# EXPERIMENTAL INFARCTS OF THE KIDNEYS

## COMMUNICATION I. STUDY OF THE BLOOD SUPPLY TO THE KIDNEYS WITH INFARCT BY MEANS OF $P^{32}$ MARKED ERYTHROCYTES

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(Received February 2, 1956. Presented by Acting Member of the Acad. Med. Sci. USSR A. L. Myasnikov)

The theory of the pathogenesis of infarcts, based on the conceptions of Cohnheim concerning the terminal character of the branching of the vessels has up to now been widely circulated. However, many investigations by a number of authors have demonstrated the presence of anastomoses between the vessels in many organs, which obliges one to reconsider the theory of Cohnheim. Some authors [1, 2, 3 and others] attach great importance in the pathogenesis of infarcts to the reflex spasm of the vessels and their anastomoses, and also to the disturbance of their function upon atherosclerosis and general blood circulation disturbances.

When one of us (I. M. Shapiro) studied the morphology and pathogenesis of infarcts of the kidneys, a number of questions arose connected with blood supply of the kidneys upon the development of this pathological process. In order to clarify these questions, experiments were conducted in which, with the aid of marked erythrocytes, the dynamics of the blood supply to the kidneys after ligaturing the branch of the renal artery were studied.

## EXPERIMENTAL METHODS

The experiments were conducted on white rats (21 experiments), in which under ether narcosis, the kidney was approached from the rear and the left posterior renal pelvis artery was ligatured. The animals were killed 10, 30-40 minutes, and at 6, 9 and 24 hours after ligature of the artery. A suspension of marked rat erythrocytes in physiological solution was introduced intravenously, 5-10 minutes before sacrifice.* The degree of saturation by radioactive phosphorus of the marked erythrocytes, introduced in the blood, did not change in the course of 60 minutes [6]. This allows one to consider that the radioactivity of the tissues in our experiments was basically caused by the marked erythrocytes entering into it. The saturation of the erythrocytes by the radioactive phosphorus was carried according to the method described by Nylin and Hedlung and Malm [6, 7] with slight modifications. After centrifuging 3-5 ml of the citrated blood of healthy animals, the plasma was drawn off, 1-2 ml physiological solution was added and 0.1 mC radioactive phosphorus introduced. The vessel was placed in a thermostat at 37° C for 2-3 hours. The contents of the vessel were shaken several times. Then the erythrocytes were washed 10-12 times (with centrifugation) with physiological solution. The washed liquid was shown to be almost 100 times less radioactive than the residual erythrocytes. After washing, 2-4 ml physiological solution was added to the erythrocytes and the activity of the suspension obtained determined. The erythrocytes were introduced into the animals calculated at the rate of 1000-2000 impulses per 1 g of body weight.

* For complete admixture of the marked erythrocytes with the blood of the recipient 5 minutes is sufficient [5].

After sacrifice of the animals, the vascular stem of the kidney was ligatured, the kidneys extracted, carefully washed with physiological solution and removed from their capsule. In order to calculate the activity of the weighed portion, tissue was taken from the central, and in some of the experiments also from the peripheral sections of the zone of ischemia and from the symetrically situated regions of the frontal (lower) surface of both kidneys. The weighed portion was carefully pulverized and smeared at the bottom of a tin foil dish, serving as a target, on an area not exceeding 3/4 diameter of the tube of the counter and attached to a microscopic slide.*

The weight of the samples was always less than 40 mg/cm.

The calculation of the radioactivity of the samples and interpretation of the findings was conducted in accordance with the generally accepted rules. In order to calculate the activity, we used the apparatus of type B, equipped with counter AS-2. In order to compare the state of blood supply of the different regions of the kidneys, a conversion was made on the number of impulses to 1 g of tissue: 100 units was nominally taken as the number of impulses per 1 g of tissue of the right kidney.

## EXPERIMENTAL RESULTS

The experiments showed that 10 minutes after ligaturing the left posterior renal pelvic artery, 5-8 times less blood entered the ischemic area than entered the right kidney (12-20 units). Only in one experiment (No. 20a) did the blood supply of the ischemic area correspond to 39 conventional units. The healthy parts of the left kidney receiving blood from the system of the frontal renal pelvic artery, under these conditions received a quantity of blood less than half that received by the right kidney (39-40 units), and only in experiment No. 20a, was the level of blood supply equal to 73 units. The results of all the groups of experiments are presented in Table 1.

Within 20-40 minutes, the blood supply picture of the left kidney changed considerably. The entry of blood in the ischemic area increased somewhat, reaching 26-31 units. Blood supply of the healthy parts of the left kidney increased almost twice: it varied from 77-87 units.

In the control experiments (Nos.12, 14, 29 and 13), we repeated all the phases of the operation: introduction to the kidney was by means of incision, the ligature was placed under the vessel (but not tightened), then the ligature was removed, the kidney was placed in position and the wound stitched up. Within 10 minutes, the entry of blood in the parts of the kidney supplied by the posterior renal pelvic artery decreased somewhat; however, it never once dropped to the level of blood supply of this part after ligaturing the artery. In one of the experiments (No. 12), a small decrease in blood supply of the regions fed by the frontal renal pelvic artery was observed. With 30-40 minutes, these changes disappeared (Table 1).

The entry of blood in the region of the infarct again fell 6-9 hours after ligaturing the branch of the renal artery, varying from 11 to 22 units, and towards 24 hours it degenerated still further (Table 1). Blood supply of the healthy parts of the left kidney within 6-24 hours remained at the former level. Only in one experiment did it reach 112 units within 6 hours, and in experiment No. 30 (lasting 24 hours) it fell to 69 units.

The peripheral sections of the region of infarct in these periods received 1½-2 times more blood than the central sections.** This concurs with the findings of Z. Z. Dorofeeva, who showed that the center of the zone of ischemia in the myocardium receives less blood than the peripheral sections.

The dynamics of the changes in blood supply of the healthy parts of the left kidney in the early periods, in our view, may be explained by the spasm of the vessels in the system of the frontal renal pelvic artery arising after ligaturing the posterior renal pelvic artery. The spasm leads to a sharp fall in the amount of blood entering the healthy parts of the left kidney as compared with the right one. ***

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* Weighing of weighed portions was conducted by torsion scales.

** Determination of blood supply of the peripheral sections of the area of ischemia in the early stages of development of infarct was not carried out, owing to insufficient distinctness of the borders of this region.

*** In the Experiment No. 20, the spasm of the vessels was apparently weakly marked. The level of blood supply of the ischemic region was correspondingly higher.

Within 30-40 minutes the spasm of the vessels significantly fell. A. V. Lebedinsky, V. I. Medvedev, and I. A. Peimer recorded by means of diathermal meters the spasm of the right coronary artery of the heart after ligaturing the branch of the left one.

The control experiments show that even a slight trauma of the vascular stem during the operation can produce spastic manifestations on the part of the renal vessels, although considerably less marked than with ligature of the artery.

The disparity in blood supply of the healthy parts of the left kidney as compared with the coreesponding parts of the right one in later periods (6-24 hours) is apparently related to the compensatory hyperemia of the right kidney.

It is of interest to clarify the causes of the appearance of spasm of the vessels of the system of the frontal renal pelvic artery after ligaturing the posterior one.

The published findings allow one to put forward the hypothesis that the spasm of the vessels is of reflex character, and caused by stimulation of the nerve formations located in the wall of the posterior renal pelvic artery, and in the ischemic section of the kidney (V. N. Chernigovsky, Trueta, etc.). If this hypothesis is correct, one would expect that denervation of the kidneys would remove or at least basically reduce the manifestations of spasm. Therefore, it was interesting to establish how denervation of the kidneys influences the state of their blood supply upon experimental infarct.

The experiments were conducted on 16 white rats in which, 7-9 days before ligaturing the left posterior renal pelvic artery, a bilateral denervation of the kidneys was performed. For this purpose, the kidneys were approached from the rear, the vascular stem was carefully cleansed of the surrounding cellular tissue, and the fatty cellular tissue together with the nerve ganglia at the site of the emergence of the renal artery was removed. Then the vessels and the upper quarter of the ureter were treated with a 2% solution of phenol, and washed out with physiological solution. After this, the fibrose capsule of the kidney was removed. Apart from this, the method of conducting the experiments was similar to that descrived above.

Ten minutes after ligaturing the left posterior renal pelvic artery, the blood supply of the area of ischemia was 3-5 times lower than that of the right kidney, and varied from 32-41 units. Only in one experiment (No. 38) was it equal to 19 units.

The level of blood supply to the healthy parts of the left kidney remained fairly high (79-81 units). Only in Experiment No. 48 did it fall to 68 units. The results of all the groups of experiments of this series are presented in Table 2.

The blood supply picture of the kidneys changed little 30-40 minutes after ligaturing the artery. The entry of blood in the region of the ischemia fluctuated between 21-42 units; in one experiment (No. 47) it amounted to 16 units. The blood supply of the healthy parts of the left kidney also remained at the former level (74-84 units in Experiments No. 32, 39, 47) or rose a little (up to 98-103 units in Experiments No. 41 and 42).

After 3-4 hours the blood supply of the central sections of the area of ischemia fell to 13-15 units. The peripheral zone of the ischemia receiving $1^1/_2$ 2 times more blood than the central sections. Entry of the blood in the healthy parts of the left kidney was 10-15 units less than the right kidney.

Thus, denervation of the kidneys prevents, to a significant degree, manifestations of spasm of the vessels of the system of the frontal renal pelvic artery after ligaturing the posterior one, which confirms the hypothesis of its reflex nature. Blood supply to the healthy and ischemic sections of the left kidney in conditions of denervation 10 minutes after ligaturing the kidney was twice as high as their blood supply with unimpaired innervation (see Figure).

In later periods, after ligaturing the posterior renal pelvic artery (from 30 minutes to 3-4 hours), no essential differences from what had been observed with unimpaired innervation could be established.

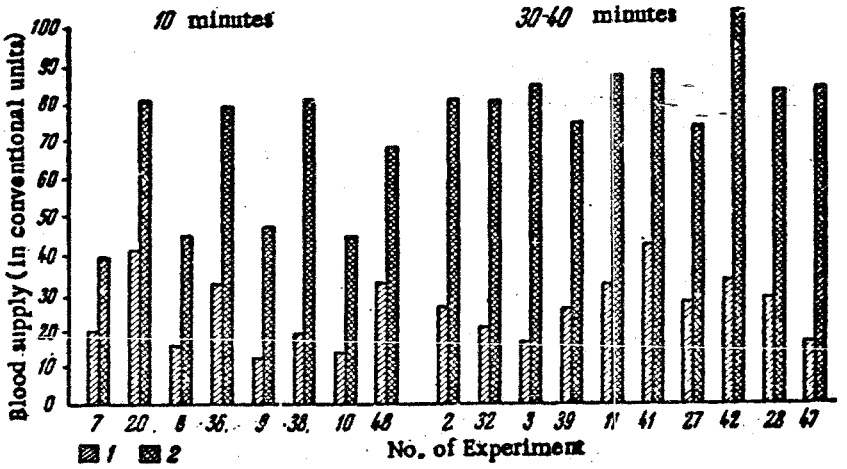
In the control experiments with reproduction of all the phases of the operation, with the exception of ligature of the artery (Nos. 18, 21, 46, 49) denervation prevented the appearance of small spasm of the vessels which had developed as a result of operational trauma with unimpaired denervation.

TABLE 1

Blood Supply to the Kidneys 10, 30-40 Minutes and 6, 9, 24 Hours after Ligaturing Left Posterior Renal Pelvic Artery.

(In impulses per 1 g tissue. Number of impulses per 1 g right kidney taken as 100).

| No. of Experiment | Duration of Experiment | Left kidney | | | | | | Right kidney |
|---|---|---|---|---|---|---|---|---|
| | | Region of infarct | | | | Healthy parts | | |
| | | Central parts | | Peripheral parts | | | | |
| | | Number of impulses | In conventional units | Number of impulses | In conventional units | Number of impulses | In conventional units | Number of impulses |
| 7 | 10 Min | 1 628 | 20 | — | — | 3 159 | 39 | 8 200 |
| 8 | 10 » | 1 758 | 16 | — | — | 4 526 | 45 | 10 100 |
| 9 | 10 » | 1 027 | 11,5 | — | — | 4 101 | 46 | 8 900 |
| 10 | 10 » | 1 167 | 14 | — | — | 3 580 | 44 | 8 162 |
| 20a | 10 » | 1 668 | 39 | — | — | 3 108 | 73 | 4 247 |
| 2 | 30 » | 1 003 | 26 | — | — | 3 154 | 80 | 3 919 |
| 3 | 40 » | 758 | 16 | — | — | 3 884 | 84 | 4 606 |
| 11 | 35 » | 2 200 | 31 | — | — | 6 175 | 87 | 7 125 |
| 27 | 30 » | 1 754 | 26 | — | — | 5 239 | 77 | 6 764 |
| 28 | 40 » | 1 610 | 27 | — | — | 5 041 | 84 | 5 980 |
| 12 | Control 10 min | 5 000 | 66 | — | — | 6 315 | 84 | 7 534 |
| 14 | Control 10 min | 2 860 | 71 | — | — | 4 065 | 100 | 4 039 |
| 29 | Control 30 min | 4 648 | 90 | — | — | 5 100 | 97 | 5 194 |
| 13 | Control 40 min | 5 205 | 99 | — | — | 5 263 | 100 | 5 236 |
| 4 | 6 Hours | 1 385 | 22,5 | 1 930 | 31 | 5 000 | 81 | 6 164 |
| 15 | 6 » | 1 219 | 19 | 1 230 | 19 | 7 349 | 112 | 6 538 |
| 22 | 9 » | 762 | 12 | 1 365 | 22 | 4 871 | 80 | 6 125 |
| 23 | 9 » | 872 | 11 | 1 515 | 20 | 6 602 | 86 | 7 656 |
| 30 | 24 » | 868 | 9 | 886 | 9 | 6 392 | 69 | 9 316 |
| 31 | 24 » | 1 271 | 17 | 2 267 | 30 | 6 591 | 86 | 7 650 |
| 33 | 24 » | 1 044 | 11 | 2 283 | 24 | 8 105 | 86 | 9 427 |




Blood supply to left kidney 10, 30-40 minutes after ligaturing left posterior renal artery.

D) Experiment with denervation; 1) Area of ischemia; 2) Healthy parts.

TABLE 2

Blood Supply to Denervated Kidneys 10, 30-40 Minutes and 3-4 Hours after Ligaturing Left Posterior Renal Pelvic Artery.
(In impulses per 1 g tissue. No. of impulses per 1 g of right kidney taken as 100).

| No. of Experiment | Duration of Experiment | Left kidney | | | | | | Right kidney |
|---|---|---|---|---|---|---|---|---|
| | | Region of Ischemia | | | | Healthy parts | | |
| | | Central parts | | Peripheral parts | | | | |
| | | Number of impulses | In conventional units | Number of impulses | In conventional units | Number of impulses | In conventional units | Number of impulses |
| 20 | 10 Min | 2 118 | 41 | — | — | 4 218 | 81 | 5 185 |
| 36 | 10 » | 4 598 | 37 | — | — | 9 960 | 79 | 12 584 |
| 38 | 10 » | 3 410 | 19 | — | — | 14 665 | 81 | 18 158 |
| 48 | 10 » | 1 512 | 32 | — | — | 3 232 | 68 | 4 727 |
| 18 | Control 10 Min | 2 255 | 94 | — | — | 2 530 | 105 | 2 400 |
| | Control | | | | | | | |
| 21 | 10 Min | 3 019 | 97 | — | — | 2 871 | 92 | 3 120 |
| 32 | 30 » | 892 | 21 | — | — | 3 300 | 80 | 4 119 |
| 39 | 30 » | 1 680 | 25 | — | — | 5 015 | 74 | 6 735 |
| 41 | 40 » | 6 360 | 42 | — | — | 14 575 | 98 | 14 810 |
| 42 | 30 » | 1 785 | 31 | — | — | 5 930 | 103 | 5 695 |
| 47 | 40 » | 754 | 16 | — | — | 3 885 | 84 | 4 615 |
| 46 | Control 30 Min | 4 720 | 96 | — | — | 5 073 | 103 | 4 925 |
| 49 | Control 40 Min | 5 075 | 99 | — | — | 4 736 | 93 | 5 120 |
| 43 | 3 Hours | 1 550 | 13 | 3 420 | 29 | 8 870 | 87 | 10 229 |
| 44 | 4 » | 1 340 | 14 | 2 265 | 22 | 8 840 | 91 | 9 680 |
| 45 | 4 » | 890 | 13 | 1 570 | 24 | 5 802 | 88 | 6 600 |

The appearance of marked erythrocytes after ligaturing the posterior renal pelvic artery, in the region supplied by this artery, gives grounds for concluding that the vessels of the kidneys are not terminal.

The capacity of the detour channel is small; even in the absence of considerable spasm of the vessels of the system of the frontal renal pelvic artery, only 1/3 -1/4 of that amount of blood received by 1 g of tissue of the right kidney enters through the anastomoses into the area of ischemia (calculated for 1 g tissue). This is plainly insufficient for the maintenance of the normal vital activity of the tissue. In the early stages, there is a relationship between the state of blood supply of the healthy parts and the area of ischemia in the left kidney; reduction of the amount of blood entering through the system of the frontal renal pelvic artery (in the experiments lasting 10 minutes) leads to deterioration of blood supply of the ischemic area; increase in the amount of blood received by the healthy parts (within 30-40 minutes) produced improvement in blood supply of the area of ischemia (see Fig.)

Statistical treatment of the findings (calculation of the coefficient of the correlation) confirmed the correctness of the conclusion drawn.

In the later stages this realtionship disappears as a result of persistent disturbances of the blood circulation in the region of infarct and at its periphery.

In the pathogenesis of infarct, the reflex spasm of the vessels and of their anastomoses is of importance and arises upon blood circulation disturbance in any part of the organ. Spasm of the vessels leads to deterioration of feeding of the ischemic tissue and contributes to the development of infarct. Together with this, the blood supply of the healthy parts of the affected organ also deteriorates. Manifestations of spasm of the vessels in the development of infarct may be of greater or less significance, depending on the capacity of their detour channel.

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* In Russian