anastomosis of the central end of the vagus with the renal nerves. The opening of the ureter of the transplanted kidney was brought out onto the skin of the chest, and that of the inact kidney onto the skin of the

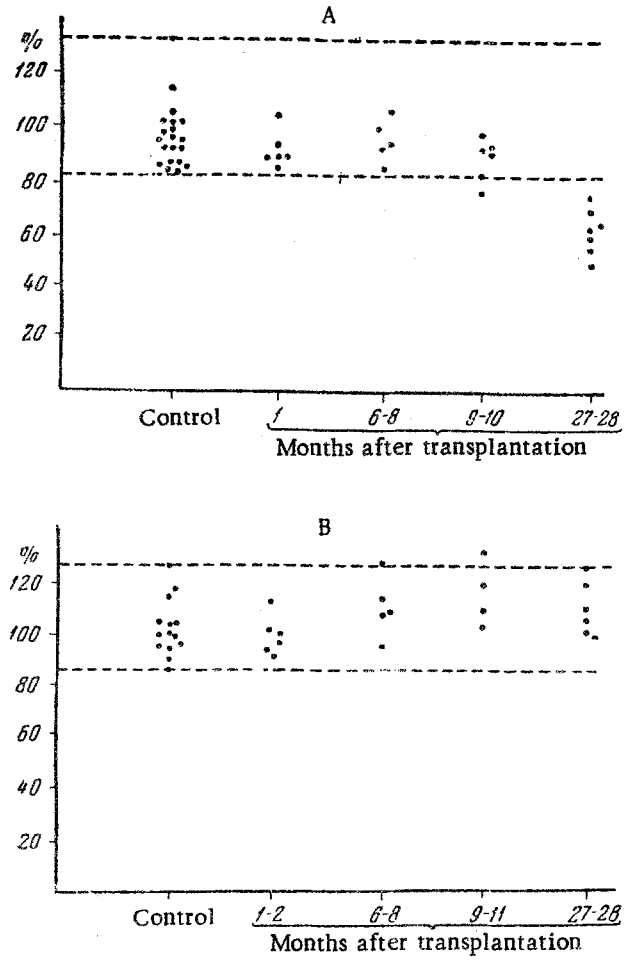


Fig. 2. Filtration of the transplanted reinnervated kidney as a percentage of the filtration of the intact organ as control in (A) Daisy and (B) Zhulik at various times after division of the anastomosed vagus.

belly. During the post-operational period, fibers of the vagus nerve grew out along the degenerating fibers of the renal nerves to enter the parenchyma of the transplanted kidney so as to innervate it. Previously [4,5] we have demonstrated the growth of afferent and efferent fibers into the parenchyma of the kidney, and the role of the latter in regulating renal function.

A study was made of the intact kidneys on 3 dogs (Al'fa, Mary, and Lyuks) in which the openings of the ureters were brought out on to the anterior abdominal wall. Next, the right kidney was transplanted into the neck, and reinnervated from the central end of the vagus. A study of the transplanted kidney was made for 8 months, starting a few days after the operation. In the remaining 7 dogs, a comparative study was made of the functions of the transplanted reinnervated and the intact kidneys at a time long after the operation.

The functions studied included filtration (in terms of inulin, and in many experiments with use of endogenous creatinine), reabsorption (water, glucose, $Na^{24}$). Tubular excretion was measured with phenol red. Inulin, glucose, and phenol red were given as a continuous intravenous drip. The concentration of these substances in the plasma and urine was measured, and the indices were calculated from the usual formulas. The values obtained were referred to one square meter of body surface.

## RESULTS

In the 3 dogs (Al'fa, Mary, and Lyuks), renal filtration and reabsorption was studied by means of inulin. After the operation there was a change in the diuresis of the transplanted and of the intact kidney. In the first 2 months after transplantation, there was a period of variable diuresis, as was observed also by G. M. Shpuga [7] in experiments with the usual type of transplanted kidney.

Figure 1 shows the filtration of the right transplanted kidney as a percentage of the left. It can be seen that the filtration of the reinnervated kidney is low during the first month after transplantation in comparison with the value for that kidney before operation. During the second, and particularly during the fourth to eighth months, filtration returned to the normal values.

It is interesting to compare these results with the rate of growth of vagal fibers into the parenchyma of the transplanted kidney. The first indication of the growth of afferent vagal fibers into the renal parenchyma is that a cough is produced in response to a light massage of the transplanted kidney [4]. This effect was shown at the end of the first month after transplantation, and functional recovery of the reinnervated kidney began at the end of the second month after transplantation.

Our experiments have therefore demonstrated the recovery of function in a transplanted reinnervated kidney occurring long after transplantation, an effect which is not found in dogs with the normal type of transplantation. Further, it has been shown in our laboratory that with the normal method of transplantation, renal function shows a continuous decrease with time [9].

A study of renal function long after the transplantation showed that there was very little difference in the filtration and reabsorption of the transplanted and intact kidneys. Reabsorption of glucose (in Daisy and Zhulik), reabsorption of $Na^{24}$ (Al'fa, Mary, Lyuks), excretion of phenol red (dogs Al'fa, Mary, Lyuks, Daisy, and Zhulik), also showed

no essential difference between the transplanted reinnervated and the intact kidneys. Only in one of the 10 experimental dogs (Avva) was there some reduction of filtration, reabsorption of glucose, and excretion of phenol red in the transplanted reinnervated kidney.

The disturbed function of the transplanted kidney in this dog was apparently due to the considerable operational trauma: The ischemia of the transplanted kidney lasted for about an hour while the vascular connection was being made. Probably the subsequent regeneration of the vagus was unable to restore renal function to the original level.

In the last set of experiments on two dogs (Daisy and Zhulik), the anastomosed vagus was divided 6 months after transplantation. By then, the function of the transplanted kidney had already become established, and in neither dog did it differ significantly from that of the intact kidney.

From Fig. 2 it can be seen that in the months following division of the anastomosed vagus there was no appreciable difference between the function of the transplanted and control kidneys. In Daisy, long after the division of the vagus, there was a considerable reduction in the function of the transplanted kidney, whereas in Zhulik there was no change.

Our results indicate that renal function is disturbed for a short period after transplantation. The impairment of function appears to be associated with trauma to the kidney at operation, and by the arrest of blood for 20-30 min while the vessels are sutured, etc. [10]. Renal function in a transplanted kidney supplied with vascular anastomosis only deteriorates further after a prolonged period [9, 11]. However, the function of a transplanted reinnervated kidney which is disturbed for one month after the operation, recovers to the original level. The conclusion is that innervation plays a great part in the recovery of renal function.

In the last set of experiments it was shown that in the first few months, division of the anastomosed vagus causes no deterioration of function of the transplanted reinnervated kidney. This method of "secondary" denervation has much in common with that of denervating a kidney in its normal position, which is used to study the role of the efferent nerves in renal function. The results on this subject are extremely contradictory. Some authors maintain that after denervation there is a fundamental disturbance of renal function and morphology, while others are inclined to the view that denervation with the kidney in position causes no essential functional changes [2].

Probably denervation of a kidney does not influence its function under all conditions. If denervation of an intact or of a transplanted reinnervated kidney is made a long time after transplantation, there may be no functional change. On the other hand, if the denervation is made at the same time that the kidney is transplanted, there is no recovery of the function of the kidney impaired through transplantation, and even atrophy may occur [9]. Recovery of innervation is a necessary condition for recovery of renal function impaired through transplantation.

This interpretation is confirmed by many other investigations. Kaiserling and Mathies [12], and S. D. Reizel'man [6] found that a pathological process resembling nephritis runs a very severe course in the denervated kidney and brings about sclerotic changes, whereas, in the intact kidney, the changes are insignificant. I. S. Beritov [1], in summing up the published reports on the effects of denervation on the function of organs, points out that in denervated tissues, the recovery of the normal condition is delayed, particularly when trauma has been inflicted. All these considerations support our conclusion that functional recovery of the transplanted kidney may be brought about by recovery of the innervation of the transplant.

## SUMMARY

In dogs, an autografted kidney was reinnervated by anastomosis of the central end of the vagus with the peripheral end of the renal nerve. Glomerular filtration and tubular water reabsorption determined by the inulin method showed no essential difference between the transplanted reinnervated and intact kidneys. There were no significant differences either between the transplanted reinnervated and intact kidneys with respect to phenol red excretion or glucose and sodium isotope tubular reabsorption. Reinnervation from the central end of the vagus improved renal function in the autografted kidney disturbed by transplantation.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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